Modern Medical Imaging and Radiation Therapy

Cyber Security | Big Data | AI

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Open MedScience

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More About the Book

This comprehensive guide provides in-depth coverage of the principles and practices of Modern Medical Imaging and Radiation Therapy. It is designed for medical professionals, students, and researchers who are seeking an authoritative source of information in these fields.

Key Features:

Fundamental Concepts:

Provides an introduction to the basics of medical imaging and radiotherapy, covering fundamental principles, techniques, and technologies.

Imaging Modalities:

- Discusses various imaging modalities, including X-ray, CT, MRI, ultrasound, and nuclear medicine.
- Offers detailed insights into the physics, equipment, image acquisition protocols, and clinical applications of each modality.

Radiotherapy Techniques:

- Explores different radiotherapy techniques such as external beam radiotherapy (EBRT), brachytherapy, and proton therapy.
- Examines treatment planning, dose calculation, and the use of modern technologies like image-guided radiotherapy (IGRT) and stereotactic body radiotherapy (SBRT).

Advanced Technologies:

- Covers cutting-edge technologies like artificial intelligence (AI), machine learning, and their role in improving imaging quality and treatment precision.

Target Audience:

- Radiologists and Radiation Oncologists
- Medical Physicists and Dosimetrists
- Radiographers and Technologists
- Medical Students and Residents
- Researchers and Academic Professionals

Preface

Medical imaging and radiation therapy are two paramount pillars of modern healthcare, bridging the gap between diagnosis and treatment and offering unique insights into the human body that have revolutionized how we approach disease. This preface introduces you to our upcoming exploration of these rapidly evolving fields, laying the groundwork for the following detailed exploration.

Over the last century, medical imaging technology has evolved in leaps and bounds, from the discovery of X-rays in 1895 to the incredible sophistication of modern MRI, PET, and ultrasound technologies. These tools have provided clinicians unprecedented access to the intricacies of the human body, demystifying its functioning and malfunctions. They have enabled the early detection of diseases, guided surgical procedures, and facilitated the monitoring of treatment outcomes, dramatically enhancing patient care.

Radiation therapy, on the other hand, represents the therapeutic application of radiology, primarily in the battle against cancer. It uses high-energy radiation to damage cancer cells' DNA, inhibiting their ability to grow and divide. With technological advancements, this therapeutic approach has seen significant refinement, allowing treatments to be targeted more precisely, reducing harm to surrounding healthy tissues and leading to better patient outcomes.

This book, Modern Medical Imaging and Radiation Therapy aims to shed light on the multifaceted world of medical imaging and radiation therapy. We will take you on a journey to demystify the science behind these powerful tools, delve into their historical roots, explore their current applications, and project their potential future directions.

We will examine how advancements in artificial intelligence, machine learning, and big data are reshaping these fields, pushing the boundaries of what we once thought possible. From AI-guided diagnostics to personalized radiation therapy plans, we are moving towards an era of precision medicine, where treatments are tailored to the individual patient's genetic makeup, lifestyle, and environment.

In our endeavour to discuss these complex topics, we have striven to make the content accessible to a broad audience. We believe that knowledge should be shared as broadly as possible, and hence, while healthcare professionals may find this book a valuable resource for updating their knowledge, we have ensured that the content remains comprehensible for non-specialists as well.

This book, therefore, is for anyone interested in understanding the dynamic interplay between technology and medicine. It is for the curious minds eager to understand how these powerful tools work, how they are applied, and what future they could shape in healthcare.

We hope you find this exploration both enlightening and inspiring, providing a glimpse into the profound impact of medical imaging and radiation therapy on human health and well-being. Ultimately, we aim to leave you with a greater appreciation of how far we have come and anticipate the future in these remarkable fields.

Welcome to the fascinating world of Modern Medical Imaging and Radiation Therapy.

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1 Overview of Modern Medical Imaging and Radiation Therapy

Medical imaging and radiation therapy are crucial in diagnosing and treating diseases, utilising advanced technology for understanding human anatomy, monitoring conditions, and delivering targeted cancer treatments.

1.1 Introduction

Medical imaging and radiation therapy are two essential pillars within modern healthcare, serving as vital tools in diagnosing, monitoring, and treating various diseases, including cancer. They represent a fusion of advanced technology, science, and medicine, uniting to provide crucial insight into the intricacies of the human body. The advent of these fields marked a significant step forward in our ability to understand, diagnose, and treat a vast array of health conditions, allowing us to peer into the body's depths without invasive procedures.

Medical imaging, a term encompassing a wide range of techniques, has revolutionised how healthcare professionals examine and understand the human body. Technologies such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, and positron emission tomography (PET) each offer unique benefits in the visualisation of the body's structure and function. The generated images serve as a roadmap, helping doctors navigate the complex terrain of the human anatomy and identifying irregularities that may signal disease or injury.

X-rays and CT scans are invaluable for visualising bone and other dense tissues, while MRI is optimal for soft tissue imaging, like muscles, brain, and heart. Ultrasound provides real-time imaging ideal for monitoring fetal development and diagnosing conditions in the heart and blood vessels.

PET scans, part of nuclear medicine, enable viewing of cellular-level metabolic changes often preceding structural changes, playing a pivotal role in early disease detection.

The images these modalities generate can reveal vital information about a patient's health status, from fractures and tumours to infections and degenerative conditions. They contribute significantly to medical decision-making, guiding everything from diagnosis to treatment plans, resulting in more personalised and effective patient care.

On the other hand, radiation therapy stands as one of the key weapons in the war against cancer. This therapeutic modality involves using high-energy radiation to kill cancer cells and shrink tumours. It harnesses the power of X-rays, gamma rays,

electron beams, or protons to target and damage the DNA of cancer cells, inhibiting their ability to grow and divide. It can be used alone or in conjunction with other treatments, such as surgery and chemotherapy, depending on the type and stage of cancer.

Fusing medical imaging with radiation therapy has led to a significant advancement in cancer treatment. Medical imaging helps map the tumour's exact location, size, and shape, allowing the radiation oncologist to develop a treatment plan that maximises the effect on cancer cells while minimising exposure to normal tissue.

Medical imaging has significantly transformed the healthcare landscape, offering a non-invasive method to visualise and analyse the body's internal structure and function. This remarkable concept began with the discovery of X-rays by Wilhelm Conrad Roentgen in 1895, a groundbreaking event that sparked the birth of radiology. This marked a monumental shift in medicine, providing the ability to peer into the human body without the need for invasive procedures.

Today, medical imaging has expanded far beyond X-rays, encompassing a wide array of modalities with unique applications and capabilities.

1.2 X-rays

Medical imaging, therefore, represents a critical component of modern medicine. From the discovery of X-rays to the development of sophisticated imaging technologies, medical imaging continues to evolve, offering unprecedented insights into the human body. As technology continues to advance, we can expect the field of medical imaging to refine its ability to aid in the detection, diagnosis, and treatment of disease, enhancing patient care and outcomes.

X-rays and computed tomography (CT) scans represent two foundational techniques in medical imaging. They provide essential information about the body's internal structure, primarily visualising bone and other dense tissues like tumours and blood vessels.

Both X-rays and CT scans operate based on the principle of differential absorption. In simpler terms, various tissues in the body absorb differing amounts of X-ray radiation due to their unique density and composition. Since bones are dense structures, they absorb more radiation and appear white on the radiograph. In contrast, less dense tissues, like muscles and organs, absorb fewer X-rays and occur in varying shades of grey, while air-filled spaces like the lungs appear black.

While an X-ray produces a 2-dimensional image, a CT scan, essentially a more sophisticated form of X-ray imaging, takes multiple X-ray images from different angles around the body. A computer then processes this data to generate a detailed 3D image of the body's structures. This 3D representation provides a much more comprehensive view, helping healthcare professionals discern fine details and more effectively diagnose and plan treatments for various conditions.

However, it's important to note that both X-rays and CT scans utilise ionising radiation. This type of radiation carries enough energy to detach electrons from atoms or molecules, which can lead to damage at the cellular level and may increase the risk of cancer over time. For this reason, medical professionals always weigh the potential risks against the benefits of these imaging tests.

Ongoing advancements aim to reduce the radiation dose required for these scans, improving their safety profiles. Techniques like low-dose CT and iterative reconstruction algorithms are already making a significant impact. Ultimately, while ionising radiation presents a particular risk, the diagnostic and therapeutic benefits of X-rays and CT scans are undeniable, often proving lifesaving in many scenarios.

1.3 Ultrasound

Ultrasound imaging, also known as sonography, is a vital modality in medical imaging. Unlike X-rays, CT scans, and MRI, which can be complex and time-consuming, ultrasound offers a quick, non-invasive, and real-time imaging solution. Ultrasound utilises high-frequency sound waves, far beyond the range of human hearing, to visualise internal body structures.

During an ultrasound scan, a device called a transducer is used. This transducer both emits and receives sound waves. It releases high-frequency sound waves into the body, bouncing off internal structures. These returning echoes are detected by the transducer and translated into images by a computer.

One of the most widely recognised applications of ultrasound imaging is within obstetrics. Ultrasound provides a safe means of monitoring fetal development throughout pregnancy. It allows healthcare providers to visualise the fetus, assess its growth and position, and even identify potential abnormalities or complications.

However, the uses of ultrasound extend far beyond obstetrics. It's an incredibly versatile tool used in various diagnostic and therapeutic applications across many areas of medicine. For instance, in cardiology, an echocardiogram uses ultrasound waves to produce images of the heart, helping diagnose conditions such as heart valve diseases and congestive heart failure.

Ultrasound is also extensively used in imaging abdominal organs like the liver, kidneys, gallbladder, and spleen, aiding in diagnosing conditions such as gallstones, kidney stones, or liver disease. In addition, ultrasound can guide procedures such as needle biopsies, where a needle is inserted into a specific area to collect tissue samples.

The real-time nature of ultrasound imaging, its safety profile (as it uses sound waves rather than ionising radiation), and its versatility make it an invaluable tool in medical imaging. It exemplifies how technology can be harnessed to enhance patient care across various medical disciplines.

1.3 Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is an advanced imaging modality that offers unique benefits in the world of medical imaging. Unlike X-rays and CT scans, which use ionising radiation, MRI uses powerful magnetic fields and radiofrequency waves to generate detailed images of the body's internal structures, exceptionally soft tissues.

In an MRI scan, the patient is placed inside a large cylindrical machine that produces a strong magnetic field around the body. This field aligns the protons within the body's water molecules in a specific direction. These protons are temporarily knocked out of alignment when radiofrequency waves are applied. Returning to their original alignment, they emit signals that the MRI machine's sensors detect and convert into images.

The detailed images produced by MRI allow for exceptional visualisation of soft tissues such as the brain, spinal cord, muscles, tendons, and heart. This makes MRI particularly valuable in diagnosing conditions related to these structures. For instance, it's extensively used for brain imaging to detect abnormalities such as tumours, strokes, or neurodegenerative diseases. In musculoskeletal imaging, MRI can reveal damage in ligaments and tendons, herniated disks, or arthritis.

Additionally, MRI has a pivotal role in cardiovascular imaging. It can help visualise the anatomy and function of the heart and blood vessels, helping detect conditions such as congenital heart defects, coronary heart disease, or heart failure.

MRI's ability to differentiate between different types of soft tissues, and even between normal and abnormal tissue within the same organ, sets it apart from other imaging modalities. While it doesn't replace X-rays or CT scans, MRI adds valuable information, providing unique insights that often make a critical difference in diagnosis and treatment planning. The fusion of high-resolution images and non-ionising radiation technology makes MRI a vital tool in modern medicine's diagnostic arsenal.

1.4 Nuclear Medicine

Nuclear medicine and positron emission tomography (PET) scans represent an intriguing subset of medical imaging. Instead of solely depicting the physical structure of body tissues, these modalities provide insights into physiological processes occurring at the cellular level. This is achieved using radioactive substances known as radiotracers, which are injected into the bloodstream, swallowed, or inhaled.

These radiotracers travel to specific areas of the body, where they emit gamma rays. A special camera detects these rays and produces images highlighting the tracer's distribution within the body, giving physicians a detailed view of how organs and tissues function.

Nuclear medicine scans can be applied to various organ systems. For instance, a cardiac nuclear medicine scan can evaluate the heart's health and diagnose conditions like coronary artery disease. Similarly, a bone scan can identify fractures, infections, or tumours in the bone that might not be visible in other imaging studies.

PET scans, a specific type of nuclear medicine scan, are especially useful in oncology. They help detect cancer and monitor the body's response to cancer treatment by highlighting areas of increased metabolic activity, often indicative of rapidly dividing cancer cells. PET scans can also detect changes in brain function, aiding in diagnosing and managing neurological disorders such as Alzheimer's disease and epilepsy.

It's crucial to note that while the radioactive tracers used in nuclear medicine and PET scans might sound concerning, the doses are generally low and are carefully controlled to minimise risk. Moreover, the benefits of these scans often outweigh the potential risks, as they can provide critical diagnostic information that can't be obtained from other imaging modalities.

While each modality has its strengths, often a combination is used to get the most accurate diagnosis, as each provides a different perspective. This demonstrates the importance of having a diverse toolbox of imaging technologies at our disposal.

1.5 Radiation Therapy

Radiation therapy has revolutionised cancer treatment. It uses high-energy particles or waves, such as X-rays, gamma rays, electron beams, or protons, to destroy or damage cancer cells. Radiation therapy can be delivered externally, where the radiation source is outside the body, or internally, where radioactive material is placed in the body near cancer cells (brachytherapy). There's also systemic radiation therapy, where a radioactive substance is swallowed or injected and travels through the blood to kill cancer cells.

Radiation therapy can be curative, where the goal is to eliminate all cancer cells and cure the patient, or palliative, which aims to reduce symptoms and improve the quality of life for patients with advanced or terminal cancer.

Radiation therapy is an integral component of cancer treatment, used in over half of all cancer cases. It works on the principle of directing high-energy particles or waves, such as X-rays, gamma rays, or proton beams, to destroy or damage cancer cells. The radiation disrupts the DNA within cancer cells, inhibiting their ability to grow and divide. However, the use of radiation in therapy is a double-edged sword. While it effectively targets cancer cells, it can also harm healthy cells and tissues, leading to side effects. Thus, it's crucial to ensure that radiation therapy is administered judiciously and precisely.

Over the years, technological advancements have made radiation therapy more precise, minimising its impact on healthy tissues. Two such advancements are intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT).

IMRT represents a significant advancement in the delivery of radiotherapy. Unlike conventional radiotherapy, which delivers a uniform dose of radiation to the entire treatment area, IMRT modulates the intensity of the radiation beams. It uses computer-controlled linear accelerators to deliver radiation doses that conform to the tumour's shape. This means that different areas can receive different radiation doses.

Higher doses are directed toward the tumour, while lower doses are directed toward the surrounding healthy tissues, reducing collateral damage.

IMRT involves rigorous planning before treatment. A computer uses data from imaging scans to create a 3D tumour model. This model allows radiation oncologists to adjust the intensity of the radiation beams and shape them to match the tumour, ensuring optimal targeting. IMRT is particularly beneficial in treating tumours located near critical organs and structures.

IGRT, on the other hand, enhances the precision of radiotherapy by utilising imaging technology just before or even during the radiation treatment. This allows for real-time monitoring and tracking of the tumour, leading to more accurate radiation delivery. IGRT is especially valuable in treating tumours that can move between or during treatments due to breathing or other body motions. With IGRT, the patient's position and the tumour's location can be verified before each dose of radiation, allowing adjustments to target the tumour precisely.

Technologies such as IMRT and IGRT exemplify the strides made in radiation therapy. By making radiation delivery more precise, these technologies minimise radiation exposure to healthy tissues, potentially reducing side effects and improving patient outcomes. However, like all medical interventions, they are not without their challenges. They require specialised equipment, rigorous planning, and a team of highly trained professionals, including radiation oncologists, medical physicists, and radiation therapists.

Nonetheless, the rise of precision radiation therapy underscores the exciting potential of technology in improving cancer treatment. As research progresses and technologies evolve, radiation therapy will likely become even more refined, providing safer, more effective treatment options for patients with cancer. It's a testament to the power of combining medical knowledge with technological innovation to enhance patient care.

1.6 The Role of Cybersecurity in Medical Imaging and Radiation Therapy

In the modern healthcare landscape, medical imaging and radiation therapy play crucial roles in diagnosing and treating various medical conditions. The need for robust cybersecurity measures has become paramount with the rapid advancement of technology and the integration of digital systems in medical practices. Protecting patient data, ensuring the integrity of medical images, and safeguarding radiation therapy devices are essential aspects that demand special attention to maintain the quality and safety of healthcare services.

One of the primary concerns in medical imaging is the protection of patient data and electronic health records (EHRs). These records contain sensitive and private patient information, including their medical history, test results, and personal identification details. Cyberattacks, such as ransomware, phishing, and data breaches, pose significant threats to the confidentiality and privacy of this information. Strong

encryption, access controls, and regular security audits can help prevent unauthorized access and protect patient data from falling into the wrong hands.

In medical imaging, the integrity of images is critical for accurate diagnoses and treatment planning. Any tampering or altering medical images can lead to misdiagnoses and potentially harm patients. Healthcare facilities must employ cybersecurity solutions that detect and prevent image manipulation to ensure image integrity. Watermarking techniques and digital signatures can also help authenticate medical images, assuring their validity and origin.

Radiation therapy, on the other hand, involves using complex devices to target and treat cancerous tumours with precision. These devices are often integrated into networked systems, making them vulnerable to cyber threats. A cyber-attack on radiation therapy equipment could have severe consequences, potentially compromising patient safety and treatment outcomes. Robust cybersecurity protocols and regular device monitoring can help identify and address any vulnerabilities in these systems, reducing the risk of cyber incidents.

Moreover, healthcare professionals and staff must be educated about cybersecurity best practices. Implementing training programs can raise awareness about potential threats, such as social engineering attacks, and teach employees how to recognize and respond to suspicious activities effectively.

1.7 AI and Big Data in Medical Imaging and Radiation Therapy

Integrating artificial intelligence (AI) and big data analytics has revolutionized medical imaging and radiation therapy, ushering in a new era of precision medicine and improved patient outcomes. These cutting-edge technologies offer unprecedented capabilities to analyse vast amounts of medical data and assist healthcare professionals in making more accurate diagnoses, personalized treatment plans, and enhancing overall patient care.

In medical imaging, AI algorithms have proven invaluable in interpreting and analysing images from various modalities, such as X-rays, MRI, CT scans, and ultrasound. Deep learning algorithms can accurately identify patterns and anomalies in medical images, assisting radiologists in detecting early signs of diseases, including cancer, cardiovascular disorders, and neurological conditions. AI can highlight subtle features that might be overlooked by human observers, leading to earlier and more accurate diagnoses.

Furthermore, AI-driven image segmentation and registration tools can precisely outline organs and tumours, allowing radiation oncologists to develop highly targeted treatment plans. This optimises treatment efficacy and minimizes radiation exposure to healthy tissues, reducing potential side effects for patients undergoing radiation therapy.

Big data analytics complement AI in medical imaging by providing a vast repository of patient data, medical records, and research findings. Analysing this wealth of information can identify trends and correlations that can inform treatment decisions

and medical research. By leveraging big data, healthcare professionals can access evidence-based insights, compare treatment outcomes across a diverse patient population, and adopt more personalized and data-driven approaches to patient care.

Moreover, AI and big data analytics facilitate the integration of multi-modal data, where patient information from different sources is combined, such as genomics, medical imaging, and electronic health records. This comprehensive approach enables a deeper understanding of the patient's condition, leading to tailored treatment strategies considering individual variations in disease progression and treatment response.

However, while AI and big data hold immense potential, several challenges must be addressed. Ensuring data privacy and security is critical, as medical data is highly sensitive and subject to stringent regulatory requirements. Additionally, integrating AI algorithms into existing healthcare systems requires careful validation and standardization to guarantee their safety and efficacy.

1.8 Conclusion

Medical imaging and radiation therapy are two key disciplines that converge significantly, especially in the context of cancer treatment. This intersection, often referred to as image-guided radiation therapy (IGRT), forms the bedrock of modern precision radiotherapy, as high-quality imaging is vital to every step of the radiation therapy process.

The fusion of medical imaging with radiation therapy begins with the diagnosis. Various imaging modalities like X-ray, CT, MRI, and PET scans help identify the presence of a tumour, its exact location, size, shape, and even the stage of the disease. The resultant data is vital for the oncologist in planning the subsequent treatment strategy.

The planning phase of radiation therapy, known as treatment planning, relies heavily on medical imaging. CT scans are typically used in this phase to create a three-dimensional model of the tumour and the surrounding tissues. These images help the radiation oncologist to identify the 'target volume' (the tumour and a small margin around it to account for any microscopic spread of disease) and the 'organs at risk' (healthy organs close to the tumour that need to be protected).

These detailed, 3D images are then imported into a sophisticated computer program that helps design the most effective radiation treatment plan. This plan involves determining the radiation dose, the direction of the radiation beams, and the number of treatment sessions, all in a way to maximise tumour cell kill and minimise damage to healthy tissues.

MRI, known for its superior soft tissue contrast, often supplements CT in treatment planning. MRI is beneficial in the brain, spinal cord, and prostate tumours, providing more detailed information about the tumour and its relationship with the surrounding structures.

Additionally, PET scans can also play a role in treatment planning. By showing areas of increased metabolic activity, PET scans can help identify the primary tumour and any spread of the disease to lymph nodes or distant organs. This information can help the radiation oncologist determine the areas that need to be targeted by radiation.

Furthermore, medical imaging is crucial even during radiation therapy. Imaging techniques are employed to verify the patient's position and ensure the tumour is accurately targeted. Changes in the size or position of the tumour during treatment can also be monitored with the help of imaging.

Cybersecurity plays a critical role in ensuring the reliability, confidentiality, and safety of medical imaging and radiation therapy practices. Implementing comprehensive security measures, protecting patient data, and ensuring the integrity of medical images are paramount in providing high-quality healthcare services and protecting patient welfare in an increasingly digital healthcare environment. Healthcare providers must stay proactive and vigilant in their cybersecurity efforts to mitigate potential risks and maintain the trust of patients and the broader medical community.

Furthermore, AI and big data have become indispensable tools in medical imaging and radiation therapy, empowering healthcare professionals to make more informed decisions, improve diagnostic accuracy, and optimize treatment planning. Embracing these transformative technologies holds the promise of advancing patient care, driving medical research, and ultimately improving health outcomes for countless individuals around the world.

Reading the following chapters on Modern Medical Imaging and Radiation Therapy can provide invaluable insights into the fundamental principles, advanced technologies, and applications that play a pivotal role in modern healthcare. Each chapter serves as a gateway to a specific aspect of the field, contributing to a comprehensive understanding of medical imaging and radiation therapy.

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2 A Dive into the World of 3D Medical Imaging

3D Medical Imaging transforms diagnostics, treatment, and patient education through enhanced visualisation, precise localisation, and emerging AI integration.

2.1 Introduction

3D Medical Imaging has radically transformed over the past century, driven by constant innovation and technological advancements. 3D imaging has marked a significant turning point in radiology and nuclear medicine by providing healthcare professionals with a powerful and versatile tool for diagnosing, monitoring, and treating various disease states. The evolution from the rudimentary X-ray technology of the past to the sophisticated 3D imaging modalities employed today has genuinely transformed medicine, ultimately leading to improved patient outcomes.

To fully comprehend the significance of 3D medical imaging, it is essential to understand its roots in earlier imaging technologies. Traditional X-ray technology, first discovered in 1895, provided a 2D representation of the human body's internal structures. Although its limitations, X-ray technology was revolutionary for its time and laid the groundwork for more advanced imaging modalities, such as Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Ultrasound.

The development of 3D imaging techniques has taken these modalities to new horizons, offering healthcare professionals detailed, volumetric information that significantly enhances their ability to diagnose and treat various medical conditions. Creating a 3D image involves the reconstruction of multiple 2D slices or projections, which are then combined to form a comprehensive view of the body's internal structures.

These 3D imaging technologies are employed in various medical applications. For example, they allow for more precise localisation and characterisation of tumours, improved diagnosis, and management of cardiovascular diseases. They also enhance surgical planning for orthopaedic procedures and better visualisation of the brain's anatomy and function. Furthermore, 3D imaging has emerged as an invaluable tool for patient education, enabling healthcare professionals to communicate complex medical information to their patients and foster informed decision-making.

The future of 3D medical imaging is promising, as it is poised for numerous innovations and advancements in the near future. Integrating artificial intelligence (AI) and machine learning algorithms with 3D imaging is fascinating. This combination

will transform medical imaging by automating image analysis, enhancing diagnostic accuracy, and personalising treatment planning. Furthermore, the fusion of 3D imaging with augmented reality (AR) and virtual reality (VR) technologies promises to revolutionise medical education, surgical planning, and patient engagement by offering immersive, interactive experiences.

2.2 The Evolution of 3D Medical Imaging

In recent years, advancements in medical imaging technology have continued to evolve, incorporating new techniques and applications that enhance the diagnostic capabilities of existing modalities. These significant breakthroughs include:

- Digital radiography has replaced traditional film-based X-rays, offering improved image quality, faster processing times, and reduced radiation exposure for patients. In addition, digital images can be easily stored, shared, and analysed using specialised software.
- 3D ultrasound creates three-dimensional images of internal structures, while 4D ultrasound offers real-time 3D imaging, allowing physicians to observe the movement of organs and systems. This technology benefits obstetrics and fetal imaging, enabling clinicians to assess fetal development and identify abnormalities more effectively.
- Functional MRI measures changes in blood flow related to neural activity, allowing researchers and clinicians to map brain function and observe how different brain areas are involved in various tasks or stimuli. This technology has become essential in understanding brain disorders and planning brain surgeries.
- Positron Emission Tomography (PET) scans utilise radioactive tracers to create three-dimensional images of the body's internal processes, including metabolism and blood flow. PET scans are often used with CT or MRI scans to provide a more comprehensive view of a patient's condition.
- Optical Coherence Tomography (OCT) is a non-invasive imaging technique that uses light to create high-resolution, cross-sectional images of biological tissues. It has become an essential tool in ophthalmology for diagnosing and monitoring various eye conditions, including age-related macular degeneration and diabetic retinopathy.
- AI and Machine Learning algorithms are increasingly integrated into medical imaging to improve image analysis, reduce the risk of human error, and increase efficiency. These technologies can help radiologists detect patterns and abnormalities more accurately and support decision-making in patient care.
- Image-Guided therapy, or interventional radiology, combines real-time imaging with minimally invasive procedures to diagnose and treat various conditions, including cancer, vascular diseases, and musculoskeletal disorders. Image-

guided therapies often result in faster recovery and fewer complications than traditional surgical methods.

2.2 The Science Behind 3D Imaging

3D imaging involves the creation of a detailed 3D representation of an object, typically derived from a series of 2D images or data points. In medical imaging, 3D images are often reconstructed from multiple 2D slices or projections, providing clinicians with a comprehensive view of the body's internal structures.

There are several techniques used to create 3D medical images, and these include:

- Volume Rendering is a technique that involves the conversion of 2D data (such as CT or MRI slices) into a 3D volume, with each voxel (3D pixel) assigned a specific colour and opacity based on its density or other properties. The final 3D image is then generated by compositing these voxels, allowing clinicians to visualise complex anatomical structures.
- Surface rendering involves extracting the surfaces of structures of interest from 2D data, creating a 3D mesh of the surface. This technique is beneficial for visualising the shape and size of organs or other anatomical features.
- Multiplanar Reconstruction (MPR) involves the reformatting of 2D image data into different planes, allowing for the creation of 3D images that can be viewed from various angles.

3D imaging in medicine has transformed how healthcare professionals diagnose, monitor, and treat various conditions, especially in oncology, cardiology, orthopaedics, neurology, dentistry, obstetrics, and gynaecology.

2.3 The Impact of 3D Imaging on Cancer Care

Oncology, focused on the study and treatment of cancer, has witnessed a remarkable transformation in recent years. The most promising advancement is the integration of 3D imaging technology, which has emerged as a critical tool in the precise localisation and characterisation of tumours. This innovative approach is revolutionising how oncologists manage cancer care, allowing for more accurate staging, treatment planning, and monitoring of cancer progression or response to therapy.

3D imaging involves various techniques, such as CT, MRI, and PET, to generate detailed, multi-dimensional images of tumours within the body. These high-resolution images provide valuable insights into the tumours' size, shape, and density, enabling clinicians to differentiate between benign and malignant lesions more effectively.

This level of precision is crucial for accurate cancer staging, which is essential for determining the best course of treatment. In addition, by understanding the extent and spread of cancer, oncologists can develop tailored treatment plans that consider the unique characteristics of each patient's tumour.

Furthermore, 3D imaging allows for more accurate treatment planning, particularly in the case of radiotherapy. By mapping the tumour's exact location and surrounding healthy tissue, radiation oncologists can deliver targeted radiation doses, minimising damage to healthy tissues and reducing the risk of side effects.

Finally, 3D imaging is vital in monitoring cancer progression and response to therapy. As treatment progresses, these detailed images enable clinicians to evaluate the effectiveness of the therapy, detect any changes in tumour size, and identify potential recurrences at an early stage. This timely assessment allows for adjustments in treatment plans, ultimately improving patient outcomes and overall survival rates.

2.4 Unveiling the Heart's Secrets with 3D Imaging Technology

Cardiology, the branch of medicine that deals with diagnosing and treating heart diseases, has been transformed by 3D imaging technology. This state-of-the-art innovation allows for a detailed examination of the heart's structure and function, offering invaluable insights that aid in diagnosing and managing a wide range of cardiovascular diseases.

3D imaging techniques, such as echocardiography, cardiac MRI, and CT, provide high-resolution, real-time images of the heart, enabling clinicians to visualise its complex anatomy and assess its functionality. These images allow for a more accurate assessment of the heart's size, shape, and contractile function and the identification of any abnormalities or defects within the heart's valves and chambers.

One of the primary advantages of 3D imaging in cardiology is the ability to understand the heart's function and blood flow. This is particularly crucial in diagnosing and managing conditions like valvular heart disease, congenital heart defects, and cardiomyopathies. In addition, by providing a precise evaluation of these conditions, 3D imaging assists in determining the most appropriate course of treatment and monitoring the patient's response to therapy.

Furthermore, 3D imaging plays a significant role in the planning and execution of minimally invasive cardiac procedures, such as transcatheter aortic valve replacement (TAVR) and transcatheter mitral valve repair (TMVR). By facilitating accurate measurements and visualisations, these advanced imaging techniques help to reduce the risk of complications during these procedures, ultimately improving patient outcomes.

In addition to diagnosis and treatment planning, 3D imaging is invaluable for monitoring patients with cardiovascular diseases. Regular assessments enable clinicians to track disease progression, evaluate the effectiveness of prescribed treatments, and make any necessary adjustments to the treatment plan, ensuring optimal patient care.

2.4 Orthopaedic Breakthroughs: Enhancing Patient Care with 3D Imaging Technology

Orthopaedics, the branch of medicine concerned with diagnosing, treating, and preventing musculoskeletal disorders, has greatly benefitted from advancements in

3D imaging technology. This cutting-edge innovation transforms the planning and execution of orthopaedic surgeries, including joint replacement, spinal fusion, and fracture repair, ultimately improving patient outcomes and overall quality of care.

3D imaging techniques, such as CT and MRI, generate detailed images of bones, joints, and soft tissues, providing invaluable insights for orthopaedic surgeons. These high-resolution images enable a comprehensive understanding of the patient's anatomy, allowing for precise surgical planning and minimising potential complications.

In joint replacement surgeries, such as hip and knee arthroplasty, 3D imaging facilitates accurate measurements of joint components and customisation of prosthetic implants. By ensuring optimal sizing and alignment, surgeons can improve the longevity of the implant, reduce the risk of complications, and enhance postoperative function and patient satisfaction.

Spinal fusion surgeries also benefit from 3D imaging technology. The detailed visualisation of the spine's anatomy, including the vertebrae, discs, and surrounding soft tissues, enables surgeons to make more informed decisions regarding the optimal approach and techniques for spinal stabilisation. This level of precision contributes to a higher success rate and a reduced risk of complications, such as nerve damage or spinal instability.

In fracture repair, 3D imaging assists in identifying complex fractures and assessing surrounding soft tissue damage. This information is critical in determining the most appropriate method of fracture fixation, whether internal or external. Furthermore, 3D imaging helps to guide the surgical procedure, ensuring proper alignment and stabilisation of the fractured bone and promoting successful healing and recovery.

2.5 Neurology Transformed by 3D Imaging Technology

Neurology is focused on diagnosing and treating neurological disorders and has been significantly advanced by integrating 3D imaging technology. This groundbreaking innovation offers detailed views of the brain's anatomy and function, playing a crucial role in diagnosing and treating various neurological disorders, including brain tumours, aneurysms, and neurodegenerative diseases.

3D imaging techniques, such as MRI, CT, and PET, generate high-resolution images of the brain's structure and function. These detailed images enable neurologists and neurosurgeons to identify and assess abnormalities, such as tumours or vascular malformations, with unprecedented precision.

In the case of brain tumours, 3D imaging provides essential information regarding the size, location, and extent of the lesion. This information is critical for accurate diagnosis, staging, and treatment planning, whether it involves surgery, radiation therapy, or chemotherapy. Moreover, 3D imaging assists in differentiating between benign and malignant tumours and monitors treatment response and potential recurrence.

For patients with cerebral aneurysms, 3D imaging offers crucial insights into the size, shape, and location, enabling clinicians to determine the risk of rupture and the most appropriate treatment approach, such as endovascular coiling or surgical clipping. By providing a comprehensive understanding of the aneurysm's characteristics, 3D imaging helps to reduce the risk of complications and improve patient outcomes.

In neurodegenerative diseases like Alzheimer's, Parkinson's, and multiple sclerosis, 3D imaging contributes to a greater understanding of the disease's underlying pathological processes and progression. These insights facilitate early diagnosis and intervention and the development of targeted therapies that may slow or halt disease progression.

2.6 The Role of 3D Ultrasound in Obstetrics and Gynaecology

Obstetrics and Gynaecology, the branch of medicine focusing on the female reproductive system and prenatal care, has experienced significant advancements with the introduction of 3D ultrasound imaging technology. This innovative technology enables clinicians to visualise the developing fetus, assess fetal health, and detect abnormalities in the placenta, uterus, and other pelvic structures, improving prenatal care and patient outcomes.

3D ultrasound imaging is a non-invasive diagnostic tool that generates detailed, real-time images of the fetus and its surroundings using sound waves. Unlike traditional 2D ultrasound, 3D ultrasound offers a more comprehensive view of the fetus, providing information about its anatomy, growth, and overall health. This technique also allows for better visualisation of the placenta, umbilical cord, and amniotic fluid, essential for fetal well-being.

One of the primary benefits of 3D ultrasound in obstetrics and gynaecology is the early detection of congenital abnormalities, such as cleft lip, heart defects, and skeletal anomalies. By identifying these issues in the prenatal stage, clinicians can provide appropriate counselling, plan for necessary interventions, and improve the overall prognosis for the affected infants.

In addition to its use in prenatal care, 3D ultrasound imaging is valuable in diagnosing and managing gynaecological conditions, such as uterine fibroids, endometriosis, and ovarian cysts. By offering a detailed view of the uterus, ovaries, and other pelvic structures, this technology aids in determining the most effective course of treatment and monitoring response to therapy.

Moreover, 3D ultrasound is useful for assessing the position and presentation of the fetus in the later stages of pregnancy, guiding decisions regarding the mode of delivery and reducing the risk of complications during labour and birth.

2.7 The Impact of 3D Imaging on Modern Dentistry

Dentistry, the branch of medicine that focuses on diagnosing, treating, and preventing oral health conditions, has greatly benefitted from introducing 3D imaging technologies. Cone-beam computed tomography (CBCT) is one such technology that provides comprehensive information about the teeth, jaws, and surrounding

structures, significantly improving treatment planning for dental procedures and oral surgery.

CBCT is a specialised form of X-ray imaging that generates high-resolution, 3D images of the teeth, jaws, and associated structures with minimal radiation exposure. This advanced imaging technique offers a more comprehensive view of the patient's oral anatomy than traditional 2D X-rays, allowing for enhanced diagnostic accuracy and precision in treatment planning.

One of the primary applications of CBCT in dentistry is in the planning and execution of dental implant procedures by providing detailed information about bone density, quality, and available space for implant placement. CBCT enables dentists to ensure optimal implant positioning and avoid potential complications like nerve or sinus damage.

Additionally, 3D imaging is invaluable in diagnosing and treating orthodontic issues, such as malocclusion and impacted teeth. CBCT allows orthodontists to assess tooth and jaw alignment, plan for braces or precise aligner therapy, and monitor the progress of orthodontic treatment more effectively.

3D imaging is also essential in oral and maxillofacial surgery, including corrective jaw surgery, wisdom tooth extraction, and treating temporomandibular joint (TMJ) disorders. CBCT provides critical insights into the patient's anatomy, enabling surgeons to minimise the risk of complications and optimise surgical outcomes.

Furthermore, CBCT aids in identifying and managing dental pathologies, such as cysts, tumours, and infections, by offering detailed images of the affected areas and assisting in developing targeted treatment plans.

2.8 Advantages of 3D Imaging in Medicine

3D images provide a more accurate and comprehensive view of internal structures, allowing healthcare professionals to understand complex anatomical relationships better and identify abnormalities that may not be apparent in 2D images.

By offering a complete picture of the body's internal structures, 3D imaging can improve diagnostic accuracy, leading to more targeted and effective treatments.

3D images can be used to create detailed surgical plans, reducing the risk of complications and improving surgical outcomes. In some cases, 3D images can also be used during surgery to provide real-time guidance and ensure the accurate placement of surgical instruments.

3D images can help patients better understand their medical condition and the proposed treatment plan, increasing patient engagement and satisfaction.

2.9 Limitations and Challenges of 3D Imaging in Medicine

Although its numerous advantages, 3D medical imaging is not without its limitations and challenges:

The generation and manipulation of 3D images require substantial computing power and specialised software, which can be expensive and time-consuming.

Some 3D imaging techniques, such as CT scans, involve exposure to ionising radiation. While efforts are continuously being made to minimise radiation doses, the risk of radiation exposure must always be considered, particularly in pregnant women and children.

The quality of 3D images can be affected by various factors, including patient movement, image noise, and artefacts. These issues can potentially impact the diagnostic accuracy and utility of 3D imaging.

The interpretation of 3D images can be more complex than traditional 2D images, requiring additional training and expertise from healthcare professionals.

2.10 Future Trends in 3D Imaging in Medicine

In the coming years, integrating AI and machine learning algorithms is expected to revolutionise 3D imaging in medicine. These advanced technologies have the potential to significantly enhance the speed and accuracy of image processing, segmentation, and analysis. This will allow healthcare professionals to quickly identify abnormalities and make informed decisions regarding diagnosis and treatment. Furthermore, AI-driven algorithms can be trained to recognise patterns in complex datasets, facilitating early detection of diseases and improving patient outcomes.

Advancements in visualisation techniques, such as holography and virtual reality (VR), are also expected to reshape how medical professionals interact with 3D images. Holography enables the creation of 3D images without special glasses, while VR allows for an immersive, interactive experience in a simulated environment. These technologies can provide healthcare practitioners with more intuitive and effective ways to explore and manipulate 3D medical images, enhancing their understanding of the underlying anatomy and pathology.

Another emerging trend in 3D imaging is the fusion of multiple imaging modalities, such as PET/CT or PET/MRI, to provide more comprehensive and accurate diagnostic information. By combining the strengths of different imaging techniques, healthcare professionals can better understand a patient's condition, particularly in complex cases or when multiple physiological processes need to be assessed simultaneously. This can lead to more accurate diagnoses and tailored treatment plans, ultimately improving patient care and outcomes.

The development of personalised medicine is another area where 3D imaging is poised to make a significant impact. 3D imaging can help tailor treatments to each patient's needs by offering detailed insights into an individual's unique anatomy and

physiology. This personalised approach can lead to more effective therapies, reduced side effects, and improved patient satisfaction.

Finally, advancements in 3D imaging technology are expected to enhance the field of telemedicine, enabling remote consultations and collaboration between healthcare professionals across the globe. Specialists in different locations can share and analyse high-quality, real-time 3D images, facilitating expert opinions and improving patient care, even in remote or underserved areas.

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3 The Da Vinci Technology: Pioneering a New Era in Medical Imaging and Patient Care

Da Vinci technology transforms medical imaging through robotics, artificial intelligence, and advanced equipment, enhancing diagnostics and patient treatment.

3.1 Introduction

Medical imaging has radically transformed since the first X-ray was taken in 1895. The rapid evolution of technology in recent years has led to more accurate and efficient diagnostic techniques, significantly impacting the healthcare industry. Among the various innovations in medical imaging, the Da Vinci technology stands out as a revolutionary development. Drawing inspiration from the genius of Leonardo da Vinci, this technology combines robotics, artificial intelligence (AI), and advanced imaging equipment to change how physicians diagnose and treat a myriad of diseases.

The Da Vinci technology enhances medical imaging by integrating state-of-the-art imaging systems with robotic assistance, providing unprecedented precision and control during diagnostic and surgical procedures. This groundbreaking approach has far-reaching applications across various medical specialities, including radiology, oncology, cardiology, and gastroenterology. With improved diagnostic capabilities and minimally invasive procedures, Da Vinci technology significantly benefits surgeons and patients.

Incorporating AI within the Da Vinci system enables advanced image analysis, surgical planning, and real-time adjustments based on the patient's specific anatomy and physiology. These modifications ensure optimal surgical outcomes, improving patient experiences and recovery times. Furthermore, the system's use of AI and machine learning continues to evolve, promising even more significant advancements in medical imaging capabilities.

As the technology continues to develop and become more widespread, costs are expected to decrease, making it accessible to a broader range of healthcare providers. Additionally, new applications and innovations will likely emerge, pushing the boundaries of medical imaging even further.

3.2 The Da Vinci Technology

The Da Vinci technology represents a groundbreaking medical imaging and surgical procedure innovation. As a state-of-the-art robotic surgical system, it integrates advanced imaging with robotic assistance to deliver enhanced precision and control during various medical procedures. The fusion of these technologies allows for unparalleled accuracy and efficiency in diagnostic imaging, which has far-reaching implications for patient care.

One of the most significant benefits of the Da Vinci technology is its ability to facilitate minimally invasive surgical procedures. By combining high-definition 3D imaging with precise robotic assistance, surgeons can perform intricate procedures with smaller incisions, less blood loss, and a reduced risk of complications. This approach results in shorter hospital stays, faster recovery times, and improved patient outcomes.

3.2.1 Components of the Da Vinci System

The Da Vinci system has several components that work harmoniously to deliver unparalleled imaging capabilities and enhanced surgical precision.

These features include multiple robotic arms equipped with cameras and surgical instruments. A surgeon can control these arms from a console, allowing precise movements and manipulation during procedures. In addition, the robotic arms enable unparalleled agility and accuracy, which translates to improved patient outcomes.

Also, the system employs cutting-edge 3D imaging technology, providing a highly detailed, real-time view of the surgical area. This advanced visualisation offers a comprehensive understanding of the patient's anatomy and enables improved diagnostic capabilities. With a clear view of the surgical site, surgeons can perform more accurately and precisely, leading to fewer complications and improved patient recovery.

The incorporation of AI into the Da Vinci system significantly enhances its capabilities. AI allows for advanced image analysis, surgical planning, and real-time adjustments based on the patient's unique anatomy and physiology. By leveraging AI, the system can identify critical structures, predict potential complications, and optimise surgical techniques, ensuring optimal outcomes for each patient.

Furthermore, the integration of AI and advanced imaging technologies enables a high level of instrumentation in the Da Vinci system. This personalised approach tailors surgical plans to the specific needs of each patient. These factors include the patient's medical history, anatomical variations, and potential risk factors. This level of technology ultimately results in more effective treatment and faster recovery times.

3.3 Applications of Da Vinci Technology in Medical Imaging

In radiology, Da Vinci technology offers a transformative potential for diagnostic imaging by providing improved image quality and accuracy. The system's high-definition 3D imaging capabilities enable radiologists to detect abnormalities with greater confidence and precision, ultimately leading to faster diagnoses and treatments. In addition, this enhanced imaging technology ensures that even the most minor and subtle irregularities can be identified, allowing for early intervention and improved patient outcomes.

Cancer detection and treatment have also benefited significantly from the Da Vinci technology. The advanced imaging capabilities of the system allow for superior tumour visualisation and localisation, enabling more targeted therapies and minimally invasive surgical procedures. Precise imaging facilitates the removal of cancerous

tissue while minimising damage to surrounding healthy tissue, resulting in improved recovery rates and reduced complications.

The field of cardiology has seen successful applications of Da Vinci technology, particularly in treating heart valve diseases and coronary artery bypass grafting. High-definition 3D imaging offers precise visualisation of the heart's structure, allowing cardiologists and cardiac surgeons to make more accurate diagnoses and implement effective surgical interventions. This increased accuracy improves surgical outcomes and patient care in cardiac health.

In gastroenterology, the Da Vinci system has been utilised to perform minimally invasive surgeries on the gastrointestinal tract. The enhanced imaging capabilities provided by the system allow for greater visualisation of the digestive organs, resulting in more accurate diagnoses and targeted treatments.

Furthermore, by enabling a clearer view of the gastrointestinal structures, surgeons can perform procedures with increased precision and minimal disruption to healthy tissue, leading to faster recovery and fewer patient complications.

3.5 Benefits of Da Vinci Technology in Medical Imaging

One of the primary advantages of Da Vinci technology is the increased precision and control it offers in medical imaging and surgical procedures. This revolutionary system, designed by Intuitive Surgical, combines robotic arms with high-definition 3D imaging, providing physicians with unprecedented accuracy and dexterity in diagnosing and treating various medical conditions. The advent of the Da Vinci system has brought about significant advancements in the field of minimally invasive surgery, leading to improved patient outcomes and overall healthcare experiences.

The robotic arms of the Da Vinci system are engineered to mimic the subtle movements of human hands, which allows for a more delicate and precise manipulation of surgical instruments. This heightened level of control results in smaller incisions, which reduces blood loss during surgery. With less invasive procedures, patients experience less pain and discomfort and quicker recovery times, allowing them to return to their daily lives faster. Additionally, the minimised invasiveness of these surgeries reduces the likelihood of complications, such as infections and scarring, further enhancing patient outcomes.

A key aspect of the Da Vinci system's success lies in the integration of artificial AI into its operations. AI algorithms help analyse and interpret the vast amounts of data collected during medical imaging and diagnostic procedures, enabling the development of highly personalised treatment plans. Considering the patient's unique anatomy and physiology, the AI-driven Da Vinci system can tailor the surgical approach to best suit each individual's needs. This ensures that patients receive the most appropriate and effective care possible, ultimately improving their chances of a successful recovery.

3.6 Da Vinci Technology: Overcoming Cost & Training Challenges for Global Healthcare Impact

One of the significant challenges associated with Da Vinci technology is its high costs, which can limit accessibility for some medical facilities, particularly in low-income countries. The initial investment required to purchase and install the system and ongoing maintenance costs can be prohibitive for healthcare providers with limited resources. However, as technology advances and becomes more widespread, costs are expected to decrease, making it more accessible to a broader range of healthcare providers, ultimately benefiting patients worldwide.

Another challenge facing the widespread adoption of Da Vinci technology is the need for specialised training for healthcare professionals. The system involves complex components and procedures, which require a steep learning curve for physicians and other healthcare providers. Therefore, adequate training and skill development are essential to ensure the safe and effective use of the technology and maximise its potential benefits. With the increasing popularity of the Da Vinci system, more training programs are being developed to facilitate its adoption. These programs aim to provide healthcare professionals with the necessary skills and knowledge to operate the system confidently and competently, ultimately leading to favourable patient outcomes.

The future of medical imaging and surgical procedures using Da Vinci technology looks promising. As technology advances, it is expected that new applications and innovations will emerge, further revolutionising the field of medical imaging and minimally invasive surgery. For instance, developing smaller and more versatile robotic arms could enable the system to be used for an even more comprehensive range of procedures, thereby expanding its scope and impact.

Additionally, machine learning and AI integration will continue to enhance the system's capabilities, making it even more precise and efficient. These advanced algorithms will allow for improved diagnostic accuracy and more customised and targeted surgical interventions. By harnessing the power of AI, Da Vinci, technology will continue to evolve and adapt to the ever-changing landscape of healthcare, ultimately leading to improved patient care and outcomes.

3.7 Conclusion

The Da Vinci technology has revolutionised medical imaging by offering enhanced precision and control in diagnostic and surgical procedures. Its applications in various medical specialities, such as radiology, oncology, cardiology, and gastroenterology, have improved patient outcomes and satisfaction. The system's ability to provide detailed, high-definition 3D imaging, coupled with its robotic arms, has enabled physicians to perform minimally invasive surgeries with unprecedented accuracy and control.

As the technology becomes more accessible, its applications are expected to expand, benefiting patients and healthcare providers. Additionally, the integration of AI and

machine learning will continue to refine and enhance the system's capabilities, making it even more efficient and effective.

As healthcare continues to evolve, Da Vinci technology is poised to play a crucial role in shaping the future of medical imaging and patient care. Its groundbreaking advancements are set to redefine the standards of precision and efficiency in surgical procedures, ultimately leading to improved patient outcomes and a more streamlined healthcare experience.

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4 Medical Imaging of the Human Skeleton

Medical imaging revolutionises healthcare by offering profound insight into human anatomy, with skeletal imaging specifically aiding diagnosis, treatment, and understanding of structural intricacies and functions.

4.1 Introduction

Medical imaging is essential to modern healthcare, providing valuable information about the human body's structure, function, and health. Among the various tissues and systems of the body, the human skeleton plays a critical role in supporting and protecting our organs, enabling movement, and serving as a reservoir for minerals such as calcium and phosphorus.

Conventional radiography, commonly known as X-ray imaging, has been the cornerstone of medical imaging since its inception in 1895 by Wilhelm Conrad Röntgen. This revolutionary technique has transformed how healthcare professionals visualise the internal structures of the human body, particularly the skeletal system. As the oldest and most widely utilised imaging modality, X-ray imaging has continued to play a vital role in diagnosing and monitoring a broad range of medical conditions.

The principle of X-ray imaging relies on the differential absorption of X-rays by various tissues within the body. When X-ray beams pass through a body part, they are absorbed by tissues to varying degrees, depending on the density and composition of the tissues. For example, denser structures, such as bones, absorb more X-rays and appear lighter on the radiographic image, while less dense tissues like muscles and fat absorb fewer X-rays and appear darker. This contrast in absorption allows for the creation of detailed images of the internal structures, enabling healthcare providers to identify and assess potential abnormalities.

Since X-rays are the oldest imaging modality, conventional radiography has maintained its relevance in modern medicine due to its numerous advantages. It is a quick, non-invasive, and cost-effective diagnostic tool, making it accessible to a vast population worldwide. In addition, the technology has evolved significantly, with digital radiography systems replacing traditional film-based systems, enhancing image quality and reducing radiation exposure.

However, X-ray imaging has limitations, such as being less sensitive in detecting soft tissue abnormalities than other advanced imaging modalities compared to computed tomography (CT) or magnetic resonance imaging (MRI). Despite these limitations, conventional radiography remains an indispensable tool in modern medicine for

assessing the human skeleton, providing valuable information for clinical decision-making and treatment planning.

4.2 Computed Tomography: Diagnostic Imaging with Advanced Visualisation and Expanding Applications

Computed tomography (CT) is a sophisticated X-ray-based imaging modality that has revolutionised diagnostic imaging since its invention in the 1970s. By applying computer algorithms, CT scans generate detailed cross-sectional images of the body, offering superior contrast and resolution compared to conventional radiography. The enhanced image quality provided by CT scans has expanded the scope of medical imaging, enabling healthcare professionals to visualise intricate structures and diagnose a broader range of conditions with increased accuracy.

In a CT scan, an X-ray source and detector rotate around the patient, capturing numerous projections from various angles. These projections are subsequently reconstructed into a series of two-dimensional cross-sectional images, which can be combined to generate a comprehensive three-dimensional representation of the body. This advanced imaging technology allows for improved visualisation of complex fractures, spinal injuries, joint disorders, and other skeletal abnormalities.

Beyond its application in musculoskeletal imaging, CT scans have proven invaluable in assessing bone tumours, infections, and degenerative conditions such as osteoporosis. In addition, the ability to visualise soft tissues in addition to bone has further broadened the utility of CT scans, making them essential tools for detecting and evaluating a wide array of pathologies, including those affecting the lungs, abdomen, and pelvis.

CT scans have also gained traction in interventional radiology, frequently employed to guide procedures such as biopsies, drainages, and ablations. By providing real-time, high-resolution images, CT scans facilitate precise targeting and positioning, which can significantly improve the safety and efficacy of these minimally invasive procedures.

Despite the numerous advantages of CT scans, some drawbacks exist. CT scans generally involve higher radiation doses than conventional radiography, which may raise concerns about long-term radiation exposure, especially in paediatric patients and individuals who require frequent imaging. Additionally, CT scans are more expensive, which can limit their accessibility and availability, particularly in resource-constrained healthcare settings.

4.3 Magnetic Resonance Imaging: Unveiling Soft Tissues and Skeletal Insights with Non-Ionising Diagnostic Precision

Magnetic Resonance Imaging (MRI) is a groundbreaking non-ionising imaging modality that revolutionised the field of diagnostic medicine. Developed in the 1970s, MRI uses a combination of powerful magnetic fields, radiofrequency pulses, and sophisticated computer algorithms to generate detailed images of the body's internal

structures. The technique is particularly effective for visualising soft tissues, providing valuable insights into various medical conditions and enabling accurate diagnoses.

In an MRI procedure, hydrogen nuclei present in the body are aligned within a strong magnetic field. Then, radiofrequency pulses are applied, causing these nuclei to absorb energy and change their alignment. As the nuclei gradually return to their original state, they release energy, which is detected and subsequently used to create images of the body's internal structures.

Although MRI is not primarily used for skeletal imaging, it can offer valuable information about bone marrow and surrounding soft tissues. This modality evaluates bone tumours, infections, and metabolic bone diseases. Additionally, MRI effectively visualises cartilage, tendons, and ligaments, making it a powerful tool for diagnosing and monitoring joint disorders such as osteoarthritis, rheumatoid arthritis, and sports injuries.

The primary advantage of MRI is its ability to visualise soft tissues in detail without exposing patients to ionising radiation, which can pose health risks with prolonged exposure. Moreover, MRI images can be acquired in multiple planes, allowing for enhanced visualisation of complex anatomical structures that might otherwise be challenging to observe using other imaging techniques.

Notwithstanding its numerous advantages, MRI also has certain limitations; for example, the procedure is generally more expensive and time-consuming than other imaging modalities, such as X-rays and CT scans. Furthermore, MRI is contraindicated for patients with specific implanted devices, like pacemakers and certain metallic implants, as the strong magnetic fields could interfere with their function or cause harm to the patient.

4.4 Bone Scintigraphy: Harnessing Nuclear Medicine for Early Detection and Monitoring of Skeletal Disorders

Nuclear medicine imaging, or bone scintigraphy, is a functional imaging technique that has revolutionised how physicians diagnose and treat various bone-related disorders. Pioneered in the 1950s, it employed small amounts of radioactive substances to visualise the metabolic activity within the skeleton, allowing for the detection of changes in bone metabolism before they are discernible through other imaging techniques.

Bone scintigraphy begins with injecting a radiopharmaceutical, typically technetium-99m-labelled diphosphonate, into the patient's bloodstream. This compound exhibits a predilection for areas of high bone turnover, such as sites of injury, infection, or tumour growth. A gamma camera subsequently captures the emitted radiation, generating images depicting the radiopharmaceutical distribution within the skeletal system.

This imaging modality is instrumental in detecting and monitoring metastatic bone disease, primary bone tumours, and infections. Furthermore, evaluating treatment response and identifying the source of unexplained bone pain is crucial. With its ability

to provide whole-body imaging and high sensitivity for detecting early changes in bone metabolism, bone scintigraphy has become an indispensable tool in the medical field.

Despite its numerous advantages, bone scintigraphy does possess certain limitations. Its specificity is somewhat restricted, as various conditions can produce similar uptake patterns, potentially leading to misinterpretation. Moreover, this imaging technique involves exposure to ionising radiation, raising concerns about the cumulative effects of radiation exposure, especially in patients requiring multiple scans. Additionally, bone scintigraphy offers limited anatomical detail compared to other imaging modalities, such as CT and MRI.

4.5 Ultrasound in Skeletal Imaging: Applications, Advantages, and Limitations of a Non-Invasive Diagnostic Approach

Ultrasound, or sonography, is a non-invasive imaging technique that employs high-frequency sound waves to generate images of the body's internal organs and structures. This technology was developed in the 1940s; ultrasound has become an essential diagnostic tool in modern medicine. However, primarily used for imaging soft tissues, such as organs, muscles, and blood vessels, ultrasound has limited applications for skeletal imaging due to its inability to penetrate dense bone structures effectively.

The ultrasound imaging process involves placing a transducer on the skin, which emits sound waves that penetrate the body and reflect off internal structures. The returning echoes are detected by the transducer and used to create real-time images that can be viewed on a monitor. This real-time visualisation allows healthcare professionals to observe the function and movement of internal structures, making ultrasound particularly useful for guiding procedures such as needle biopsies and catheter insertions.

While not as effective for imaging dense bones as other modalities like X-ray or CT, ultrasound can evaluate superficial bones such as the ribs and certain joints like the shoulder and knee. It is also useful for assessing bone healing, particularly in infants and children whose bones are less dense and more sonolucent. Furthermore, ultrasound can be employed to diagnose soft tissue injuries, such as tendon or ligament tears, and to monitor the progress of bone fractures during the healing process.

Ultrasound provides multiple benefits compared to other imaging methods. As a non-ionising technique, it avoids subjecting patients to the potentially harmful ionising radiation found in X-rays and CT scans. Additionally, ultrasound is portable and economical, making it an appealing choice for imaging in specific circumstances, especially in rural or isolated regions with restricted access to more sophisticated imaging technology.

However, ultrasound does have some limitations. For example, its penetration depth is limited, and it cannot effectively visualise deeper bones or the internal structure of bone. Additionally, the quality of the images depends on the operator's skill, and

certain factors, such as the presence of gas or obesity, can impede the transmission of sound waves and reduce image quality.

4.6 Navigating the Evolution of Skeletal Imaging: Advancements, Modalities, and Their Impact on Modern Patient Care

In summary, medical imaging of the human skeleton has undergone a remarkable transformation over the years, with numerous modalities available to diagnose and monitor skeletal disorders. The evolution of these imaging techniques has significantly enhanced our ability to detect and manage a wide range of bone and joint conditions. However, each imaging modality has unique advantages and limitations, and the choice of the most appropriate technique depends on the clinical scenario, patient factors, and available resources.

Radiography, or X-ray imaging, has been the cornerstone of skeletal imaging since its discovery in 1895. It is a simple, cost-effective, and widely available method for detecting fractures, dislocations, and other bone abnormalities. However, its limited sensitivity for soft tissue structures and the potential risks associated with ionising radiation are important considerations.

CT scans provide high-resolution, cross-sectional skeletal system images, making this technique ideal for detecting subtle fractures, assessing complex anatomical structures, and planning surgical interventions. Despite its higher radiation dose than conventional X-rays, CT scans offer more detailed information on bone and joint pathologies.

MRI has revolutionised skeletal imaging by providing exceptional detail of bone and soft tissue structures without ionising radiation. MRI is particularly valuable for evaluating bone marrow disorders, infections, tumours, and joint conditions. However, the major limitations of MRI include its high cost, longer scanning times, and contraindications in patients with certain implanted devices.

Besides these traditional imaging methods, promising modalities like Positron Emission Tomography (PET) and Optical Imaging are emerging, offering the potential for even greater accuracy and specificity in diagnostic capabilities. As technology advances, we can anticipate further improvements in the quality, safety, and accessibility of skeletal imaging. These advancements will inevitably enhance our capacity to diagnose and treat many bone and joint conditions, ultimately improving patient care and outcomes.

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5 Medical Imaging of the Liver: Techniques and Applications

Advanced medical imaging has revolutionised liver disease detection, diagnosis, and management, improving diagnostic accuracy and personalised therapeutic interventions.

5.1 Introduction

The liver, a vital organ in the human body, performs essential functions such as metabolism, detoxification, and synthesis of proteins. Therefore, detecting and diagnosing liver diseases is crucial for appropriate treatment and management. Advanced medical imaging techniques are pivotal in detecting, diagnosing, and monitoring liver diseases. Several advanced imaging techniques are used in the assessment of the liver and their clinical applications.

A non-invasive imaging technique for liver evaluation is ultrasonography which uses high-frequency sound waves to produce images of internal organs and structures, such as the liver. This imaging modality has undergone numerous advancements, significantly improving its diagnostic capabilities. The ultrasound toolbox consists of Conventional ultrasonography, or B-mode ultrasound, commonly used as the first-line imaging modality for liver evaluation. It can identify morphological changes such as liver cirrhosis or tumours and assess the liver's size, shape, and echogenicity. This non-invasive technique is cost-effective, widely available, and has no known harmful effects. Furthermore, it can be performed in real-time, allowing for a dynamic assessment of the liver and its vasculature.

However, conventional ultrasonography has its limitations. It is operator-dependent, which means that the accuracy of the examination heavily relies on the expertise of the sonographer. Moreover, its sensitivity in detecting small lesions, mainly those less than 1 cm in diameter, is limited. This may lead to missed or delayed diagnoses, especially in the early stages of liver diseases.

Throughout the years, numerous advancements in ultrasonography have emerged to address its limitations and augment its diagnostic prowess.

Doppler Ultrasonography is used to assess blood flow within the liver's vessels. It helps evaluate portal hypertension, liver vascular disorders, and the detection of vascular invasion by tumours. Doppler ultrasonography has become an essential tool

in liver transplantation, where it is used to evaluate the patency and flow within hepatic vessels.

Contrast-Enhanced Ultrasonography (CEUS) involves using microbubble contrast agents, which are injected intravenously to enhance the visualisation of blood vessels and tissues. This technique improves the detection and characterisation of liver lesions, including hepatocellular carcinoma, metastases, and focal nodular hyperplasia. CEUS can also monitor the treatment response in patients undergoing locoregional therapy for the liver.

5.2 Non-Invasive Assessment of Liver Fibrosis Using Strain and Shear Wave Elastography

Liver fibrosis and cirrhosis represent severe conditions that may result in liver failure, potentially necessitating a liver transplant. Therefore, early diagnosis and monitoring are crucial for managing these conditions and reducing complications. Elastography is a non-invasive imaging technique that measures the stiffness of liver tissue, which can indicate the presence of fibrosis or cirrhosis. Two main types of elastography are used for liver assessment:

Strain elastography, also known as compression elastography or static elastography, is the first generation of elastography techniques. It involves manually applying pressure to the tissue of interest with an ultrasound transducer, causing the tissue to deform. The deformation of the tissue is then measured by comparing the pre-compression and post-compression ultrasound images. The degree of deformation indicates tissue stiffness; less deformation means stiffer tissue, which can indicate liver fibrosis or cirrhosis.

However, strain elastography has limitations, such as being operator-dependent and highly susceptible to external factors like patient movement or breathing. Additionally, strain elastography does not provide absolute measurements of tissue stiffness, making it challenging to compare results across different examinations or patients.

Shear wave elastography, a more advanced form of elastography, overcomes many of the limitations of strain elastography. This technique uses specialised ultrasound transducers to generate acoustic radiation force impulses (ARFI) within the tissue.

These impulses create shear waves that propagate through the tissue, and the velocity of these waves is directly related to the tissue's stiffness. The faster the shear waves travel, the stiffer the tissue. Shear wave elastography has several advantages over strain elastography.

First, it is less operator-dependent, as the ultrasound transducer generates the ARFI rather than relying on manual compression. Second, shear wave elastography provides quantitative measurements of tissue stiffness, which can be compared across different examinations or patients. Finally, this technique is less susceptible to external factors like patient movement or breathing, making it more reliable and accurate.

Elastography has various clinical applications, particularly in assessing and monitoring liver fibrosis and cirrhosis. In addition, it can be used to:

Assess patients susceptible to liver fibrosis or cirrhosis, including individuals with chronic hepatitis B or C, non-alcoholic fatty liver disease (NAFLD), or alcohol-associated liver disease. Monitor disease progression in patients with established liver fibrosis or cirrhosis, providing valuable information to guide treatment decisions and adjust therapy as needed.

Assess treatment response in patients receiving antiviral therapy or other treatments for liver disease, helping to determine the effectiveness of the intervention and inform ongoing management.

5.3 Computed Tomography: A Powerful Tool for Liver Imaging and Intervention

Computed tomography (CT) is an advanced medical imaging technique that uses X-ray technology to produce detailed, cross-sectional images of the body's internal structures. One of the primary applications of CT is the imaging and evaluation of the liver, where it has become an indispensable tool for clinicians. Conventional CT assesses liver anatomy, detect and characterises liver lesions, and stage liver malignancies. Furthermore, it plays a significant role in planning and monitoring various interventions, such as ablations or transarterial chemoembolisation (TACE).

The liver is a complex organ with various anatomical structures and functional units. Therefore, an accurate assessment of liver anatomy is essential for diagnosing and managing liver diseases. CT provides a non-invasive method for visualising liver anatomy, including assessing the liver size, shape, and structural abnormalities. In addition, it allows for identifying liver lobes, segments, and vascular structures, such as the hepatic artery, portal vein, and hepatic veins. By providing detailed images of the liver, CT aids in evaluating underlying liver diseases and helps guide appropriate treatment plans.

Liver lesions refer to atypical growths or regions of tissue injury within the liver, which can be either benign or malignant. Characterisation is vital for establishing the proper course of treatment. CT is a powerful diagnostic tool for detecting and characterising liver lesions. It can identify various liver lesions, such as cysts, haemangiomas, focal nodular hyperplasia, and malignant tumours.

Using contrast-enhanced CT, radiologists can evaluate the enhancement patterns of liver lesions, which is essential for characterising the lesion and differentiating between benign and malignant growths. For example, hepatocellular carcinoma (HCC), the most common primary liver cancer, typically shows arterial enhancement and washout in the venous phase. These characteristic patterns help radiologists and clinicians establish a diagnosis and select the most suitable management approach.

Accurate staging of liver malignancies is vital for determining prognosis and guiding treatment decisions. CT is widely used for this purpose, as it can provide detailed information about the extent of the tumour. Also, its involvement in liver vasculature and the presence of extrahepatic metastases. The TNM (Tumour, Node, Metastasis)

staging system is used for liver malignancies, and CT plays a significant role in determining each component of the staging system. By providing comprehensive information about tumour size, number, and location, as well as the involvement of lymph nodes and distant metastases, CT is an essential tool for liver cancer staging.

CT is valuable for diagnostic purposes and crucial for planning and monitoring liver interventions. Ablation therapy involves using heat or cold to destroy tumour cells and is a minimally invasive treatment option for patients with small liver tumours. CT guidance ensures precise tumour targeting and minimises damage to surrounding healthy tissue. Moreover, CT is used to monitor the effectiveness of the treatment and assess for any complications.

Transarterial chemoembolisation (TACE) is another liver-directed therapy primarily used to treat hepatocellular carcinoma. TACE involves the injection of chemotherapy drugs and embolic agents directly into the blood vessels supplying the tumour, leading to tumour ischemia and necrosis. CT is used to identify the appropriate blood vessels for catheter placement and to monitor the treatment response.

5.4 Dual-Energy Computed Tomography: A Game Changer Tumour Liver Imaging

Dual-Energy Computed Tomography (DECT) is an advanced medical imaging technique that acquires images at two different X-ray energy levels, enabling the differentiation of various tissue types and enhancing the detection of small liver lesions. DECT is beneficial for characterising liver tumours, assessing liver steatosis, and identifying liver inflammation. This technology has revolutionised liver imaging, offering several advantages over traditional single-energy computed tomography (SECT).

DECT leverages that different tissue types absorb and scatter X-ray photons differently at varying energy levels. By acquiring images at two different energy levels, DECT can generate material-specific images that enhance the differentiation of various tissue types. This ability to distinguish between tissues has proven advantageous in detecting small liver lesions, which may otherwise be missed or misdiagnosed on conventional imaging modalities.

DECT plays a crucial role in characterising liver tumours by offering a more precise and accurate evaluation of the tumour composition. This is particularly important for differentiating between benign and malignant liver tumours, which can significantly impact treatment planning and patient prognosis. DECT's ability to generate iodine-specific images has also made it possible to identify and quantify iodine uptake within liver tumours. This quantitative information can provide valuable insights into tumour vascularity and response to therapy, further improving the clinical management of patients with liver cancer.

Fatty liver, also referred to as liver steatosis, is a widespread condition characterised by excessive fat accumulation in the liver. Left untreated, it can progress to more severe liver diseases, such as non-alcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma. DECT has emerged as a powerful diagnostic tool for

assessing liver steatosis, providing a non-invasive means to quantify the degree of fat infiltration. In addition, with the ability to differentiate between water and fat components in the liver, DECT can accurately measure the liver fat content and monitor the progression of steatosis over time.

Liver inflammation, frequently resulting from viral hepatitis, autoimmune disorders, or drug-induced liver injury, has the potential to cause substantial liver damage and may eventually lead to liver failure. Therefore, early identification and appropriate management of liver inflammation are crucial to prevent further deterioration of liver function. DECT has shown promise in detecting and quantifying liver inflammation by generating virtual non-contrast images highlighting inflammation-related tissue changes.

This technique enables clinicians to differentiate inflammatory changes from other causes of liver damage, such as fibrosis or steatosis, facilitating prompt and accurate diagnosis.

DECT offers several advantages over traditional SECT in liver imaging. These include DECT's ability to generate material-specific images results in improved image quality with increased contrast resolution and reduced beam-hardening artefacts. By simultaneously acquiring images at two different energy levels, DECT can achieve comparable or even lower radiation doses than SECT while maintaining diagnostic accuracy. DECT allows for advanced post-processing techniques, such as virtual non-contrast imaging and material decomposition, enabling more accurate and detailed evaluations of liver diseases. The additional information DECT provides radiologists makes more confident diagnoses, reducing the need for invasive diagnostic procedures, such as liver biopsy.

5.5 The Versatility of Magnetic Resonance Imaging in Liver Assessment

Magnetic Resonance Imaging (MRI) is a non-invasive medical imaging technique that utilises powerful magnets and radiofrequency waves to generate detailed images of the liver without employing ionising radiation. Conventional MRI offers high spatial resolution for visualising liver anatomy and pathology, rendering it an invaluable resource for assessing liver size, detecting focal liver lesions, and evaluating biliary structures.

Various MRI sequences, such as T1-weighted, T2-weighted, and fat-suppressed sequences, are used to obtain detailed liver images. In addition, advanced MRI techniques, such as Contrast-Enhanced MRI (CE-MRI) and Diffusion-Weighted Imaging (DWI), further improve the diagnostic capabilities of MRI in liver assessment.

Contrast-Enhanced MRI (CE-MRI) uses gadolinium-based contrast agents to improve the visualisation of liver lesions and blood vessels. By enhancing the contrast between healthy and abnormal liver tissue, contrast-enhanced MRI (CE-MRI) facilitates more accurate detection and characterisation of liver lesions.

Additionally, it is beneficial in identifying and characterising liver tumours, as the contrast agents assist in distinguishing between benign and malignant lesions

according to their enhancement patterns. This information is crucial for determining the appropriate treatment strategies and predicting patient outcomes.

CE-MRI is also valuable in assessing liver fibrosis, a condition characterised by the excessive accumulation of fibrous tissue in the liver. Using contrast agents enables the visualisation of liver parenchymal changes and the degree of fibrosis, aiding in diagnosing and staging liver diseases, such as chronic hepatitis and cirrhosis.

Furthermore, CE-MRI can be used to evaluate the post-treatment response of liver tumours. By comparing the enhancement patterns before and after treatment, clinicians can assess the effectiveness of various therapies, such as chemotherapy, radiotherapy, and liver resection, in eradicating or reducing the tumour burden.

Diffusion-Weighted Imaging (DWI) is an advanced MRI technique that measures the diffusion of water molecules within tissues. By examining the movement of water molecules, DWI can provide valuable information on the microstructural properties of liver tissue, allowing for better differentiation between normal and abnormal tissue.

DWI is useful for detecting small liver lesions that conventional MRI sequences may miss, as these lesions often exhibit restricted diffusion due to their higher cellularity. The ability to detect small lesions is essential in the early diagnosis of liver cancer, as it enables timely treatment and improves patient prognosis.

In addition to lesion detection, DWI can characterise liver tumours. By analysing the apparent diffusion coefficient (ADC) values, representing the degree of water molecule diffusion within a given tissue, radiologists can differentiate between benign and malignant liver lesions. Lower ADC values are typically associated with malignant tumours, as they exhibit higher cellularity and restricted water diffusion.

DWI is also beneficial in evaluating liver fibrosis, as the diffusion of water molecules is affected by the presence of fibrous tissue. In addition, studies have demonstrated a correlation between decreased ADC values and increased liver fibrosis stages, suggesting that DWI can be used as a non-invasive tool for fibrosis assessment and staging.

5.6 Liver Malignancy Diagnosis: The Power of PET/CT and PET/MRI Imaging in Assessing Metabolic Activity and Anatomical Details

Positron Emission Tomography (PET) is a nuclear medicine imaging technique that has revolutionised the field of medical diagnostics by providing vital insights into cellular metabolic activity. This is achieved by tracking a radiotracer, usually fluorodeoxyglucose (FDG), which allows for visualising physiological processes that cannot be observed through conventional imaging modalities. PET/CT and PET/MRI are hybrid imaging techniques that amalgamate the functional information derived from PET with the anatomical details obtained from CT or MRI scans. These advanced imaging modalities have proven exceptionally useful in diagnosing, staging, and restaging liver malignancies, assessing treatment response, and detecting recurrent disease.

Liver malignancies represent a significant challenge in medical diagnostics due to their complexity and heterogeneity. The liver, a crucial organ with numerous metabolic and detoxification roles, is vulnerable to various diseases, including cancer. Primary liver cancers, including hepatocellular carcinoma (HCC), cholangiocarcinoma, and metastatic liver lesions stemming from colorectal, breast, or lung cancer, represent the most prevalent liver malignancies. Therefore, accurate diagnosis and staging of liver malignancies are essential for determining the appropriate treatment strategy and predicting the disease's prognosis.

PET/CT and PET/MRI have emerged as powerful imaging tools that provide complementary information to traditional imaging techniques, such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Combining the metabolic data from PET with the anatomical precision of CT or MRI, these hybrid imaging modalities offer a more comprehensive and accurate assessment of liver malignancies.

The key to PET imaging lies in its ability to detect the metabolic activity of cells by tracking the uptake of radiotracers. In the case of liver malignancies, FDG is the most commonly used radiotracer. FDG is a glucose analogue that accumulates in cells with high metabolic activity, such as tumour cells. This differential uptake of FDG allows for identifying malignant lesions, as they display increased metabolic activity compared to healthy liver tissue. In addition, PET imaging can provide valuable information regarding tumour aggressiveness, as highly aggressive tumours tend to exhibit higher FDG uptake.

PET/CT and PET/MRI offer several advantages for staging and restaging liver malignancies. They provide a comprehensive assessment of the tumour burden in the liver, as well as identify extrahepatic metastases that may impact treatment planning. Furthermore, these hybrid imaging modalities can evaluate the response to various treatment modalities, including surgery, chemotherapy, and targeted therapies. By comparing pre- and post-treatment PET scans, clinicians can determine the effectiveness of the treatment and make informed decisions regarding the need for further intervention or the modification of the treatment plan.

A major obstacle in managing liver malignancies is identifying instances of recurring disease. Patients who undergo surgical resection or other curative treatments risk developing recurrent tumours within the liver or other organs. PET/CT and PET/MRI have proven to be highly sensitive in detecting recurrent liver malignancies, enabling early intervention and improving patient outcomes.

Despite the numerous advantages of PET/CT and PET/MRI in managing liver malignancies, these imaging techniques also have some limitations. The high cost of these modalities and limited availability in some regions may restrict their widespread use. Furthermore, PET imaging relies on the differential uptake of radiotracers, which may not always accurately reflect the metabolic activity of all tumour types.

5.7 Hepatobiliary-Specific PET Radiotracers

In recent years, nuclear medicine has witnessed significant advancements in developing new and improved radiotracers for positron emission tomography (PET) imaging. These advances have shown great potential in detecting and characterising liver lesions, particularly in the context of hepatocellular carcinoma (HCC). Two notable hepatobiliary-specific PET radiotracers that have garnered significant attention are ^{18}F-fluorocholine and ^{11}C-acetate. These novel radiotracers have improved sensitivity and specificity for liver lesion detection, offering promising alternatives to conventional imaging modalities.

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy, with its worldwide incidence continually increasing. Thus, early and precise detection of HCC is essential for optimal patient care and enhanced prognosis. Traditional imaging techniques, like computed tomography (CT) and magnetic resonance imaging (MRI), are extensively employed to detect and characterise liver lesions. However, these approaches may be limited, particularly when lesions are small, indeterminate, or masked by preexisting liver disease.

^{18}F-Fluorocholine, a radiolabelled choline analogue, is a newer hepatobiliary-specific PET radiotracer promising in detecting liver lesions. Choline is a precursor of phosphatidylcholine, a major component of cell membranes. Malignant cells, including HCC, exhibit increased choline uptake and metabolism, which can be exploited for imaging. Early studies of ^{18}F-fluorocholine PET imaging have demonstrated improved sensitivity and specificity for detecting HCC compared to traditional imaging techniques. Furthermore, this radiotracer has shown potential for differentiating between benign and malignant liver lesions and assessing treatment response in HCC patients.

Another emerging radiotracer, ^{11}C-acetate, has demonstrated potential for detecting and characterising liver lesions. Acetate is involved in lipid synthesis and is preferentially taken up by HCC cells due to their enhanced lipogenesis. ^{11}C-acetate PET imaging has shown promising results in detecting HCC, especially in cases where traditional imaging modalities have yielded inconclusive results. Moreover, ^{11}C-acetate PET has helped identify extrahepatic metastases, which can significantly impact patient management and treatment planning.

5.8 Ablation Techniques for Liver Tumours

Ablation techniques have revolutionised the treatment of liver tumours, providing a minimally invasive and highly effective alternative to traditional surgery. These cutting-edge procedures, including radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation, utilise imaging guidance to precisely target and destroy tumour tissue while preserving healthy liver tissue. This approach is particularly advantageous for patients with unresectable liver tumours or those who are not suitable candidates for liver transplantation.

Radiofrequency ablation (RFA) is the most commonly utilised ablation method for treating liver tumours. It employs high-frequency electrical currents to generate heat,

which causes coagulative necrosis of the targeted tissue. This method is generally safe, with minimal complications, and can be performed using local anaesthesia or conscious sedation. RFA is effective for treating small to medium-sized tumours, and several sessions may be required for larger tumours.

Microwave ablation (MWA) is another heat-based ablation technique that uses electromagnetic waves to create friction within the tumour cells, generating heat and leading to cellular death. MWA is known for its rapid heating and larger ablation zones, making it suitable for treating more extensive tumours. It also has a reduced risk of heat-sink effect compared to RFA, which can improve treatment outcomes.

Cryoablation, on the other hand, employs extremely cold temperatures to destroy tumour cells. This technique uses argon gas to create an ice ball around the tumour, freezing and ultimately destroying the cells. Cryoablation is advantageous in some instances, as it preserves the extracellular matrix and reduces the risk of haemorrhage, which can be crucial for patients with compromised liver function.

5.9 Transarterial Therapies for Liver Malignancies

Transarterial therapies, including transarterial chemoembolisation (TACE) and transarterial radioembolisation (TARE), have revolutionised the treatment of liver malignancies by providing minimally invasive, targeted therapy to patients suffering from unresectable hepatocellular carcinoma (HCC) or liver metastases. These advanced techniques have emerged as a viable alternative to traditional surgical resection, offering several advantages, such as reduced morbidity and faster recovery time.

TACE is a procedure that combines the administration of chemotherapy drugs with embolisation, a process that obstructs blood flow to the tumour. The chemotherapy agent is injected directly into the hepatic artery, delivering a high drug concentration to the tumour while minimising systemic side effects. Simultaneously, embolic agents are introduced to block the blood supply, starving the tumour of essential nutrients and oxygen. This dual approach maximises the therapeutic effect while minimising damage to healthy liver tissue.

Conversely, TARE involves the delivery of radioactive microspheres, commonly known as Yttrium-90 (Y-90), into the hepatic artery. These microspheres emit beta radiation, selectively targeting and destroying cancer cells in the liver. By delivering radiation directly to the tumour, TARE spares healthy tissue and has been associated with fewer side effects compared to conventional external beam radiation therapy.

Both TACE and TARE offer significant benefits in controlling tumour growth and alleviating symptoms for patients with unresectable HCC or liver metastases. While they are not curative, these therapies can prolong survival and improve quality of life, making them a valuable addition to the treatment arsenal for liver cancer patients.

5.10 Conclusion

Advanced medical imaging techniques have profoundly transformed the liver disease detection, diagnosis, and management landscape. Technologies such as ultrasonography, CT, MRI, PET, and interventional radiology have provided clinicians with a comprehensive toolkit to evaluate liver function, characterise lesions, assess fibrosis, and monitor treatment response. These innovations have enhanced diagnostic accuracy and facilitated more personalised and targeted therapeutic interventions, ultimately improving patient outcomes. As research and technological advancements progress, we can anticipate even more sophisticated liver imaging capabilities, paving the way for further breakthroughs in preventing, diagnosing, and treating liver diseases. The future of liver imaging is bright, and with it comes the promise of better, more efficient healthcare for patients worldwide.

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6 Digital Defences in Radiology: Cyber Security in Medical Imaging Systems

The increasing connectivity of medical devices highlights the need for robust cyber security measures.

6.1 Introduction

Cyber security in medical imaging refers to the measures taken to protect medical images, patient information, and medical devices used in imaging from cyber attacks, data breaches, and unauthorised access.

Radiology departments use various medical modalities, such as X-rays, Computed Tomography, and Magnetic Resonance Imaging, to diagnose and treat patients. Unfortunately, when these images are produced, they contain sensitive patient information, such as their name, date of birth, and medical history, making them a valuable target for cyber criminals.

To ensure cyber security, access to medical photos and patient data should only be restricted to authorised personnel. This can be achieved by using strong passwords, multi-factor authentication, and role-based access control. Also, all medical images and patient data should be encrypted during transmission and storage to prevent unauthorised access. In addition, all the medical devices are linked to other servers, such as DICOM (Digital Imaging and Communications in Medicine) and PACS (Picture Archiving and Communication System). It is important that these servers are updated regularly with the latest security patches to protect against known vulnerabilities.

These measures extend to the network used to transmit medical images, and patient information should be secured using firewalls, intrusion detection and prevention systems, and other security measures. It is important that healthcare personnel should be trained on the importance of cyber security and the best practices for protecting medical images and patient information. In the event of a security violation or cyber attack, healthcare organisations should have a well-defined incident response plan to minimise damage and quickly recover from the attack.

By implementing these measures, healthcare organisations can ensure the confidentiality, integrity, and availability of medical images and patient data and protect against cyber threats.

PACS systems have several components, including imaging modalities (such as X-ray machines and CT scanners) and radiologist workstations. These systems enable healthcare professionals to view and interpret the images, servers and storage devices

for storing and retrieving images, and network infrastructure for transmitting the images between these components.

DICOM is a standard for managing medical images and related information. It is a file format and communication protocol that enables exchanging of medical images, such as X-rays, MRIs, and CT scans, between different imaging devices and software applications. It is used by healthcare organisations, medical device manufacturers, and software vendors worldwide. It plays a critical role in supporting clinical decision-making and improving patient outcomes.

6.2 When Cyber Security Fails: The Consequences of Cyber Attacks on the National Health Service

Several cyber-attacks have targeted the NHS (National Health Service) in recent years. These attacks have caused significant disruption to healthcare services and put patient data at risk.

One of the most notable cyber attacks on the NHS was the WannaCry ransomware in 2017, affecting over 200,000 computers in 150 countries. The attack exploited a vulnerability in older versions of Microsoft Windows, affecting many NHS hospitals and clinics. The attack disrupted services, causing cancellations of appointments and surgeries and delayed processing of test results and referrals.

In 2021, the NHS experienced another cyber attack that affected several hospitals and healthcare organisations. The attack was attributed to a Chinese hacking group, and it targeted vulnerabilities in virtual private network (VPN) systems used by the affected organisations. The attack disrupted services and caused delays in patient care.

The NHS has taken steps to improve cyber security in response to these attacks. This will include investing in new technology and training staff to be more aware of the risks of cyber attacks. The NHS has also established a dedicated cyber security centre to monitor and respond to threats.

However, the threat of cyber attacks on the NHS remains high. Healthcare organisations must continue to be vigilant and proactive in their efforts to protect patient data and ensure the availability of critical services.

6.3 Hijacked Imaging: The Threat of Cyber Criminals Controlling Medical Scanners

Cyber criminals can take control of medical imaging scanners, although it is not a common occurrence. Medical imaging scanners can be vulnerable to cyber attacks like all connected devices if they are not adequately secured. If a scanner is compromised, a cyber criminal could gain access to the images it produces, modify them, or even interfere with its operation.

One example of a vulnerability that cyber criminals could exploit is using default login credentials on the scanner's web interface or operating system. If these credentials are not changed, an attacker could use them to gain unauthorised access to the scanner.

Another potential vulnerability is outdated software or firmware on the scanner, which may contain known security vulnerabilities that cyber criminals can exploit. Therefore, following best practices for cyber security is important to reduce the risk of cyber attacks on medical imaging devices. These include regularly updating software and firmware, using strong passwords and multi-factor authentication, and limiting scanner access to authorised personnel. Furthermore, organisations must have a plan for responding to a cyber attack, including regular backups of patient data and a system for quickly detecting and responding to security incidents.

6.4 Layers of Protection: Building a Robust Security Framework for Medical Imaging Device

Protecting medical scanners from cyber criminals involves a multi-layered approach that includes both technical and administrative safeguards, for example:

- Regularly update the scanner's operating system, software, and firmware to fix known vulnerabilities and protect the scanner against the latest cyber threats.
- Ensure that strong passwords are used for all accounts. If possible, enable two-factor authentication to add an extra layer of security.
- Install firewalls and antivirus software to protect the scanner from Malware and other cyber threats.
- Limit access to the scanner to authorised personnel only. Restrict physical access to the scanner by implementing access controls, such as keycards or biometric authentication.
- Conduct regular security evaluations to identify vulnerabilities and ensure all security controls work effectively.
- Apply encryption to protect sensitive data stored on the scanner or transmitted over the network.
- Train staff on identifying and responding to cyber threats, including phishing attacks and social engineering.

The future of cyber security will likely be shaped by several emerging technologies and trends, as well as ongoing threats and challenges. For example, artificial intelligence and machine learning are already used to enhance cyber security, such as identifying and preventing cyber attacks. However, the associated security risks will increase as more devices connect to the internet. Therefore, ensuring the security of IoT devices will be crucial in the future.

Furthermore, quantum computing has the potential to break many of the cryptographic algorithms used to secure data today. This means that new, quantum-resistant encryption methods will need to be developed. The use of cloud computing is increasing, so securing cloud environments will become more critical. As more companies move their data and applications to the cloud, cloud security will become a significant concern.

However, human behaviour will play a crucial role in cyber security. Educating people on how to stay safe online will be essential, as will ensuring that employees are adequately trained to recognise and respond to cyber threats.

6.5 Digital Hostage: Analysing the Impact of the WannaCry Ransomware Attack on Healthcare Organisations

Cyber attacks in medical imaging include the WannaCry ransomware attack in May 2017, which affected more than 200,000 computers in 150 countries, particularly in healthcare organisations. This attack exploited a vulnerability in Microsoft Windows operating systems and demanded ransom payments for data restoration. A further raid in June 2017 involved NotPetya Malware which targeted healthcare facilities.

However, In May 2019, Microsoft warned about a critical vulnerability in its Remote Desktop Services that attackers could exploit to execute code remotely. This vulnerability, known as BlueKeep, could allow attackers to spread Malware and take over systems. Healthcare organisations that use medical imaging systems were among the many potentially affected organisations. Another cyber attack in 2021 involved the Ryuk ransomware, which affected Universal Health Services, causing significant disruption and forcing the organisation to temporarily shut down some of its systems. In 2021, the cyber security firm Check Point discovered a new strain of Malware called DarkRadiation, specifically designed to target medical imaging devices. This Malware could potentially allow attackers to gain access to sensitive patient data or even disrupt the functioning of these devices.

6.6 Vision 2030: The Future of Cyber Security in Medical Imaging Devices

The future of cyber security will be complex and challenging. However, with the right strategies and technologies in place, we can work to ensure that our digital lives remain safe and secure.

Cyber attacks involving IoT are becoming increasingly common as more devices connect to the internet. Unfortunately, these devices are often designed with limited security features, making them easy targets for cyber criminals looking to exploit vulnerabilities and gain unauthorised access. For example, Botnets can use distributed denial of service (DDoS) attacks and comprise the device due to weak security and internet connection. Also, Malware can be used to infect IoT devices and therefore gain access to sensitive data and steal passwords to take control of the device. In addition, a cyber attacker can intercept communication between two devices and steal data or inject malicious code.

However, physical attacks involve accessing the IoT device to steal or modify data, install Malware, or even destroy the device. Therefore, protecting IoT devices from cyber attacks is vital by implementing strong security measures, such as using complex passwords, keeping software up-to-date, and regularly monitoring suspicious activity. Additionally, manufacturers can design devices with more robust security features like encryption and two-factor authentication.

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7 SPECT Imaging Technology: From Single Photon Emission Tomography to Hybrids

SPECT imaging provides valuable functional information, aiding clinicians in diagnosing, planning treatments, and monitoring progress

7.1 Introduction

SPECT (Single Photon Emission Computed Tomography) is a medical imaging modality that uses gamma rays emitted by radiotracers to create 3-D images of organs and tissues in the human body. These SPECT scanners use a rotating gamma camera to detect gamma rays emitted by the radiotracer to generate a series of 2-D images which are then converted using algorithms to produce 3-D images of the target area. This scanning technique SPECT is used in nuclear medicine departments to diagnose and monitor conditions such as cardiology, oncology, and neurology disorders.

SPECT-CT hybrid scanners allow for integrating the functional information obtained from SPECT with the anatomical information obtained from CT. This results in more accurate localisation of the radiotracer and improved image quality.

Conventional SPECT detectors use scintillation crystals to detect gamma rays, but newer SPECT systems use cadmium zinc telluride (CZT) detectors. CZT detectors have higher sensitivity and energy resolution, so they can detect and differentiate photons more accurately, resulting in better image quality.

TOF technology improves the temporal resolution of SPECT imaging. By measuring the time taken for a gamma ray to travel from the radiotracer to the detector, TOF technology can more accurately determine the location of the radiotracer and produce better images.

SPECT images are reconstructed from the data acquired by the detectors. Iterative reconstruction algorithms use statistical methods to iteratively refine the reconstructed image iteratively, resulting in improved image quality and reduced imaging time.

The development of new radiotracers has expanded the clinical applications of SPECT imaging. Radiotracers are molecules labelled with a radioactive isotope and used to target specific organs or tissues. New radiotracers have been developed for various applications, such as detecting Alzheimer's, cancer, and cardiac diseases.

These technological advances have made SPECT imaging a more accurate and efficient diagnostic tool, enabling earlier disease detection and improved treatment outcomes.

7.2 Multi-Detector SPECT Scanner Configurations

Several types of SPECT scanners can be classified based on their design, configuration, and imaging capabilities. These scanners are capable of implementing the following diagnostic imaging:

- Dedicated SPECT scanners are designed for specific imaging applications, such as cardiac or brain SPECT. They are optimised for high sensitivity and resolution in the targeted area of the body.
- SPECT scanners are designed to perform a variety of imaging studies across different body parts. They are flexible and can be used for various clinical applications.
- Stand-alone SPECT scanners comprise a gamma camera and a computer system for image reconstruction. They are typically used in smaller clinics or medical facilities.
- SPECT-CT hybrid scanners combine SPECT with CT (Computed Tomography) technology to provide functional and anatomical imaging in a single scan. They offer improved accuracy and specificity by combining the benefits of both technologies.
- SPECT-MRI hybrid scanners combine SPECT with MRI (Magnetic Resonance Imaging) technology to provide functional and anatomical imaging in a single scan. They are particularly useful for studying brain disorders and other conditions that require high spatial resolution.
- Mobile SPECT scanners are designed to be transported to various locations for on-site imaging studies. They are often used in emergency departments, intensive care units, and other clinical settings requiring rapid imaging.

Each SPECT scanner type has unique advantages and disadvantages, depending on the clinical application and imaging requirements.

7.3 CZT SPECT Scanners: Improving Image Quality and Reducing Radiation Dose

The most advanced is the CZT-based SPECT scanner. CZT stands for cadmium zinc telluride, a semiconductor material used as the detector material in these scanners. CZT-based SPECT scanners have several advantages over conventional SPECT scanners.

CZT detectors are more sensitive to gamma rays than conventional scintillation detectors. This means that CZT-based SPECT scanners require less radiation dose to obtain high-quality images. These detectors have better energy resolution than conventional scintillation detectors and allow CZT-based SPECT scanners to distinguish between photons of different energy levels, resulting in higher image quality and better diagnostic accuracy.

Also, CZT-based SPECT scanners can acquire images faster than conventional SPECT scanners. This means that patients spend less time undergoing the scan, and the imaging department can serve more patients in a given time period. In addition, CZT detectors have better spatial resolution than conventional scintillation detectors and can produce more detailed images, which is particularly useful for small lesions or structures.

One example of a CZT-based SPECT scanner is the Discovery NM/CT 670 CZT scanner developed by GE Healthcare. This scanner uses CZT detectors and advanced reconstruction algorithms to produce high-quality images with improved spatial resolution and diagnostic accuracy.

SPECT scanners are used for various medical imaging applications and use radiotracers, which are molecules labelled with a radioactive isotope and injected into the patient's bloodstream. The radiotracer emits gamma rays detected by the SPECT scanner, allowing for the production of 3-D images of the inner structures and functions of the body. The areas of clinical applications of SPECT imaging include studying various brain disorders, such as Alzheimer's disease, Parkinson's disease, and epilepsy. It can help diagnose, stage, and monitor these conditions. Also used to evaluate blood flow in the heart and diagnose heart conditions, such as coronary artery disease and heart failure. It may also be used to assess the effectiveness of treatment and predict the risk of future heart problems.

Furthermore, SPECT imaging is used to detect and stage cancer and monitor the response to treatment, including localising tumours and guiding biopsy procedures. Moreover, SPECT imaging can evaluate bone disorders such as fractures, infections, and tumours.

7.4 Radiopharmaceuticals in SPECT Imaging

Radiopharmaceuticals contain a radioactive tracer and are used in medical imaging to diagnose and treat diseases. For example, in SPECT imaging, these radiotracers emit gamma rays and are detected by the SPECT scanner to create 3-D images of internal organs and tissues. The following radiotracers are used in SPECT imaging:

- Technetium-99m (Tc-99m, $t_{1/2}$= 6 hrs) is the most commonly used radiopharmaceutical in SPECT imaging. It is attached to various compounds depending on the organ or tissue being imaged, such as the heart, brain, bone, and kidneys.
- Iodine-123 (I-123, $t_{1/2}$= 13.2 hrs) is used to image the thyroid gland and often diagnoses thyroid disorders such as hyperthyroidism and hypothyroidism.
- Thallium-201 (Tl-201, $t_{1/2}$= 73 hrs) is used to evaluate blood flow to the heart muscle and can help diagnose coronary artery disease.
- Gallium-67 (Ga-67, $t_{1/2}$= 78 hrs) is used to detect inflammation and infection in the body and is often used in diagnosing and monitoring cancer.

- Indium-111 (In-111, $t_{1/2}$= 67 hrs) is used to evaluate inflammation and infection in the body and can also image certain types of tumours.

Radiotracers used in SPECT imaging are generally safe and well tolerated, but as with any medical procedure involving radiation, there is a small risk of radiation exposure. Therefore, the scanning procedures are discussed with the patient before imaging is performed.

7.5 Next-Generation SPECT Systems: Enhancing Sensitivity, Resolution, and Speed

The future of SPECT imaging will likely involve advancements in hardware and software that will improve image quality and increase the accuracy and specificity of SPECT scans.

One area of development in SPECT imaging is new radiotracers, which are substances injected into the body and emit gamma rays that the SPECT scanner can detect. Researchers are exploring the use of radiotracers specific to certain types of cells or tissues, which could improve the ability of SPECT scans to detect and diagnose diseases.

Another development area is using hybrid imaging techniques that combine SPECT with other imaging modalities, such as computerised Tomography (CT) or magnetic resonance imaging (MRI). These hybrid techniques can provide more detailed and precise images by combining the strengths of each imaging modality.

Advancements in SPECT hardware and software are also likely to play a role in the future of SPECT imaging. For example, improvements in detector technology could increase the sensitivity and resolution of SPECT scanners, while advancements in image reconstruction algorithms could improve image quality and reduce image artefacts.

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8 Why Cybersecurity is Non-Negotiable for Medical Devices in 2023

Cyber threats have become a critical concern for every industry, including healthcare, as the world becomes increasingly connected.

8.1 Introduction

Cyber threats have become a critical concern for every industry, including healthcare, as the world becomes increasingly connected. In fact, according to recent statistics, the healthcare industry experiences more data breaches than any other industry, and medical devices are one of the top targets for cybercriminals.

In 2020, medical device security incidents increased by 45%, and the average cost of a healthcare data breach was over $7 million.

As we move into 2023, healthcare providers must prioritize cybersecurity measures. These measures will protect patients' sensitive data and prevent potentially life-threatening cyber attacks on medical devices.

8.2 Threats to Medical Devices

Medical devices are increasingly becoming connected, which has made them vulnerable to cyber threats. The threat landscape for medical devices includes hackers, malicious insiders, and nation-states, who can physically access the devices through the network. These cyber threats to medical devices can result in data breaches, ransomware attacks, device malfunction, and patient harm.

8.3 Types of Cybersecurity Threats in Healthcare

The use of medical devices in healthcare has made patient care easy, but with technology, integration comes the increased risk of cybersecurity threats. Medical devices are exposed to a range of cyber threats, including:

Malware attacks: Malware attacks occur when malicious software is installed on a device, allowing cybercriminals to access sensitive data, modify device functionality, or cause physical harm to patients.

Ransomware attacks: Ransomware attacks involve encrypting device data, and cybercriminals demand payment to restore access to the data.

Denial-of-service attacks: occur when cybercriminals flood a device with requests, causing it to crash and become unavailable.

Man-in-the-middle attacks occur when cybercriminals intercept data transmitted between devices, allowing them to access sensitive data or modify device functionality.

Physical attacks occur when cybercriminals gain access to a device physically, allowing them to install malicious software or modify device functionality.

Insider threats: Insider threats involve employees or contractors with access to medical devices which intentionally or unintentionally compromise the devices' security.

8.4 Consequences of Cyber Attacks on Medical Devices

Cyber attacks on medical devices can have severe effects, including patient harm, loss of sensitive information, and damage to the reputation of healthcare providers. Cybercriminals can have different ways to access sensitive patient information, such as medical history, social security numbers, and financial information.

They can also modify the device's functionality, causing physical harm to patients. Moreover, a cyber attack on a medical device can result in costly downtime for healthcare providers, leading to significant financial losses.

8.5 Why Data Protection Is Vital to Reduce the Risk of Cybersecurity in Healthcare?

Data protection has to be the major concern in reducing the risk of cybersecurity threats in healthcare. Patient data is one of the most valuable assets in the healthcare industry, making it a prime target for cybercriminals.

Cyber attacks on medical devices can result in stolen patient data, unauthorized access to sensitive medical information, and even physical harm to patients. Thus, healthcare providers must opt for effective data protection measures to safeguard against these threats.

These measures include data encryption, access controls, and regular data backups. Encryption converts sensitive data into unreadable code, making it challenging for cybercriminals to access and decipher patient data. Access controls limit who can access patient data and what actions they can perform, reducing the risk of unauthorized access. Moreover, regular data backups ensure that patient data is recoverable in the event of a cyber-attack or system failure.

While you take measures to protect data, make sure it is easily accessible to the staff members. Simplifying data will help make patient analysis and critical aid therapies accessible and deployable.

Whether it is a Windows PC or an Apple computer, everything can be converted into a different format to make it compatible with the hardware you use. For example, you can always click here https://setapp.com/how-to/convert-numbers-to-excel-on-mac to convert your Numbers documents to a Windows-compatible tool quite easily. This ensures that the most useful clinical tools are available to you and your staff members without any delay.

In addition to protecting patient data, data protection measures also help healthcare providers comply with regulatory requirements such as HIPAA, GDPR, and other data privacy laws. By prioritizing data protection, healthcare providers can reduce the risk of cybersecurity threats, safeguard patient data, and maintain compliance with regulatory requirements.

8.6 Best Practices for Cybersecurity in Medical Devices

To protect against cybersecurity threats for medical devices in healthcare, there are several steps healthcare providers can take. Here are some tips to help avoid cybersecurity threats:

Implement robust security measures: Healthcare providers should ensure that all medical devices are equipped with robust security measures, including firewalls, encryption, and access controls.

Regularly update software: Medical devices should be updated regularly to ensure that they have the latest security patches and software updates. This will help to protect against known vulnerabilities and reduce the risk of cyber attacks.

Train employees: Healthcare providers should provide regular training to employees on how to identify and respond to cybersecurity threats. This should include training on how to recognize phishing emails and suspicious links, as well as how to report any potential security incidents.

Use secure networks: Medical devices should be connected to secure networks that are regularly monitored and maintained. This will help to reduce the risk of unauthorized access and data breaches.

Conduct regular risk assessments: Healthcare providers should conduct regular risk assessments to identify any vulnerabilities or potential security threats. This will allow them to take proactive steps to address any issues before they can be exploited by cybercriminals.

Develop a response plan: Healthcare providers should develop a comprehensive response plan in the event of a cybersecurity incident. This plan should outline the steps to be taken in the event of a breach, including who to contact and how to contain the incident.

8.7 Regulatory Requirements for Cybersecurity

Regulatory bodies around the world have recognized the importance of cybersecurity for medical devices and have implemented regulations to ensure patient safety.

One example of regulatory requirements for cybersecurity in healthcare is the Health Insurance Portability and Accountability Act (HIPAA). Under the HIPAA act, it is mandatory for healthcare organizations to take measures to ensure the confidentiality, integrity, and availability of patient information. This includes implementing administrative, physical, and technical safeguards to protect electronic protected health information (ePHI).

Another example is the Medical Device Regulation (MDR) and In-Vitro Diagnostic Regulation (IVDR) in the European Union. These regulations require medical device manufacturers to ensure that their products are secure and do not compromise patient safety. Manufacturers must also provide evidence that their devices meet specific cybersecurity requirements before they can be approved for use in the EU.

In the United States, the Food and Drug Administration (FDA) has also issued guidelines on cybersecurity for medical devices. These guidelines outline the steps that medical device manufacturers should take to ensure that their products are secure from cyber-attacks.

Compliance with regulatory requirements for cybersecurity is essential for healthcare organizations to avoid legal and financial repercussions.

Non-compliance can result in significant fines and damage to an organization's reputation. Adherence to these regulations also helps to build trust with patients and healthcare providers, as they can be assured that their information and medical devices are secure.

8.8 Future of Cybersecurity in Medical Devices

The future of cybersecurity in medical devices is rapidly evolving as the healthcare industry continues to rely on technology to improve patient care. As more medical devices become connected to the internet, the risk of cybersecurity threats increases, making it critical to prioritize cybersecurity measures.

Integration of AI and ML

One trend in the future of medical device cybersecurity is the integration of artificial intelligence (AI) and machine learning (ML) technologies. AI and ML can help healthcare providers identify and respond to potential cybersecurity threats in real-time, improving response times and reducing the risk of data breaches.

Use of blockchain technology

Another trend is the use of blockchain technology to secure patient data. Blockchain technology offers an immutable and decentralized method of storing patient data, making it difficult for cybercriminals to gain unauthorized access to sensitive information.

Stricter regulatory requirements

The implementation of stricter regulatory requirements is also expected in the future of medical device cybersecurity. Regulatory bodies such as the FDA and European Union have already released guidelines and regulations for medical device cybersecurity, and it is likely that these requirements will become even more stringent in the future.

Integration with the design and development of medical devices

Lastly, the integration of cybersecurity into the design and development of medical devices is expected to become standard practice. Cybersecurity will be considered at every stage of the device lifecycle, from design to implementation and beyond.

Cybersecurity is non-negotiable for medical devices in 2023. Cyber threats to medical devices significantly risk patient safety and healthcare providers' reputation. Manufacturers and healthcare providers must adopt best practices and comply with regulatory requirements to mitigate cybersecurity risks. As the use of medical devices continues to grow, the importance of cybersecurity will only increase.

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9 Personalised Theranostics for Cancer: A New Era in Precision Medicine

Theranostics is a cutting-edge approach that integrates diagnosis and therapy, enabling personalised and precise disease management.

9.1 Introduction

Theranostics has shown promise in various fields, including oncology, neurology, and cardiovascular disease. It is an advancing research area that will revolutionise how we approach the treatment of various diseases. This emerging field in nuclear medicine combines diagnostic and therapeutic techniques into a single approach and aims to develop personalised patient treatment plans based on their medical needs. This approach relies on technologies such as genetic testing, biomarker analysis, and electronic health records to collect and analyse data about an individual's health status, disease risk, and response to treatment.

The goal of personalised medicine is to move away from a 'uniform' approach to medical care and instead create targeted therapies that are more effective, efficient, and affordable. This approach is particularly relevant in cancer treatment, where genetic testing can identify specific mutations that drive tumour growth and guide the selection of targeted therapies that are more likely to be effective.

The personalised medicine approach can be achieved by applying theranostics, which involves using diagnostic tests to find specific biomarkers or molecular targets associated with a particular disease or condition. Once these targets have been identified, therapeutic agents can be designed to target them, selectively providing more effective and precise treatment.

For example, theranostics can be used to identify patients with specific genetic mutations or protein expression patterns that are associated with cancer. Once these biomarkers have been identified, targeted therapies can be developed to attack the cancer cells while sparing healthy cells. This approach can reduce the side effects of conventional cancer treatments such as radiation and chemotherapy.

9.2 Personalised Theranostics in Oncology: Current Status and Future Perspectives

Targeted radionuclide therapy is one of the most promising applications of theranostics in cancer treatment. This involves the use of radioactive isotopes attached to cancer-targeting molecules that are delivered directly to cancer cells. The radioactive isotopes emit radiation that kills the cancer cells while sparing healthy tissue.

Theranostic approaches can also be used to monitor the effectiveness of cancer treatments. For example, positron emission tomography (PET) imaging can be used to visualise the distribution of a therapeutic agent within the body and track how it affects the cancer cells.

Furthermore, theranostics has shown encouraging results in treating various cancers, including neuroendocrine tumours, prostate cancer, and breast cancer. The approach can improve treatment outcomes and reduce the side effects of traditional cancer treatments such as chemotherapy and radiation.

9.3 Non-Invasive Imaging-Guided Theranostics for Atherosclerosis Management

Also, theranostics has the potential to play a vital role in the diagnosis and treatment of cardiovascular diseases. The approach involves the use of diagnostic tests to identify specific biomarkers or molecular targets that are associated with cardiovascular disease. Once these targets have been identified, therapeutic agents can be designed to target them, selectively providing more effective and precise treatment.

One of the most promising applications of theranostics in cardiovascular disease is using imaging techniques to identify vulnerable plaques in the arteries that can lead to strokes and heart attacks. For example, intravascular ultrasound and optical coherence tomography can be used to visualise the structure of arterial plaques and identify those most likely to rupture.

Theranostic approaches can also be used to monitor the effectiveness of cardiovascular treatments by enabling magnetic resonance imaging (MRI) to visualise changes in the heart and blood vessels following treatment. In addition, theranostics has shown promising results in diagnosing and treating cardiovascular diseases such as atherosclerosis, hypertension, and heart failure.

9.4 Molecular Imaging-Guided Theranostics for Neurodegenerative Diseases

Theranostics is used in the diagnosis and treatment of neurological disorders. The approach involves using diagnostic tests to identify specific biomarkers or molecular targets associated with neurological conditions such as Parkinson’s disease, Alzheimer’s disease and multiple sclerosis. Once these targets have been identified, therapeutic agents can be designed to target them, selectively providing more effective and precise treatment.

One of the most promising applications of theranostics in neurological disorders is the use of imaging techniques to visualise changes in the brain that occur during the

progression of the disease. For example, PET imaging can detect the accumulation of amyloid plaques in the brain, a hallmark of Alzheimer's disease.

Theranostic approaches can also be used to monitor the effectiveness of neurological treatments. For instance, theranostic approaches have been used to develop targeted therapies for multiple sclerosis that selectively target immune cells that attack the nervous system while sparing healthy cells. The approach can improve treatment outcomes and reduce the side effects of traditional neurological treatments.

9.5 Theranostic Radionuclides in Nuclear Medicine: From Diagnosis to Treatment

Radiopharmaceuticals contain a radioactive substance that can be used for diagnostic or therapeutic purposes. For example, radiopharmaceuticals selectively target specific biomarkers or molecular targets associated with a particular disease or condition in theranostics. This allows for more precise and effective treatment.

Theranostic radiopharmaceuticals can be used for both diagnosis and therapy. For example, a radiopharmaceutical can bind specifically to cancer cells expressing a particular protein. The radioactive substance in the drug emits radiation that kills the cancer cells while sparing healthy tissue. The same radiopharmaceutical can be used for diagnostic purposes by attaching a diagnostic molecule to the radioactive substance, allowing for the visualisation of the cancer cells using imaging techniques such as PET or SPECT.

One example of a theranostic radiopharmaceutical is lutetium-177 DOTATATE, which is used in treating neuroendocrine tumours. The radiopharmaceutical is designed to bind specifically to somatostatin receptors on the surface of neuroendocrine tumour cells. The radioactive substance in the drug emits radiation that kills the cancer cells while sparing healthy tissue. The same radiopharmaceutical can be used for diagnostic purposes by attaching a diagnostic molecule to the radioactive substance, allowing for the visualisation of the neuroendocrine tumours using imaging techniques such as PET or SPECT.

Theranostic radiopharmaceuticals have shown promising results in treating cancer, cardiovascular disease, and neurological disorders. The approach can potentially improve treatment outcomes and reduce the side effects associated with traditional treatments such as chemotherapy and radiation.

Examples of theranostic radiopharmaceuticals include:

- Lutetium-177 PSMA-617 is used for the treatment of metastatic prostate cancer. It selectively targets prostate-specific membrane antigen (PSMA) expressed on prostate cancer cells.
- Iodine-131 metaiodobenzylguanidine (MIBG) treats neuroendocrine tumours like pheochromocytoma and neuroblastoma. It selectively targets the norepinephrine transporter expressed on the surface of these tumours.

- Yttrium-90 ibritumomab tiuxetan is used for the treatment of non-Hodgkin lymphoma. It selectively targets CD20, a protein expressed on the surface of B-cell lymphoma cells.
- Iodine-131 tositumomab is used for the treatment of non-Hodgkin lymphoma. It selectively targets CD20, a protein expressed on the surface of B-cell lymphoma cells.
- Lutetium-177 DOTATATE is used for the treatment of neuroendocrine tumours. It selectively targets somatostatin receptors expressed on the surface of these tumours.
- Gallium-68 DOTATOC is used for the diagnosis and staging of neuroendocrine tumours. It selectively targets somatostatin receptors expressed on the surface of these tumours.
- Copper-64 PET tracers are used for the diagnosis and staging of prostate cancer.
- Fluorine-18 FDG is used to diagnose and stage various cancers, including lung, lymphoma, and breast cancer. A glucose analogue accumulates in cancer cells due to their increased metabolic activity.

9.6 Artificial Intelligence and Machine Learning in Theranostics: Opportunities and Challenges

The future of theranostics is very promising, as this approach can revolutionise how we diagnose and treat a broad range of diseases and conditions.

The development of new and improved imaging techniques, such as PET/MRI and PET/CT scanners, is helping to improve the accuracy and sensitivity of theranostic imaging. This will enable us to detect diseases earlier and more accurately and to monitor treatment response more effectively.

The use of AI and machine learning is helping to identify new disease biomarkers and to develop more effective theranostic approaches. AI can also be used to analyse vast datasets of patient information to identify patterns and trends that can help to guide treatment decisions.

The development of new radiopharmaceuticals, such as alpha particle-emitting agents, is expanding the range of diseases and conditions that can be treated with theranostics. These new agents have the potential to deliver more precise and targeted therapy to cancer cells while minimising damage to healthy tissue.

9.7 Personalised Zevalin Therapy: Combining Imaging and Treatment for Optimised Outcomes

Zevalin is a theranostic radiopharmaceutical used for the treatment of non-Hodgkin's lymphoma. It consists of two components: a monoclonal antibody called rituximab, which targets the CD20 antigen expressed on the surface of B-cell lymphoma cells,

and a radioisotope called yttrium-90, which delivers radiation therapy to the cancer cells.

Zevalin's theranostic aspect involves using a diagnostic agent called Indium-111 Zevalin. This agent is administered to the patient before treatment with Zevalin, and it allows doctors to determine the extent of disease involvement and the appropriate dose of Zevalin to use.

Indium-111 Zevalin is injected into the patient's bloodstream during the diagnostic phase, which binds to the CD20 antigen on B-cell lymphoma cells. Next, the patient undergoes imaging with a gamma camera, which detects the radioactive emissions from the Indium-111. This allows doctors to determine the distribution of the lymphoma cells throughout the body and assess the degree of CD20 expression.

Based on the diagnostic imaging results, doctors can calculate the appropriate dose of Zevalin for treatment. The rituximab component of Zevalin targets the CD20 antigen on the surface of the cancer cells, delivering the yttrium-90 directly to the cancer cells and sparing healthy tissue. In addition, the yttrium-90 emits beta radiation, which damages the DNA in the cancer cells and causes cell death.

Using Zevalin as a theranostic radiopharmaceutical allows for more precise and personalised treatment of non-Hodgkin's lymphoma, improving outcomes and reducing side effects.

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10 Visual Evoked Potentials and Their Clinical Applications

Visual Evoked Potentials are brain responses to visual stimuli used for diagnosis and research.

10.1 Introduction

Visual evoked potential (VEP) is an electrophysiological test that measures the electrical activity of the visual system in response to visual stimuli, typically flashes or light patterns. The test evaluates the integrity and function of the visual system, including the retina, optic nerve, and visual pathways in the brain.

During the VEP test, the patient wears a special electrode cap or electrodes placed on the scalp to record electrical signals from the brain's visual cortex. Then, the patient is subjected to visual stimuli, such as flashes of light or patterns on a computer screen, and the electrical responses from the visual cortex are recorded.

The recorded signals are then analysed to determine the latency and amplitude of the response, which can provide information about the health and function of the visual system.

10.1 Visual-Evoked Potentials in Multiple Sclerosis

VEP testing can help diagnose various conditions that affect the visual system, including optic neuritis, multiple sclerosis, glaucoma, and amblyopia. Optic nerve inflammation can result in vision problems resulting in blurred or double vision, including pain with eye movement.

During VEP testing for MS, the patient is shown a series of visual stimuli, such as flashes of light or checkerboard patterns. At the same time, electrodes record the electrical signals from the brain's visual cortex. The recorded signals are then analysed to determine the latency and amplitude of the response.

In MS patients with optic neuritis, VEP testing can show delayed latency and reduced visual response amplitude, indicating that the optic nerve and visual pathways are not functioning correctly. However, VEP testing alone is insufficient to diagnose MS and should be combined with other clinical and diagnostic tests.

10.2 Clinical Applications of Visual-Evoked Potentials

Visual evoked potential (VEP) testing can diagnose various conditions affecting the visual system. For example, amblyopia, known as lazy eye, is when the brain ignores or suppresses input from one eye. VEP testing can evaluate the function of each eye and determine if there is a problem with the visual pathways in the brain.

Glaucoma damages the optic nerve, which can lead to vision loss. VEP testing can help diagnose and monitor the progression of glaucoma by measuring the electrical responses from the visual cortex in response to visual stimuli.

Brain tumours affecting visual pathways can cause vision problems. VEP testing can help diagnose and monitor the progression of these tumours by measuring the electrical responses from the visual cortex.

VEP testing can also diagnose and monitor certain retinal disorders, such as optic disc drusen and macular degeneration, by evaluating the electrical responses from the visual cortex to visual stimuli.

10.3 Assessment of Visual Function Using Visual-Evoked Potentials

Visual evoked potential (VEP) data is typically analysed by measuring the latency and amplitude of the electrical responses from the visual cortex in response to visual stimuli. The analysis of VEP data involves several steps, including VEP signals being recorded using an electrode cap or individual electrodes placed on the scalp. The recorded signals are then amplified and filtered to remove noise. VEP signals are usually averaged over multiple trials or visual stimulus presentations.

The latency of the VEP response is measured as the time from the onset of the visual stimulus to the peak of the evoked response. Latency analysis can provide information about the speed of neural transmission along the visual pathways.

The amplitude of the VEP response is measured as the magnitude of the peak-to-peak voltage of the evoked response. Amplitude analysis can provide information about the strength of neural activity in the visual cortex.

VEP data is often compared to normative data from healthy individuals to determine any abnormalities in the VEP response. Deviations from normal values can indicate underlying pathology or dysfunction of the visual system.

The analysis of VEP data is a complex process that requires specialised equipment and expertise. As a result, trained healthcare professionals or specialised laboratories often perform it.

10.4 The Future of Visual-Evoked Potentials in Ophthalmology

The future of VEP testing looks promising, as it continues to be an essential tool for evaluating the visual system's function and diagnosing a wide range of conditions. While VEPs and MRI are different types of tests, they can be used together to gain a complete picture of brain function. For example, researchers may use VEPs to study the brain's visual processing pathways while using MRI to identify the certain brain regions involved in those pathways.

In some cases, VEPs can also be used during an MRI scan to help map the visual cortex and identify brain areas that may be affected by disease or injury. This type of technique is known as functional MRI (fMRI) and can provide valuable information for research and clinical applications. VEP testing may be used for the early detection of Alzheimer's and Parkinson's disease. VEP testing can better understand individual

differences in the visual system, which can help healthcare professionals tailor treatment plans to each patient's unique needs.

Advances in technology, such as high-density electrode arrays and wearable devices, may improve the accuracy and efficiency of VEP testing and make it more accessible to patients. VEP testing may be integrated with other medical imaging modalities, such as positron emission tomography PET and magnetic resonance imaging, to evaluate the visual system and brain function. Therefore, combining VEPs and MRI can provide a powerful tool for studying brain function and identifying abnormalities or changes in the brain's visual processing pathways.

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11 Medical Imaging of the Heart: From Diagnosis to Treatment

Heart imaging provides non-invasive ways to diagnose, treat, and monitor heart disease for better outcomes.

11.1 Introduction

Medical imaging of the heart is used to diagnose and prevent heart disease, a leading cause of death worldwide. In addition, imaging can help improve patient outcomes and quality of life by providing detailed and accurate information about the heart. For example, heart imaging can investigate the following:

- Heart imaging can help diagnose various heart conditions, such as coronary artery disease, congenital heart defects, heart valve disease, and heart failure.
- Monitor heart disease progression and assess treatments' effectiveness.
- Healthcare providers can determine the best course of treatment for heart conditions, such as medication, surgery, or lifestyle changes.
- Identify risk factors for heart disease, such as plaque build-up in the arteries or heart enlargement, allowing for early intervention and prevention of heart disease.

11.2 Advances in Medical Imaging of the Heart: Applications in Diagnosis, Treatment, and Prevention of Heart Disease

Medical imaging of the heart can be performed using several different modalities, including:

Echocardiography is a non-invasive imaging modality that uses ultrasound waves to generate images of the heart. It is a commonly used diagnostic tool for assessing the structure and function of the heart and diagnosing various heart conditions.

During an echocardiogram, a trained technician or physician places a small, hand-held device called a transducer on the chest, which emits high-frequency sound waves. These sound waves bounce off the heart's structures and create images displayed on a monitor.

There are several types of echocardiograms, including:

The transducer is placed on the chest in a transthoracic echocardiogram (TTE) to create heart images.

Transesophageal echocardiogram (TEE) uses a small probe with a transducer passed down the throat and into the oesophagus to create more detailed images of the heart.

Stress echocardiogram involves performing an echocardiogram before and after exercise to assess the heart's function during physical activity.

11.3 Cardiac CT Imaging: Diagnosis of Cardiovascular Disease

During a cardiac CT scan, the patient lies on a table that travels through a large, doughnut-shaped machine called a CT scanner. The scanner emits X-rays detected by a series of detectors, which create detailed images of the heart and surrounding blood vessels.

There are different types of cardiac CT scans, including:

Calcium scoring involves a non-contrast CT scan that detects the presence of calcium in the coronary arteries, which is an indication of coronary artery disease.

Coronary CT angiography (CTA) involves a contrast-enhanced CT scan that provides detailed images of the coronary arteries to detect blockages or narrowing.

Cardiac CT for pulmonary embolism involves a contrast-enhanced CT scan that detects the presence of blood clots in the pulmonary arteries.

Cardiac CT scanning is safe but exposes the patient to a small amount of radiation. In addition, patients with kidney disease or allergies to contrast dye may not be candidates for cardiac CT.

11.4 Cardiac Magnetic Resonance Imaging: Diagnosis of Cardiovascular Disease

Magnetic resonance imaging (MRI) is valuable for diagnosing various heart conditions, including heart valve disease, heart failure, and congenital heart defects.

During a cardiac MRI, the patient lies on a table that travels through a large, doughnut-shaped machine. The patient is subjected to a strong magnetic field and radio waves to create images of the heart and surrounding blood vessels.

There are different types of cardiac MRI scans, including:

- Cine MRI involves creating a series of images that show the heart's movement over time. It can provide information about the heart's size, shape, and function.
- Cardiac MRI with contrast involves the injection of a contrast dye into the bloodstream, which enhances the images of the heart and blood vessels.
- Magnetic resonance angiography (MRA) involves the creation of detailed images of the blood vessels in and around the heart.
- Cardiac MRI is generally safe, but it is not recommended for patients with certain types of metallic implants or devices, such as pacemakers or defibrillators. In addition, patients with kidney disease may also not be candidates for cardiac MRI with contrast. Therefore, discussing any concerns with a healthcare provider before undergoing a cardiac MRI is essential.

11.5 Myocardial Perfusion Imaging in the Evaluation of Coronary Artery Disease

Myocardial perfusion imaging is a non-invasive diagnostic imaging technique that uses a small amount of radioactive material to create images of blood flow to the heart muscle. It is also known as nuclear stress testing or radionuclide myocardial perfusion imaging (MPI).

During a myocardial perfusion imaging test, a small amount of radioactive tracer material is injected into the patient's bloodstream, which is then taken up by the heart muscle. The patient then undergoes a series of images through SPECT (single-photon emission computed tomography) or PET (positron emission tomography) imaging to visualise the blood flow to the heart muscle.

The test is typically performed while the patient rests and again while exercising or under stress. By comparing the images obtained at rest with those obtained under stress, doctors can identify areas of reduced blood flow to the heart, which may indicate a heart condition such as coronary artery disease.

Myocardial perfusion imaging is generally considered a safe procedure with few risks or side effects. However, it may not be suitable for patients with certain medical conditions, such as pregnancy or kidney disease. Therefore, discussing any concerns with a healthcare provider before undergoing a myocardial perfusion imaging test is imperative.

Myoview is a brand name for a radioactive tracer material used in myocardial perfusion imaging (MPI). The tracer material is a small amount of a radioactive substance called technetium-99m, which is injected into the patient's bloodstream during the imaging procedure.

Once injected, the Myoview tracer is taken up by the heart muscle, allowing doctors to visualise blood flow to the heart and detect any areas of reduced blood flow or blockages in the coronary arteries.

Myoview is commonly used with either SPECT (single-photon emission computed tomography) or PET (positron emission tomography) imaging to produce detailed images of the heart muscle and surrounding blood vessels.

As with any imaging procedure involving radioactive material, there is a small risk of radiation exposure associated with Myoview imaging. However, the dose of radiation used in MPI is generally considered safe, and the benefits of the test in diagnosing and treating heart disease typically outweigh the risks.

11.6 Coronary Angiography: Imaging in Cardiovascular Disease

Angiography of the heart, also known as coronary angiography, is an imaging test that uses X-ray technology and a contrast dye to visualise the heart's blood vessels, including the coronary arteries. It is used to diagnose and evaluate heart conditions such as heart valve disease, coronary artery disease and congenital heart defects.

During coronary angiography, a catheter is inserted into an artery, usually in the groin or wrist, and threaded up to the heart. Then a contrast dye is injected through the

catheter and into the coronary arteries. X-ray images are taken as the dye flows through the arteries, allowing doctors to visualise any blockages or narrowing in the arteries.

Coronary angiography is generally a safe procedure, but it does carry some risks, including infection, bleeding and damage to the artery or surrounding tissue. There is also a possible risk of an allergic reaction from the contrast dye during the procedure.

Depending on the angiography results, further treatment may be necessary, such as angioplasty to open blocked arteries or surgery to repair or replace a heart valve.

During a CT angiography, the patient lies on a table that moves through a CT scanner. The scanner uses X-rays to create detailed images of the heart and surrounding blood vessels. Then, a contrast dye is injected into the patient's bloodstream to enhance the images of the blood vessels.

CT angiography is generally considered safe, but it does carry some risks, including allergic reactions to the contrast dye, radiation exposure, and kidney damage in patients with pre-existing kidney problems.

CT angiography may not be suitable for patients with certain medical conditions, such as pregnancy or kidney disease, or for those who cannot lie still for an extended period.

The choice of imaging modality will depend on the specific clinical situation and the information required by the healthcare provider.

11.7 Emerging Technologies in Cardiac Imaging: The Next Frontier in Cardiovascular Diagnosis and Treatment

The future of heart imaging will likely involve continued advancements in technology and techniques that provide more detailed and accurate information about the structure and function of the heart. Some possible future developments include:

Artificial intelligence and machine learning both these technologies can be used to analyse vast amounts of imaging data and provide insights into heart function and disease.

Advanced imaging techniques that allow for detailed 3D and even 4D (3D plus time) heart images can provide better visualisation and understanding of heart function and abnormalities.

Techniques that allow for the visualisation of specific molecules in the heart, such as proteins or enzymes, can provide information about disease processes at a cellular level.

Miniature sensors that can be worn or implanted in the body can continuously monitor heart function, potentially allowing for earlier detection of heart disease and personalised treatment.

Advancements in non-invasive imaging techniques such as MRI and CT may allow for more accurate and detailed heart imaging without requiring invasive procedures.

The future of heart imaging is likely to focus on more personalised and precise diagnosis and treatment of heart disease, leading to improved patient outcomes and quality of life.

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12 Revolutionising Healthcare: A Historical Perspective on Medical Imaging

Medical imaging has evolved over centuries, starting with X-rays in 1895 and progressing to CT, MRI, and PET scans.

12.1 Introduction

Medical imaging can create visual representations of the internal workings of the human body. Medical professionals use these images to diagnose and treat different health conditions. Modern medical imaging has a long and fascinating history that spans 128 years, and some of the key developments include:

In 1895, German physicist Wilhelm Conrad Röntgen discovered X-rays, a type of electromagnetic radiation that can penetrate through materials and create images of the internal structures of the human body. This discovery revolutionised medicine and paved the way for the development of medical imaging.

The invention of the X-ray machine in 1896 by British physicist Sir William Crookes made it possible to generate and control X-rays for medical imaging.

In the early 1900s, radiography became a common technique for producing X-ray images of the human body. This technique was used to diagnose fractures, detect foreign objects, and identify diseases such as tuberculosis.

In the 1970s, the first computed tomography (CT) scanner produced detailed cross-sectional images of the human body.

In the 1980s, magnetic resonance imaging (MRI) applied magnetic fields and radio waves to generate detailed images of the body's soft tissues.

In the 1990s, positron emission tomography (PET) became widely used to diagnose cancer and used a small amount of radioactive material to create images of metabolic processes.

Medical imaging continues to evolve with new techniques and technologies such as 3D imaging, digital radiography, and molecular imaging. These advances have greatly improved our ability to diagnose and treat various medical conditions.

12.2 Nuclear Medicine: A Vital Tool in Modern Healthcare

Nuclear medicine is a medical speciality that uses radioactive substances to diagnose and treat various medical conditions.

The history of nuclear medicine dates back to the early 20th century when scientists first discovered that certain substances could emit radiation. Then, in the 1930s, scientists began to explore using radioactive substances for medical purposes.

In the 1940s and 1950s, advances in nuclear technology led to the development of the first nuclear medicine techniques, including using radioactive isotopes to visualise internal organs and tissues. For example, in 1946, the first radioisotope tracer was used to diagnose a patient with thyroid disease. Then in 1951, the first radionuclide imaging scan was performed on a patient.

Over the next few decades, nuclear medicine technology continued to evolve with the development of new radiotracers and imaging techniques. Nuclear medicine diagnoses and treats various medical conditions, including cancer, heart disease, and neurological disorders.

Nuclear medicine procedures typically involve the injection or ingestion of a radiopharmaceutical, which contains a radioactive isotope. The radiopharmaceutical travels through the body and emits radiation, which is detected by a special camera that creates images of the internal structures.

Nuclear medicine has become an essential tool in modern medicine, providing clinicians with valuable information about the internal structures and functions of the human body. While the use of radioactive substances in medical practice carries some risks, the benefits of nuclear medicine have been shown to outweigh the risks for most patients.

12.3 The Invisible Light: A Journey Through the History of X-rays

The discovery of X-rays by the German physicist Wilhelm Conrad Röntgen conducted experiments using cathode rays in 1895. He observed that a screen coated with a fluorescent material placed near a cathode ray tube emitted a bright green glow when the tube was functioning.

Röntgen understood this glow was generated by a new type of ray emitted from the cathode ray tube. He called these rays ‘X-rays’, as he did not know what they were and wanted to denote their unknown nature.

Röntgen conducted further experiments to understand the properties of X-rays, including their ability to penetrate different materials and their effects on living tissue. He soon concluded that X-rays could be a powerful tool for medical diagnosis, as they allowed doctors to see inside the body without requiring invasive procedures.

The discovery of X-rays revolutionised medical imaging and profoundly impacted medical practice. Within months of Röntgen’s discovery, X-ray machines began to be utilised in hospitals and clinics worldwide, and the field of radiology was born.

12.4 CT Scans: A Breakthrough in Medical Technology

Computed tomography (CT) uses X-rays and computer algorithms to generate detailed human body images.

The history of CT began in the late 1800s when scientists began experimenting with using X-rays to see inside the body. However, it wasn't until the 1960s that British engineer Godfrey Hounsfield and American physicist Allan Cormack developed the first CT scanner.

Hounsfield and Cormack's invention used X-rays to create multiple images of the human body from different angles, which were combined using computer algorithms to create 3-D images of the internal structures of the human body. The first CT scanner was installed at Atkinson Morley's Hospital in Wimbledon, London, in 1972.

The development of CT revolutionised medical imaging, allowing doctors to see inside the body with much greater detail and accuracy than ever before. Over the years, CT technology has continued to evolve, with advances in computer processing power and imaging technology leading to faster and more detailed scans. Today, CT scans are widely used in medical practice and have become an essential tool for diagnosis and treatment in many fields of medicine.

12.5 PET Scans: A Powerful Tool for Disease Detection and Treatment

The history of PET began in the 1950s when scientists first discovered positrons, which are the antimatter counterpart of electrons. Then, in the 1960s, scientists realised that positrons could be applied to study the body's biological processes.

In 1975, Edward J. Hoffman and Michael E. Phelps developed the first PET scanner at the University of California, Los Angeles (UCLA). The scanner used a rotating ring of detectors to measure the distribution of positrons emitted by a radioactive tracer in the body. However, the first PET scan was performed on a human patient in 1976.

PET technology continued to evolve over the next few decades, with imaging technology improvements and new radiotracers' development. Today, PET scanners can produce highly detailed images of the internal structures and biochemical processes, making them an important tool for diagnosing and treating various medical conditions, including cancer, heart disease, and neurological disorders.

12.6 MRI: Pioneering the Way to Advanced Medical Diagnostics

Magnetic resonance imaging (MRI) uses radio waves in a strong magnetic field to produce internal body images.

The history of MRI began in the 1930s when scientists began to study the phenomenon of nuclear magnetic resonance (NMR). In the 1970s, scientists working in the field of NMR started to realise this technology could be used to create images of the human body.

In 1977, the first human MRI scan was performed by British physicist Peter Mansfield and American chemist Paul Lauterbur. Mansfield and Lauterbur's work used gradient

magnetic fields to construct internal images of the body with much greater detail and accuracy than ever before.

Over the next few decades, MRI technology continued to evolve, with advances in computer processing power and imaging technology leading to faster and more detailed scans. MRI is often combined with other imaging modalities to form positron emission tomography (PET) hybrids to provide more detailed and precise information about the human body's internal structures and functions. The continued development of MRI technology will lead to even more powerful and versatile imaging tools in the future.

12.7 The Power of Sound: A Journey Through the History of Ultrasound

The imaging modality, ultrasound, uses high-frequency sound waves to produce images of the internal structures of the human body.

The history of ultrasound dates back to the early 19th century when scientists first discovered that sound waves could detect objects hidden underwater. In the 1940s, researchers began to explore using ultrasound for medical purposes.

In 1955, Scottish obstetrician Ian Donald used ultrasound to detect the presence of fluid-filled cysts in the human body. These observations led to the development of the first commercial ultrasound scanner in the 1960s, primarily used for obstetric imaging.

Over the next few decades, ultrasound technology continued to evolve, with improvements in imaging technology and new image processing and analysis techniques.

Ultrasound is used to help diagnose cardiovascular disease, musculoskeletal injuries, and abdominal and pelvic disorders. In addition, it is commonly used during pregnancy to monitor foetal development and detect abnormalities.

The continued development of ultrasound technology will lead to even more powerful and versatile imaging tools, potentially revolutionising how many medical conditions are diagnosed and treated.

12.8 Conclusion

Modern medical imaging continues to be shaped by artificial intelligence and machine learning to analyse and interpret imaging data. These technologies can identify patterns and trends in large amounts of imaging data, helping clinicians make more accurate diagnoses and treatment decisions.

For example, molecular imaging visualises specific molecules within the body. In contrast, functional imaging can study how different organs and tissues function in real-time.

In addition, advances in imaging technology, such as the development of higher-resolution scanners and faster data processing, are expected to further improve the accuracy and speed of medical imaging. These imaging modalities will allow

clinicians to diagnose and treat medical conditions more quickly and effectively, leading to better patient outcomes.

Overall, the future of medical imaging is bright, with continued technological advancements expected to drive improvements in the accuracy, speed, and versatility of imaging techniques to diagnose various diseases.

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13 Revolutionising Medical Imaging with AI and Big Data Analytics

AI can revolutionise medical imaging by improving accuracy, speed, and clinical decision-making, improving patient outcomes.

13.1 Introduction

Artificial intelligence (AI) is increasingly being used to improve image interpretation and analysis in medical imaging. AI algorithms can be trained to analyse medical images and detect abnormalities or subtle changes that may be difficult for humans to detect, leading to more accurate and efficient diagnosis and treatment of various conditions.

AI algorithms can detect early signs of breast cancer on mammograms, lung nodules on CT scans, and detect signs of Alzheimer's disease on MRI scans. AI can also be used to analyse echocardiograms to assess heart function and diagnose heart disease.

In addition, AI can be used to improve the accuracy and efficiency of radiology reports by automatically generating preliminary information based on the analysis of medical images. This can help reduce the workload of radiologists and improve patient care by providing faster and more accurate reports.

Therefore, it is vital to ensure that AI algorithms are developed and used with human healthcare providers to provide the best possible patient care.

13.2 The Role of AI in Improving Medical Imaging Diagnostics

AI is increasingly being used to automate routine tasks in medical imaging, such as image processing, quality control, and data management. By automating these tasks, AI can help improve the efficiency and accuracy of medical imaging, leading to better patient care.

AI can automatically segment and label structures in medical images, such as organs and tumours, reducing the time and effort required by human healthcare providers. AI can also perform quality control checks on medical images, ensuring they meet the necessary standards for diagnosis and treatment.

In addition, AI can be used to manage and organise large amounts of medical imaging data, making it easier for healthcare providers to access and analyse this data. This can help improve the accuracy and efficiency of diagnosis and treatment by providing

healthcare providers with a more comprehensive view of the patient's medical history and imaging data.

By automating routine tasks in medical imaging, AI can help reduce healthcare providers' workload and improve patient care quality. However, it is vital to ensure that AI algorithms are developed and used responsibly and ethically, with a focus on patient privacy and safety.

13.3 From Image to Diagnosis: AI-Powered Medical Imaging Techniques

With the advancement of technology, AI is increasingly being used to assist in the prediction and risk assessment of medical imaging.

One area where AI is being used is in the analysis of medical images to identify potential health risks or predict the likelihood of certain conditions developing. For example, AI can be used to analyse CT or MRI scans to identify cancer signs or detect the early stages of Alzheimer's disease.

Another way AI is used in medical imaging is in risk assessment. AI models can be trained on large datasets of medical images and associated patient data to identify risk factors that may lead to certain medical conditions. Healthcare providers can then use this information to make more informed decisions about treatment options or take preventative measures to reduce the risk of certain conditions developing.

One of the advantages of using AI in medical imaging is that it can analyse large amounts of data quickly and accurately.

However, it is essential to note that AI does not replace healthcare providers. While AI can assist in analysing medical images, it is ultimately up to the healthcare provider to make the final diagnosis and treatment decisions based on all available information.

13.4 AI-Enabled Personalised Medicine: Revolutionising Patient Care

Personalised treatment planning involves tailoring medical treatments to individual patients based on their unique characteristics, such as their genetic makeup, medical history, and lifestyle factors. AI is increasingly being used in personalised treatment planning to help healthcare providers make more informed decisions about treatment options.

One way AI is used in personalised treatment planning is through predictive modelling. AI algorithms can analyse large datasets of patient information to identify patterns and predict how a patient is likely to respond to different treatments.

Another way AI is used is through image analysis. For example, AI algorithms can analyse medical images, such as CT or MRI scans, to identify specific features indicating a particular condition. This can help healthcare providers diagnose conditions earlier and more accurately, which can lead to more effective treatment outcomes.

AI can also be used in combination with electronic health records (EHRs) to provide more personalised treatment recommendations. EHRs contain a wealth of information about a patient's medical history, including past diagnoses, treatments, and medications. AI algorithms can analyse this information to identify potential risks and recommend personalised treatment plans based on the patient's unique health profile.

Overall, the use of AI in personalised treatment planning has the potential to improve patient outcomes by tailoring medical treatments to the individual needs of each patient. However, it is important to note that AI should not replace healthcare providers but rather be used as a tool to help support their decision-making processes.

13.5 Advances in Medical Imaging through AI and Computer Vision

AI can help researchers analyse large datasets of medical images and identify patterns or trends that may be difficult or impossible for humans to detect.

One area where AI is being used is in the development of new imaging modalities. For example, researchers use AI to analyse data from different imaging modalities, such as CT, MRI, and PET scans, to identify the strengths and weaknesses of each modality and determine how they can be combined to improve diagnostic accuracy.

AI is also being used to improve the accuracy of existing imaging modalities. For example, researchers are using AI to develop algorithms that can automatically correct image distortion and reduce noise in medical images, which can improve the quality and accuracy of the images.

Another way AI is being used in medical imaging research is through image analysis. AI algorithms can analyse medical images to identify specific features that may indicate a particular condition or disease, such as cancer. This can help researchers develop more accurate diagnostic tools and improve treatment outcomes.

13.6 Artificial Intelligence and Robotics in Healthcare: The Emergence of Robot Doctors

Currently, no robot doctor is capable of diagnosing patients on their own. While there are some robots being developed for use in healthcare, such as surgical robots, they are typically used in conjunction with human healthcare providers. They are not capable of diagnosing patients independently.

However, AI has shown promise in diagnosing certain conditions based on medical imaging data and other patient information. AI algorithms can be trained to analyse medical images and detect abnormalities or subtle changes that may be difficult for humans to detect, leading to more accurate diagnoses and improved patient outcomes.

It is important to note that AI algorithms cannot replace human healthcare providers. While they can provide valuable insights and support in diagnosing and treating certain conditions, they do not have the same level of clinical judgment and experience as

human healthcare providers. Therefore, AI should be used as a tool to support healthcare providers rather than replace them.

13.7 Emerging Applications of AI in Medical Imaging: Opportunities and Challenges

The future of AI in medical imaging is expected to bring significant advancements in diagnosis, treatment, and personalised care. The key areas where AI is expected to have an impact include:

AI algorithms can quickly analyse large datasets of medical images and identify patterns or abnormalities that may be difficult for humans to detect. This can lead to earlier and more accurate diagnoses, improving patient outcomes.

AI can help healthcare providers develop personalised treatment plans based on a patient's unique characteristics, such as genetics, medical history, and lifestyle factors. This can lead to more effective and efficient treatments tailored to each patient's needs.

AI can help researchers develop new imaging modalities or improve the accuracy of existing ones, leading to more precise and efficient diagnostic tools.

AI can analyse data from EHRs, such as past diagnoses, treatments, and medications, to identify potential risks and develop personalised treatment plans.

AI can be used to analyse medical images taken at home, allowing healthcare providers to monitor patients remotely and detect potential health issues early on.

Overall, the future of AI in medical imaging is expected to bring significant advancements in diagnosis, treatment, and personalised care, leading to improved patient outcomes and better overall healthcare. However, it is important to note that the development and validation of AI algorithms require careful testing and validation to ensure their accuracy and safety.

13.8 The Power of Big Data and AI

AI and data science are being used in medical imaging:

AI algorithms can analyse medical images to identify patterns and abnormalities that may not be visible to the human eye. This can help healthcare providers make more accurate and timely diagnoses.

AI algorithms can be trained to identify specific features in medical images that may be indicative of certain conditions, such as cancer. This can help healthcare providers detect potential health issues earlier and improve treatment outcomes.

Data science can be used to analyse large datasets of patient information, including medical images, to develop personalised treatment plans based on a patient's unique characteristics.

Data science can be used to analyse large datasets of medical images and other clinical data to identify trends and patterns that can inform clinical decision-making and improve patient outcomes.

AI and data science can be used to develop predictive models that can forecast the likelihood of certain health outcomes based on patient data, such as medical images, laboratory test results, and genetic information.

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14 The Future of Robotic Technologies in Medical Imaging

Robots are used in medical imaging and surgery to enhance precision, reduce risk, and improve patient outcomes.

14.1 Introduction

In 2019, a robot developed by Chinese researchers reportedly outperformed human doctors on a national medical licensing exam, scoring 456 points out of 600. The robot was trained to analyse and interpret medical images, such as computed tomography (CT) scans and X-rays, to give a diagnosis.

Several robots are currently being used in medicine and include:

Da Vinci Surgical System performs minimally invasive surgery. It allows surgeons to operate with greater precision and control, resulting in smaller incisions, less pain, and faster patient recovery times.

Hospitals use the RP-VITA robot to allow doctors to interact remotely with patients. It has a video screen that can display a live video feed of the doctor, allowing them to communicate with patients from another location.

CyberKnife is used to perform radiosurgery, a radiation therapy to treat tumours and other medical conditions. It uses a robotic arm to deliver high doses of radiation to specific areas of the body.

MiroSurge robotic system can perform highly precise microsurgery, allowing surgeons to operate on delicate tissues with greater accuracy and control.

Rex is a robotic exoskeleton used to help people with mobility impairments to walk. Also, mimicking the human body's movements allows users to walk more naturally and with greater ease.

Robotic surgery has become increasingly common in recent years. Surgeons can use robots to perform minimally invasive procedures with greater precision and control. In addition, these procedures can reduce pain, scarring, and recovery time for patients.

14.2 The Role of Robotics in Minimally Invasive Surgery

Robotic surgery has several advantages over traditional open surgery and other minimally invasive procedures, such as laparoscopic surgery. These advantages include the following:

The robotic arms can move in ways human hands cannot, allowing for greater accuracy and control during surgery.

Robotic surgery uses smaller incisions than traditional open surgery, which can lead to less pain, scarring and a quicker recovery time for the patient.

Robotic surgery is less invasive and can result in less blood loss during the procedure.

Patients who undergo robotic surgery have shorter hospital stays and a quicker recovery time than traditional surgery.

Robotic surgery is used in the prostate, gynaecologic, cardiac, and orthopaedic surgery. However, it is essential to note that not all surgeries can be carried out using robotic systems. Therefore, a qualified surgeon should decide to use robotic surgery based on the patient's medical condition and individual needs.

The da Vinci Surgical System consists of a console where the surgeon sits and controls the robot and a patient-side cart that holds the robotic arms and surgical instruments. The system uses advanced 3D visualisation and precision instruments to enable surgeons to perform complex surgical procedures with greater precision and control than traditional surgical methods. The surgeon controls the robotic arms using hand and foot controls at the console while looking through a high-definition 3D camera that provides a magnified view of the surgical site.

Da Vinci robotic surgery can perform various procedures, including prostatectomy, hysterectomy, and colorectal and thoracic surgeries. The benefits of da Vinci's robotic surgery include:

The da Vinci system gives the surgeon greater precision and control than traditional surgical methods, which can lead to better surgical outcomes.

Da Vinci's robotic surgery uses smaller incisions than traditional surgery, which can lead to less pain, scarring and a quicker recovery time for the patient.

The da Vinci robotic surgery is less invasive and can result in less blood loss during the procedure.

Patients who undergo da Vinci robotic surgery have shorter hospital stays and a quicker recovery time than traditional surgery.

14.3 The Role of Robotics in Automated Medical Imaging Analysis

Robots can analyse medical imaging scans such as X-rays, CT scans, MRI scans, and ultrasounds. However, these scans generate large amounts of data, making it difficult for doctors to analyse and interpret the information. By using artificial intelligence (AI) and machine learning algorithms, robots can help physicians to analyse and interpret medical images more accurately and quickly.

For example, AI algorithms can be trained to detect specific abnormalities or patterns in medical images, such as tumours or areas of inflammation. Therefore, AI can help physicians make more accurate diagnoses and effective treatment plans.

Robots can also analyse medical images in real-time during surgical procedures. For example, during brain surgery, a robot can analyse MRI scans to help the surgeon identify the tumour's precise location or other abnormalities, improving the procedure's accuracy and safety.

In addition to analysing medical images, robots can generate 3D models of organs or tissues based on medical images. These 3D models can be used to plan and simulate surgical procedures, which can help improve the procedure's accuracy and safety.

Robots are becoming increasingly important in medical imaging analysis, as they can help physicians analyse and interpret large amounts of data more accurately and quickly, leading to better patient outcomes.

14.4 The Benefits of the Lokomat Robotic Device in Physical Therapy

Robots are increasingly used in physical therapy to assist patients with rehabilitation and recovery. For example, robotic devices can help patients to regain mobility, strength, and coordination following an injury, surgery, or other medical condition.

One example of a robotic device used in physical therapy is the Lokomat, a robotic gait training system that helps patients relearn how to walk. The Lokomat uses robotic leg braces to support the patient's weight and robotic motors to move the patient's legs in a natural walking pattern. In addition, the Lokomat can be programmed to adjust the support and resistance level based on the patient's abilities and progress.

Another example of a robotic device used in physical therapy is the Armeo. This robotic arm exoskeleton helps patients regain movement and coordination in their arms following a stroke or other neurological injury. The Armeo can be programmed to provide varying levels of assistance and resistance to help patients to regain strength and control in their arms.

Robotic devices can also provide feedback and monitoring during physical therapy exercises. For example, a robotic device can measure the force and movement of a patient's muscles during an exercise, which can help the therapist track the patient's progress and adjust the therapy program as needed.

Robotic devices are becoming increasingly important in physical therapy, as they can help patients recover more quickly and effectively than traditional therapy methods. While robotic devices can be expensive and unsuitable for all patients, they offer a promising new approach to rehabilitation and recovery.

14.5 Robotics and Precision Medicine: Enhancing Drug Delivery Outcomes

Robots are increasingly used in drug delivery to improve drug administration's accuracy, efficiency, and safety. One example of a robotic device used in drug delivery is the i.v.STATION is an automated system for preparing and dispensing intravenous (IV) medications.

The i.v.STATION uses robotic arms to prepare and label IV medications, which helps to minimise the risk of medication errors and contamination. The system can be

programmed to ensure that the correct dose and concentration of medication are dispensed, which helps to improve the accuracy and safety of drug administration.

Another example of a robotic device used in drug delivery is the RIVA (Robotic IV Automation) system, an automated system for compounding sterile IV medications. The RIVA system uses robotic arms and advanced imaging technology to prepare IV medications in a sterile environment, which helps to minimise the risk of contamination and infection.

Robots can also deliver drugs directly to targeted areas of the body, such as tumours or diseased organs. For example, tiny robotic devices known as nanobots can be programmed to deliver drugs directly to cancer cells, which can help to minimise the side effects of chemotherapy and improve the effectiveness of treatment.

Furthermore, robots are becoming increasingly important in drug delivery, as they can help to improve the accuracy, efficiency, and safety of drug administration. While robotic devices can be expensive and unsuitable for all patients, they offer a promising new drug delivery approach that could help improve patient outcomes and reduce healthcare costs.

Robots can help provide care to patients, especially those who are elderly or have limited mobility. For example, robots can assist with activities of daily living such as feeding, bathing, and dressing.

Robots are increasingly used in patient care in a variety of ways, for example:

Surgeons use surgical robots to perform minimally invasive procedures with greater precision and control, resulting in reduced patient pain, scarring, and recovery time.

Rehabilitation robots help patients recover from injuries or disabilities by assisting them with exercises and movements.

Telepresence robots allow remote doctors or specialists to communicate with patients and healthcare providers, providing virtual consultations, check-ins, and diagnoses.

Delivery robots transport medication, lab specimens, or other items throughout healthcare facilities, reducing the risk of human error and increasing efficiency.

Companion robots provide emotional support and companionship to patients, especially those in long-term care facilities or hospices.

Cleaning robots sanitise and disinfect patient rooms, common areas, and equipment, reducing the risk of infection and disease transmission.

14.6 Robotics and Telemedicine: Enhancing Access to Healthcare

Robots are used in telemedicine to enable remote consultations between physicians and patients. This technology allows doctors to diagnose and treat patients far away or in remote areas.

Robots are increasingly being used in telemedicine to provide remote healthcare services to patients in various ways and including:

Telepresence robots enable healthcare providers to connect remotely with patients, providing virtual consultations, check-ins, and diagnoses. These robots, equipped with cameras and screens, allow doctors to see and communicate with patients in real-time, regardless of location.

Diagnostic robots perform medical tests remotely, such as taking blood samples or measuring vital signs, allowing doctors to diagnose and treat patients from a distance.

Pharmacy robots dispense medication remotely, providing patients with prescriptions without physical contact with a pharmacist.

Surgical robots perform complex surgeries remotely, allowing surgeons to operate on patients from another location.

Health monitoring robots track patients' health remotely, such as their heart rate, blood pressure, and other vital signs, allowing doctors to detect any changes in their health and intervene as necessary.

Telemedicine robots can improve patient access to healthcare services, especially in remote or underserved areas, while reducing healthcare costs and increasing efficiency.

14.7 The Future of Medical Imaging: Advancements in Robotics

The future of robots in medical imaging is expected to be highly transformative. Robotic technology has already made significant strides in medical imaging, and it is projected to play a critical role in the future.

One of the most significant advantages of using robots in medical imaging is their ability to perform exact and accurate procedures. Robots are programmed to perform highly complex and delicate operations, such as surgery or biopsy, with high accuracy and precision, leading to better patient outcomes and reduced risks.

Another advantage of using robots in medical imaging is their ability to work nonstop without needing rest or breaks. This can help increase productivity and reduce patient wait times, improving healthcare efficiency.

Robots can also be equipped with advanced imaging technology, such as high-resolution cameras and sensors, to provide highly detailed and accurate human body images. This can help doctors and clinicians make more informed patient care and treatment decisions.

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15 Breaking New Ground: Proton Therapy and the Future of Cancer Care

Proton therapy is a type of radiation therapy that uses protons to treat cancer by targeting tumours with high precision.

15.1 Introduction

Proton therapy uses high-energy proton beams to target and destroy cancer cells. During proton therapy, a cyclotron or synchrotron accelerates protons to high speeds and directs them towards the tumour. As a result, the protons deposit most of their energy at the tumour site, sparing the surrounding healthy tissue from damage.

Proton therapy is particularly effective for treating cancers resistant to conventional radiation therapy, such as those located in the brain, spine, or prostate gland. Also, proton therapy can be used in conjunction with surgery or chemotherapy.

The availability of proton therapy is limited to certain hospitals and treatment centres, which may make it difficult for some patients to access it. Proton therapy is available in the UK at the Christie NHS Foundation Trust in Manchester and the University College London Hospitals.

Both these centres provide proton therapy for various cancer types, including brain, eye, spinal, and prostate tumours. The treatment is usually recommended for patients with cancer close to vital organs, where conventional radiation therapy may cause significant damage to surrounding healthy tissue.

Before treatment, a team of radiation oncologists and medical physicists will create a detailed treatment plan based on the patient's needs using various imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). The aim is to determine the precise location and size of the tumour. The treatment plan will also consider the patient's overall health and the specific characteristics of their cancer.

The patient lies on a table during treatment while the proton beam is geared toward the tumour from different angles. The treatment is painless; the patient can usually go home immediately after each session.

Proton therapy is typically delivered over several weeks, each lasting only a few minutes. The total number of treatments will depend on the size and location of the tumour and the individual characteristics of the patient's cancer.

15.2 Proton Therapy: A Versatile Treatment Option for Different Cancer Types

Proton therapy is being used to treat various cancer types, including brain tumours, eye tumours, head and neck cancers, lung cancer, prostate cancer, and certain types of paediatric cancer. The main advantage of proton therapy is that protons deposit most of their energy at the tumour site, sparing the surrounding healthy tissue from damage.

Brain tumours can be challenging to treat with conventional radiation therapy because the brain is a sensitive organ, and radiation can cause damage to healthy brain tissue, leading to long-term side effects. Proton therapy can help to reduce the risk of damage to healthy brain tissue, which can help to minimise side effects.

In addition, proton therapy can treat tumours in critical areas of the brain, such as the brainstem or optic nerve, where surgery may not be an option.

The cost of proton therapy machines can vary widely depending on the type of machine and the manufacturer. The cost of a single proton therapy machine can range from tens of millions of dollars to over $200 million.

One of the reasons why proton therapy machines are so expensive is that they are highly complex and require advanced technology to produce and maintain high-energy proton beams. In addition, proton therapy machines require specialised facilities, including radiation shielding and high-tech monitoring and control systems, which can add to the overall cost of the treatment.

The cost of proton therapy machines can be a barrier to their widespread adoption, particularly in countries with limited healthcare budgets. However, some healthcare systems and governments have made significant investments in proton therapy technology in recent years, recognising the potential benefits of this advanced cancer treatment.

It is worth noting that the cost of proton therapy is not only related to the cost of the machine but also to the cost of the entire treatment, which includes the personnel, facility, and other related expenses. In some cases, insurance companies or national healthcare systems may cover the cost of proton therapy for eligible patients. However, this can vary depending on the country and the specific circumstances of the patient's case.

15.3 Types of Brain Cancer that Respond to Proton Therapy

Gliomas are tumours that develop from the glial cells in the brain, which provide support and nourishment to the neurons. Gliomas can be either low-grade or high-grade, and proton therapy can treat both types.

Meningiomas are tumours that develop from the meninges, the membranes covering the brain and spinal cord. Meningiomas are usually benign but can still cause significant symptoms and may require treatment with proton therapy.

Proton therapy can treat these tumours, which can cause hormonal imbalances and other symptoms.

Medulloblastomas are more common in children, and proton therapy can be an effective treatment option for these tumours.

Metastatic brain tumours spread to the brain from other parts of the body. Proton therapy can be used to treat these tumours, which can be challenging to treat with traditional radiation therapy due to their location in the brain.

15.4 Proton Therapy and Beyond: The Future of Radiation Oncology

The future of proton therapy looks promising as this treatment option continues to gain popularity and acceptance among patients and healthcare providers. Proton therapy technology is evolving rapidly, with new proton therapy machines and techniques being developed to make the treatment more precise and effective. One of the key advancements is the development of pencil beam scanning, which enables the proton beam to be delivered in a highly precise manner, allowing for better targeting of tumours while minimizing damage to healthy tissue.

As more proton therapy centres are being established worldwide, proton therapy is becoming more accessible to patients. This is due to the decreasing cost of proton therapy machines and the increasing number of healthcare providers offering this treatment option. In addition, the development of proton therapy is being driven by collaboration and research between healthcare providers and researchers worldwide. This has led to the sharing of best practices, the development of new treatment protocols, and the creation of international standards for proton therapy.

Proton therapy is well-suited to personalised medicine, which tailors cancer treatments to individual patients based on their genetic makeup and other factors. As a result, healthcare providers can deliver more effective treatments while minimizing side effects by using proton therapy to target tumours highly precisely. In addition, proton therapy is used with other cancer treatments, such as chemotherapy and immunotherapy, to enhance their effectiveness. This is called combination therapy and has shown promising results in clinical trials.

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16 Nuclear Medicine Techniques for Bone Imaging and Cancer Diagnosis

Bone imaging is an essential diagnostic tool for detecting bone diseases, injuries, and disorders.

16.1 Introduction

Bone scans use a radioactive tracer to create images of the bones. The tracer is injected into the bloodstream, accumulating in areas of the bone undergoing active growth or repair. Bone scans can detect bone fractures, infections, tumours, and conditions such as osteoporosis and Paget's disease.

Bone imaging is a valuable tool for diagnosing and monitoring Paget's disease. Paget's disease is a bone disorder characterized by abnormal bone remodelling, leading to weakened bones, deformities, and pain. The following imaging modalities help to diagnose and monitor Paget's disease:

X-rays can detect the characteristic changes in bone structure in Paget's disease. These changes include areas of increased bone density, called sclerotic lesions, and areas of bone thinning or osteoporosis circumscripta. X-rays can also detect deformities and fractures associated with Paget's disease.

Using radiopharmaceuticals, such as technetium-99m or fluorine-18, can provide a more comprehensive view of bone involvement in Paget's disease. These scans can detect areas of increased bone turnover and activity and areas of decreased blood flow or avascular necrosis that can occur in advanced cases.

CT scans can provide more detailed images of the bones affected by Paget's disease, including bone deformity, thinning, or thickening. CT scans are beneficial for evaluating the spine and other areas where X-rays may not provide a complete picture.

MRI can provide detailed images of soft tissue, which can help detect nerve or spinal cord compression associated with advanced Paget's disease. MRI is also useful for detecting areas of bone marrow oedema, indicating areas of increased bone activity or inflammation.

16.2 Bone Imaging with Technetium-99m

Technetium-99m (Tc-99m) is a radioisotope commonly used in bone imaging. A medical cyclotron or generator produces it from its parent isotope, molybdenum-99 (Mo-99). Tc-99m has a short half-life of about 6 hours, making it ideal for medical imaging because it allows imaging studies to be completed within a reasonable time.

In bone imaging, Tc-99m is typically injected intravenously, accumulating in areas of the bone undergoing active growth or repair. This makes it useful for detecting various bone conditions, including fractures, infections, tumours, and degenerative bone diseases.

Tc-99m bone imaging can be achieved in several ways, including planar imaging, SPECT (single-photon emission computed tomography), and hybrid imaging (such as SPECT/CT or SPECT/MRI). Planar imaging involves taking two-dimensional images of the bone, while SPECT imaging involves three-dimensional images that can provide more detailed information about the bone structure and function.

16.3 Strontium-89 for the Palliative Treatment of Bone Pain in Metastatic Cancer

Strontium-89 (Sr-89) is not used in bone imaging but rather as a treatment for metastatic bone cancer to relieve bone pain. Sr-89 is a radioactive isotope similar in structure to calcium, especially taken up by bone tissue. Once injected into the bloodstream, it accumulates in areas of the bone undergoing active growth or repair, such as those affected by bone metastases.

The radioactive decay of Sr-89 emits beta particles, which can penetrate the bone tissue and destroy the cancer cells within the bone. This can lead to pain relief and improved quality of life for patients with metastatic bone cancer.

While Sr-89 is not used for diagnostic bone imaging, it can be imaged using nuclear medicine techniques such as gamma camera imaging, confirming the radioactive isotope uptake in the bone tissue.

Furthermore, Sr-89 is a valuable treatment option for patients with metastatic bone cancer who are experiencing bone pain, and it can provide significant pain relief and improved quality of life.

16.4 Samarium-153 for the Treatment of Bone Pain in Metastatic Cancer

Samarium-153 (Sm-153) is not typically used in bone imaging but rather as a treatment for bone pain associated with metastatic bone cancer. Sm-153 is a radioactive isotope similar in structure to calcium, preferentially taken up by bone tissue. Once injected into the bloodstream, it accumulates in areas of the bone undergoing active growth or repair, such as those affected by bone metastases.

The radioactive decay of Sm-153 emits beta particles, which can penetrate the bone tissue and destroy the cancer cells within the bone. This can lead to pain relief and improved quality of life for patients with metastatic bone cancer.

Consequently, Sm-153 is not used for diagnostic bone imaging. It can be imaged using nuclear medicine techniques such as gamma camera imaging, confirming the radioactive isotope uptake in the bone tissue.

However, Sm-153 is a valuable treatment option for patients with metastatic bone cancer who are experiencing bone pain, and it can provide significant pain relief and improved quality of life.

16.5 Fluorine-18 as a Tracer in PET Bone Imaging

Fluorine-18 (F-18) is not typically used as the primary imaging agent in bone imaging but as a tracer in PET (positron emission tomography) bone imaging. F-18 is a radioisotope commonly used in PET imaging due to its short half-life of about 110 minutes, which allows imaging studies to be completed relatively quickly.

In PET bone imaging, F-18 is typically administered intravenously, and the bone tissue takes it up in a manner similar to Tc-99m. However, F-18 detects bone metastases in cancer patients and evaluates treatment effectiveness.

PET imaging using F-18 can provide valuable information about the structure and function of the bone tissue, and it can help to detect bone abnormalities at an earlier stage than other imaging modalities.

F-18 PET bone imaging can be combined with other imaging modalities, such as CT (computed tomography) or MRI (magnetic resonance imaging), to provide more detailed information about the bone tissue and surrounding structures.

Overall, F-18 PET bone imaging is a valuable tool for detecting bone metastases and other bone abnormalities, and it can provide vital information to guide treatment decisions and monitor disease progression.

16.6 Radiopharmaceuticals used in Bone Imaging

Several new imaging agents in bone imaging have shown promise in preclinical and clinical studies. These agents can provide more accurate and specific information about bone structure and function, improving the diagnosis and treatment of bone disorders, for example:

Sodium fluoride (NaF) PET is a promising imaging agent to detect increased bone activity and remodelling areas. This makes it particularly useful for the detection of bone metastases in cancer patients, as well as for the evaluation of bone mineral density and turnover in osteoporosis and other metabolic bone disorders.

Radium-223 (Ra-223) dichloride is a radiopharmaceutical that can selectively target areas of bone affected by metastatic prostate cancer. It emits alpha particles that can penetrate bone tissue and kill cancer cells while sparing surrounding healthy tissue. Ra-223 has been shown to improve survival in patients with metastatic prostate cancer and has been approved by the FDA for this indication.

Gadolinium-based contrast agents (GBCAs) for MRI are commonly used in MRI to enhance the contrast between tissues and improve the accuracy of diagnosis. Newer GBCAs that target specific molecular markers associated with bone diseases, such as integrins and osteoclasts, are being developed and tested in preclinical and clinical studies.

Osteocalcin-targeted imaging agents: Osteocalcin is a protein produced by bone-forming cells called osteoblasts. Targeted imaging agents that bind specifically to osteocalcin, such as radiolabelled antibodies and peptides, are being developed and tested to detect bone metastases and other bone disorders.

16.7 The Future of Bone Imaging: An Overview of Emerging Technologies and Applications

The future of bone imaging is promising, with ongoing advancements in imaging technology and the development of new imaging agents. The key trends and developments in the field include:

There is growing interest in using molecular imaging techniques to detect bone disease at an earlier stage and monitor treatment response more accurately. This includes using targeted imaging agents that can bind specifically to molecules associated with bone diseases, such as cancer cells or inflammatory markers.

Artificial intelligence (AI) and machine learning algorithms are being developed to analyse large amounts of imaging data and extract meaningful information about bone structure and function. This could help to improve the accuracy and speed of diagnosis and treatment planning.

Combining multiple imaging modalities, such as PET/CT or MRI/SPECT, is becoming increasingly popular for bone imaging. These hybrid scanners provide more comprehensive and accurate information about bone tissue and surrounding structures.

Advances in 3D printing technology are being used to create anatomically accurate models of bone tissue for surgical planning and educational purposes. These models can be customized to each patient's specific anatomy and can help improve surgical procedures' accuracy and safety.

Portable bone imaging devices are being developed to be used at the point of care, such as in emergency departments or remote locations. This could help to improve access to bone imaging for patients who may not have easy access to traditional imaging facilities.

The future of bone imaging is exciting, with technological advancements and the development of new imaging agents that can improve the accuracy and speed of diagnosis and treatment planning for a wide range of bone conditions and injuries. For example, radioisotopes are a valuable tool in bone imaging because they allow for the detection of bone abnormalities at a molecular level, which can lead to earlier detection and treatment of bone conditions.

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17 Security and Privacy Considerations in Picture Archiving and Communication Systems

Picture Archiving and Communication Systems (PACS) streamline medical imaging storage, sharing, and access, enhancing patient care.

17.1 Introduction

Picture Archiving and Communication Systems (PACS) development began in the 1960s when digital imaging technologies became apparent in radiology. However, until the 1980s and 1990s, PACS emerged as a comprehensive solution for managing and storing medical imaging data.

In the early days of PACS, this technology was primarily used for storing and displaying digital images. Consequently, replacing traditional film-based X-rays with digital images viewed on computer screens. However, these early systems were expensive and complex, requiring specialised hardware and software.

As PACS technology advanced, new features and capabilities were added, such as image analysis tools, 3D imaging, and advanced networking capabilities. In addition, in the 2000s and 2010s, PACS began to move to a web-based model, allowing for more efficient and accessible storage and management of medical imaging data.

Today, PACS is an essential component of modern radiology departments, providing healthcare providers with fast and reliable access to patient imaging data, improving diagnosis and treatment planning, and reducing the need for physical storage of medical images. In addition, PACS has evolved to incorporate artificial intelligence (AI) and machine learning, enabling more advanced analysis and interpretation of medical images.

PACS integrates into healthcare facilities such as hospitals and clinics to store and manage medical images, such as X-rays, CT scans, MRIs, and ultrasounds.

PACS typically includes software tools and hardware components, including image acquisition devices, image display workstations, image storage servers, and network infrastructure. The system streamlines the management of medical images by allowing healthcare professionals to access and review images from any location within the healthcare facility and remotely via a secure network.

The benefits of PACS include improved patient care through faster and more accurate diagnosis, increased efficiency of healthcare delivery, reduced costs associated with film-based imaging, and enhanced collaboration and communication among

healthcare professionals. PACS has become an essential tool in modern healthcare, enabling faster and more efficient access to medical images and improving the overall quality of patient care.

17.1 From Film to PACS: The Transition to Digital Medical Imaging

PACS offers several advantages over traditional film-based medical imaging systems and includes the following:

PACS eliminates the need for manual film processing and storage, which can significantly reduce the time and effort required to manage and retrieve medical images. Instead, images can be viewed, accessed, and shared quickly and easily from any location with secure network access.

PACS eliminates the need for costly film and film processing equipment and physical storage space for film-based images, resulting in significant cost savings for healthcare facilities.

PACS enables healthcare professionals to access and review medical images quickly, allowing for faster and more accurate diagnosis and treatment planning. It also improves communication and collaboration among healthcare professionals involved in a patient's care.

PACS includes robust security features to protect patient data and ensure that authorised healthcare professionals only access images. These procedures will help to prevent data breaches and protect patient privacy.

PACS allows healthcare professionals to view and manage medical images more efficiently, reducing the time and effort required for image retrieval, viewing, and interpretation. These functions can improve productivity and workflow for radiology departments and other healthcare professionals involved in patient care.

PACS has revolutionised how medical images are stored, managed, and shared, improving efficiency, reducing costs, and enhancing patient care.

17.2 Transforming Paediatric Radiology: The Advantages of Picture Archiving and Communication Systems

PACS offers several advantages in paediatrics, specifically:

Children are more susceptible to radiation than adults, and PACS allows for lower-dose imaging techniques. This can help reduce the radiation exposure children receive during medical imaging procedures.

PACS enables healthcare professionals in different locations to quickly and easily access and share medical images, facilitating collaboration and communication among healthcare providers involved in a child's care.

PACS allows for faster and more accurate diagnosis and treatment planning, which can lead to improved outcomes for paediatric patients.

PACS, there is no risk of losing or misplacing film-based images, which can help to ensure that paediatric patients receive the appropriate care and treatment promptly.

PACS allows family members to view and discuss their child's medical images with healthcare providers, which can help to enhance family-centred care and improve patient satisfaction.

Furthermore, PACS can help improve paediatric patients' medical imaging procedures' safety, quality, and efficiency while facilitating collaboration and communication among healthcare providers and families involved in a child's care.

17.3 The Role of Prefetching in PACS: Improving Radiology Workflow and Patient Care

Prefetching is a feature of PACS that automatically retrieves and stores medical images and patient information before a radiologist or clinician's request. This reduces the time required to access and view medical images during patient care, thereby improving the efficiency of healthcare delivery.

Prefetching involves analysing a patient's electronic medical record and identifying upcoming appointments or scheduled procedures. The PACS system then automatically retrieves and stores the relevant medical images and patient information in advance to be readily available when needed.

Prefetching can help reduce the time healthcare professionals spend waiting for medical images to load, which can be particularly important in time-sensitive situations. It can also help reduce the workload of radiology departments and other healthcare professionals by automating the image retrieval and storage process.

Furthermore, prefetching is a valuable feature of PACS that can help to improve the efficiency and quality of patient care by reducing the time required to access and view medical images during diagnosis and treatment planning.

17.4 The Role of Default Display Protocols and Hanging Protocols in PACS: Enhancing Patient Care and Provider Productivity

Default Display Protocols and Hanging Protocols are two important features of PACS that help to ensure that medical images are displayed consistently and efficiently.

Default Display Protocols are the default settings for how medical images are shown in PACS. These protocols specify things like the orientation of the image, the colour and brightness settings, and the type of image processing applied. Default Display Protocols help ensure that medical images are displayed consistently and accurately, which is essential for accurate diagnosis and treatment planning.

Hanging Protocols, on the other hand, specify how multiple medical images should be arranged and displayed on a viewing workstation. Hanging Protocols can be modified based on the radiologist's or clinician's specific needs. For example, they can display multiple images side-by-side, in different orientations, or in any other configuration that is most useful for interpretation.

Hanging Protocols are beneficial for multi-modality imaging studies, such as CT scans and MRIs, which often require displaying multiple images in a specific order for accurate diagnosis. By automating the image arrangement and display process, Hanging Protocols can help improve the efficiency and accuracy of image interpretation.

Overall, Default Display Protocols and Hanging Protocols are important features of PACS that help to ensure that medical images are displayed consistently and efficiently, improving the accuracy and speed of diagnosis and treatment planning.

17.5 Challenges and Limitations of PACS: Potential Drawbacks and Solutions

While PACS offers many advantages over traditional film-based medical imaging systems, there are also some disadvantages. Some of the potential drawbacks of PACS include the following:

Implementing a PACS system can be expensive, requiring significant hardware, software, and staff training investment. Additionally, ongoing maintenance and upgrades can be costly.

PACS systems rely on complex technology, and technical problems such as system failures, data loss, and software glitches can occur. This can result in downtime and delays in patient care.

PACS requires specialised training for radiology staff and other healthcare professionals involved in patient care. This can be time-consuming and costly and may require ongoing training to keep up with new technologies and updates.

In addition to the increasing use of electronic medical records and the growing threat of cyber attacks, there are concerns about the security of patient data stored in PACS systems. Maintaining data security requires robust security measures and ongoing monitoring.

Implementing a new PACS system can disrupt existing workflows and processes, requiring staff to adjust to new working methods. This can result in initial decreases in efficiency and productivity.

While PACS offers many benefits for managing medical images, some potential disadvantages should be considered when deciding whether to implement a PACS system. Proper planning, training, and ongoing maintenance can help minimise these disadvantages and ensure the successful implementation and use of a PACS system.

17.6 The Future is Digital: The Advantages of Electronic Patient Record (EPR) in Healthcare

Electronic Patient Record (EPR) is a digital record of a patient's medical history, including diagnoses, treatments, medications, and test results. EPRs are electronic versions of traditional paper-based medical records, and they are used to store and manage patient data in a secure and accessible way.

EPRs provide several benefits over traditional paper-based records, including:

EPRs are stored electronically and can be retrieved from anywhere with an internet connection. This makes it easier for healthcare providers to access patient information, regardless of location.

EPRs reduce the risk of errors and inconsistencies with paper-based records. Electronic records can be updated in real-time and reduce the number of errors due to outdated or missing information.

EPRs streamline managing patient data, reducing the time and effort required to retrieve, update, and share medical records.

EPRs provide a comprehensive view of a patient's medical history, enabling healthcare providers to make more informed decisions about diagnosis and treatment.

EPRs are stored in secure databases that can be protected with encryption and other security measures. These procedures will reduce the risk of data breaches and help to protect patient privacy.

17.7 Hospital Information System (HIS): A Comprehensive Solution for Hospital Management

A Hospital Information System (HIS) is a comprehensive software solution designed to manage and streamline a healthcare facility's administrative and clinical operations. HIS systems typically include modules for patient registration, scheduling, billing, electronic medical records (EMRs), and other features such as inventory management, pharmacy management, and human resources management.

In a healthcare organisation that uses PACS and RIS, the HIS system must be bidirectionally linked to both approaches. This allows for seamless patient data integration between the three systems, ensuring that patient records are up-to-date and accurate across all departments.

Some of the key benefits of bidirectional integration between HIS, PACS, and RIS include:

In conjunction with bidirectional integration, patient data can be shared between systems in real-time, reducing the risk of errors and discrepancies.

Bidirectional integration allows for the seamless transfer of patient data between systems, reducing the time and effort required to manage patient records and removing the need for manual data entry.

With all patient data accessible from a single system, healthcare providers can make more informed decisions about diagnosis and treatment, improving patient outcomes.

Bidirectional integration between HIS, PACS, and RIS can help to reduce administrative burdens, allowing healthcare providers to focus on patient care.

Overall, bidirectional integration between HIS, PACS, and RIS ensures efficient, accurate, and high-quality patient care. By integrating these systems, healthcare

organisations can streamline operations, improve data accuracy, and provide better patient care.

An Electronic Patient Record (EPR) system is designed to store and manage a patient's medical data in digital format, including radiology imaging data from PACS and reports from Radiology Information Systems (RIS) such as radiology orders, exam results, and interpretations.

17.8 Beyond Records: How Electronic Patient Record (EPR) Systems can Incorporate Other Digital Clinical Data

In addition to these data types, an EPR system can incorporate other digital clinical data such as pathology reports, clinical photographs, electrocardiograms, and different diagnostic test results. Integrating these various types of data into a single EPR system provides healthcare providers with a comprehensive and holistic view of a patient's medical history, allowing for more informed decision-making and improved patient care.

By incorporating PACS and RIS into the EPR system, radiology and imaging data can be seamlessly integrated into the patient's overall medical record, reducing the risk of errors or discrepancies and ensuring all providers have access to the same up-to-date information. In addition, this can improve efficiency and collaboration between healthcare teams, resulting in better patient outcomes.

17.9 Revolutionizing Healthcare Delivery: The Potential of Modern PACS Systems in Telemedicine and Remote Patient Care

Many PACS systems are available on the market, and the system chosen will depend on the healthcare organisation's specific needs. Some modern PACS systems include:

Agfa HealthCare Enterprise Imaging creates a comprehensive solution for managing medical images across the healthcare enterprise.

Carestream Health Vue PACS system offers a web-based platform for storing, viewing and sharing medical images and reports.

Fujifilm Synapse PACS is intended to provide a flexible and scalable solution for managing medical images in large healthcare organisations.

GE Healthcare Centricity PACS system is created to provide a comprehensive solution for managing medical images across the healthcare enterprise.

McKesson Radiology provides a fully integrated solution for managing medical images and reports.

Philips IntelliSpace PACS offers a web-based platform for storing, viewing and sharing medical images and reports.

Siemens Healthineers syngo.via the system is a comprehensive solution for managing medical images and reports, with advanced features such as 3D image reconstruction and advanced visualisation tools.

These are just a few examples of modern PACS systems. Therefore, it is vital for healthcare organisations to carefully evaluate their needs and select a PACS system capable of meeting those needs cost-effectively and efficiently.

17.10 Future Directions in PACS: Meeting the Needs of a Changing Healthcare Landscape

The future of PACS is anticipated to be shaped by technological advances, changing healthcare needs, and evolving regulatory and reimbursement requirements. Several key trends and developments that are projected to shape the future of PACS include:

Artificial Intelligence (AI) and Machine Learning will continue to play an increasingly important role in PACS, enabling automated image analysis, diagnosis, and treatment planning. AI algorithms can help to identify subtle changes in medical images that might be missed by human readers, improving diagnostic accuracy and reducing the time required for image interpretation.

Cloud-based PACS systems are becoming more common, offering increased accessibility, scalability, and flexibility. In addition, cloud based PACS systems can be accessed from anywhere via the internet, allowing radiologists and clinicians to access medical images and patient data remotely, improving collaboration and patient care.

Interoperability between different PACS systems, electronic medical records, and other healthcare systems is becoming increasingly important, enabling the seamless exchange of patient data and medical images between various providers and systems. This can help to improve patient care and reduce costs.

Virtual and augmented reality technologies are being explored for their potential use in PACS, enabling radiologists and clinicians to visualise and interact with medical images in new and innovative ways. This can improve diagnostic accuracy, treatment planning, and patient engagement and education.

The future of PACS will be characterised by ongoing technological innovation and the growing importance of data interoperability, automation, and AI. These developments can transform how medical images are managed, interpreted, and used in patient care, improving patient outcomes and reducing costs.

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18 Surgical Innovation in The 19th Century: Anaesthesia, Antiseptics, and More

Anaesthesia and antiseptics transformed surgery in the 19th century. Scientific advancements, war, and innovation led to modern techniques.

18.1 Introduction

The history of modern surgery can be traced back to the 19th century, when anaesthesia was first introduced to the field of surgery to perform operations without pain.

During the last two hundred years, advances in antiseptic and aseptic techniques were developed, significantly reducing the risk of infection during surgery. This led to a rapid expansion of surgical procedures, with surgeons able to operate on a broader range of patients and conditions.

In the 20th century, the development of antibiotics further reduced the risk of infections during surgery and allowed more complex procedures. In addition, the introduction of blood transfusions, intravenous fluids, and other supportive measures also improved patient outcomes and reduced mortality rates. Furthermore, the development of new technologies and surgical techniques revolutionised the field of surgery. The use of lasers, laparoscopic surgery, and robotic surgery allowed for more precise and minimally invasive procedures, reducing the trauma to the patient, and promoting faster recovery.

18.2 Microsurgery, laparoscopy, and robotics are recent advances

The key features of modern surgery include:

Minimally invasive surgery (MIS) is a less invasive technique than traditional open surgery. For example, laparoscopic surgery involves making small incisions in the abdomen and inserting a thin tube with a camera and light to visualise the surgical site. Surgical instruments are then inserted through other small incisions to perform the surgery.

Furthermore, endoscopic surgery, or minimally invasive surgery, is a surgical technique that uses a small camera and specialised instruments to perform procedures through small incisions or natural orifices.

The following are types of endoscopic surgery:

Laparoscopy operates inside the abdominal cavity and is used for gallbladder removal, appendectomy, and hernia repair.

Arthroscopy investigates joints such as the knee, shoulder, and ankle. In addition, it is used to diagnose and treat conditions such as torn ligaments, cartilage damage, and arthritis.

Hysteroscopy is used to operate on the uterus and to diagnose and treat fibroids, polyps, and abnormal bleeding.

Bronchoscopy is used on the lungs to diagnose and treat lung cancer, infections, and blockages.

Endoscopic sinus surgery is performed on the sinuses to treat conditions such as chronic sinusitis, nasal polyps, and sinus blockages.

The advantage of endoscopic surgery is often associated with less pain, smaller incisions, faster recovery, and fewer complications than traditional open surgery.

18.3 Laparoscopic Surgery Goes High-Tech with Robotic Arms

However, laparoscopic surgery uses robotic arms that a surgeon can control from a console to produce 3-D images of the surgical site.

Several robotic surgical systems are available on the market, each with unique features and capabilities. These known robotic surgical systems include:

The da Vinci Surgical System is designed for minimally invasive surgery and is used in urologic and gynecologic procedures.

The Mako system is used for joint replacement surgeries and utilises a robotic arm to help the surgeon perform more accurate and precise implant placement.

The Robotic Surgical Assistant (ROSA) system is used in neurosurgery and can assist surgeons in performing complex brain and spinal surgeries.

The Senhance system is designed for laparoscopic surgeries and uses robotic arms to assist with surgical procedures.

The Versius system is a relatively new robotic surgical system designed for various laparoscopic procedures. It features a modular design allowing greater flexibility and ease of use.

18.4 Arthroscopic Surgery: The Role of Imaging and Visualisation

Arthroscopic surgery is a minimally invasive endoscopic surgery performed on joints like the knee, shoulder, hip, wrist, ankle, and elbow. It is used to diagnose and treat various joint conditions, including torn ligaments, cartilage damage, and arthritis.

During arthroscopic surgery, a small camera called an arthroscope is inserted into the joint through a small incision. The arthroscope provides a clear view of the joint, allowing the surgeon to visualise any damage or abnormalities. Specialised instruments are then used to make repairs or remove damaged tissue.

Arthroscopic surgery is less invasive than conventional open surgery, typically resulting in less pain and discomfort for the patient. In addition, since arthroscopic surgery involves smaller incisions, patients generally experience a faster recovery time than traditional open surgery. Because arthroscopic surgery uses smaller incisions, the resulting scars are typically smaller and less noticeable than in conventional open surgery. Arthroscopic surgery allows for greater precision and accuracy in diagnosing and treating joint conditions. Arthroscopic surgery generally treats various joint conditions, including meniscus tears, rotator cuff tears, ACL tears, carpal tunnel syndrome, and tennis elbow.

18.5 TORS: A Promising Treatment for Oropharyngeal Cancer

Transoral robotic surgery (TORS) is a minimally invasive surgery performed using a robotic system. This surgical technique involves using a small, flexible robotic arm inserted into the mouth to perform surgery on the throat, mouth, and other head and neck areas. During TORS, the surgeon sits at a console and controls the robotic arm using a computer. In addition, the robotic arm is equipped with small, precision instruments and a camera, which provide a magnified, three-dimensional view of the surgical area. This allows the surgeon to perform complex procedures with greater precision and control than conventional surgical techniques.

TORS often treats head and neck cancer, such as tongue, tonsils, and pharynx tumours. It can also be used to remove benign tumours or to perform reconstructive surgery in the head and neck region.

Benefits of TORS include reduced pain, less scarring, shorter hospital stays, and faster recovery times compared to traditional surgery. However, TORS is unsuitable for all types of surgeries and patients, and discussing the risks and benefits with a qualified healthcare provider is essential.

18.6 The Advantages of Minimally Invasive Techniques for Patients and Surgeons

Minimally invasive techniques have many advantages over traditional open surgery, including reduced pain, shorter hospital stays, and faster recovery times. However, they may not be suitable for all patients or all types of surgeries. Therefore, the decision to use minimally invasive techniques depends on the individual patient and their specific medical condition.

Modern surgery also benefits from advanced imaging and visualisation tools like MRI, CT scans, ultrasound, and virtual reality technology. These tools allow surgeons to accurately locate and target the affected area, improving the precision and safety of the surgery.

Advanced imaging and visualisation tools have greatly improved the accuracy and safety of surgical procedures. Some typical imaging and visualisation tools used in surgery include:

Magnetic Resonance Imaging (MRI) uses a powerful magnetic field and radio waves to create detailed images of the body. MRI is often used to visualise soft tissues, such as the brain and spinal cord, and can help guide surgical planning.

Computed Tomography (CT) uses X-rays and computer technology to create detailed body images. CT is often used to visualise bones and internal organs and can help guide surgical planning.

Ultrasound is often used during surgeries to guide needle placement and to visualise organs and blood vessels in real-time.

Endoscopy is a procedure that involves inserting a thin, flexible tube with a camera and light attached to the body. Endoscopy is often used to visualise the digestive, respiratory, and urinary tract and can help diagnose and treat various conditions.

Virtual reality (VR) technology allows surgeons to visualise the surgical site in a three-dimensional virtual environment. This technology can help surgeons plan complex surgeries and simulate different surgical approaches.

Advanced imaging and visualisation tools have revolutionised the field of surgery, allowing surgeons to perform more accurate and precise procedures with fewer complications. These tools have also improved patient outcomes, reduced hospital stays, and minimised recovery times.

Computer-assisted surgery (CAS) refers to using computer technology to aid in planning, guiding, and performing surgical procedures. CAS is also known as computer-guided surgery, robotic surgery, or surgical navigation.

CAS uses advanced imaging techniques such as CT scans, MRI, and 3D ultrasound to create a virtual 3D model of the patient's anatomy. This model is then used to plan and simulate different surgical scenarios.

During the surgical procedure, the surgeon uses a computer system to track the position and movement of surgical instruments in real-time, allowing for precise and accurate placement of implants, removal of tissue, and other surgical actions. This tracking system can also help the surgeon avoid critical structures and reduce the risk of complications.

CAS can be used in various surgical specialities, including orthopaedics, neurosurgery, ENT (ear, nose, and throat) surgery, and more. Some examples of CAS procedures include spinal fusion, joint replacement, tumour removal, and cranial surgery.

The benefits of CAS include improved surgical accuracy and precision, reduced risk of complications, shorter recovery times, and improved patient outcomes. However, CAS requires specialised training and can be more expensive than traditional surgical methods.

Advanced materials and implants are increasingly used in surgery to improve patient outcomes and reduce the risk of complications. Some examples of advanced materials and implants used in surgery include:

Titanium implants are strong, lightweight, biocompatible metal that does not harm living tissue. Titanium implants, such as joint replacements and spinal fusion, are commonly used in orthopaedic surgery.

Bioresorbable materials are materials absorbed by the body over time. These materials, such as screws and plates, are used in surgical implants and can reduce the risk of complications associated with permanent implants.

Ceramic materials are strong and durable and can be used in various surgical implants, such as hip and knee replacements. In addition, ceramic implants have the advantage of being wear-resistant and can potentially last longer than traditional metal implants.

Hydrogels are a soft, water-containing material that can be used in various surgical applications, such as wound dressings and drug delivery systems. Hydrogels can also create scaffolds for tissue engineering and regenerative medicine.

3D printing technology allows custom implants tailored to a patient's specific anatomy. 3D-printed implants can be used in various surgical applications, such as spinal fusion and cranial reconstruction.

18.7 Precision Surgery: Personalised Treatments and Techniques

The future of modern surgery is rapidly evolving, driven by advances in technology and innovation. Here are some of the key areas that are likely to shape the future of surgery:

Minimally invasive surgery techniques, such as laparoscopic and robotic surgery, have revolutionised surgical practice. In the future, improvements in these techniques, new technologies, and approaches will allow for even less invasive procedures.

Robotics and automation are already being used in surgery, and this trend will likely continue. Robotic systems can enhance surgeons' visualisation, agility, and precision, potentially reducing the risk of complications.

Augmented reality technology can provide surgeons with real-time, 3D images of the surgical site overlaid with the patient's anatomy. This technology can potentially improve surgical accuracy and reduce the risk of complications.

Nanotechnology involves using tiny particles, often on the scale of nanometres, to deliver drugs and other therapies to specific targets in the body. For example, nanotechnology could deliver drugs to specific tissues or create scaffolds for tissue regeneration in surgery.

Advances in genomics and other areas of personalised medicine will likely impact surgery in the future. Personalised medicine approaches can help identify patients at higher risk of complications and tailor treatments to individual patient needs.

The future of modern surgery is likely to be characterised by a continued focus on patient-centred care, enhanced precision and safety, and greater use of technology and innovation to improve surgical outcomes.

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19 A Closer Look At Radiotherapy: A Powerful Tool Against Cancer

Radiotherapy machines are advanced tools that deliver high-energy radiation to treat cancer. From linear accelerators to cyberKnife and tomotherapy.

19.1 Introduction

Radiotherapy machines use high-energy X-rays or other types of radiation to destroy cancer cells by damaging their DNA.

External beam radiation therapy is the most common type of radiotherapy, and it involves directing a beam of high-energy radiation from a machine outside the body towards the tumour. The radiation is targeted to ensure that it affects only the cancer cells and limits damage to the surrounding healthy tissue as possible. This type of radiotherapy is usually delivered over several weeks, with each treatment session lasting only a few minutes.

Internal radiation therapy, or brachytherapy, involves placing a small radioactive source inside the body near the tumour. This allows a higher radiation dose to be delivered directly to the cancer cells while limiting damage to surrounding healthy tissue.

Radiotherapy may be used alone or with other cancer treatments, such as chemotherapy or surgery. The treatment plan doctors will depend on the type and stage of cancer, the patient's overall health and other medical conditions.

19.2 Linear Accelerators: A Vital Tool in Radiation Oncology

Linear accelerators (LINACs) are one of the most commonly used radiotherapy machines to treat cancer. They use electricity to accelerate electrons to very high speeds and collide them into a heavy metal target, creating high-energy X-rays. These X-rays are then shaped into a beam directed at the cancerous cells.

LINACs offer several advantages over other types of radiotherapy machines. They can deliver radiation with high precision, allowing doctors to target cancerous cells while reducing damage to nearby healthy tissue. Linear accelerators can deliver different types of radiation, including photons, electrons, and protons, depending on the type of cancer and the treatment plan. The radiation is delivered quickly and is important for patients receiving radiation as part of their primary cancer treatment. In addition, LINACs are non-invasive and, therefore, can reduce the risk of infection and other complications. In general, LINACs are an essential tool in the fight against cancer, and they continue to be a key component of many cancer treatment plans.

19.3 Gamma Knife Radiosurgery: An Advanced Technique for Treating Brain Tumours

Gamma Knife is a type of radiosurgery machine that uses gamma rays to treat tumours in the brain. It uses multiple sources of gamma radiation to deliver a highly focused dose of radiation to the tumour while minimising radiation exposure to the surrounding healthy tissue.

The Gamma Knife machine has a frame attached to the patient's head to keep it still during the procedure. The head frame is attached to a machine that delivers a precise radiation dose to the tumour site. The machine uses 192 individual beams of gamma radiation to target the tumour from different angles while limiting exposure to the surrounding healthy tissue. The entire procedure is typically completed in a single session, and the patient can usually go home the same day.

Gamma Knife is particularly effective for treating tumours in the brain that are difficult to remove surgically or for patients who are not good candidates for surgery due to other health issues. It can also be used to treat tumours that have recurred after previous treatment or as a primary treatment option for small tumours.

19.4 Proton Therapy: A Powerful Tool for Fighting Cancer

Proton therapy machines use protons to deliver radiation therapy. Protons are positively charged particles that can be directed to the tumour site with greater precision than X-rays. This results in less damage to healthy tissue surrounding the tumour.

Proton therapy machines use a particle accelerator to generate high-energy protons, which are then directed at the tumour using a system of magnets. The protons penetrate the tumour and deposit their energy directly into the tumour cells, causing damage to the DNA and ultimately killing the cancer cells.

One of the key advantages of proton therapy is that it delivers radiation with a high degree of precision, which allows doctors to target the tumour while reducing exposure to healthy tissue. This is because protons have a characteristic depth-dose curve, meaning they deposit most of their energy at a specific depth in the tissue. By adjusting the energy of the protons, doctors can control the depth at which the energy is deposited, allowing them to target the tumour precisely.

Proton therapy is beneficial for treating tumours that are located near sensitive structures, such as the spinal cord, brainstem, or eyes. It can also be used to treat tumours in children, as it has been shown to cause less damage to surrounding tissues than traditional radiation therapy.

There are several types of proton therapy machines, including cyclotron-based and synchrotron-based machines. These machines differ in how they generate and accelerate the protons, but they all work using a system of magnets to direct the protons to the tumour.

Proton therapy is a safe and effective treatment option for many patients with cancer, and it offers several advantages over traditional radiation therapy.

19.5 Cyberknife Radiosurgery: A Non-Invasive Treatment for Cancer and Tumours

CyberKnife is a type of radiosurgery machine that uses advanced robotics technology to treat tumours in the brain and other parts of the body. It uses a combination of advanced imaging technology and robotics to deliver a highly precise dose of radiation to the tumour while minimising radiation exposure to the surrounding healthy tissue. The machine uses a small linear accelerator that can move in multiple directions, allowing it to target the tumour from various angles.

One of the key advantages of CyberKnife is that it can adjust for small movements of the patient during treatment. This is particularly important when treating tumours in the brain, as even small movements of the patient's head can cause the tumour to move relative to the treatment beam. CyberKnife uses advanced tracking technology to monitor the position of the tumour during treatment continuously, and it adjusts the position of the treatment beam in real-time to ensure that the tumour is always in the target zone.

19.6 Tomotherapy: A Unique Approach to Radiation Therapy for Cancer Treatment

Tomotherapy is a radiation therapy machine that combines a linear accelerator with a computed tomography (CT) scanner. This allows for highly targeted radiation delivery while reducing exposure to healthy tissue.

Tomotherapy is a type of radiation therapy used in cancer treatment. It is a specialised form of intensity-modulated radiation therapy (IMRT) that combines CT scanning and radiation therapy delivery to target cancer cells while precisely limiting damage to healthy tissue.

During tomotherapy, the patient lies on a table that moves slowly through a CT scanner while a radiation beam is directed at the tumour from multiple angles. The CT images are used to create a 3-D of the tumour and surrounding tissue, allowing the radiation oncologist to tailor the radiation dose to the specific shape and size of the tumour.

One of the advantages of tomotherapy is its ability to deliver high doses of radiation to the tumour while sparing nearby healthy tissue. This is particularly important in treating tumours in areas such as the brain, spine, and lungs, where minimising damage to healthy tissue is critical.

While tomotherapy is generally safe and effective, it can cause side effects such as fatigue, skin irritation, and nausea. Patients may also experience long-term side effects such as scarring and tissue damage. Therefore, patients must discuss the potential risks and benefits of tomotherapy with their doctor before undergoing treatment.

19.7 Brachytherapy: Delivering Radiation Therapy from the Inside Out

Brachytherapy is a type of radiation therapy used in cancer treatment that involves placing radioactive sources directly into or near the tumour. Several types of brachytherapy machines are used in this treatment and include:

High-Dose Rate (HDR) Brachytherapy Machine delivers a high dose of radiation to the tumour for a short period of time. The machine contains a tiny radioactive source inserted into a catheter or applicator placed near the tumour. The radioactive source is moved to different positions to deliver the radiation dose in a precise manner. HDR brachytherapy is commonly used to treat cervix, prostate, and breast cancers.

Low-Dose Rate (LDR) Brachytherapy Machine delivers a continuous low dose of radiation to the tumour over a more extended period of time. The machine contains tiny radioactive seeds implanted directly into the tumour or surrounding tissue. Depending on the specific treatment plan, the seeds release radiation over several weeks or months. LDR brachytherapy is commonly used to treat prostate cancer.

Electronic Brachytherapy Machine delivers low-energy X-rays to the tumour through a small applicator. The portable machine can be used in a doctor's office or outpatient setting. Electronic brachytherapy is commonly used to treat skin cancers.

Pulsed-Dose Rate (PDR) Brachytherapy Machine delivers radiation to the tumour in pulses, with short periods of high radiation followed by extended periods of no radiation. The machine contains a radioactive source that is placed near the tumour and is moved to different positions to deliver the radiation dose in a precise manner. PDR brachytherapy is commonly used to treat gynaecological cancers.

Brachytherapy is a highly effective cancer treatment that can provide targeted radiation therapy to the tumour while reducing damage to surrounding healthy tissue. The specific type of brachytherapy machine used will depend on the type and location of the tumour being treated.

19.8 The Future of Radiotherapy Machines: Trends, Challenges, and Opportunities

The future of radiotherapy machines in cancer treatment is promising, as new technologies and advancements in existing technologies are being developed to improve the effectiveness and efficiency of cancer treatment.

One of the most significant advancements in radiotherapy technology is the development of intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT). Both use advanced computer algorithms and software to deliver highly targeted radiation to cancer cells while minimising damage to surrounding healthy tissues. This allows higher doses of radiation to be delivered to the tumour, resulting in better patient outcomes.

Another promising technology is proton therapy, which uses protons instead of photons to deliver radiation to cancer cells. Protons have a unique energy deposition profile that allows for more precise targeting of cancer cells while sparing surrounding

healthy tissue. Proton therapy is beneficial for treating tumours in sensitive areas such as the brain, spine, and prostate.

There are also emerging technologies such as carbon ion therapy, which is even more precise and powerful than proton therapy but is currently only available in a few specialised centres worldwide.

In addition to these technological advancements, there is a growing trend towards personalised medicine, where treatment plans are tailored to individual patients based on their genetic and molecular characteristics. This approach is expected to become more common and will likely lead to better patient outcomes.

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20 Frankenstein to Modern Anatomy of the Human Body

Modern anatomy has evolved rapidly through today's technology, and human anatomical structures are more understood since the publication of Frankenstein.

20.1 Introduction

To study the internal structures of the human body, anatomists require a lawfully donated body to a medical school. However, medical history has shown this is not always the case and resulted in limiting the knowledge about the internal anatomy of the human body.

During the late medieval period, the anatomist Leonardo da Vinci (1452-1519) and Andreas Vesalius (1514-1564) published detailed anatomical drawings to express an interest in human anatomy. These drawings set the foundation for medical schools to teach anatomy by human dissection supported by illegally obtaining corpses.

Interestingly, the human anatomy has always been part of fictional stories; for example, Victor Frankenstein was a young scientist who created 'The Monster' using unconventional scientific experiments. This story was created by the English author Mary Shelley (1797-1851) in the eighteenth century. Frankenstein created the monster over two years by meticulously constructing the body using anatomical parts brought to life.

During the study of anatomy in England, the Age of Enlightenment become infamous for body snatching from graveyards to provide an adequate supply of corpses. Consequently, it was a factor because the teaching of medicine and surgery was becoming more established through medical schools. There was a shortage of corpses legally available for anatomy classes. The lack of corpses forced the anatomy teachers to pay for bodies from London gangs who dug them up from graveyards.

To help and circumvent the shortage of corpses, the 1752 Murder Act was passed by Parliament to allow the bodies of executed murderers and be used to study anatomy.

In the notorious case of William Burke and William Hare murdered 16 people over about ten months in Edinburgh in 1828. They sold these corpses to the renowned lecturer of anatomy Robert Knox (1791-1862) at the University of Edinburgh for dissection lectures.

However, these murders met the requirements for bodies for medical research and contributed to the passing of the Anatomy Act of 1832. This Act of Parliament

authorised physicians, anatomy lecturers and medical students to dissect donated bodies. It was legislated in response to the public disgust at the illegal trade in corpses.

The Anatomy Act 1832 was first presented in 1828 because acquiring bodies for medical research was scrutinised by the House of Commons, but an initial attempt at legislation failed.

However, the Anatomy Act of 1832 gave surgeons and medical students legal access to bodies from workhouses, hospitals and prisons that were unclaimed 48 hours after death.

20.2 Modern Anatomy

Modern anatomy has evolved rapidly through today's technology, and human anatomical structures have been more understood since the publication of Frankenstein. For example, the muscles and bone structures are more understood, and plastic surgery has improved through skin grafts being more successful operations. Furthermore, the secrets of the nervous system on how electricity can cause muscle spasms since the time of Galvani.

Since Shelley's writing of Frankenstein, the understanding of human anatomy may be accurate at the surface, but little was known about the human body's inner workings. However, Frankenstein created a sinister monster that is today recognised throughout the world over 200 years ago.

The Stone Age

Ancient skulls from the late Palaeolithic period have shown evidence of cutting a hole in the skull. This practice is thought to have been carried out to release 'evil spirits' from people suffering from mental health disorders.

The Ancient Egyptians

The early Egyptian physicians had limited knowledge of anatomy, and their drawings and sculptures demonstrated this. In addition, the mummification practices, which required the disembowelment of human bodies, did not provide them with an exact knowledge of internal organs.

The Ancient Greeks

The ancient Greeks made scientific advances in the field of anatomy. For example, it is alleged that Alcmaeon of Croton practised human dissection. However, Hippocrates also contributed to anatomy, and Aristotle made investigations into anatomy and embryology. Aristotle's anatomical studies led him to conclude that the soul was the body's life source.

The Ancient Romans

Ancient Roman physicians gained much of their anatomical knowledge of the human body by treating wounded gladiators. Galen is known for his anatomical observations

and experimental approaches in emphasising the interrelationships between physiology and anatomy.

The Islamic Golden Age

Muhammad Al-Razi (862-930) to the field of neuroanatomy.

Ibn Al-Haytham (965-1040) provided new insight into optics.

Avicenna or Abu ibn (980-1037) famously wrote the Canon of Medicine.

Ibn Al-Nafis (1210-1288) explained pulmonary circulation, paving the way for William Harvey (1578-1657) many centuries later.

The Late Middle Ages

Thaddeus Alderoti (1206-1295) was the most active anatomist in this field. The first human dissection manual ever written, the corporis, was produced by one of the students, de Luzzi (also known as Mundinus), in approximately 1316.

The Renaissance

During the Renaissance period, various anatomical sketches of the human body were made by artists such as Leonardo Da Vinci and, to a lesser extent, Michelangelo di Buonarroti, Rembrandt van Rijn, Albrecht Dürer and Raphael da Urbino. These sketches contributed to anatomical knowledge but were later disregarded with the production of newer, updated anatomical drawings.

7th–20th Century

Named anatomical procedures include:

• Antonio Pacchioni (Pacchioni’s granulations)

• Antonio Scarpa (Scarpa's fascia and Scarpa's fluid, among many others)

• Alfonso Giacomo Gaspare Corti (organ of Corti),

• Filippo Pacini (Pacinian corpuscles)

• Camillo Golgi (Golgi apparatus)

• Johann Friedrich Meckel (Meckel’s diverticulum)

• Leopold Auerbach (Auerbach’s plexus)

• Georg Meissner (Meissner’s plexus)

• Ludwig Edinger (Edinger's tract)

• Heinrich Lissauer (tract of Lissauer)

• Johann Christian Reil (Reil's finger and the Islands of Reil, among many others)

• Anders Retzius (Cave of Retzius or Retzius' space)

• Alfred Wilhelm Volkmann (Volkmann's canals)

• Franciscus Sylvius (Sylvian fissure and Sylvian aqueduct)

• François Magendie (foramen of Magendie)

• Pierre Paul Broca (Broca's area)

• Charles-Édouard Brown-Séquard (Brown-Séquard syndrome)

• Jean-Martin Charcot (Charcot disease)

• Vladimir Betz (pyramidal cells of Betz)

• William Edwards Horner (Horner's muscle)

• Santiago Ramón y Cajal (interstitial cell of Cajal)

• Thomas Willis (circle of Willis)

• Alexander Monro secundus (foramen of Monro)

• Sir Charles Bell (Bell's palsy).

The advancement of the microscope by Anton van Leeuwenhoek (1632-1723) and Marcello Malpighi helped to progress anatomical research and led to some scientific discoveries:

Van Leeuwenhoek was able to magnify the fine details of various tissues and was the founder of microscopic anatomy known as histology.

Robert Hooke (1635-1703) was the first to recognise and name cells in the tissues.

Robert Brown (1773-1858) recognised the presence of nuclei.

In the 1830s, Theodor Schleiden and Matthias Schwann proposed that cells are universal in all tissues and play a vital role. This theory is the basis for modern histology, embryology and pathology concepts.

In 1761, Giovanni Battista Morgagni, an Italian researcher, made several discoveries and was the first pathologist.

Today, anatomical education has been more constructive and beneficial since the Age of Enlightenment due to the advancements in digital technology, web-based resources and computer-aided learning. For example, a wide range of 3-D virtual reality models such as Visible Body; Primal Pictures; 3D4Medical; Cyber Anatomy HolographicTM; BodyViz; are the most prevalent and influential.

This technology platform enables teachers and students of anatomy to engage in the illustrations and information they need to conduct anatomical research.

In the twentieth century, further advances in radiological techniques have permitted researchers to make remarkable connections between anatomy and physiology. In

addition, these imaging modalities allowed for the integration of anatomy with genetics, biochemistry and biophysics.

Furthermore, microscopy and the discovery of X-rays have set the foundation of advanced technologies such as PET, MRI and CT scanners to allow a non-invasive look inside the human body.

Furthermore, anatomy books are much more different from when Gray's Anatomy was first published in 1858. An earlier book on anatomy by Claudius Galenus was a 15-volume collection on De Anatomicis Administrationibus (Galen on Anatomical Procedures). This book gave an account of the achievements and failures of surgeons between 129 and 198 AD. The book provided experimental details on the phrenic nerves and the diaphragm from numerous dissections.

The history of anatomy, especially in the medieval period, was reported by the Italian anatomist Mondino de Luzzi (1270-1326) from the University of Bologna. His teachings on dissection even influenced Leonardo da Vinci. Furthermore, Andreas Vesalius (1514-1564) published the De humani corporis fabrica (On the Structure of the Human Body), and other ancient texts of Aristotle and Galen were still used in medical schools of Europe. However, Vesalius discovered inaccuracies in the ancient texts, and the De humani corporis fabrica became an authoritative textbook on anatomy.

The De humani corporis fabrica contained over 200 engravings by various artists, including Jan Steven van Calcar (1499-1546). One of these illustrations shows Vesalius lecturing to a large crowd while dissecting a corpse.

20.3 Conclusion

Modern medical students use the modern Gray's Anatomy with its colour artwork, which has become the gold standard. In addition, the modern Gray's contains MRI, X-ray, and PET scans which would have been unimaginable in Henry Gray's time.

Interestingly, the American educator Abraham Flexner (1866-1959) wrote a famous report on medical education reform and the importance of the basic medical sciences. The report concluded that anatomy is an essential science for basic medical training. Today, the human body or parts are preserved techniques to ensure adequate material for future medical students.

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21 Insights of Big Data and Artificial Intelligence

The healthcare sector is transforming through the convergence of technology, digitalisation, and 3-D modelling.

21.1 Introduction

In the past decade, new trends in diagnostic radiology through artificial intelligence, machine learning, virtual reality, wearable medical devices, and 3-D modelling have revolutionised the healthcare sector. Today, these technological platforms will have a more significant impact on patient management.

Future healthcare innovations to medical devices will be more modular and flexible to improve the patient experience. For example, 3-D printing and virtual simulations create new opportunities to improve quality and safety, especially optimising. However, 3-D printing can also offer faster prototypes and the creation of personalised prosthetics. Furthermore, 3-D printing adjusts tablet porosity to produce personalised medicines at the point of care.

The COVID-19 pandemic has accelerated virtual healthcare technology due to consumers and providers finding ways to deliver aspects of healthcare. These digital interface systems allow patients to connect remotely with healthcare professionals using video conferencing or mobile apps. Therefore, future general practices will decline due to the expansion and production of innovative medical devices.

21.2 Exploring Structured, Unstructured, and Semi-Structured Data

Structured Data: This refers to ordered data already stored in the traditional matrix databases and accounts for about 20% of the total data. The data is useful in programming and computer-related applications.

Unstructured Data: This type of data has no clear format in storage and accounts for about 80% of the unstructured data. This data is more assessable and is just stored and analysed manually.

Semi-Structured Data: The type of unstructured and semi-structured data is sometimes not apparent to the user because most semi-structured data appear unstructured when first encountered. For example, NoSQL documents are considered semi-structured because they contain keywords used to process the document.

21.2.1 Difference between Structured, Semi-structured and Unstructured data

Parameter	Structured Data	Semi-structured Data	Unstructured Data
Organisation	Structured data is organised with the highest level of organisation	Semi-structured data is partially organised; hence the level of organisation is less than structured data but higher than unstructured data	Unstructured data is unorganised
Flexibility	Structured data is part of an interactive database. It is schema dependent, resulting in a less flexible database and challenging to scale	Semi-structured data is more flexible and less complicated to scale than structured data	Unstructured data does not have a schema. Therefore, the data becomes more flexible
Versioning	Structured data is based on an interactive database. Versioning is performed over tuples, rows and tables	Semi-structured data, tuples or graphs are possible as only a partial database is supported	Unstructured data, versioning is likely as whole data with no database support
Transaction Management	Structured data, data concurrency is available and therefore, usually preferred for the multitasking process	Semi-structured data transactions get adapted from Database Management System, but still, data concurrency is not available	Unstructured data, neither transaction management nor data concurrency, is present

21.3 Internet of Medical Things

The healthcare sector is transforming through the convergence of technology, digitalisation, and 3-D modelling. These changes have created technological development through innovation and market expansion through the robotic revolution. Robotic process automation can carry out basic and repetitive tasks in the healthcare setting while allowing healthcare professionals to concentrate more on high-value projects.

Big Data is creating a digital revolution that needs more analytics, equating to 2.5 quintillion bytes of data every day. Big Data is becoming part of the everyday industry today, which is the driving force behind the worldwide success of organisations.

The internet of medical things (IoMT) refers to the network that connects intelligent medical devices via the internet.

The next healthcare interaction will involve a medical device, for example, a blood pressure monitor, a continuous glucose monitor or a medical scanner. Today there are over 500,000 available medical technologies. These medical devices provide internet-connected services that can improve efficiencies and improve patient treatment plans. Furthermore, increased computer power and wireless capabilities will force healthcare organisations towards more IoMTs.

IoMT devices will be able to accumulate, analyse, and transmit healthcare data, especially for clinicians to evaluate the patient's chronic illnesses and evolve the future of care.

Big Data, Artificial Intelligence and Algorithms all play a role in medical diagnostics towards personalised medicine. Big Data brings a vast amount of data generated from several sources. Also, Big Data needs to be automated and stored in the correct category to find correlations, hidden patterns, and other valuable insights. The categorisation of mixed heterogeneous data is known as data classification based on predefined features.

However, in the last decade, the healthcare sector has expanded and generated enormous amounts of volume, velocity, variety, and veracity data. All these Big Data practices in healthcare can increase the business value and improve healthcare services.

21.4 Big Data is a highly complex dataset characterised by the 'V' attributes

Big Data four Vs – Volume, Velocity, Variety and Veracity

Volume

The datasets generated by radiology procedures are high in volume due to the pixel image size from computed tomography, magnetic resonance imaging, computed tomography angiography, x-rays, PET and SPECT imaging and mammography.

Velocity

Data is processed at speed. Radiology procedures produce vast amounts of data at high speed. MRI and CT scanners provide continuous datasets into the PACS networks, and the images are then stored using the Vendor Neutral Archives (VNA). All the data is generated in real-time.

Variety

The images produced by the radiology data are generated from a range of modalities, for example, computed radiography, conventional radiography, interventional radiology, digital radiography, PET and SPECT imaging, MRI, and ultrasound.

Veracity

The integrity of the dataset is paramount in any project. However, a systematic analysis of data is required to make sure the input datasets are accurate results. Therefore, scans with motion artefacts and low quality can be eliminated from the study group. In addition, the checks maintain the uniformity of datasets.

21.5 Big Data Analytics

Big Data analytics manage and analyse massive data volumes. Another way to characterise Big Data more effectively is to apply the HACE (Huge, Autonomous, Complex, Evolving) approach.

Big data utilises large and heterogeneous data volumes. This approach includes independent sources to enable distribution and reorganised controls to explore complex and evolving relationships with the data.

Big Data incorporates parametric and non-parametric measures, such as diagnosis, demographics, treatment, and disease prevention. All these attributes stem from a variety of sources by applying incongruent sampling.

This approach produces structured data focusing on genotype, proteomic or clinical scores compared to unstructured data, including clinical notes, medical imaging, prescriptions, lifestyle, environmental and health economics data.

Healthcare professionals should strive toward harnessing Big Data in imaging, which can lead to advanced clinical support, personalised diagnostic and prognostic tools, and the ability to optimise individual patient outcomes in previously impossible ways.

Big Data analytics implies the evaluation of large, the identification of clusters and the correlation between datasets leading to the development of predictive models using data mining techniques.

21.6 Revolutionising Radiology: A Journey Through the Evolution and Expansion of Diagnostic Imaging

The diagnostic imaging sector has undergone significant growth both in terms of technological development and market expansion. This growth leads to the increased production of a vast amount of data that puts diagnostic imaging in Big Data storage in the context of healthcare. Consequently, it is necessary to build digital platforms and medical devices that facilitate diagnostic images using Big Data.

Big Data users need new advancing procedures incorporating cloud computing, teleradiology from a site far from the acquisition scanner or finalised second-look activities to check the quality and advice for specialist reports.

All these technological procedures require transmitting thousands of images to other locations. Moreover, it must facilitate download/upload velocity, data integrity and security at the terminals. Also, the handling of data must comply with privacy laws.

Furthermore, applying various algorithmic tools and converting raw data to large datasets will enable a better understanding of the radiological data to gain new knowledge and insights into a medical problem.

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22 From Pixels to Patterns: Big Data and AI Transforming Medical Imaging

Big Data will be the foundation for personalised healthcare, especially the application of algorithmic tools capable of converting raw data.

22.1 Introduction

Big Data will be beneficial in the planning and implementing of radiological procedures in radiology departments. Therefore, the potential future applications of Big Data are scheduling scans, creating patient-specific personalised scanning protocols, radiologist decision support, emergency reporting, and virtual quality assurance for the radiologist.

The analytic process can support the targeted use of Big Data on images. In addition, several screening software tools designed to handle Big Data can be used to find correlations among the datasets. For example, slight changes in the parenchymal density, solitary pulmonary nodule, and focal hepatic lesions of a multidimensional anatomical image.

Running more complex applications such as 3-D multiplanar reconstructions (MPR) and volumetric rendering (VR) is possible in this situation. In addition, a curved planar reconstruction consumes higher system resources on targeted data subsets than querying the complete cross-sectional imaging dataset.

This preventative selection of the dataset can significantly reduce system requirements, such as system memory, server load, and the ability to provide rapid results.

Big Data should not become garbage data resulting from secondary analysis and not reasonably storing non-structured data.

Big Data will be the foundation for personalised healthcare, especially the application of algorithmic tools capable of converting raw data to large datasets. Therefore, it is possible to understand radiology data to gain insights into the medical problem.

However, focusing big data applications on medical images will support the analytic process. Big Data screening software tools are used to identify a region of interest. For example, these tools can evaluate the small changes in the parenchymal density by plotting multidimensional anatomical images. Furthermore, more complex applications can be performed using 3-D multiplanar reconstructions (MPR), volumetric rendering (VR), and curved planar reconstruction.

22.2 The 6-Cs of Big Data Analytics: Shaping the Future of Medical Imaging

Big Data analytics consists of 6-Cs: Connection, Cloud, Cyber, Content, Community, and Customisation. By applying Big Data, radiology departments' planning and implementation of radiological procedures have been significantly boosted. The future applications of Big Data are creating patient-specific personalised scanning protocols, scheduling scans, emergency reporting, radiologist decision support and virtual quality assurance for the radiologist.

Connection

Radiology Departments must have robust networks between the imaging modalities CT, MRI, Ultrasound and Radiography. This is because the patients' data generated from these medical scanners is transferred into the Hospital Information System (HIS), Radiology Information System (RIS), Picture Archiving and Communication System (PACS).

Cloud

The cloud stores radiological data in remote servers and connects them to hospital computers for fast access, processing, and distribution of large data.

Cyber

Cyber relates to the computer processing power and memory required to process the query to obtain specific answers. Therefore, a complex question requires sizeable mainframe computers and higher processing power to achieve desired real-time results.

Content

This refers to the Digital Imaging and Communications in Medicine (DICOM) datasets. This system can be searched to obtain information relevant to a medical decision to help alter the patient line of management.

Community

Distribution of data to other healthcare organisations will allow for providing a solution to a particular problem. For example, the sharing of radiology data could help regarding infectious diseases. The data would be in the form of chest radiographs during H1N1 influenza. Therefore, the analysis of Big Data may help in the diagnosis based on diagnostic imaging.

Customisation

The radiology data query should be customised using algorithms to facilitate a solution to a medical problem. The idea is to create a technology of clinical relevance and allow personalised healthcare.

22.2 AI-Driven Big Data: A New Paradigm for Diagnostic Problem Solving

Artificial Intelligence and Big Data are used in conjunction with each other to solve diagnostic problems. The relationship works because AI requires vast data to build intelligence through machine learning concepts. For example, machine learning image recognition evaluates thousands of medical images to learn what constitutes a medical image to recognise these types in the future.

Therefore, Big Data is needed; however, to train the application, the data needs to be structured and easily integrated so machines can identify valuable patterns in the data.

Big Data uses vast data, and you must separate the useless data. However, the data used in AI and ML is already clean by removing duplicate and unnecessary data. This approach will provide successful AI applications through Big Data providing data to train and learn algorithms. In this case, there are two types of data learning. This involves the initial training, which primes the data, followed by collecting the valuable data. Once the initial training is complete, the AI apps will continue to learn. The AI app will continue taking in new data and evaluating the changes.

Big Data's role in AI is made possible by vast arrays of parallel processors such as graphics processing units (GPUs). These processors contain thousands of cores compared to several CPUs, speeding up the existing AI algorithms.

The Big Data flows into the parallel processors to facilitate the machine learning algorithms to repeat a specific behaviour. Also, during these processes, data is collected to make a high-velocity machine. Furthermore, AI cannot deduce conclusions compared to humans; instead, it learns through trial and error, requiring massive amounts of data to teach AI.

Consequently, more data evaluated by AI apps will produce a more accurate outcome. However, in the early development of AI, the result was limited due to the slow processors and small data sets. These limitations were attributed to the lack of sensors. For example, today's cars have a multitude of sensors to perform certain functions. Also, in the 1980s, the internet was not widely available to obtain real-time data.

Today we have fast processors, smart input devices, networks and vast amounts of data sets.

22.3 No Artificial Intelligence without Big Data

Big Data analytics identifies patterns by applying sequential analysis on cold or not recent data.

The Hadoop software is used to store and process large datasets efficiently. It is the basic framework for Big Data analysis and is a batch process initially designed to run at night during low server utilisation.

Moreover, ML learns from collected data and keeps accumulating the data. For example, a self-driving car will always collect data and keep learning the processes of the vehicle. Thus, new data is always coming in fresh and always acted upon.

The disadvantage of Big Data is that you can generate too much of it. For example, people avoided past formats like pictures, video, or voice formats. This is because they could not utilise it and an additional cost of storing it. So, artificial intelligence and Big Data began to work together. However, the only way to efficiently deal with this amount of data is to manage it with data-scanning and to use AI software algorithms.

22.4 The Future of Diagnostics: How AI and Big Data Are Shaping the Medical Landscape

Big Data has the potential to usher in the era of personalised and individualised healthcare. It starts with a systematic collection of data and ends with proper processing to obtain accurate and timely results. Big Data is the logical next step in the evolution of radiology departments. It can transform busy radiology departments, help inefficient management, and provide intelligent and innovative patient care options. It can improve the quality of performed scans, assist radiologists in decision support, and act as a virtual quality control tool. Over a period, it can self-learn to find hidden information within the reports and images that are somewhat difficult to interconnect or find a relationship using the standard routine or conventional protocols. Here lies the real advantage of this technology. In the near future, big Data will work to assist radiologists by providing intelligent and targeted decision support rather than replacing radiologists.

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23 Unravelling the Potential of FFR-CT: A New Frontier in Cardiovascular Imaging

The new technologies emerging in the clinical setting include fractional flow reserve (FFR)-CT, CT perfusion imaging, and coronary plaque assessment.

23.1 Introduction

Since introducing the standard 64-slice CT scanners, today's cardiac computed tomography imaging can examine a patient using a very low radiation dose to obtain a cardiac scan not exceeding 3 mSv. This is only possible through the technological advancements of more sensitive detectors and faster gantry speed rotation. Also, image reconstruction software enables low-radiation dose scans to produce in-depth resolution diagnostic quality images compared to high x-ray doses in older cardiac CT scanners.

The new technologies emerging in the clinical setting include fractional flow reserve (FFR)-CT, CT perfusion imaging and coronary plaque assessment. These breakthroughs will bring CT beyond the anatomical evaluation to allow physiological evaluation without the patient undergoing nuclear perfusion scans or invasive diagnostic angiography. Especially the more advanced automated visualisation software used in an invasive examination in the cath lab where an FFR is performed, and intravascular ultrasound imaging is used to evaluate the lesions. However, CT offers a non-invasive way to achieve these same assessments.

FFR-CT has been approved by the US Food and Drug Administration (FDA) for the non-invasive hemodynamic assessment of the entire coronary tree. This imaging modality can create a 3-D model of the coronary arteries using colour codes based on computational fluid dynamics. These colour codes will show low-flow areas correlated to the coronary lesions. The aim is to identify lesions that may lead to ischemic chest pain or a heart attack. However, the FFR-CT technology can take several hours to return a result. The processing time will be reduced, and FFR-CT will be broadly used in the clinical setting.

23.2 The Role of Computed Tomography in Preventative Medicine and Risk Assessment

Modern CT machines have the potential for serial imaging due to very low-dose radiation not exceeding one mSv during patient scanning. Therefore, the older 64-slice CT systems must be upgraded with more sensitive detectors, including advanced image reconstruction software.

CTCA will be the leading imaging modality to identify early coronary disease

These new coronary-CT scanners aim to identify early plaque before it leads to advanced coronary disease. Stress testing does not show early plaque until you have a reasonable amount of coronary disease compared to CT scanning. CT scanning will allow the patient to personalise the treatment plan to prevent a heart attack. Furthermore, cardiac CT as a risk assessment tool already sees growth with calcium scoring. Numerous clinical trials have shown a correlation between the amount of calcified plaque in coronary vessels and a patient's risk for a heart attack. CT calcium scoring can also be used to convince patients to go on statin therapy and calcium scoring to be performed at least every five years.

23.3 Cardiac CT Evolves: Uncovering New Areas of Usage in Cardiology

The latest CT cardiac scanners can determine structural heart evaluation and procedural planning. In addition, these scanners are also able to do precise imaging based on advanced visualisation software. These new technologies will bring state-of-the-art cardiac imaging in transcatheter aortic valve replacement (TAVR) in addition to left atrial appendage (LAA) occlusion and transcatheter mitral repair.

23.4 CT Scanners Reimagined: The Impact of Modern Technology on Medical Imaging

Over the past decade, the most significant advances in CT scanners have been delivering low-dose radiation to the patient. This can be achieved by upgrading the older CT scanners to high-slice systems, including faster gantry speeds to freeze cardiac motion. Furthermore, modern CT scanners can perform complete anatomical coverage in one rotation. The problem with the 64-slice scanners was that it usually took two rotations to image the heart. New scanner technology will lower CT cardiac exams to 3 mSv or below. However, some centres already perform routine cardiac CT exams one mSv or below using the newest scanners and image reconstruction software.

Also, the advancements in the detector resolution will increase the image sharpness and resolution by 0.2 mm. This will enable defining the smaller structures of the plaque composition and stents inside coronary vessels. In addition, the volume spectral CT technology improves tissue characterisation, small lesion detection and metal artefact reduction.

Another improvement to CT scanners is the Whisper Drive technology, allowing high-speed scans to produce diagnostic imaging of the heart in one heartbeat. This is possible using a high-speed X-ray tube that circles the patient up to five times per second. Also, a 30-degree bidirectional gantry tilt capability enables angled scanning to avoid dosing radiosensitive organs.

Furthermore, the 80-detector row (160-slice) system is designed to perform whole-body imaging and volumetric scanning. These improvements are found in the high-end CT scanners for a superior patient experience. They can provide faster reconstruction speeds of up to 50 images per second at full resolution. In addition, it

optimises workflow and patient comfort with thin slices at 0.5 mm and a 78 cm bore. Moreover, these CT scanners use SURESubtraction and Single Energy Metal Artifact Reduction (SEMAR) and can be installed on 40 to 80 to 160 slices. These technological advances in CT machines enable faster scanning speeds that allow to perform of sedation-free paediatric exams and freeze cardiac motion.

23.5 Next-Generation Cardiac Imaging: The Emergence of PET and CTCA in Cardiovascular Disease Detection

Positron emission tomography (PET) scanning combined with Computed Tomography Coronary Angiogram CTCA is on the horizon to detect cardiovascular diseases.

A PET scan uses a small dose of a radiopharmaceutical imaging agent injected into the patient before PET scanning. As with CTCA, PET imaging involves a scanning machine to obtain the images. The cardiologist and radiologist then interpret the images to evaluate biological functions, such as blood flow and glucose metabolism of the heart.

Fractional flow reserve (FFR) derived from data obtained during the computed tomography coronary angiogram provides critical information to the cardiology medical team without exposing the patient to unnecessary risk. Previously, FFR data was acquired by subjecting the patient to an invasive cardiac catheterisation. During this procedure, a reduction in contrast agent was used and gave improved diagnostic imaging. However, there are several problems in the routine use of FFR in the cardiac catheterisation lab. First, fractional flow reserve CT values from computational fluid dynamics can be acquired using resting 3-D coronary CTA images. This technology has been demonstrated from several clinical trials that Fractional flow reserve CT is a superior diagnostic imaging modality to the traditional coronary CTA in detecting coronary artery disease. Therefore, the future of Fractional flow reserve CT will depend on the interpretation of data from artificial intelligence and its evaluation of ischemic heart disease. Furthermore, non-invasive diagnostic imaging identifies the significant lesions to distinguish between patients who can safely avoid invasive coronary angiography and those requiring revascularization. Artificial Intelligence (AI), fused with big data, will potentially solve many key clinical trial challenges.

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24 Diagnostic Accuracy of Computed Tomography Coronary Angiogram in Heart Disease

CTCA imaging has revolutionised how physicians detect coronary artery disease due to its exceptional sensitivity.

24.1 Introduction

Computed Tomography Coronary Angiogram (CTCA) is a diagnostic imaging technique to evaluate coronary arteries. Computed tomography, known as a CT scan, utilises X-rays to produce cross-sectional images of the human body. Cardiac CT is an imaging technique that uses CT technology to visualise heart anatomy, coronary circulation, the aorta, pulmonary veins and arteries.

FACT: Cardiovascular diseases are the leading cause of death and account for 17.9 million lives globally each year, and 52.5% is contributed to coronary heart disease.

The primary function of the coronary arteries is to supply blood to the heart muscle. Therefore, the patient would require an injection of a contrast medium to image the arteries to show the blood vessels. Other diagnostic tests for coronary heart disease include invasive coronary angiography and non-invasive computed tomography (CT) coronary angiography.

CTCA imaging has revolutionised how physicians detect coronary artery disease due to its exceptional sensitivity.

Also, advancements in CTCA scanners in the clinical setting include increased gantry spin times and fast single-heartbeat scanning to improve image resolution and, most importantly, reduce the patient's radiation exposure. Furthermore, developing specific algorithms has improved multidetector technology to facilitate scanning the entire heart volume in a single beat. These new CT coronary angiography scanners contain detector rows to enable 256 and 320-slice images to perform coverage of the whole heart in a single acquisition. This was possible by increasing the gantry spin times, which reduced the time for one rotation of an X-ray tube. The addition of a second x-ray tube further reduced the gantry spin times.

To limit unnecessary invasive coronary angiography on patients, the best approach would be to use at least a 64-slice CTCA scanner to rule out patients' obstructive coronary stenoses and possibly coronary heart disease.

The advantage of these CTCA techniques is that the X-ray tube is only on for a short time, reducing stitching artefacts while acquiring the whole image in one sequence.

Today, the leading CT vendors have incorporated technology to scan the entire heart volume in a single beat. Another important factor when carrying out a CTCA is for the patient not to have a high heart rate and keep the effective radiation dose down. For example, the effective radiation dose given to a patient doubles when their heart rate increases from 55 to 60 beats per minute.

24.2 The Impact of the SCOT-HEART Trial on Clinical Decision-Making in Cardiology

The SCOT-HEART investigation concluded that patients who undergo CTA, when referred to a cardiology clinic, resulted in a lower risk of death from coronary heart disease. Also, patients benefited from CTCA from not having long-term use of invasive coronary angiography.

In the clinical setting, several types of CT scans can be used to diagnose heart disease, including calcium-score screening heart scan, coronary CT angiography (CTA) and total body CT scan.

Recent advances in CTCA include:

- Coronary artery calcium scoring (CACS) is used with stratification algorithms to assess risk.
- Development of CT-derived fractional flow reserve (FFR).
- Understanding plaque morphology and plaque characteristics.
- Development of machine learning (ML).
- Coronary Artery Calcium Score (CACS)

Atherosclerosis results from coronary plaque leading to inflammation of the arterial intima, which leads to several heart diseases. However, the amount of coronary calcium can be used to predict any future heart problems, enabling the patient to make any necessary lifestyle changes to reduce their risk. For example, plaque formation can result from the calcification of the artery and the calcium score will estimate the extent of coronary artery disease. The calcium score considers the density of calcified coronary plaques in the coronary arteries.

The Agatston score can be used to quantify the level of calcification.

Agatston Calcium Score	Density in Hounsfield Units (HU)
1	130 - 199
2	200 - 299
3	300 - 399
4	>400

Note: The weighted score is multiplied by the area (mm^2)

Furthermore, if calcium is not present during the CTCA scan, it does not mean that you do not have any form of coronary disease. In some cases, soft plaque atherosclerosis could be present, which cannot be detected during a CT scan.

24.3 Fractional Flow Reserve (FFR): A Modern Approach to Assessing Coronary Artery Disease

Fractional Flow Reserve – Computed Tomography (FFR-CT) uses computational fluid dynamics to predict the functional significance of coronary artery lesions. It is a non-invasive procedure that uses HeartFlow® Analysis to provide the physician with a 3-D model of the coronary arteries to determine any potential blockages.

These blockages are generally due to coronary artery disease (CAD), which results from the arteries leading to the heart becoming narrow or blocked (atherosclerosis). This reduces blood flow to the heart, possibly leading to a heart attack.

The data obtained from a standard CTCA are further analysed using the coronary tree with CT-derived FFR results reported in all coronary segments. However, combining an anatomical and functional test will lead to a more accurate diagnosis and prevent a heart attack. Furthermore, invasive FFR is a well-established technique for quantifying lesion-specific ischaemia comparable to functional imaging.

Fractional flow reserve (FFR) is limited to a few dedicated centres in the UK. However, as CT-derived FFR technology advances over the coming years, it is expected to become increasingly available across the NHS. This diagnostic FFR test could be used in approximately 40,000 patients annually, saving the NHS £9.1 million annually. Therefore, the future of CT-derived FFR will be in the diagnostic array.

24.4 Plaque Morphology and Cardiovascular Disease

Understanding plaque morphology in cardiovascular diseases is becoming more important with the ability to visualise the entire vessel using CTCA scanning. The advantage of assessing plaque is establishing its nature using CT imaging to identify vulnerable plaque and its risk of developing acute coronary syndrome.

24.5 Empowering Cardiovascular Diagnostics with Machine Learning

Machine Learning (ML) applies computer-based algorithms to evaluate a decision based on the relationship between multiple variables. These algorithms are used in diagnostic imaging to analyse large data sets and extract the relevant data. Therefore, analysis of CTCA data sets can potentially improve diagnoses and predicate lesions. In addition, ML will quantify markers, including calcium scoring, liver Hounsfield units, and epicardial fat volumes.

Integrating ML into clinical settings will help in the risk prediction of the patient towards cardiovascular diseases. For example, ML-based fractional flow reserve has been demonstrated in predicting ischaemic lesions.

24.6 The Future of Non-Invasive Cardiology

Techniques using CT have improved non-invasive diagnostic cardiology significantly over the past decade. CT based on FFR is highly likely to become increasingly prevalent to increase the accuracy of patients requiring invasive assessment/revascularization. In addition, in the subset of patients with previous percutaneous coronary intervention, CT perfusion techniques are currently being investigated. The most significant role of CTCA is in a primary prevention setting.

Adding a calcium score when using calculators (Astro-CHARM and MESA) will enhance the accuracy of coronary intervention.

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25 From Theory to Reality: The Development of the First Lasers

Modern medical lasers are used in various clinical applications, including cancer therapy and ophthalmology.

25.1 Introduction

Max Planck showed that light is released in specific amounts of energy known as quanta and is related to radiation frequency (f). This discovery led to the equation E=hf, where h is Planck's constant (6.6262 x 10 -34 Joule·second) and is fundamental to medical lasers.

Electromagnetic radiation is emitted from a charged particle (electron) that irradiates energy when it falls from a higher to a lower energy state. Its frequency or wavelength determines the colour of light. The shorter wavelengths are ultraviolet, and the longer wavelengths are infrared.

Quantum mechanics describes the smallest particle of light energy as a photon. The energy (E) of a photon is determined by its frequency (f) and Planck's constant (h). The difference in energy levels across which an excited electron fall determines the wavelength of the emitted light.

The Planck equation set the foundation of the LASER (Light Amplification Stimulated Emission Radiation), and Albert Einstein 1916 described it as the theory of stimulated emission. This process involved an incoming photon of a specific frequency interacting with an excited atomic electron, causing it to relax back to a lower energy level. These fundamental discoveries of stimulated emission were the basis of the creation of modern lasers. However, it was not until 1960 that Maiman, a physicist at Bell Laboratories, generated a laser from ruby crystal (λ = 694 nm).

However, its practical capabilities began to emerge in the 1940s in the work of Charles Townes and Arthur Schawlow on the development of microwave spectroscopy.

This research led to the invention of the MASER (Microwave Amplification by Stimulated Emission of Radiation). First, however, Theodore Maiman created the first laser using an electrical source to energise a solid ruby.

More lasers were discovered, including the CO_2 (carbon dioxide) laser, emitting a concentrated ray of light and absorbing water to vaporise tissue. In addition, the neodymium-yttrium aluminium garnet (Nd-YAG) laser-induced coagulative necrosis within the tissue. Also, visible light lasers were used to produce haemostasis.

Modern medical lasers are used in various clinical applications, including cancer therapy, ophthalmology, nerve stimulation, dermatology, plastic surgery, wound healing and dentistry.

However, the more advanced medical lasers based on the diode are used in cancer therapy. For example, these diode lasers are used in surgical procedures, including soft tissue cutting, coagulation and cancer thermal therapy.

Currently, different types of lasers are capable of undertaking invasive and non-invasive procedures at different depths. The type of laser depends on the region of the electromagnetic spectrum: UV (200-400) μm, visible (400-700) nm, near-IR (700-2900) nm and mid-IR (3-5) μm.

Since the conception of lasers, they have been classified according to the following characteristics:

- The laser medium where the amplification occurs can be a solid, liquid, or gas. These types of lasers are referred to as solid-state lasers, liquid lasers, or gas lasers.
- Gas lasers, including carbon dioxide, excimer (XeF) and argon, are used in medical lasers.
- Dye lasers are examples of liquid lasers, and ruby or yttrium aluminium garnet doped with neodymium lasers are solid-state lasers.
- Lasers can emit radiation at different wavelengths in the electromagnetic spectrum's UV, visible, and IR parts. These are classified as UV lasers, visible lasers, and IR lasers.
- Lasers that emit radiation continuously are called continuous-wave (CW) lasers.
- Lasers that emit bursts of radiation are called pulsed lasers.

Lasers produce deeper tissue penetration depths in the near-infrared (750-1200) nm than visible lasers. Therefore, procedures that require deep penetrations, such as nano-gold mediated cancer therapy.

The visible lasers (430-680) nm have strong absorption in blood and have been used for oral cancer and retina decreases phototherapy.

Mid-IR lasers (1.9-3.0) μm and (9.3 -10.6) μm have strong absorption in water and tissue. This enables them to remove soft and hard tissue, a procedure known as ablation.

IR lasers (1.3-1.6) μm have been used for minimally invasive procedures such as resurfacing due to their more negligible tissue absorption.

Type of Laser	Wavelength (nm)	Medical Applications
Ruby	694	Dermatology
Nd-YAG	1064	Broad application
Er-YAG	2940	Surgery
Diode	630-980	Surgery, Photodynamic therapy
Argon	350-514	Surgery, Photodynamic therapy, Ophthalmology, Dermatology
Carbon dioxide	10600	Surgery
Pumped-dye	504-690	Photodynamic therapy, Dermatology

25.2 Photoacoustic Imaging

Photoacoustic imaging is a hybrid imaging technique based on the photoacoustic effect. It delivers non-ionising laser pulses to tissues and produces heat which initiates thermoelastic expansion to generate an ultrasonic wave. These waves can be detected using ultrasound imaging equipment. This technique can be used to show organs and blood vessels to tumours. Also, more advanced photoacoustic imaging can picture 3-D images of internal body parts and differentiate cancerous cells from healthy cells. This technology platform is called Photoacoustic Topography Through an Ergodic Relay (PATER).

25.3 Clinical Applications of Medical Laser Technology

Clinical Application	Medical Procedure
Oncology	Laser interstitial thermal therapy (LITT) is used on patients who are not ideal surgical candidates. LITT is used to treat several cancer types, such as gliomas and meningiomas. Also, mucosal ablation techniques use lasers to treat gastrointestinal cancers, superficial oesophageal cancer, colorectal adenoma and Barrett's oesophagus. Moreover, photodynamic therapy utilises lasers to treat lung cancer lesions.
Laser Lithotripsy	Laser lithotripsy is a technique used to break up urinary and biliary stones. The most popular shockwave lasers used in lithotripsy are based on the one-microsecond pulsed-dye laser. They work by the excitation of coumarin dye to produce monochromatic light.
Oral Surgery	The lasers used in oral surgery include CO_2, Er-YAG, Diode and Nd-YAG. They are also used in disinfection and healing.
Endoscopic Gastrointestinal Surgery	The Nd-YAG laser is used to produce coagulation of gastrointestinal bleeding. It is also used to treat benign small mucosal lesions. Also, the laser is used as a soothing treatment for malignant gastrointestinal disorders in addition to incision treatment for anatomical lesions such as stenosis or cysts.

Cataract Surgery	The parameters of the ophthalmic laser are set at a specific wavelength, duration, pulse pattern, energy, repetition rate and spot size. These settings produce a monochromatic laser beam that is capable of hitting the same spot within the eye. Therefore, changing the parameters will produce a different absorption in the type of tissue. For example, when using the argon laser, local thermal effects such as photocoagulation can result. Other lasers, such as excimer lasers, for instance, Nd-YAG, can be applied in refractive surgery.
Cardiovascular Surgery	The trans-myocardial laser revascularisation (TMLR), laser vascular anastomosis and laser angioplasty in peripheral arterial diseases are used to improve blood flow to the heart. TMLR is the only treatment procedure for severe angina and is used in coronary artery bypass grafting. In TMLR, the CO_2 laser or the Ho-YAG laser are delivered directly to the target areas of the heart muscle.
Dermatology and Reconstructive Surgery	The lasers based on the Nd-YAG and diodes are mainly emitted by infra-red light. These systems target the water in the dermis and heat the collagen in the process to initiate regeneration.

25.4 Timeline of Laser Inventions

YEAR	INVENTORS/COMPANY	DISCOVERY
1953	Charles Townes, James Gordon, Herbert Zeiger (Columbia University).	The first laser was known as the MASER (microwave amplification by stimulated emission of radiation).
1954	Charles Townes, Herbert Zeiger, James Gordon (Columbia University).	The ammonia MASER obtained the first amplification and generation of electromagnetic waves by stimulated emission.
1955	Nikolai Basov, Alexander Prokhorov (P. N. Lebedev Physical of Institute in Moscow).	They designed and built oscillators and proposed the production of a negative absorption that was called the pumping method.
1956	Nicolaas Bloembergen (Harvard University).	Development of the microwave solid-state MASER.
1957	Gordon Gould.	Coined the acronym LASER.
1958	Charles Townes and Arthur Schawlow (Bell Labs).	The MASERS were able to operate in the optical and infrared regions.
1960	Charles Townes and Arthur Schawlow (Bell Labs).	US patent granted (number 2,929,922) for the optical MASER.
1960	Theodore Maiman (Hughes Research Laboratories).	The first laser was constructed with a cylinder of synthetic ruby.

1960	Peter Sorokin and Mirek Stevenson (IBM Thomas J. Watson Research).	Demonstrated the uranium laser, a four-stage solid-state device.
1960	Ali Javan, William Bennett and Donald Herriott (Bell Labs).	Developed the helium-neon laser.
1961	Trion Instruments, Perkin Elmer and Spectra-Physics.	Lasers began to appear on the commercial market.
1961	Elias Snitzer (American ed Company).	The first operation of a neodymium glass.
1961	Charles Campbell (Institute of Ophthalmology at ed Medical), Charles Koester (American Optical Co. at Columbia-Presbyterian Hospital in Manhattan).	The first medical treatment was used to destroy a retinal tumour using the ruby laser.
1962	Fred McClung	Contributed to the theory of lasers.
1962	Groups at GE and MIT Lincoln Laboratory.	Development of the gallium-arsenide laser.
1962	Nick Holonyak (General Electric).	Gallium arsenide phosphide laser diode.
1963	Logan Hargrove, Richard Fork and M Pollack.	The introduction of the mode-locked laser.
1963	Herbert Kroemer (University of California), Rudolf Kazarinov and Zhores Alferov (A.F. Ioffe Physico-Technical Institute in St. Petersburg, Russia).	The idea of semiconductor lasers was introduced.
1964	William Bridges (Hughes Research Labs).	The invention of the pulsed argon-ion laser.
1964	Townes, Basov, and Prokhorov.	Nobel Prize in physics for quantum electronics and the construction of oscillators and amplifiers based on the maser-laser principle.
1964	Kumar Patel (Bell Labs).	The invention of the carbon dioxide laser.
1964	Joseph Geusic and Richard Smith (Bell Labs).	The neodymium doped YAG laser.
1965	Bell Laboratories.	Two lasers were phase-locked for the first time.
1965	Jerome Kasper and George Pimentel (University of California, Berkeley).	Development of the first chemical laser based on a 3.7 μm hydrogen chloride instrument.
1966	Mary L. Spaeth (Hughes Research Labs).	The invention of the dye laser pumped by a ruby laser.
1966	Charles K. Kao, George Hockham (Standard Telecommunication Laboratories in Harlow, UK).	A breakthrough in fibre optics.

1966	Alfred Kastler	Nobel Prize in physics for the method of stimulating atoms to higher energy states. This technique was known as optical pumping and was influential in developing the MASER and the laser.
1967	Bernard Soffer and Bill McFarland (Korad Corp. in Santa Monica, Calif).	The invention of the dye laser.
1970	Basov, Danilychev (Lebedev Physical Institute).	Development of the excimer laser.
1970	Alferov's group (Ioffe Physico-Technical Institute), Mort Panish, Izuo Hayashi (Bell Labs).	Produced the first continuous-wave room-temperature semiconductor lasers, which led to fibre optic communications.
1970	Arthur Ashkin (Bell Labs).	The invention of optical trapping.
1971	Hayashi, Morton B Panish (Bell Labs).	The first semiconductor laser operated continuously at ambient temperature.
1972	Charles H. Henry	The invention of the quantum well laser.
1972	Bell Labs.	A laser beam to form electronic circuit patterns on ceramic.
1974	Wrigley's	A packet of Wrigley's chewing gum was the first product to be read by a barcode scanner.
1975	NJ Metuchen (Laser Diode Labs Inc).	Engineers develop the first commercial continuous-wave semiconductor laser operating at room temperature.
1975	an der Ziel, Dingle, Miller, Wiegman, Nordland.	The first quantum well laser operation.
1976	Bell Labs.	A semiconductor laser operating continuously at ambient temperature with a wavelength greater than 1 μm.
1976	John M.J. Madey (Stanford University).	The first free-electron laser (FEL).
1977	Bell Labs.	The first commercial installation of a fibre optic lightwave communications system is completed under the streets of Chicago.
1977	Gordon Gould.	A patent was granted for optical pumping.
1978	LaserDisc.	LaserDisc hits the home video market.

1978	Philips.	The launch of the compact disc project.
1979	Gordon Gould.	A patent was granted to cover a broad range of laser applications.
1981	Nobel Prize in Physics.	Schawlow and Bloembergen received the Nobel Prize in physics for their contributions to the development of laser spectroscopy.
1982	Peter F. Moulton (MIT Lincoln Laboratory).	Development of the titanium-sapphire laser.
1982	Audio CD.	The first audio CD was released.
1985	Steven Chu (Bell Labs).	Laser light is used to manipulate atoms.
1987	David Payne (University of Southampton).	Optical amplifiers are used to boost light signals.
1994	Faist, Capasso, Sivco, Sirtori, Hutchinson, Cho (Bell Labs).	The first semiconductor laser was able to emit light, known as the quantum cascade laser, simultaneously.
1994	Nikolai Ledentsov (A.F. Ioffe Physico-Technical Institute).	The first quantum dot laser.
1996	Wolfgang Ketterle (MIT).	The first pulsed atom laser, which used matter instead of light.
1997	Shuji Nakamura, Steven P. DenBaars, James S. Speck (University of California, Santa Barbara).	The development of a gallium-nitride laser was able to emit pulses of bright blue-violet light.
1997	Wind Tunnel Facility (Marshall Space Flight Center).	The application of lasers to measure the velocity and gradient of distortion during a cold-flow propulsion research test.
2003	NASA.	Successfully flies the first laser-powered aircraft.
2004	Ozdal Boyraz, Bahram Jalali (University of California, Los Angeles).	Electronic switching in a Raman laser.
2006	John Bowers (University of California, Santa Barbara), Mario Paniccia (Intel Corp's Photonics Technology Lab in Santa Clara).	The first electrical powered hybrid silicon laser used in the silicon manufacturing process.
2007	John Bowers, Brian Koch (University of California, Santa Barbara).	The first mode-locked silicon evanescent laser.
2009	Chunlei Guo (University of Rochester in NY).	A new process that used femtosecond laser pulses to generate regular incandescent light bulbs.

2009	National Ignition Facility (Lawrence Livermore National Laboratory in Livermore).	Built the largest and highest-energy laser in the world.
2009	NASA.	NASA launched the Lunar Reconnaissance Orbiter.
2009	Intel.	Lasers enter household PCs with Intel's announcement of its Light Peak optical fibre technology.
2009	Nanfang Yu, Federico Capasso (Harvard School of Engineering and Applied Sciences), Hirofumi Kan (Laser Group at Hamamatsu Photonics), Jérôme Faist (ETH Zürich).	Demonstrated the compact, multibeam and multiwavelength lasers emitting in the IR.
2009	Global laser market.	In 2010 the global laser market will grow by about 11% and generate total revenue of $5.9 billion.
2010	University of Konstanz. National Nuclear Security Administration. Manijeh Razeghi (Northwestern University). Rainer Blatt, Piet O. Schmidt (University of Innsbruck in Austria). Lawrence Livermore National Laboratory.	Generation of a 4.3-fs single-cycle pulse of light at 1.5-μm wavelength from an erbium-doped fibre laser. NIF was able to deliver 1 MJ of laser energy to a target. Quantum cascade laser efficiency increased to 53%. Demonstrated using a single-atom laser with and without threshold behaviour by tuning the strength of atom-light field coupling. The use of ultrafast laser pulses to probe basic material properties.
2011	Hans Zogg (ETH Zürich). Malte Gather, Seok Hyun Yun (Harvard University). Jianlin Liu (University of California, Riverside).	Developed a vertical external-cavity surface-emitting laser (VECSEL) that operated in the mid-IR at about 5 μm. Demonstrated a laser was able to genetically engineer cells to produce a novel material called green fluorescent protein (GFP) Produced zinc oxide nanowire waveguide lasers.

2012	Yale University. Lawrence Livermore National Laboratory. NASA's Curiosity Rover.	Development of the random laser. 192 UV laser beams produced a peak power above 500 trillion watts. A rock on mars was zapped with a laser.
2013	Stefan Rotter (Vienna University of Technology). Camille Brès, Luc Thévenaz (Ecole Polytechnique Fédérale de Lausanne). Benedikt Mayer (Technical University of Munich).	A laser control layout was developed using granular material to determine the emission direction. Laser pulses travelling down fibre optic cables carry the world's information. Demonstrated the use of room temperature laser nanowires that emitted in the near-IR.
2014	Yuri Rezunkov and Alexander Schmidt. European Space Agency. European Space Agency. Lawrence Berkeley National Laboratory. Berkeley Lab Laser Accelerator.	Reported a boost from lasers. This laser ablation has long been proposed for rocket propulsion. Lasers are used to generate a gigabit transmission between a satellite in low Earth orbit and one in geosynchronous orbit (about 45,000 km). A laser from Tenerife connects with a satellite in orbit, providing an optical data path. A new world record for a tabletop particle accelerator (4.25 GeV). A 9 cm long capillary discharge waveguide to generate multi-GeV electron beams.
2015	Brett Hokr (Texas A&M University). Anders Kristensen (Technical University of Denmark).	Report on a random Raman laser capable of producing a wide-field, speckle-free image with a strobe time of about a nanosecond. Created a 50 μm wide reproduction of the Mona Lisa.

	University of St Andrews and Harvard Medical School.	Research involving cells swallowing microresonators.
2016	ASML. Cardiff University, University College London, University of Sheffield.	EUV (extreme ultraviolet) lithography technology results in a wavelength much shorter than the 193 nm deep UV lasers used in semiconductor production. Produced quantum dot lasers on silicon.
2017	Jet Propulsion Laboratory. Lockheed Martin. The University of St Andrews, University of Wurzburg, Technical University of Dresden.	Lasers could give space communications broadband. A system produced a single laser beam of 58 kW. Created a fluorescent protein polariton laser.
2018	Lawrence Livermore National Laboratory. National Institute of Standards and Technology. Shanghai Super intense Ultrafast Laser Facility.	The National Ignition Facility laser system set a new record of 2.15 MJ. Showed that a commercial laser could produce 3D images of objects as they melted in a fire. The generation of a 10-petawatt laser burst.
2019	MIT.	Scientists used a 1.9 μm wavelength thulium laser to excite water molecules near a microphone, which transmits an audible signal.

25.5 World's Most Powerful Laser

The Thales and ELI-NP (Extreme Light Infrastructure for Nuclear Physics) projects have developed the world's most powerful laser. The ultra-high-intensity laser system can produce a pulse at a peak power level of 10 petawatts (1015 W). This laser system is designed to generate twin laser beams of 10 PW and is used in nuclear physics. For example, this type of laser can be used to study key nuclear reactions relevant to nucleosynthesis. In particular, the fusion of α particles and carbon nuclei to produce oxygen ($^4He + ^{12}C \rightarrow ^{16}O$) is central to life on Earth.

The main features of the laser system are:

- The high-power laser system (HPLS) consists of two 10 PW beams that can deliver a laser pulse of up to 225 J in each arm during a laser pulse duration of 15–22.5 fs. The wavelength region is 814 – 825 nm.
- The maximum focal spot intensity is I0 ~ 1023 W cm^{-2}.
- The laser system can deliver lower powers at 100 TW and 1 PW.
- The Variable-Energy Gamma Ray (VEGA) system at ELI-NP can deliver monoenergetic gamma rays with up to 19.5 MeV.
- The primary performance parameters are a photon density of ~104 s−1 eV−1, with a high degree of linear polarisation of >95%.
- The laser will be able to study the extreme states in gases, solids and plasma.
- The laser configuration can be altered to investigate systems that involve non-linear quantum electrodynamics (QED). In addition to vacuum birefringence, relativistically induced transparency (RIT) and nuclear resonance fluorescence (NRF). Including photoactivation, photonuclear reactions and photofission.

25.6 Laser Frontiers: The Convergence of Innovation in Medical, Industrial, and Defence Applications

The next generation of lasers will generate powerful beam sources at precisely the right wavelength for all medical and industrial applications. Since the laser conception, they are becoming smaller devices due to the advancement of semiconductors and direct diode lasers. This technology platform led to the Extreme Light Infrastructure for Nuclear Physics (ELI-NP) project, which uses the ultra-high intensity laser system to generate pulses at a peak power level of 10 petawatts. However, laser weapons based on electro-optical systems can increase the lethal power. For example, a high-energy laser system mounted on a US Army Boeing AH-64 Apache attack helicopter. Furthermore, the US Navy has developed solid-state lasers, including the Solid-State Laser Technology Maturation (SSL-TM) effort and High Energy Laser Counter-ASCM Program (HELCAP). However, continued research into LLLT on how to relate the dose to treat a range of clinical conditions in patients in a safe manner.

LASER TYPE	WAVELENGTH (nm)
Argon fluoride	193
Xenon chloride	308 and 459
Xenon fluoride	353 and 459
Helium cadmium	325 - 442
Rhodamine 6G	450 - 650
Copper vapour	511 and 578
Argon	457 - 528
Nd:YAG	532
Helium-neon	543, 594, 612, and 632.8
Krypton	337.5 - 799.3 (647.1 - 676.4 most used)
Ruby	694.3
Laser diodes	630 - 950
Ti-Sapphire	690 - 960
Alexandrite	720 - 780
Nd-YAG	1064
Hydrogen fluoride	2600 - 3000
Erbium: Glass	1540
Carbon monoxide	5000 - 6000
Carbon dioxide	10600

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26 Electron Microscopy: What Does Coronavirus Look Like?

The structures of a virus can be elucidated by using the high-resolving power of scanning electron microscopy.

26.1 Introduction

Virus particles are invisible to the human eye and live in the nanoscale world of biology. However, a virus inside structures can be elucidated using the high-resolving power of scanning electron microscopy (SEM).

The visualisation of a virus was only possible through the invention of the first electron microscope in 1931 by Ernst Ruska and Max Knoll. However, in 1939, scientists Ruska, Kausche and Pfankuch became the first to visualise viruses such as the tobacco mosaic virus using the technique of electron microscopy. These developments led to Ruska sharing the 1986 Nobel Prize with Binnig and Rohr for inventing the scanning tunnelling electron microscope.

Electron microscopy has been used to visualise organisms smaller than bacteria and viruses. In the clinical setting, it is valuable in surveilling emerging diseases and potential bioterrorism viruses. Other imaging modalities used to elucidate the structural components of viruses and provide information for treatment and vaccine strategies include immunoelectron microscopy, cryo-electron microscopy and electron tomography.

Other milestones of electron microscopy have enabled the discovery of new viruses. For example, in 1948, electron microscopy could differentiate between the virus that causes smallpox and chickenpox. Another milestone using electron microscopy was its ability in 1952 to obtain the first image of the poliovirus.

The advantage of using electron microscopy to obtain a viral diagnosis is that it does not require biological reagents of specific probes to identify the pathogenic agent. Furthermore, an unknown disease requires a particular reagent to identify the pathogen. Conversely, electron microscopy allows an open view of what is causing the disease compared to molecular tests, which would require an understanding of the agents to determine the correct diagnostic investigation.

EM is a mainstay in detecting new and unusual outbreaks. For example, norovirus (Norwalk agent) was discovered by EM, and EM continues to serve to confirm infection in quality control of molecular techniques.

Electron microscopy was used to identify the viral agent that caused Zaire's first Ebola virus outbreak in 1976. Also, in 1999, the skin infection trichodysplasia spinulosa was

identified by electron microscopy as a polyomavirus in an immunosuppressed patient. Furthermore, the Henipavirus outbreaks in Australia and Asia were first described using electron microscopy in 2003. They identified the lymphocytic choriomeningitis virus that caused fatalities of recipients of organs transplanted from a single donor.

However, electron microscopy was used to identify the severe acute respiratory syndrome (SARS) agent before it was classified as a coronavirus. Also, the cause of the monkeypox outbreaks in the United States in 2003 was discovered by electron microscopy and identified as the poxvirus.

Other methods to identify a virus require growing culture and may be unsuitable for molecular testing because the virus solution has been stored over time. In these cases, electron microscopy does not require a live virus and has been used to identify the variola virus in infected tissue preserved for several decades.

26.2 Electron Microscopy and the Battle against Coronavirus: The Key to Understanding its Structure

During the coronavirus outbreak, electron microscopy has been an essential tool for virus detection available to virologists. In the media, we have seen artists' impressions of the SARS-CoV-2 coronavirus. However, electron microscopy has been used to obtain real images of COVID-19 and shows the SARS-CoV-2 virus resembling a small pepperoni pizza.

Viruses are too small to see using conventional microscopes, mainly used to identify bacterial and fungal infections. This is because viruses come in different sizes; the most significant ones are about 500 nm. So in the conventional microscope, they would appear as dots. However, the smallest is around 20 nm, so you could never see them in a light microscope.

The SARS-CoV2 is detected using a PCR test that identifies certain viral strains from the samples obtained from individuals with suspected COVID-19.

The new images of COVID-19 obtained by electron microscopy use electrons and magnets to focus and produce images, rather than using a conventional microscope based on the application of light and glass lenses.

The shape of the virus can be determined by electron microscopy and is used to classify the virus type. The scanning electron microscopy images produce a 3-D structure of the COVID-19 viruses, which shows the nucleocapsid protein (N-protein), and the spike protein, which appears to be blurry on the outside of the coat.

The two main types of electron microscopes produce different images. Transmission electron microscopes produce a flat image, and scanning electron microscopes create 3D-like pictures. All the images from all types of electron microscopes are black and white. The images obtained of the coronavirus have been artificially coloured. These images were obtained by the transmission electron microscope, which was isolated from the first U.S. case of COVID-19.

26.3 The Diversity of Electron Microscopes: A Comparison of Techniques and Uses

Type of Electron Microscope	Description
Transmission Electron Microscope (TEM)	The transmission electron microscope (TEM) works by applying a high voltage to a beam of electrons instead of light in a traditional microscope. The electrons pass through the specimen to produce the magnified image. These images are created on a photographic film, fluorescent screen or using CCD camera. The TEM generates black and white 2-D images of the specimen. In addition, the more advanced instruments are capable of producing 3-D images of the material from the ptychography technology invented by Hoppe and Fourier.
Scanning Electron Microscope (SEM)	The scanning electron microscope (SEM) focuses a high-voltage electron beam onto a narrow region to create a raster image. In 1937 the first SEM was developed and further modified thirty years later by Sir Charles Oatley. The advantage of SEM over TEM is its ability to image wet samples. This is because SEM scans the surface, whereas TEM detects the transmission of the electron beam through the sample. Furthermore, SEM can image samples in a low vacuum and is referred to as an environmental scanning electron microscope (ESEM). However, both SEM and ESEM are capable of producing high-quality 3-D images of the sample.
Reflection Electron Microscope (REM)	The Reflection Electron Microscope (REM) uses scattered electrons that reflect from the sample's surface to create an image. REM is a similar operation to SEM and makes use of secondary electrons. REM uses reflection high-energy electron diffraction (RHEED) or sometimes known as reflection high-energy loss spectroscopy (RHELS).
Scanning Transmission Electron Microscope (STEM)	Widely considered a high-resolution version of the SEM, the scanning transmission electron microscope (STEM) focuses on a narrow spot and produces an image by scanning the sample in a raster. However, it also "picks up" the electrons that go through the specimen and delivers a resolution comparable to the TEM using the SEM technique.
Low-Voltage Electron Microscope (LVEM)	The Low-Voltage Electron Microscope (LVEM) is a combination of TEM, SEM and STEM. This microscope uses low-voltage and is useful for imaging biological and organic samples.

26.4 Electron Microscopy and the Battle against Coronavirus: The Key to Understanding its Structure

The invention of the electron microscope has contributed to the understanding of cells, molecules and the identification of micro-organisms. Also, it has helped to

determine the structure of metals and crystals, including other chemical compounds. The more advanced electron microscopes can magnify samples up to 2 million times and produce high-quality images.

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27 Molecular Imaging Technology: Use of PET in Clinical Microdose Studies

PET imaging is used in oncology, neurology, and cardiology.

27.1 Introduction

The powerful in vivo non-invasive imaging technique called positron emission tomography (PET) can generate dynamic information on biochemical processes in the human body. PET imaging is primarily used in oncology, neurology and cardiology. PET is an ultra-sensitive technique that can be used in human microdose studies.

A human Phase, 0 microdose study, is performed at the earliest stage of drug development. This approach enables preliminary data to be compiled on a human drug candidate before the commencement of Phase I clinical trials. PET imaging relies on detecting gamma radiation emitted from positrons during the annihilation of an electron.

27.2 PET Imaging in Humans: Exploring the Dual Roles of FDG and Drug Candidate Labelling

- The most common PET studies are performed with the radiotracer [^{18}F]-fluorodeoxyglucose (FDG).
- The other type of PET study uses the labelling of a drug candidate.

PET studies in humans are carried out using a low dose of the drug (micrograms) administered intravenously. The microdose study aims to provide information about the rate at which the drug passes through the blood-brain barrier (disposition of the drug) and gain insight into human pharmacodynamics and pharmacokinetics. Advances in PET technology have significantly contributed to the drug discovery process by compiling more accurate data on drug efficacy and targeting the efficiency of potential lead compounds. The potential benefits of introducing PET imaging in the early phase of drug discovery will reduce the time spent on poor lead compounds as potential drug candidates. Also, PET imaging is used in late-stage drug discovery to investigate the toxicity and dosing studies, including tracking the response.

However, the main problem of PET imaging is the ability to synthesise be-spoke PET probes to investigate a particular disease. This is because of the challenge to develop feasible synthesis routes to incorporate the short-lived radiolabel to obtain probes in a reasonable radiochemical yield within the timescale associated with the short half-lives of PET radionuclides. Developing these synthesis methods is beneficial when using the shorter-lived isotopes (carbon-11, half-life = 20.3 minutes) in applying a

broad range of targeting agents as probes. Automation will be vital in a novel probe containing fluorine-18 (half-life = 109.7 minutes) and carbon-11 PET isotopes. Enhancing the range of synthetic precursors labelled with PET isotopes also allows access to a broader range of specially designed molecular imaging agents with specific purposes, either to enhance specificity and sensitivity or to broaden the range of disease states that can be imaged.

Currently, 80% of clinical PET imaging and research uses FDG. However, the use of radiometals in PET imaging, particularly copper-64 (half-life = 12.7 hours), gallium-68 (half-life = 68 minutes) and yttrium-90 (half-life = 64.1 hours). Copper-64 and gallium-68 are routinely used in neuro and cardiac imaging. The advantage of using gallium-68 is that it does not require a cyclotron, therefore widening PET imaging opportunities throughout the world.

27.3 Why PET Imaging? Exploring the Rationale Behind this Diagnostic Tool

PET/CT offers a means of significantly reducing the drug discovery pipeline costs by providing the following:

- More secure identification of pre-clinical candidate
- Robust means of securing a pass/fail decision in Phase I/First-in-Man trials because human bio-distribution, pharmacodynamics and pharmacokinetics can be measured.

The decision to move to Phase II is based on human data. PET/CT can provide an objective and quantitative endpoint for therapeutic efficacy in clinical trials. For example, investigating the reduction in tumour volume from FDG PET, proliferation using FLT (^{18}F-fluorothymidine) and dopamine receptor activity using ^{11}C-raclopride.

PET/CT could also reveal when drugs effectively target a selected population (a specific human phenotype) but fail when the appropriate subject is used. This opens the way for rational targeted drug design.

Pre-clinical PET/CT allows in vivo bio-distribution, pharmacodynamics, and pharmacokinetics to be measured. Receptor binding (K and B_{max}) can be established in vivo. Objective and quantitative measurements of candidate therapeutics efficacy can be determined using known radiotracers. Given appropriate animal models, drugs targeting a specific genotype can be identified.

PET/CT can be used to discover why an established drug is active in one situation but not in a similar clinical situation, for example, gemcitabine for lung cancer compared to pancreatic cancer. Similarly, a drug's complex mode of action, for example, carbamazepine, can be investigated in vivo both in animal models and in man.

27.4 PET Imaging in Drug Development: Answering Critical Early-Stage Questions

- Can a drug reach its intended target?
- Does it sufficiently bind the primary target?
- Does its interaction with the primary target affect one or more biochemical/signalling pathways?
- Is the interaction of the drug on cell or organ physiology relevant to a therapeutic effect?
- Does the drug interact with or affect other off-target tissues or organs?
- Can the drug be delivered to the target efficiently and achieve therapeutic levels?

The application and access to functional metabolic imaging have significantly enhanced the understanding of various pathological processes such as cancer. In addition, these imaging modalities have enabled the incorporation of information into patient management protocols. The leading molecular imaging tool is positron emission tomography (PET) which has emerged at the forefront of various clinical applications.

The clinical use of PET was restricted until the commercial use of medical cyclotrons in the 1980s in the field of neurology and cardiology. These cyclotron advancements made it practical to produce short-lived PET radiotracers at the hospital nuclear medicine departments. However, in the 1990s, the clinical applications of PET in oncology started with the radiotracer 18F-fluorodeoxyglucose (FDG) and, more recently, the hybrid of computed tomography (CT) fused with PET. These hybrid scanners combine the anatomic images produced by CT with the functional information of PET.

The principle of PET imaging is the ability to detect changes in cells, organs and tissues of the human body during metabolic processes. Some of these target glucose metabolism, enabling PET imaging to quantify functions within the cell. For example, in cancer cells, metabolic changes occur before the cells undergo certain changes, such as metaplasia. In the late stages of cancer, PET will follow the structural changes and detect changes in the disease state. The anatomical imaging techniques include CT and MRI, identifying any conditions in the organs.

27.5 Positron-Emitting Radioisotopes: The Stars of PET Imaging

PET Radioisotope	Half-Life	Positron Energy [MeV]
Carbon-11	20 mins	0.385
Copper-62	10 mins	1.315
Copper-64	12.7 hours	0.278
Fluorine-18	110 mins	0.250
Gallium-68	68.1 hours	0.836, 0.352
Iodine-124	4.2 days	1.691, 7.228, 1.509, 1.376
Nitrogen-13	10 mins	0.492
Oxygen-15	2 mins	0.735
Potassium-38	8 mins	1.216
Rubidium-82	1.3 mins	1.523, 1.157

The radiotracer ^{18}F-fluorodeoxyglucose (FDG) behaves as an analogue of glucose and is used in glucose metabolism. FDG-PET radiotracer enters the cells like glucose, which involves phosphorylation by hexokinase to produce FDG-6-phosphate (FDG-6-P). The FDG-6-P does not undergo further metabolism but accumulates in the cells. This is because malignant cells have a higher rate of glycolysis than healthy cells.

The PET radiotracers ^{11}C-thymidine and ^{18}F-fluorothymidine (FLT) are both analogues of thymidine and are used as probes for cellular proliferation. Subsequently, the uptake of FLT has a similar mechanism to FDG uptake. The FLT uptake by the proliferation of cells does not incorporate into the DNA and only accumulates in intracellular tumour cells. FLT also can predict the tumour grade in lung cancer and is even a predictor of the brain tumour response.

Furthermore,^{11}C-methionine has been demonstrated in the evaluation of brain tumours. In addition, ^{11}C-choline and ^{11}C-acetate have been used in the PET imaging of prostate cancer to evaluate metastatic disease.

The PET radiotracer, rubidium-82, is used to evaluate the myocardial perfusion in a similar procedure when using technetium-99m (Myoview), thallium 201 or nitrogen-13 labelled ammonia.

PET imaging of the human skeleton can be investigated using the radiotracer ^{18}F sodium fluoride and is comparable to technetium-99 labelled methylene diphosphonate.

27.6 Illuminating the Brain: PET Radiotracers and Their Role in Neuroimaging

Radiotracer	Function
$H_2{}^{15}O$	Blood flow
$^{15}O_2$	Oxygen metabolism and flow
Oxygen-15 or Carbon-11 carboxy haemoglobin	Blood volume
Carbon-11 methionine	Amino acid metabolism
Carbon-11 ephedrine	Adrenergic terminals
Carbon-11 carfentanil	Opiate receptor activity
Carbon-11 flunitrazepam	Benzodiazepine receptor activity
Carbon-11 methylspiperone	Dopamine receptor activity
Carbon-11 methylspiperone	Muscarinic cholinergic receptor activity
Fluorine-18 fluorodeoxyglucose (FDG)	Glucose metabolism
Fluorine-18 fluoro-dopa	Presynapic dopamine system
Fluorine-18 fluorothymidine (FLT)	DNA synthesis

27.7 PET Imaging in Medicine: Transforming Diagnosis and Treatment

Clinical Application	Function
Brain tumours	Gliomas are the most common primary brain tumours in adults. PET imaging studies have shown that the accumulation of FDG uptake is specific to the tumour type. FDG-PET is used for tumour grading and response to the type of therapy. Several PET radiotracers are used to investigate brain tumours and include ^{11}C-methionine and the transport amino acid FLT. In addition to ^{11}C-thymidine and ^{11}C-choline are used to study lipid metabolism.
Breast cancer	In most cases, PET imaging is not used in the initial diagnosis and screening of patients with breast cancer. However, PET can be used in the later staging of the disease, including restaging and detecting recurrent disease and therapy monitoring.
Cervical cancer	FDG-PET can detect cervical cancers and can help in the personalised patient treatment plan.
Colorectal cancer	PET imaging can detect primary colon carcinoma in at least 90% of cases compared to 60% sensitivity of computed tomography (CT).

Coronary artery	PET-MPI (myocardial perfusion imaging) is performed during the stress and rest state of a patient. Radiotracers used in these tests are rubidium-82 or ^{13}N-ammonia.
Coronary perfusion	An absolute myocardial blood flow test is used to evaluate the coronary artery lesion and assess the overall coronary vasculature.
Dementia	PET imaging can help to diagnose the type of dementia. FDG-PET shows hypometabolism in superior parieto-temporal cortices in Alzheimer's disease. PET can show dementia with Lewy bodies involvement of occipital lobes.
Epilepsy	Ictal PET imaging can show increased glucose uptake at the site of seizure.
Head & Neck tumours	PET/CT imaging can assist medical physicists in planning the radiation treatment for head and neck cancers. The most prevalent cancer of the head and neck is squamous cell carcinoma. PET can be used to find a primary tumour in patients with metastatic cervical lymphadenopathy. PET is used in follow-up for the detection of recurrent disease and any changes in the tumour.
Lung cancer	FDG-PET can be used to differentiate benign from malignant nodules in solitary pulmonary nodules (SPN). Several lung cancers accumulate FDG except for pulmonary carcinoid and bronchioloalveolar carcinoma (BAC). PET imaging is used in the determination of the nodal stage of non-small cell lung carcinoma (NSCLC). In most cases, the staging of lung cancer is based on CT imaging. FDG-PET scanning can identify positive nodes which are smaller than 10 mm in size. FDG uptake correlates with tumour proliferation in lung cancers. FDG-PET can be used to detect metastases.
Lymphoma	Lymphomas are classified as Hodgkin's and non-Hodgkin's Lymphoma (NHL). PET imaging is a useful modality for staging, monitoring therapy and restaging in lymphomas. PET is used in the evaluation of the spleen and bone marrow.
Melanoma	The survival from melanoma depends on the stage at the time of diagnosis and the thickness of the primary lesion. PET is useful in the detection of metastases.
Movement disorders	PET can image the dopaminergic receptor, and ^{18}F-fluoro DOPA scan is used to investigate Parkinson's disease.
Musculoskeletal tumours	Malignant primary bone tumours can be detected by PET imaging. Also, differentiate the giant cell tumour, eosinophilic granuloma and fibrous dysplasia in benign environments.

Myocardial perfusion	FDG-PET perfusion imaging is used to identify regions of the myocardium by comparing the regional FDG uptake with regional blood flow.
Oesophagal cancer	Squamous cell carcinoma is prevalent in the upper part of the oesophagus. The lower part of the oesophagus usually finds adenocarcinoma. The overall sensitivity of PET-CT in carcinoma oesophagus is 95%.
Oncology	PET and the hybrid PET-CT are both used in the staging of cancer. FDG is the most used radiotracer in oncology. PET imaging aims to detect any remaining lesions and the type of lesion. Also used in the development of a personalised treatment plan. PET-CT hybrid imaging is used to obtain biopsies from the active region of the tumour.
Renal, bladder and prostate cancers	PET is limited in the diagnosis of primary tumours of the prostate, bladder and kidneys because of the low uptake of FDG by the tumours. The radiotracers ^{11}C-choline ^{11}C-acetate and been used to detect a primary lesion in prostatic cancers.
Stroke	MRI and CT imaging can be used in the diagnosis of a stroke.
Testicular cancer	Both seminoma and non-seminomatous germ cell tumours are found in the retroperitoneal nodes.

27.8 Revolutionising Medical Imaging: The Future of PET Technology in Oncology, Cardiology, and Neurology

Over the last decade, PET has emerged as an important molecular imaging tool in the area of oncology, cardiology and neurology. The advancement of PET technology will produce high-resolution PET scanners with integrated multiple-row detectors of computed tomography. These PET-CT hybrid scanner aims to produce a scan under 5-min with reduced radiation that affects both the patient and radiographer. In addition, these new scanners will enhance patient comfort and minimise the effects of patient movement and increase patient throughput. The design of specific radiotracers by using automated synthesis will enable PET and PET/CT to facilitate more personalised imaging towards the patient's treatment plan.

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28 Coronavirus Spikes: CT and Ultrasound Imaging Insights

COVID-19 is caused by coronavirus virions that are enveloped by spherical-shaped virus crown spikes.

28.1 Introduction

The disease COVID-19 is caused by Coronavirus virions that are enveloped spherical-shaped virus particles with a diameter ranging from 80 to 160 nanometres (625 smaller than a single strand width of a hair). These virus particles contain surface 'crown' projections of up to 20 nm in length, covering the entire virion surface. Since viruses do not have metabolic systems and are believed to be non-living, according to some researchers, they act as intracellular parasites. They transfer RNA or DNA genomes into the host from their protective, virus-coded symmetric protein capsid: the nucleoprotein and the genome form the nucleocapsid. In enveloped viruses, the nucleocapsid is coated by a lipid bilayer which results from the modified host cell membrane and is covered with an outer layer of the viral envelope of glycoproteins.

The coronaviruses belong to the order Nidovirales of viruses with animal and human hosts and include the families Coronaviridae, Arteriviridae, Roniviridae and Mesoniviridae. Coronaviruses are classified into four genera:

The alphacoronavirus include porcine respiratory coronavirus (PRCV), porcine epidemic diarrhoea virus (PEDV), human coronavirus NL63 (HCoV-NL63) and porcine transmissible gastroenteritis coronavirus (TGEV).

The betacoronaviruses include human coronavirus OC43, Middle East respiratory syndrome-related coronavirus (MERS-CoV), severe acute respiratory syndrome-associated coronavirus (SARS-CoV), mouse hepatitis coronavirus (MHV), bovine coronavirus (BCoV) and bat coronavirus HKU4.

All these betacoronaviruses infect mammals. The gamma coronaviruses infect avian species and include avian infectious bronchitis coronavirus (IBV) and delta coronaviruses such as porcine delta coronavirus, which infect both mammalian and avian species.

Inside the coronavirus, the envelope is a helical nucleocapsid of 6-8 nm in diameter. The formation of a helical nucleocapsid in coronavirus is unexpected because a helical nucleocapsid is usually associated with viruses containing a negative-stranded RNA genome. However, coronavirus contains a positive-stranded RNA (positive-

sense) genome. In most cases, the positive-stranded RNA viruses have icosahedral nucleocapsids and may play a role in the mechanism of coronavirus RNA synthesis.

The positive-sense viral RNA genome (Group IV in Baltimore) can facilitate messenger RNA and thus can be translated into protein in the host cell. Positive-strand RNA viruses encompass over 33% of all virus genera. They include numerous pathogens such as West Nile, dengue, and hepacivirus C (HCV) and the coronaviruses SARS, MERS and SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2). In addition, a positive sense of viral RNA is present in the rhinoviruses that cause the common cold.

Note: The official names for the virus responsible for COVID-19 (previously known as 2019 novel coronavirus, 2019-nCoV) and the disease it causes are: Coronavirus disease (COVID-19); Virus: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

All coronavirus particles contain three to four structural proteins; the first is a spike protein (S) shaped like a club. This glycoprotein spike (peplomer) is formed on a viral capsid or viral envelope and has a molecular weight of 180 kilodaltons. The function of the spike protein is to mediate the coronavirus entry into host cells. The binding to a receptor on the host cell surface is facilitated through the S1 subunit and initiates the fusion of the viral and host membranes via its S2 subunit. The coronavirus family have two domains in S1 that are different and can recognise a range of host receptors leading to the attachment of the viral particle. Subsequently, the spike protein can exist in two conformations which are the prefusion and post-fusion. The conformational change from prefusion to post-fusion of the spike protein will trigger membrane fusion.

Coronaviruses have club-shaped spikes on their outer coats. Immune responses from other coronavirus studies suggest that these are a good target for a vaccine.

The second viral structural protein, M, is also an integral membrane glycoprotein. The function of this protein is unclear: it is unlike the matrix protein present in other enveloped viruses. The inside domain of the M protein may interact with the virion nucleocapsid. This interaction could be the focal point for the assembly of virus particles because virus budding appears to occur at the site of M accumulation. The monoclonal antibodies specific to the M protein do not neutralise virus infectivity. The third glycoprotein on the virion surface is HE. This protein most likely constitutes the smaller spikes observed on virus particles in some electron micrographs of coronaviruses. The fourth structural protein is an internal component of the virus. This protein, N, is a phosphoprotein of 50 kilodaltons, constituting the virus's nucleocapsid protein. The protein binds to virion RNA, providing the structural basis for the helical nucleocapsid.

Coronavirus contains a single piece of non-segmented RNA genome with an estimated molecular weight of 6-8 megadaltons. The RNA contains a 5' cap structure and 3' poly(A) tail and is infectious upon transfection (the process of delivering nucleic

acids and small proteins into eukaryotic cells) of the naked RNA into a susceptible cell line. The 5' cap protects the mRNA from degradation and facilitates ribosome binding during translation. A poly (A) tail is added to the 3' end of the pre-mRNA once elongation is complete.

The RNA also serves as a template for in vitro translation of viral proteins. Thus, this RNA is typically positive-stranded (sense-strand RNA virus). In these cases, the virus's genetic information comprises a single strand of RNA that is the positive (sense) strand that encodes messenger RNA and protein. Replication in positive-strand RNA viruses is via a negative-strand intermediate. Examples of positive-strand RNA viruses include poliovirus, Coxsackie virus and echovirus.

No negative-stranded RNA has been detected in the virion for coronavirus. The RNA is more significant than any other known viral RNA (the next smaller viral RNA is paramyxovirus RNA, which is approximately 14 kilodaltons long).

Coronaviruses generally have very restricted host ranges, infecting only cells of their host species. However, some cross-species infections do occur. For instance, BCV can infect bovine, human, and rat cells. In 1965, Tyrrell and Bynoe discovered the first human coronavirus (HCoV) called B814. They isolated the virus from the respiratory tract of an adult with a common cold. However, Tyrrell and Bynoe could not grow the agent in tissue culture, and eventually, Hamre and Procknow successfully grew the virus.

28.2 From Ground Zero to Worldwide Turmoil: The Emergence of the Coronavirus Outbreak

In December 2019, Wuhan, the capital of Central China's Hubei province – a population of over 18 million people, became the epicentre for an outbreak of pneumonia of unknown origin. At the time, this outbreak was reported to the WHO (World Health Organisation) and the Chinese health authorities, who implemented an investigation to identify the source of infection and to control the disease. These measures involved isolating people suspected to have the disease and closely monitoring contacts. Further measures included collecting and analysing epidemiological and clinical data from patients, including developing diagnostic and treatment plans to address this outbreak.

Then on 7 January 2020, Chinese scientists isolated a novel coronavirus (CoV) from patients in Wuhan. The patients were experiencing symptoms similar to those caused by severe acute respiratory syndrome coronavirus (SARS-CoV). Since the SARS outbreak in 2002, investigations have continued into the interaction of the SARS-CoV spike protein receptor-binding domain (RBD) with the host receptor angiotensin-converting enzyme 2 (ACE2).

This interaction between the two receptors regulates the cross-species and human-to-human transmissions of SARS-CoV.

Therefore, the analyses of the potential receptor usage by SARS-CoV-2 are based on knowledge about SARS-CoV and the newly released sequence of 2019-nCoV.

28.3 Coronavirus Uncovered: Understanding the Distinctive Properties and Behaviour

- The sequence of the 2019-nCoV receptor-binding domain identified the interaction between the receptor-binding motif (RBM) and ACE2. This interaction is similar to that of SARS-CoV, and evidence suggests that 2019-nCoV uses ACE2 as its receptor.
- Several amino acid residues in 2019-nCoV RBM, such as Gln493, provide favourable interactions with human ACE2. Therefore, this observation is consistent with the 2019-nCoV ability to infect human cells.
- Also, the amino acid residue Asn501 in 2019-nCoV RBM unusually binds human ACE2. This suggests that 2019-nCoV has acquired some ability for human-to-human transmission.
- However, phylogenetic analysis indicates a bat origin of 2019-nCoV, but 2019-nCoV potentially recognises ACE2 from a diverse range of animal species except for mice and rats. Therefore, this implicates these animal species as possible intermediate hosts or animal models for 2019-nCoV infections.
- These analyses provide insights into the receptor usage, cell entry, host cell infectivity and animal origin of 2019-nCoV and may help epidemic surveillance and preventive measures against 2019-nCoV.

The genetic sequence (GenBank: MN908947.3) of the 2019 novel coronavirus (2019-nCoV) enabled the rapid development of point-of-care real-time polymerase chain reaction (PCR) diagnostic tests specific for 2019-nCoV. These tests were based on full genome sequence data. The analysis of all cases diagnosed as of 11 February 2020, by using China's Infectious Disease Information System gave the following results from a total of 72314 patient records: 44672 (61.8%) confirmed cases of COVID-19, and 16,186 (22.4%) suspected COVID-19 cases, in addition to, 10567 (14.6%) clinically diagnosed cases (Hubei only) and 889 asymptomatic cases (1.2%)-contributed data for the analysis.

The clinical features of the first 41 patients (see table below) admitted to a hospital in Wuhan were confirmed to be infected with 2019-nCoV by January 2020. The symptoms resulting from the 2019-nCoV infection were non-specific, including fever, dry cough and sickness.

28.4 Characteristics of patients infected with SARS-CoV-2, MERS-CoV, and SARS-CoV

Demographic	SARS-CoV-2	MERS-CoV	SARS-CoV
Date	December 2019	June 2012	November 2002
Location of the first detection	Wuhan, China	Jeddah, Saudi Arabia	Guangdong, China
Age, years (range)	49 (21–76)	56 (14–94)	39.9 (1–91)
Male: female sex ratio	2.7:1	3.3:1	1.1:25
Confirmed cases (Data as of 20 January 2020)	835	2494	8096
Mortality (Data as of 23 Jan 2020)	25 (2.9%)	858 (37%)	744 (10%)
Health-care workers (Data as of 21 January 2020)	16	9.8%	23.1%
Symptoms			
Fever	40 (98%)	98%	99-100%
Dry cough	31 (76%)	47%	29-75%
Dyspnoea	22 (55%)	72%	40-42%
Diarrhoea	1 (3%)	26%<	20-25%
Sore throat	0	21%	13-25%
Ventilation support	9.8%	80%	14-20%

28.5 Symptoms of COVID-19

Common Symptoms	fever (85-90%), cough (65-70%), fatigue (35-40%), sputum production (30-35%), and shortness of breath (15-20%).
Less Common Symptoms	myalgia/arthralgia (10-15%), headaches (10-15%), sore throat (10-15%), chills (10-12%), and pleuritic pain.
Rare Symptoms	nausea, vomiting, nasal congestion (<10%), diarrhoea (<5%), palpitations, and chest tightness.
Other Symptoms	Possible loss of smell and taste, including anosmia, hyposmia, ageusia and dysgeusia. Also, patients with the disease may have symptoms of conjunctivitis, and those affected may have positive viral PCR in their conjunctival fluid.

28.6 COVID-19 Radiographic Features: Unravelling Atypical Pneumonia through Chest Radiographs and CT Imaging

The radiographic features of COVID-19 using chest radiographs and Computed Tomography (CT) are those of atypical pneumonia. However, imaging has limited sensitivity for COVID-19, and up to 18% demonstrated normal chest radiographs or CT subjected to mild or early disease course. This decreases to 3% in severe diseases. Bilateral and multilobar involvement is frequent. The application of a plain radiograph is less sensitive than a chest CT. However, chest radiography is usually the first-line imaging modality for patients with suspected COVID-19. The chest radiographs may be normal in early or mild disease. Of patients with COVID-19 requiring hospitalisation, 69% of initial admissions gave an abnormal chest radiograph. Also, 80% of hospital patients indicated some form of radiographic abnormalities. These observations were found to be more prominent after 10-12 days from the onset of symptoms. The most common findings were airspace opacities compared to the less frequent pulmonary ground-glass opacity. The distribution of COVID-19 in the chest is bilateral and peripheral, with the lower region being predominant. This is in contrast to multiple lung parenchymal abnormalities and associated pleural effusion, which is rare.

28.7 Decoding COVID-19 in Adults: The Role of Computed Tomography (CT) Imaging

Observations	Notes
Ground-Glass Opacities (GGO).	GGO is a radiological finding in CT consisting of a hazy opacity that does not obscure the underlying bronchial structures or pulmonary vessels. Pure GGOs are those with no solid components, whereas part solid GGOs contain both GGO and a solid component.
Crazy paving presence in GGOs and inter-and intra-lobular septal thickening.	The superimposition of a linear pattern on GGO on CT images results in a pattern that is termed crazy-paving pattern, similar to the structure of paving stones. The crazy-paving pattern is a feature of thin-section computed tomography and multidetector computed tomography.
Air space consolidation.	Air space opacification results from the filling of the pulmonary tree. This filling results in the attenuation of X-rays more than the surrounding lung parenchyma. It is one of several patterns of lung opacification and is equivalent to the pathological diagnosis of pulmonary consolidation.
Bronchovascular thickening in the lesion.	The interlobular septum defines the boundary of the secondary pulmonary lobule. The bronchus and artery, or bronchovascular bundle, run into the centre of the secondary pulmonary lobule. Therefore, analysis of the secondary pulmonary lobule is a crucial step to determine the distribution of the diffuse lung disease and narrow the differential diagnosis.

Traction Bronchiectasis.	Traction bronchiectasis results from the distortion of the airways, which is secondary to mechanical traction at the bronchi due to fibrosis of the surrounding lung parenchyma.
The ground-glass opacities and consolidative are usually bilateral, peripheral and basal in distribution.	It was found that approximately half the COVID-19 infected patients had normal CT scans up to 2 days after the onset of flu-like symptoms. Also, the COVID-19 RT-PCR sensitivity may be as low as 60-70%. Therefore, patients with pneumonia resulting from COVID-19 may have lung abnormalities on chest CT with associated negative RT-PCR. However, the lung abnormalities during the early course of COVID-19 infection usually are peripheral focal or multifocal GGOs affecting both lungs in approximately 50%–75% of patients. Furthermore, as the disease progresses, crazy paving and consolidation become the dominant CT findings. These observations start to peak between 9 and 13 days, followed by slow clearing at approximately one month and beyond.
A study of found 54% of asymptomatic patients had pneumonic changes on CT scans.	This study evaluated the chest CT findings of patients from the Diamond Princess cruise ship who contracted the COVID-19 disease. The results revealed a high incidence of subclinical CT changes in COVID-19 infected cases. Also, they indicated more GGO predominance over consolidation and milder severity on CT than symptomatic cases. The key points of the study included that the 104 cases analysed, 76 (73%) were asymptomatic and 41 (54%) showed pneumonic changes on the CT scans. Also, the other 28 (27%) cases were symptomatic, 22 (79%) of which had abnormal CT findings. However, the asymptomatic cases showed more GGO predominance over consolidation (83%) compared to symptomatic cases that may show a consolidation predominance over GGO (41%). Furthermore, asymptomatic cases indicated a milder CT severity score than symptomatic cases.
Lung Ultrasound observations in adults with COVID-19.	
Multiple B-lines indicated: A broad spectrum from focal to diffuse with spared areas.	Is it possible for a lung ultrasound to detect the early diagnosis of COVID-19 pneumonia? In the majority of patients, the ultrasound produced a diffuse B-pattern with spared areas. The chest CT scan was performed in all 12 patients and indicated a strong correlation with ultrasound. The ultrasound scans revealed bilateral lung involvement with GGO, 42% of the patients had a crazy-paving pattern, and four patients developed organising pneumonia. B lines - often non-homogenous with spared areas, increasing in number with severity, coalesced with a 'white lung' appearance with severe disease. The thickened or irregular pleural line. Small consolidations immediately below the pleural line.

Irregular, thickened pleural line with scattered discontinuities.	The non-critical COVID-19 patients had visible ultrasound characteristics in the posterior and inferior areas of the lung. A large number of B lines mainly characterised these lesions in addition to subpleural pulmonary consolidation and poor blood circulation. Lung ultrasound seems to be useful for contributing towards the clinical diagnosis of COVID-19.
Subpleural consolidations. Can be associated with a discrete, localised pleural effusion. Relatively avascular with colour flow Doppler interrogation. Pneumonic consolidation is typically related to the preservation of flow or hyperaemia.	The lung ultrasound for pneumonia at the point of patient admission gave the following conclusions. In essence, 56% of children indicated a typical pattern of lung consolidation and showed hypervascularity at colour-Doppler imaging. 44% of patients showed an association of multiple B-lines. This was an indication of interstitial involvement and small subpleural consolidations, which are consistent with small mucus plugs. However, an air bronchogram was observed in 70% of patients, and a fluid bronchogram was found in only 2 cases. 86.6% of patients indicated some pleural line abnormalities. These included thickening, irregularity, and hypoechogenicity and gave a typical granular pattern. 30% of children showed pleural effusion, and 5 with debris, including one case positive at CXR was negative at lung ultrasound.
Nuclear Medicine: PET-CT imaging in adults with COVID-19.	Notes
FDG uptake due to the increase in ground-glass opacities in those with possible COVID-19 disease. Patients with higher SUVs in lung lesions may take longer to heal.	All patients had peripheral GGOs and lung consolidations in more than two pulmonary lobes. The lung lesions were characterised by a high 18F-FDG uptake, and there was evidence of lymph node involvement. >However, the disseminated disease was absent, and this suggested that COVID-19 has pulmonary tropism. Although ^{18}F-FDG PET-CT cannot be routinely used in an emergency setting and is not recommended for infectious diseases, this study demonstrated the potential clinical use of this imaging modality in the differential diagnosis of complex cases. FDG PET-CT imaging results after COVID-19 infection found lung lesions characterised by increased FDG uptake. There was also evidence of lymph node involvement. Also, FDG PET-CT can play a vital role in the evaluation of inflammatory and infectious pulmonary diseases.

As COVID-19 spreads, efforts are being made to reduce transmission via social distancing, isolation of cases and tracing of contacts. Therefore, the current COVID-19 situation requires the development of a vaccine or antiviral drugs. Clinical trials of hydroxychloroquine already used in treating malaria, lupus erythematosus and rheumatoid arthritis are under investigation for COVID-19 pneumonia in China (NCT04261517 and NCT04307693). The first study (NCT04261517) has shown positive preliminary outcomes in terms of clinical management.

Scientists continue to investigate how the COVID-19 virus passed to humans in the first place. Even though bats are thought to be the virus's origin, bat coronaviruses differ from COVID-19. For example, the spike proteins, which bind to receptors on the surface of cells to gain access, are different in the two viruses. It was found that coronavirus RNA – isolated from pangolins encoded – spike proteins that were similar to COVID-19. However, that does not prove that the new coronavirus passed through pangolins.

28.8 Unveiling the Secrets: Exploring the Mechanism of SARS-CoV-2 Infection

The betacoronavirus genome can encode the glycosylated spike (S) protein which initiates a host immune response. Both coronavirus SARS-CoV and SARS-CoV-2, the latter casing COVID-19 disease: invade the host cell from the binding between the S protein spike at the receptor protein angiotensin-converting enzyme 2 (ACE2), which is found on the surface membrane of host cells. This binding interaction results from an invasion process and requires S protein priming facilitated by the transmembrane serine proteinase 2 (TMPRSS2, known as epitheliasin) is present in the host cell.

This proteinase was first identified in 1997 on human chromosome 21 by systematic exon-trapping experiments. It was found to be a multidomain type II transmembrane serine protease that cleaves the surface glycoprotein HA (haemagglutinin) of influenza viruses. This monobasic cleavage site is a condition for virus fusion and propagation. Also, it activates the fusion protein F of the human metapneumovirus and the spike protein S of the SARS-CoV. Therefore, TMPRSS2 is a potential target for drug design. Also, the SARS-CoV-2 viral genome encodes several non-structural proteins, such as 3-chymotrypsin-like cysteine protease (3CLpro). Therefore, this enzyme plays a role in coronavirus replication and is a proven drug discovery target for SARS-CoV and MERS-CoV.

Another important non-structural protein is RNA-dependent RNA polymerase (RdRp, also named nsp12) is an essential protein encoded in the genomes of all RNA-containing viruses with no DNA stage. This protein is central to coronaviral particles' replication/transcription machinery and, therefore, a potential primary target for the antiviral drug remdesivir an adenosine analogue, which inserts into viral RNA chains, causing their premature termination). The RdRp catalyses the synthesis of the RNA strand, which complements a given RNA template, and the molecular mechanism for this process remains unclear. However, the RNA replication process involves a two-step mechanism:

- The initiation step of RNA synthesis commences at or near the 3' end of the RNA template, facilitated by a primer-independent mechanism.
- This mechanism starts with adding nucleotide triphosphate (NTP) to the 3'-OH of the first initiating NTP. During the elongation phase, the nucleotidyl transfer reaction is repeated with subsequent NTPs to generate the complementary RNA product.

Combining zinc ions (Zn2+) and the zinc-ionophore pyrithione has been shown to inhibit nidovirus replication in cell culture. Further investigations are required for the use of zinc-ionophores as antiviral compounds. However, in vitro studies on the reversible inhibition of the RdRp by Zn2+ have provided a suitable research tool to gain more insight into the molecular details of (nido)viral RNA synthesis. It is important to reveal novel mechanistic differences between the RdRps of SARS-CoV and equine arteritis virus (EAV) in cell cultures.

The final non-structural protein papain-like protease (PLPro) from the human SARS-CoV consists of a cysteine protease located within the non-structural protein 3 (NS3) section of the viral polypeptide. The PLPro activity is required to process the viral polyprotein into functional, mature subunits. Also, PLPro cleaves a site at the amino terminus of the viral replicase part during viral protein maturation. In addition, PLPro possesses a deubiquitinating and deISGylating activity.

The SARS-CoV-2 enters the host cells; the viral genome is released as a single-stranded positive RNA (note positive-sense viral RNA genome and serves as a messenger RNA which can be translated into protein in the host cell). Consequently, the single-stranded positive RNA is translated into viral polyproteins using host cell protein translation machinery and is then cleaved into effector proteins by viral proteinases 3CLpro and PLpro. The PLpro also behaves as a deubiquitinase (a large group of proteases that cleave ubiquitin from proteins and other molecules) on specific host cell proteins. These include interferon factor 3 and NF-κB resulting in immune suppression. At this point, RNA-dependent RNA polymerase (RdRp) helps to make more viral genomic RNA containing negative-strand RNA to be used by RdRp.

The infection process initiated by coronavirus results from the interaction of viral S protein and ACE2 receptors on the host cell surface. The coronavirus binds to host cells through its trimeric spike glycoprotein, and therefore, this protein is a key target for potential therapies and diagnostic treatments. By cryo-electron microscopy, researchers have determined a 3.5-angstrom resolution structure of the SARS-CoV-2 trimeric spike protein. However, this S-protein can bind at least ten times more tightly than the corresponding spike protein of SARS-CoV to the common host cell receptor (ACE2). This binding has been shown for the RBD-specific monoclonal antibodies S230, m396 and 80R in SARS-CoV.

Therefore, this may be a reason why SARS-CoV-2 is of higher transmissible and contagious than SARS-CoV. Therapeutic agents are required to target the conserved proteins associated with SARS-CoV and SARS-CoV-2. Consequently, both RdRp and 3CLpro protease of SARS-CoV-2 share over 95% of sequence similarity with those of

SARS-CoV. However, both these viruses demonstrate only 79% sequence similarity at the genomic level. On further investigation, it was found by applying sequence and homology modelling that both SARS-CoV and SARS-CoV-2 share a highly conserved receptor-binding domain (RBD) of the S protein with 76% in sequence similarity. Also, the PLpro sequences of SARS-CoV-2 and SARS-CoV are only 83% similar, and both viruses share a similar active site. To date, there are no SARS-CoV-2-specific antiviral agents.

28.9 Zoonotic Coronaviruses: Origins, Impacts, and the Race for Effective Vaccines

Coronaviruses belong to a large pool of viruses; some will cause illness in people, while others circulate among mammals and birds. However, it is unusual for animal coronaviruses to spread to humans and between humans. In the last decade, zoonotic coronaviruses have emerged in the human population, such as SARS-CoV-2 leading to COVID-19 disease, SARS and MERS. These betacoronaviruses lead to respiratory infection and, in some cases, gastrointestinal infections in humans. Moreover, the clinical range of these diseases varies from no symptoms or mild respiratory symptoms to severe. Further symptoms progress to pneumonia, acute respiratory distress syndrome, septic shock and multi-organ failure leading to death.

The acute respiratory infection SARS-CoV-2 was first identified in Wuhan City, Hubei Province, China, in December 2019. Since then, it has spread to over 180 countries around the World to become a pandemic which the WHO declared with a fatality rate of at least 2.3%. The respiratory tract infection caused by MERS-CoV was first identified in Saudi Arabia in 2012, and the case fatality rate was approximately 37%. These infectious diseases were compared to the acute viral respiratory tract infection caused by SARS-CoV, first known in the Guangdong province of Southern China in 2002. The SARS-COV epidemic affected 26 countries, resulting in more than 8000 cases and 774 deaths in 2003. However, there have been no reported cases since 2004, and the fatality rate was approximately 10%.

The World urgently needs a vaccine against SARS-CoV-2. Over the past decade, researchers have responded to other epidemics, including H1N1 influenza, Ebola virus disease (EVD, a viral haemorrhagic fever of humans and other primates caused by ebolaviruses), Zika (a member of the Flaviviridae family and originates from the Ziika Forest of Uganda, Aedes mosquitoes spread the virus) and SARS-CoV. These epidemics have produced a wealth of knowledge ranging from the discovery of pharmaceutical drugs to vaccine programmes. For example, a vaccine for H1N1 influenza was quickly developed because influenza-vaccine technology is well established. This monovalent H1N1 vaccine was available after the pandemic peaked and became a stand-alone vaccine incorporated into the seasonal influenza vaccines. However, vaccines for SARS, EVD and Zika followed a different path to H1N1 vaccine development. In this case, the SARS and Zika epidemics ended before vaccine development was completed.

Accelerating the development of vaccines to address epidemics led to the formation of the organisation known as the Coalition for Epidemic Preparedness Innovation (CEPI). This international non-governmental coalition comprises the Bill and Melinda Gates Foundation, Wellcome Trust, the European Commission and eight other countries Australia, Belgium, Canada, Ethiopia, Germany, Japan, Norway and the UK). CEPI aims to support the development of vaccines against five epidemic pathogens on the WHO list. CEPI will also support the development of a vaccine against the COVID-19 disease. Success in producing a vaccine would require support for development from viral sequencing to clinical trials and must be capable of large-scale manufacturing. In COVID-19, it is vital to manufacture vaccines based on the DNA and RNA platforms, including recombinant-subunit vaccines.

The major advantage of vaccines made from RNA and DNA is that the processes do not require culture or fermentation and only use chemical synthetic processes such as those used for oncology vaccines. However, there are no approved RNA vaccines to date, but RNA vaccines have entered clinical trials. Developing a SARS-CoV-2 vaccine will impose different challenges; for example, could the virus S spike protein be a promising immunogen for protection? or would optimising the antigen design warrant an optimal immune response? Also, is it best to target the full-length protein or only the receptor-binding domain (RBD)?

However, past research on the SARS and MERS vaccines has raised concerns about worsening lung disease or facilitating antibody-dependent enhancement. These effects could be associated with type 2 helper T-cell (TH2) response, and therefore, it is best to carry out tests in suitable animal models. Furthermore, at present, the duration of immunity is unknown, and what would be the effect of single-dose vaccines on immunity?

In April 2020, a clinical trial involving about 510 volunteers will test a new vaccine called ChAdOx1 nCoV-19 for SARS-CoV-2 (COVID-19). This vaccine is an adenovirus vector (ChAdOx1) developed by researchers at the Oxford Jenner Institute. The vaccine contains the genetic sequence of this surface spike protein inside the ChAdOx1 construct. After vaccination, the surface spike protein of the coronavirus is produced, which primes the immune system to attack the coronavirus if it later infects the body.

Zoonotic diseases contribute to about 60-75% of emerging infectious diseases throughout the World, and more than 70% have supposedly originated in wildlife species. Bats are known to be a natural pool of viruses. These highly pathogenic viruses seriously threaten human health, especially coronaviruses responsible for SARS and MERS, the paramyxoviruses such as Nipah virus, haemorrhagic Ebola and Marburg filoviruses. The most recent pandemic linked to the coronavirus known as SARS-CoV-2, which originated in Wuhan, China, in December 2019, shared 96% identity with a bat-borne coronavirus at the whole-genome level. The emergence of MERS in 2012 and the ongoing COVID-19 pandemic have accelerated the interest in detecting coronaviruses of bat origin due to public health concerns. In addition to human-

associated coronavirus, bats have also been implicated in the emergence and origin of swine acute diarrhoea syndrome (SADS), transmissible gastroenteritis virus (TGEV) in pigs and porcine epidemic diarrhoea (PED). Therefore, it is possible that bat-borne coronavirus could pose a considerable threat to human health and food production. Researchers have discovered seven new coronaviruses detected in bats in Myanmar. However, none of the viruses was closely related to SARS-CoV, MERS-CoV, or SARS-CoV-2.

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29 WannaCry Ransomware: The Vulnerability of Medical Imaging Systems

WannaCry infects computers and encrypts window files on the hard drive, making them impossible for users to access.

29.1 Introduction

Cyber security is paramount in the protection of medical imaging systems. In May 2017, a global cyber attack hit large organisations such as the UK's National Health Service (NHS). During these attacks, patient operations were cancelled, X-rays, test results and patient records became unavailable, and communication channels did not function. The WannaCry attack cost the NHS more than £92 million. These cyber hackers infected computers in 150 countries using WannaCry ransomware.

The WannaCry infects computers and encrypts window files on the hard drive, making them impossible for users to access. To access these blocked files, the hacker demands payment in bitcoin (digital gold) in order to decrypt them. The WannaCry ransomware consists of several components. The virus enters the windows system in the form of a dropper and starts to encrypt and decrypt data. The United States National Security Agency (NSA) first uncovered this windows system weakness. The ransomware attack was linked to the cyber crime organisation Lazarus Group (known as Hidden Cobra, Zinc) – a group of unknown individuals possibly linked to North Korea.

Interestingly, cyber security experts found that the programme code used to implement the WannaCry was not complicated. The mode of operation was for WannaCry to access the coded URL known as the kill switch. The ransomware hackers embedded this kill switch to check if a nonsense URL gave a live webpage response.

However, it was found that the domain name:

www[.] ifferfsodp9ifjaposdfjhgosurijfaewrwergwea[.]com was not registered and was inactive. The domain status did not affect the spreading of ransomware. When the URL was registered, it became active and killed the WannaCry virus.

The two strategies that slowed the spread of WannaCry was that Microsoft released a patch to help shield Windows XP devices; this was a rare event because Microsoft had not supported XP since 2014. This approach assisted the older computer system with unstable security, and they could download the patch before WannaCry struck.

If the patch were unsuccessful, the ransomware virus would search for the files and produce, for example, encrypted Microsoft Office files to MP3s (MPEG-1 Audio Layer-3) and MKV file extension (Matroska Video file). The result was that the user would be unable to access files, and a ransom notice would appear to demand $300 in Bitcoin to decrypt the files. The WannaCry works by abusing the Windows implementation of the Server Message Block (SMB) protocol. The function of SMB protocol is to share access to files, printers, serial ports and other resources on a network.

The NSA discovered the vulnerability in Microsoft's Windows operating system and developed a code called EternalBlue MS17-010 to exploit it. They issued a security patch before the WannaCry ransomware spread worldwide, and the updated computer systems had early protection from WannaCry.

Subsequently, the hacking tools used by NSA were stolen and published by the Shadow Brokers hacker group and appeared in the summer of 2016.

WannaCry used EternalBlue to infect computers and began spreading rapidly on May 12. Microsoft conflicted with the NSA because it did not disclose the operating system's vulnerability during this period.

In addition, a new strain of the Petya ransomware started spreading on June 27, 2017, infecting many organisations. This ransomware is similar to WannaCry but uses the EternalBlue exploit as one of the means to spread itself. Petya (known as GoldenEye; NotPetya) uses SMB (Server Message Block) networks and can spread within organisations seemingly resistant to the EternalBlue patch. The infection vector for the Petya cyber attack was MEDoc, a tax and accounting software package used by corporate networks.

Interestingly, when the computer system becomes infected with WannaCry, it will not initiate the encryption of files straightaway because the virus first tries to access the nonsense URL before going to work. Consequently, if the virus can access the domain, this would result in WannaCry shutting itself down. The possible idea behind this mechanism could be that hackers could stop the attack at any time. WannaCry attempted to contact the URL and make an analysis of the code more complicated.

Cyber researchers will run malware in a sandbox environment to enable any URL or IP address details to be reachable. Necessarily, these automated malware analysis systems, known as sandboxes, are one of the latest weapons in the arsenal for cyber security. These sandbox systems will execute an unknown malware program in an instrumented environment and monitor their execution.

29.2 From Bytes to Bites: The Story of the WannaCry Ransomware Assault

Since the destruction of WannaCry, healthcare facilities have remained concerned about protecting their digital medical systems for imaging by employing medical cyber security and information technology professionals.

Just imaging a patient undergoing a CT scan, a hacker changes the scan and diagnosis!

The majority of medical imaging systems are part of internal and external networks and are at risk of cyber-attacks which threaten the confidentiality, safety, and well-being of the patient.

The WannaCry outbreak emphasised the importance of robust cyber security practices in increasingly connected US and European healthcare sectors. In these unfortunate situations, the data was held hostage to ransomware and medical devices were compromised. These attacks highlighted the possible consequences for radiology in healthcare. The problem with IT in healthcare is that it intends to focus on patching known vulnerabilities (zero-day attacks) from the not sophisticated attacks because the regulatory requirements guide it. A zero-day vulnerability results from a software security flaw known by the software vendor. At the time, there was no patch to fix the flaw so that cyber criminals could exploit it.

The problem with some software vendors is that they do not have the expertise to address these issues. In these cases, the product remains a risk to security. For example, the FDA criticised St. Jude Medical for failing to address known security issues with some of its implantable electrophysiology devices. Nevertheless, medical device approval processes are still adjusting to changes in cyber security requirements.

29.3 Navigating the Cyber Threat Landscape: Developing Adaptive Strategies

To reduce these malware attacks on computer systems, a cyber security strategy must be in place to counteract these threats. These potential cyber-attacks can be categorised by relating the type of information the hacker wants to access or what they want to achieve. For example, untargeted information could include large quantities of personal health data compared to more targeted attacks where the hacker can control an infusion pump resulting in patient harm.

Also, healthcare providers must consider the sources of potential attacks within their organisation or external parties: if from employees or agency workers, there is already trusted access to the systems, which is a significant security threat. The drive behind external attacks is usually for financial gain and, in some cases, may result from malice towards the organisation.

The issues to consider regarding internal cyber security threats within organisations include limited encryption, system set-up configuration, applications, operational security gaps, which may contain loopholes in processes and unpatched software and lack of authentication of user login credentials. All these vulnerabilities can occur on any medical device, especially when connected to the internet, posing a real danger to the technology used in various hospital departments.

To put this into perspective, the number of devices per patient bed between 1995 and 2010 increased by 62%. Today, a patient in a hospital bed will be monitored on average using at least 13 devices.

29.4 Connected Care: Cyber Medical Devices in Modern Medicine

It is important to protect medical devices by applying imaging system acceptance testing. This approach is usually in conjunction with the medical device supplier and the cyber security department of the hospital to assess all potential vulnerabilities, which may include securing all USB ports and CD/DVD drives using validated devices: can suppliers gain remote access, are the medical devices protected using strong usernames and passwords and finally are the computer systems well maintained using the most up to date antivirus and antimalware software.

When purchasing medical equipment for patient use, all the above considerations must be evaluated on a regular basis. To help to facilitate the relationship between suppliers and providers of patient healthcare, the National Electrical Manufacturers Association (NEMA) has produced guidance documents such as PS3.15 of the DICOM standard relating to Security and System Management Profiles. Another guidance relates to the Manufacturer Disclosure Statement for Medical Device Security (MDS2), which helps the healthcare provider to perform risk assessments.

According to Dr Suzanne Schwartz, Center for Devices and Radiological Health:

Any medical device connected to a communications network, like Wi-Fi, or public or home Internet, may have cyber security vulnerabilities that could be exploited by unauthorised users.

In 2015, a phishing attack – a social engineering attack to steal user data, such as login and credit card details – was unleashed on the computer systems at UC Davis Health. The hacker(s) may have compromised the personal health information of 15,000 patients. In this case, the attack was most likely initiated when an employee responded to a phishing email with their account login details. The hacker was then able to send emails to other employees requesting bank transfers. Fortunately, the attack was stopped, and further investigation found no violation of sensitive information.

Several steps can be considered to prevent the loss of sensitive information from healthcare computer systems. They can include up-to-date cyber security training for all employees, picture archiving and communication system (PACS) on a separate system with its non-routable IP network to minimise exposure, data encryption at all points and updating Windows XP-based image acquisition devices.

The categorisation of security defences includes:

- Technical – include firewalls, encryption and secure data transmission
- Physical – the isolation of devices from each other, including backing up and restoring data in addition to proper device disposal methods
- Administrative – documenting security policies, maintaining audit trails, training staff, and incident reporting logs

Most cyber attacks' technical and physical categories result in hackers entering the device. However, computer failure is usually due to administrative safeguards and

results in a catastrophe. Healthcare providers must introduce and set minimum standards for upholding secure data policy and focus on the high-risk elements of their computer systems. Therefore, consideration to maintain healthcare systems must consider the capability to use whitelisting, which is a cyber security list only giving administrator-approved programs and IP and email addresses, system access. It is vital to ensure device functions towards best practices such as not using expired passwords and no elevated administrator privileges, including a supported operating system that third-party applications can upgrade. In addition, to no hard-coded or default passwords on the devices.

Cyber breaches in healthcare information regarding patients are on the increase. In the first six months of 2019, there was a 53% increase in breaches of health records compared to the whole of 2018. The increase in cyber breaches in healthcare is likely to continue due to the array of highly sensitive patient health information such as date of birth, social security number, credit card data, insurance information and medical records. All this information is a treasure trove for criminality, especially on the dark web.

Medical imaging is central to patient care, and all these records are increasingly becoming digitised and stored on picture archiving communication systems (PACS). The PACS system facilitates the sharing of medical images across healthcare organisations, so it is essential to implement robust cyber security. However, ProPublica – an independent, non-profit newsroom that produces investigative journalism in the public interest – showed that 5 million patients in the US had their medical imaging data exposed on the internet.

This identifiable patient information can be used for blackmail purposes. It should be protected as it was discovered that over 13.7 million medical tests, including 400,000 images (e.g. MRI scans, X-rays), were available on the internet. Consequently, these imaging records were stored on servers, including archiving systems, potentially without monitoring for unauthorised changes. All these systems should be securely configured and in compliance with regulatory standards.

To demonstrate how these vulnerabilities could be detrimental to medical imaging equipment and the networks, Israeli cyber security experts used malware that could change the information on CT scans. This was done to reflect a different diagnosis; for example, the CT scan of a healthy patient showing cancer and a sick patient indicated no disease present.

In the future, healthcare organisations must protect their PACS networks, including the digital signature of all images, to prevent malware from altering CT and MRI scans by installing end-to-end encryption. All investigations have demonstrated that future malware attacks on CT scans are a real threat, and both manufacturers and providers of medical imaging systems should not become complacent. To further emphasise this potential problem, an investigation was carried out by altering real CT lung scans using advanced malware. A group of radiologists reviewed 70 CT-altered scans and were misled into misdiagnoses. Furthermore, the radiologists reviewed another batch

of CT scans, and even though they knew this time about the malware, they were still misled by 60%. Also, on removing cancerous nodules from the CT scans, the radiologists were unsuccessful in diagnosing sick patients 87% of the time. These studies focus on the malware attack on the patient's lung cancer CT scans. However, malware can attack CT scans concerning brain tumours, bone fractures, spinal injuries and heart disease.

In the previous years, NHS Digital, which is the national provider of information, data and IT systems, has embarked on aggressive cyber security programmes in the following areas:

- Cyber monitoring, threat intelligence and incident responses
- Enhanced support and guidance for local organisations
- Improved cyber training with greater awareness and engagement to create cyber security best practices among NHS staff and organisations

29.5 The Increasing Threat of Cyber Attacks on Medical and Personal Devices: The Need for Future Cyber Security Measures

Suppose you have ever watched the cyber attack dramatisation in Chicago Med and Grey's Anatomy, where hospitals came under attack resulting in the shutdown of vital equipment. It is essential to realise these situations reflect the increasing fact that hackers are carrying out cyber attacks on medical and personal devices. For example, in 2019, the U.S. Food and Drug Administration informed patients and doctors that a specific insulin pump was at risk of cyber attacks. Also, in 2017, certain implanted heart devices were susceptible to hacking via home monitoring systems. The accumulation of cyber attacks on medical devices has forced the FDA to publish new guidelines in 2018 regarding these situations.

The future platforms in cyber security are to understand what hackers want to achieve. In most attacks, hackers obtain healthcare patient data and payment information (e.g. credit card data) for fraud. To reduce these cyber threats, Government agencies require more trained cyber professionals to intercept these hackers and limit any damage caused. On 25 May 2018, the EU's General Data Protection Regulation (GDPR) came into force and will help protect personal data and aid cyber security. Another vulnerability is the company supply chains, where hackers can infiltrate parts of systems during the construction to plant malware. Therefore, companies must think like hackers and reduce cyber attacks by creating innovative security across the supply chains.

The future of cyber security will use artificial intelligence (AI) to secure devices and systems within the internet of things (IoT). These connected devices are increasing rapidly, and the consequences lead to exposure to potential cyber-attacks. It is claimed that by 2025, there will be an estimated 75 billion internet-connected devices worldwide. Also, it is projected that ownership of smart devices could rise from 10 to 15 devices per UK household this year.

The old computer operating systems no longer have the capability to keep up with evolving security threats and depend on human surveillance to keep them in order, but this remains an ineffective approach. Further investment into intelligent automated systems will monitor, detect, manage and prevent cyber attacks in real-time situations.

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30 Artificial intelligence applications in machine medicine

Artificial intelligence (AI) and the study of algorithms, known as machine learning, will analyse complex medical imaging data from patients.

30.1 Introduction

Alan Turing features on the back of a new £50 banknote; he not only cracked the Enigma code during World War II but was a pioneer of machine learning. In 1950, he came up with the Turing test, published in a paper called 'Computing Machinery and Intelligence.' Turing proposed that a method of inquiry in the application of Artificial Intelligence (AI) must be able to determine if a computer system is capable of thinking like a human being. Moreover, Artificial Intelligence (AI), a phrase first coined by the computer scientist John McCarthy in 1955: also predicted that creating an AI machine would require '1.8 Einstein's and one-tenth the resources of the Manhattan Project.'

However, according to IBM, the four fundamental pillars of a trusted AI system are:

Fairness: The input training data and models used in AI systems should not be biased towards certain groups.

Robustness: The data and models in the AI system must be secured and not compromised.

Explainability: The output data from the AI system should be in a logical format so that the end-user can understand.

Lineage: AI systems should be audited, and all details recorded.

For several decades, researchers have been working to develop methods that capture the reasoning used by physicians to arrive at diagnoses. The application of Artificial Intelligence (AI) in the clinical setting started to expand in the 1980s and 1990s through Bayesian networks, which are artificial neural networks and hybrid intelligent systems. For example, in 1986, Dxplain was developed by the Massachusetts General Hospital in conjunction with Harvard Medical School Laboratory of Computer Science in order to create a diagnostic decision-support system. The DXplain database included 5,000 clinical indexes associated with more than 2,000 diseases. Each disease description has at least ten current references. DXplain was an early electronic textbook and medical reference system.

Since 1993, the Barnes Jewish Hospital in St. Louis has been using the GermWatcher electronic microbiology surveillance application to detect and investigate hospital-

acquired infections. In 2013, UK Babylon NHS services encompassed more than 40,000 registered user-patients who provided remote consultations with physicians via text and video messaging through its mobile application.

The Da Vinci robotic surgical system developed by the company Intuitive Surgical Inc. was given FDA approval in 2000. The robot aims to facilitate surgery using a minimally invasive approach and is controlled by a surgeon from a console. It is used in the field of surgery, especially in urological and gynaecological surgeries. Since 2018, Boston children's hospital has been working on a web interface-based AI system. These chatbots provide advice to parents regarding the symptoms of ill children and whether they require a doctor's visit.

The National Institute of Health (NIH) created an AiCure App, which monitors the use of medications by the patient via smartphone webcam access and hence reduces the rate of non-adherence.

In 2016, the Digital Mammography DREAM Challenge was carried out on several networks of computers. The aim was to establish an AI-based algorithm by reviewing 640,000 digital mammograms. In conclusion, this study demonstrated that AI has potential, but it is unlikely that AI will replace doctors outright.

In 2018, the Food and Drug Administration approved the first algorithm to make a medical decision without the need for a physician to review an image. The algorithm was developed by IDx Technology and analysed retinal images to detect diabetic retinopathy with 87% accuracy.

Using these systems won't make a bad doctor a good doctor, but it might make a good doctor a better doctor.

The healthcare revolution has begun in the area of diagnostic medical imaging through the application of Artificial Intelligence (AI). This revolution will include new technologies for image acquisition and processing. Ultimately, AI will lead to improvements in treatment plans, data storage and data mining (turning raw data into useful information), especially in the future role of the radiologist. Medical AI applies computer technology by detecting a possible association in a dataset of clinical situations to form a diagnosis and provide a suitable treatment plan for the patient and therefore create a more favourable prognosis.

Artificial intelligence (AI) and the study of algorithms, known as machine learning, will analyse complex medical imaging data from patients. These high-resolution images are mostly obtained from X-rays, computed tomography (CT) scans and magnetic resonance imaging (MRI). However, these images require time to evaluate. Consequently, AI can be a valuable asset for radiologists to increase output and improve accuracy.

30.2 Clinical application of artificial intelligence in radiology

Thoracic computed tomography (CT) is considered the gold standard for nodule detection in lung pathology. Artificial Intelligence (AI) can be applied to the screening

process to automatically identify these nodules and categorise them as benign or malignant. However, in comparison to standard chest radiography, CT is significantly more costly, and even a low-dose CT requires higher radiation dosages.

Multiphase contrast-enhanced magnetic resonance imaging (MRI) is the current modality of choice for the characterisation of liver masses incidentally detected on imaging. Contrast-enhanced computed tomography (CT) is the basis for the screening of liver metastases. The description of a liver mass by CT and MRI primarily relies on the dynamic contrast-enhancement characteristics of the mass in multiple phases. MRI and CT imaging can feature both benign and malignant liver masses, and this, coupled with relevant clinical information, allows reliable characterisation of most liver lesions. Some cases have nonspecific or overlapping features that may present a diagnostic dilemma. Artificial Intelligence (AI) may aid in characterising these lesions as benign or malignant and therefore prioritise follow-up evaluation for patients with these lesions.

Screening mammography is technically challenging to interpret expertly. Artificial Intelligence (AI) can assist in the interpretation, in part by identifying and characterising micro-calcifications which are small deposits of calcium in the breast.

30.3 Artificial intelligence and brain imaging

A brain tumour is an abnormal mass of tissue resulting from an uncontrollable growth of cells. There are more than 150 known intracranial tumours that are broadly classified as benign (e.g. chordomas, gangliocytomas) or malignant (e.g. medulloblastomas, glioblastoma multiforme), primary (craniopharyngiomas, pituitary tumours) or metastatic. Metastatic tumours in the brain affect 25% of patients with cancer, and this correlates to about 150,000 people a year compared to 40% of people with lung cancer who will develop metastatic brain tumours.

Artificial Intelligence (AI) can assist neurosurgeons by evaluating the type of brain tumour during surgery. In a clinical trial, the researchers combined stimulated Raman histology (SRH) and deep convolutional neural networks (CNNs) – the way neural networks in the human brain process information – to predict the diagnosis of the patient in the clinical setting. These CNN systems are qualified by analysing over 2.5 million SRH images which are classified into malignant glioma, lymphoma, metastatic tumours and meningioma brain tumours. The CNN system was validated using half of the 278 brain tissue samples, and a pathologist analysed the other half. The type of tumour was concluded in a few minutes using CNN compared to the pathologist, who would take much longer to ascertain a diagnosis. It is worth noting that the CNN system gave 95% accurate results compared to 94% by the pathologist. During the analysis of the samples, CNN made a correct diagnosis in all 17 cases that a pathologist got wrong. However, the pathologist got the right answer in all 14 cases in which the machine made a wrong diagnosis, and consequently, there is a need for machine medicine to work in conjunction with pathology.

Stimulated Raman histology (SRH) is the cause of the Raman effect. The Raman effect is caused when the scanning laser emits photons onto a sample and generates

a scattering pattern which can be detected by a 2-D microarray. Therefore, the application of SRH to biological tissue produces a real-time histopathological image. The advantage of this technique over traditional pathology is that the biological sample does not have to undergo freezing to acquire the pathology results. SRH allows for the fast, high-resolution acquisition of structural information through the generation of spectral images.

Hence, SRH can differentiate between the vibration of lipids, proteins and nucleic acids when exposed to the laser. The generated clinical image is observed through the microscope to provide high-resolution without modification (e.g. freezing) during a traditional pathology examination.

The deep learning process in computers involves recognising complex relationships when analysing large data sets. This process results in a network consisting of layers of information to decide on the diagnosis of a brain tumour.

The studies have demonstrated the powerful combination of SRH and AI in the real-time predictions of a patient's brain tumour diagnosis. This approach allows rapid surgical decision-making, especially when expert neuropathologists are hard to find.

Artificial Intelligence (AI) facilitates diagnostic predictions; for example, BrainScan provides an automatic search for similarly computed tomography (CT) and magnetic resonance imaging (MRI) scans in large data sets. The approach works by searching medical cases and abstracting the correct information from the database consisting of CT and MRI scans to help with the diagnosis. The retrieved scans will be obtained in a matter of minutes so the physicians can make a more accurate diagnosis.

Radiation Oncology – Radiation treatment planning can be automated by segmenting tumours for radiation dose optimisation. Furthermore, assessing responses to treatment by monitoring over time is essential for evaluating the success of radiation therapy efforts. Artificial Intelligence (AI) can perform these assessments, thereby improving accuracy and speed.

30.4 Cardiovascular disease

A leading cause of mortality in the world is cardiovascular disease (CVD) which accounted for 17.6 million deaths in 2016. Therefore, it is crucial to measure the various structures of the heart to determine if a person will develop cardiovascular disease. Also, it would be useful to have a clearer understanding of the early symptoms of CVD in order to propose a proper treatment plan for the patient.

Research into automated chest X-ray analysis, reported in 1977, used a computer system to extract optical and digital measurements from the scans to classify the severity of lung disease. This set-up consists of a film transportation system, a digital image scanner and an RSI Fraunhofer diffraction pattern sampling unit. The system can be utilised in several disease areas, such as lung disease, heart disease and cancer. For example, results have indicated higher accuracy rates for pneumoconiosis (interstitial lung diseases) comparable to visual readings of the films by expert radiologists.

The advantage of using automated chest X-rays is in the detection of abnormalities. This approach would lead to faster decision-making and fewer diagnostic errors. Automated chest X-rays can also be used as a primary screening tool for cardiomegaly (enlarged heart), which is a marker for heart disease.

30.5 Atrial fibrillation

Atrial fibrillation is a heart condition that causes an irregular heart rate. It can be asymptomatic and is associated with stroke, heart failure and death. However, the existing screening methods for atrial fibrillation requires prolonged monitoring. In these cases, the application of machine learning is used to identify patients with atrial enlargement by analysing chest X-rays. This approach would rule out other cardiac or pulmonary problems and provide suitable treatment plans for individual patients. Also, AI could automate other measurements such as carina angle measurements, pulmonary artery diameter and aortic valve analysis. The application of AI tools for the analysis of imaging data could help in the evaluation of specific muscle structures, such as the thickening of the left ventricle wall. These AI tools could also extend to changes in blood flow through the heart and arteries.

30.6 Degenerative neurological diseases

The four types of motor neurone disease (MND) depend on the type and extent of motor neurone involvement and the location of symptoms within the body. These types include progressive muscular atrophy (PMA), amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS) and progressive bulbar palsy (PBP). However, there is no medical cure for MND, and this is a devastating diagnosis for patients. Medical imaging studies are used to diagnose ALS by reviewing if specific lesions are the underlying cause.

In some cases, there may be lesions that mimic the disease and give a false positive. The development of biomarkers aims to increase the accuracy of MND diagnoses. For example, blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI) can detect areas of neuronal and synaptic activation when responding to experimental stimuli.

Currently, the technique of manual segmentation and quantitative susceptibility mapping (QSM) assessments are used to investigate motor cortex function. For example, the whole-brain landscape of iron-related abnormalities in ALS can be assessed using the in vivo MRI technique of QSM. Whole-brain MRI-QSM analysis is sensitive to tissue alterations in ALS that may be relevant to pathological changes.

The QSM process is time-consuming, and automation of this procedure with machine learning will contribute to the development of imaging biomarkers. The more advanced algorithms will be able to evaluate images that indicate evidence of ALS or PLS. Computer-assisted therapeutic management is involved in selecting the correct medication and the optimisation of dosages. This approach is also essential to decide the course of therapy needed for the patient. This system aims to decrease the adverse effects of hypersensitivity reactions and reduce costs. Also, it can change the method of data interpretation for patients with neurodegenerative disorders.

The integration of AI into the clinical setting is assisting healthcare workers with the optimisation of the treatment plan towards solving complex disorders. These technology platforms help diagnose epilepsy, stroke, ALS and SCI diseases, Alzheimer's disease, and Parkinson's disease. For example, AI-based clinical and decision-making processes can monitor neurodegenerative functions resulting in an effective diagnosis on a continual basis. Dynamic knowledge repositories are linked to AI systems to train algorithms from the vast collection of electroencephalography and electromyography reports, especially in obtaining real-time clinical data from patients' specific problems.

The introduction of AI and machine learning into the clinical setting will change the interaction between the patient and healthcare professionals. The development of non-invasive and low-cost support tools involving computer-aided diagnosis will support clinicians in the management of patients with Parkinson's disease and Alzheimer's disease.

The early stages of these degenerative neurological diseases produce exceptionally few observational changes in the patient and therefore do not provide enough information for early diagnosis. Therefore, in these cases, predictive models based on fMRI and diffusion-weighted imaging can be used to detect tiny changes in any disease patterns that can be missed by the healthcare professional.

30.7 Convolutional neural networks and diabetic retinopathy

Approximately 420 million people worldwide are diagnosed with diabetes mellitus, and approximately 33% will be diagnosed with diabetic retinopathy (DR) – a chronic eye disease that can progress to irreversible vision loss. Therefore, the early detection of DR relies on skilled readers and is both labour and time intensive.

Machine medicine has been applied to the automated detection of diabetic retinopathy. In addition, the use of convolutional neural networks (CNNs) on colour fundus images for the recognition task of diabetic retinopathy staging. These network models achieved metric test performance comparable to baseline literature results, with a validation sensitivity of 95%. Automated detection and screening offer a unique opportunity to prevent a significant proportion of vision loss in the population.

Medical images are crammed with subtle features that can be crucial for diagnosis. These images have been optimised to recognise macroscopic features which are present in the ImageNet dataset. Overall, the aim is to improve the recognition of mild disease forms and to transition to more challenging cases with the overall benefit of multi-grade disease detection.

30.8 Skin cancers

Skin cancer is the most prevalent form of cancer, classified into the following group types: basal and squamous cells; melanoma; Merkel cells; lymphoma and Kaposi sarcoma. Therefore, it is essential to identify which form of skin cancer the patient has to receive the right treatment plan. In the US, more than 9,500 people are

diagnosed with skin cancer every day. At least two people die of skin cancer every hour.

However, the most common forms of skin cancer are visually diagnosed. This process consists of an initial clinical screening, followed by dermoscopic analysis and obtaining a biopsy for histopathological examination.

AI systems could play a role in the diagnosis of the type of skin cancer by the automated classification of skin lesions. The deep convolutional neural networks (CNNs) approach may be able to distinguish between the different groups of skin cancers. The CNN was uploaded with a dataset of 129,450 clinical images consisting of 2,032 different diseases. This system was validated against the expertise of 21 dermatologists by comparing the most common skin cancers, keratinocyte carcinomas and benign seborrheic keratosis.

The latter group was between the deadliest skin cancers, malignant melanomas and benign nevi. The CNN results were just as good as the expert opinion on the diagnosis of the type of skin cancer. This study confirmed that AI was able to classify the type of skin cancer with the same ability as a qualified dermatologist. AI systems are starting to be incorporated into mobile devices, and these deep neural networks will be able to reach patients who cannot see a dermatologist face-to-face.

30.9 CheXpert pneumonia

Researchers at Stanford University have developed an AI system called CheXpert that can detect pneumonia in chest X-rays within 10 seconds compared to a radiologist, that could take 20 minutes to make the same diagnosis. Therefore, a rapid diagnosis means that the patient can undergo treatment for pneumonia without delay. CheXpert is a fully integrated automation system that can interpret chest X-rays based on AI.

In the clinical setting, CheXpert was able to accurately analyse chest X-rays and give a rapid diagnosis of pneumonia to the patient, which was confirmed by the healthcare professional. To train the AI component of CheXpert, the team provided the system with 224,316 chest radiograph files of 65,240 patients. The model was further perfected by reading 6,973 more images from several hospitals.

30.10 Multiple sclerosis

Multiple sclerosis (MS) is the most common form of inflammatory demyelinating disease of the central nervous system and affects about 2.5 million worldwide. In 2020, Public Health England released new MS prevalence data based on GP records from 2018. This data indicated that the number of people with MS in the UK was 131,720 adults and 250 children.

Researchers at UCL and King's College London have applied MRI to assist in the diagnosis of MS. This dynamic imaging modality is capable of detecting multiple lesions and new lesions on follow-up scans.

Therefore, AI systems based on MRI can be used to help in the diagnosis of relapsing-remitting MS, and this was demonstrated by analysing the brain's response to

natalizumab (brand name is Tysabri) treatment. The patient MRI scan was compared to the AI system containing a dataset of MRI brain scans. The AI system generated a result by extracting the information from the patient's MRI scan and comparing it against the dataset.

The aim is to see what changes were taking place in the white and grey matter of the brain. This approach demonstrated higher sensitivity than conventional analysis of brain scans in the diagnosis of MS.

30.11 Conclusion

Artificial Intelligence (AI) is becoming established throughout medical imaging, especially in the diagnostic area of mammography, CT scanners and digital chest X-rays. Since the discovery of X-rays by Wilhelm Conrad Röntgen 125 years ago, this high-energy electromagnetic radiation has changed the way we look at the human body. In the UK, there is currently a shortage of radiologists. In 2018, hospitals reported 379 vacant consultant radiologist posts across the UK, with 61% being unoccupied for at least a year.

Radiologists need to be aware of the basic principles of machine learning and deep learning systems, especially datasets. However, radiologists do not have to be computer scientists, but they require knowledge of how to communicate with data scientists and understand the output from these AI systems. In the future, radiologists may be replaced by robot radiologists: however, that does not mean that the radiologist will become obsolete; it just means there may not be as many in requirement.

AI will enhance the future role of the radiologist due to the ability of algorithms to replicate the skills of radiologists. On the side of caution, if the radiologist embraces AI, they may eventually replace the 'traditional' radiologist. The essence of AI algorithms is to spot detail in medical images and to devise new ways of interpreting these medical images, which the radiologist does not yet fully understand. Also, AI systems could be used to examine medical records and determine if a patient does require a scan. However, some medical imaging modalities are overused; for example, at least 80 million CT scans are performed every year in the US.

The radiologist has to accept AI systems that are currently entering the clinical setting and have the ability to reduce patient waiting time to receive treatment. Also, AI will reduce the workload of the radiologist and might eventually lead to a reduction in human radiologists. However, in the 1990s, computers were used to read radiological scans using computer-assisted diagnosis (CAD) to detect breast cancer in mammograms. At the time, CAD technology in hospitals resulted in many errors due to the difficulties in using the system. The medical AI revolution has arrived, and several surveys amongst radiologists have found that 84% of radiology clinics in the US have accepted the use of robot radiologists in the clinical setting.

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31 Spotting breast cancer – mammography and digital imaging

Medical imaging plays a vital role in the early detection of breast cancer, including those with BRCA1 or BRCA2 mutations.

31.1 Introduction

In 2016-17, a breast cancer screening programme was carried out in England, and the following facts were reported: 2.2 million over the age of 45 were screened (a 34% increase from the previous decade); 71.1% of women took up the breast imaging invitation; 18,402 women aged over 45 had cancer and correlated to 8.4 cases per 1,000 women screened.

In about 5 to 10% of patients, the origin of their breast cancer was the result of gene mutations. In some cases, the mutant forms of breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2) have been shown to play a role in the initiation of about 10% of all breast cancers. Therefore, women who possess faulty BRCA1 or BRCA2 allele (a variant form of a gene) are at higher risk of developing breast cancer within their lifetime.

It is worth noting that several studies have implicated mutated BRCA1/2 genes in the role of prostate, pancreatic and stomach cancers.

Both BRCA1 and BRCA2 genes are present in all humans, and BRCA1 is involved in the repair of DNA breaks that could lead to the formation of a tumour. Also, the BRCA genes in themselves do not cause breast cancer as they have a role in its prevention. Consequently, these genes are known as tumour suppressor genes. The reason that these genes do not work correctly and are involved in breast cancer is because of mutations within them.

Incidentally, about 0.25% of the human population carries mutated BRCA1 or BRCA2 genes. One of the most common cancer-related mutations found in BRCA1 is the 5382insC. This mutation originated from a common European ancestor about 400-500 years ago and is associated with a higher incidence of ovarian cancer (9.4%).

These damaged BRCA genes can no longer be effective at repairing broken DNA and helping to prevent breast cancer. Therefore, people with a BRCA gene mutation are more likely to develop breast cancer and pass a gene mutation down to the next generation.

Women with a BRCA1 or BRCA2 mutation who have overcome breast cancer through a treatment plan may develop secondary cancer known as a recurrence. Cancers involving BRCA1 mutations are more probable, forming aggressive triple-negative breast cancer, which is challenging to treat. Triple-negative breast cancer tests negative for oestrogen receptors, progesterone receptors and excess HER2 protein. About 10-20% of breast cancers are triple-negative breast cancers.

Today, medical imaging plays a vital role in the early detection of breast cancer, including those with BRCA1 or BRCA2 mutations. The most commonly used breast imaging techniques are positron emission tomography/computed tomography (PET/CT) imaging, ultrasound, magnetic resonance imaging (MRI), thermography and electrical impedance tomography. The objective of these medical imaging modalities is to detect breast cancer at the earliest stage.

31.2 Medical imaging modalities

31.2.1 Mammography

This technique is used in the detection of breast cancer and utilises low-dose amplitude X-rays. Screen-film mammography has proved to be the gold standard in breast screening due to its cost-effectiveness and reduction in breast cancer mortality. During mammography screening, two standard views are used, and these include the mediolateral oblique (MLO) view and the craniocaudal (CC) view. The MLO view compresses the breast along a plane of approximately 45 degrees extending from the upper inner quadrant to the lower outer quadrant. In this configuration, the X-ray tube is rotated parallel to the pectoralis muscle fibres and allows for maximum breast tissue in the MLO view. The CC view positions the breast directly on top of the X-ray cassette holder, with the X-ray tube positioned for superior and inferior imaging.

The cancerous masses and calcium deposits appear bright in the mammogram, and this technique has the ability to detect ductal carcinoma in situ (DCIS). It is vital to detect breast cancer at the earliest stage to prevent the formation of lesions from becoming evident. The generation of a 3-D mammogram will have more significant screening potential in spotting breast lesions. A study of 7300 women from the ages of 48 to 71 received a standard mammogram including both a combination of standard and 3-D imaging. It was found that a total of 59 breast cancers were detected. However, 39 were found by both standard mammograms alone and the standard plus 3-D compared to combination mammography, which found an additional 20 cancers. In September 2017, the Tomosynthesis Mammographic Imaging Screening Trial (TMIST) was opened to healthy women in order to compare and contrast the tomosynthesis (3-D mammogram) and the conventional 2-D mammogram.

31.2.2 Digital mammography

This technology uses a single or multiple detector system. The electronic image of the X-rays transmitted through the breast can be displayed, stored and communicated. Digital mammography is now a standard tool for breast cancer imaging and is replacing screen-film mammography as the preferred tool for screening.

31.2.3 Digital breast tomosynthesis – DBT

Breast tomosynthesis is an advanced form of mammography. This breast imaging uses low-dose X-rays to detect cancer early when it is at its most treatable. The technique DBT continues to expand in the clinical setting and produces a more effective mammogram based on observed increases in specificity and breast cancer detection compared with digital mammography (DM) alone. DBT will help to address the limitation caused by overlapping structures by acquiring a series of low-dose projection images. Computer reconstruction allows the radiologist to examine 1 mm single-section images for a particular volumetric set. This technique has shown improved sensitivity and specificity compared with digital mammography, especially in cases of noncalcified breast cancer, with an overall improvement of cancer visibility.

31.2.4 Ultrasound imaging

This modality works by directing high-frequency sound waves via a transducer into the breast tissues. This results in the detection of the reflected sound waves and produces 2-D images in real-time. The ultrasound approach is used to detect the location of the breast lesions.

31.2.5 Automated breast ultrasonography – ABUS

The first line of examination in the detection of breast lesions is the application of breast ultrasonography. The use of handheld ultrasonography devices is very dependent on the healthcare professional and requires a significant amount of time for the radiologist to examine the whole breast. However, the ABUS device provides improvements in higher reproducibility and less operator dependence compared to handheld ultrasonography. The ABUS system provides both a coronal and a large field of view. Several studies have indicated that ABUS is a useful screening tool for breast cancer in women with dense breast tissue.

31.2.6 Elastography

This test can be carried out in conjunction with an ultrasound examination. Elastography works using the concept that breast cancers appear to be more solid compared to the surrounding breast tissues. During the elastography process, the breast is slightly compressed, and ultrasound is targeted to a particular area to see how firm it is. This test will help to decide if the solid is likely to be cancer or a benign tumour.

31.2.7 Breast thermography

The concept behind this imaging technique makes use of the fact that cancerous tissues have a higher metabolic rate which can lead to the formation of new blood vessels to supply vital nutrients in order to grow the cancerous mass. This results in an increase in the localised temperature of the cancerous breast tissue compared to

the temperature of the surrounding healthy tissues. Furthermore, breast thermograms can detect breast cancer accurately and can be used as a screening tool to diagnose breast cancer at least ten years in advance.

31.2.8 Magnetic resonance imaging – MRI

The Indomitable was the first MRI full-body scanner invented by Raymond Damadian for human body imaging in 1977. This non-invasive technique makes use of the physical properties of the hydrogen nucleus (a single proton) to produce images. The human body is abundant in water and fat and enables the magnetic 'spin' property of the hydrogen nucleus to generate internal images. This procedure involves placing the patient on a horizontal moveable bed followed by transportation into the magnetic field.

Once inside the tunnel, a radio frequency wave is applied to create high-contrast images of the breast. Several techniques stem from MRI and include the injection of a contrast agent into the patient to produce dynamic contrast enhanced-MRI (DCE-MRI) images. The advantage of this technique is that it is more sensitive than mammography and is used to investigate the vascular changes associated with neoangiogenesis.

Also, MRI is used to assess tumour response to treatment plans and in the early detection of breast cancer. In addition, advanced MRI scanners using 3 Tesla magnets have demonstrated that MRI can achieve a higher spatial and temporal resolution to produce an improved signal-to-noise ratio and consequently improve survival rates.

31.2.9 Magnetic resonance elastography – MRE

This non-invasive medical imaging technique is based on imaging the propagation of transmission of shear waves. During this process, measurements are taken regarding the stiffness of soft tissue. Consequently, the stiffness of diseased tissue is more than that of healthy tissue in the surrounding area. MRE works by applying acoustic waves with a frequency of 100 Hz to 1 kHz and adjusting motion-sensitive phase-contrast MRI sequences. Furthermore, this gives rise to the propagation of shear waves as a function of the shear modulus of the tissue. The images are the result of shear wave propagation with variable wavelengths and are being used in the detection of breast cancer. Several studies have found that breast cancer tissue is much harder than healthy fibroglandular tissue.

31.2.10 Magnetic resonance mammography – MRM

This technique is capable of distinguishing the physiologic changes of the scar from tumour tissue due to its high sensitivity, specificity and accuracy. For example, the clinical and X-ray mammographic assessment of response to neoadjuvant chemotherapy may be inaccurate because of the replacement of the tumour with scar tissue. Also, MRM is useful in patients with recurrent disease and for the assessment of breast implants because it is more accurate than X-ray mammography and ultrasound. MRM is becoming a valuable tool in the diagnostic uncertainty of breast cancer and will become more prevalent in the clinical setting.

31.2.11 Positron emission tomography – PET

Nuclear medicine procedures can measure the metabolic activity of cells within the human body to generate 3-D images. The patient receives a radioactive tracer via injection into the bloodstream: the emitted radiation produces a pair of gamma rays which are detected. Malignant tumours will rapidly uptake glucose and provide a contrast between cancerous and healthy cells in PET images. This technique can be used in the investigation of brain and heart function and also in planning cancer treatment.

31.2.12 Single-photon emission computed tomography – SPECT

This imaging technique utilises computed tomography (CT) in conjunction with an injected radioactive tracer into the bloodstream of a patient. When the radioactive tracer is taken up by the cells, the X-rays produced are then detected by gamma cameras and provide an image. SPECT can be used to investigate blood flow to tissues and metabolism in the body. Both SPECT and PET are used to study animal models of breast cancer with direct application to human imaging. Also, MRI and PET can be used to monitor the response of medical treatment – during breast cancer assessment and pre-surgery -known as neoadjuvant chemotherapy.

31.2.13 PET/MR imaging in breast cancer

This is a combination of positron emission tomography (PET) and magnetic resonance imaging. The hybrid scanner combines the metabolic information obtained from PET imaging with the high resolution of MRI to contrast the soft tissue in a single examination of the patient. Furthermore, dynamic contrast-enhanced MRI of the breast provides higher sensitivity in the evaluation of primary breast cancers. However, PET/CT has been shown to provide information regarding loco-regional staging in women: especially with locally advanced breast cancer and the response to neoadjuvant chemotherapy. Moreover, PET/MRI has been shown to perform just as well as PET/CT imaging in patients with breast cancer, especially during the assessment of metastatic cancer.

31.2.14 Scintimammography, SPECT and PET Imaging

These imaging tools are useful in the early detection and staging of breast cancer. A disadvantage of these imaging modalities is the insufficient sensitivity to detect small (less than 1 cm) tumours. Therefore, these imaging techniques cannot replace invasive procedures. However, SMM is a useful technique in the assessment of palpable breast masses in women and PET imaging for the detection and staging of recurrent breast cancer facilitated with the radiotracer [18F]fluorodeoxyglucose. Also, PET imaging can assess the patient's response to chemotherapy.

The scintimammography imaging technique can visualise lesions of the breast by utilising in vivo injections of radiotracers. The advantage of SMM over mammography is its ability to detect breast cancer in dense breast tissue. Also, mammography can result in a high number of false positives. The radiopharmaceutical technetium-99m tetrofosmin allows improved precision in the diagnosis of women with dense breasts through this scintimammography approach. This technique demonstrated that high-

resolution scintimammography of the breasts was able to detect small (<1 cm) nonpalpable lesions. Also, the application of mammography with the scintimammography imaging agent 99mTc-MIBI was able to decrease the number of biopsies by 34% in patients with potential breast cancer.

31.2.15 Positron emission mammography – PEM

Mammography using positron emitters was first proposed in 1994 and has been demonstrated to have a higher resolution than PET-CT. The PEM set-up uses a pair of gamma radiation detectors placed above and below the breast under slight compression. The radiotracer [18F]fluorodeoxyglucose is injected into the bloodstream of the patient, and the resultant coincident of two 511 keV gamma rays, which are emitted 180 degrees from opposite directions and detected by a gamma camera. This high-resolution tomographic technique is a complementary imaging-resource in patients with a history of breast cancer with apparent abnormalities in their mammogram.

31.2.16 Optical imaging

This technique makes use of the physical property of near-infrared (NIR) wavelength light which is capable of detecting lesions inside the breast. Diffuse optical imaging is the progression from near-infrared spectroscopy and uses image reconstruction techniques to generate pictures from multiple NIRS measurements. It is primarily used in functional brain imaging and imaging for breast cancer. Diffuse optical imaging uses NIR light to penetrate the breast at wavelengths of 700 to 1000 nm. However, optical mammography uses various wavelengths of light to detect breast lesions. The advantage of diffuse optical imaging is that it is non-invasive and can be used to characterise the properties of dense tissue.

31.2.17 Electrical impedance Tomography and electrical impedance scanning

These non-invasive mobile breast screening techniques do not use ionising radiation and work by the body tissues resisting the flow of electric current. Several studies have shown that breast cancer tissue has a lower impedance compared to healthy tissues. The 2-D or 3-D images are reconstructed from a range of impedance values obtained by placing electrodes around the breast surface.

31.2.18 Microwave imaging

Several research groups have studied microwave breast imaging systems that are non-invasive for the early detection of breast cancer. The advantage of this technique is that the breast does not have to be compressed during the imaging process. Also, a microwave breast imaging system will help patients who have dense breast tissue to receive regular breast cancer screening safely and comfortably. Laser infrared thermography assisted by microwaves provides a source of heating the biological tissues in the breast to provide active dynamic thermography (ADT) in mammography.

31.2.19 Radio waves

Imaging systems are being developed that use radio waves to detect breast cancer. The advantage of this technique is that it does not involve breast compression.

31.2.20 Computed tomography

This imaging technique was introduced in 1972 and made use of X-rays to generate 2-D images (slices) of the human body. A different algorithm is applied to produce more advanced 3D anatomical images, especially in the location of lesions. The disadvantage of CT is the low-contrast images, and consequently, iodinated agents can be injected into the bloodstream to produce more pronounced images of the tumours. Also, shown that CT perfusion in breast cancer patients can identify and locate enlarged axillary lymph nodes.

31.2.21 Hybrid imaging

This technique involves combining PET and CT imaging and is especially useful in the staging of metastatic cancers. The benefits of this hybrid scanner are that CT can better define the location of the tumour while PET can indicate the metabolic activity of the cancer cells' uptake of glucose. Also, automated ultrasound systems can be combined with CT or breast MRI and would be able to assist surgeons in obtaining more accurate biopsies. Furthermore, the combination of digital breast tomosynthesis (DBT) and scintimammography, including ^{18}FDG-PET-MRI, where anatomical and functional techniques together have the potential to provide a more accurate assessment of the breast cancer patient.

31.2.22 Photoacoustic computed tomography

The concept behind this new scanner developed by Caltech is to locate tumours within 15 seconds by shining pulses of light into the breast. This scanning technique is called photoacoustic computed tomography (PACT) and primarily works by shining a near-infrared laser pulse into the breast tissue. The mode of action of detection is as the laser light diffuses through the breast, and the haemoglobin molecules in the red blood cells cause ultrasonic vibrations. These vibrations pass through the tissue and are detected by an array of 512 tiny ultrasonic sensors around the skin of the breast. The data generated from these sensors can create an image of the breast's internal structures. The advantage of PACT is that it can view structures as tiny as 0.25 mm at a depth of 4 cm. Also, mammograms are unable to provide soft-tissue contrast compared to greater details from PACT images.

31.2.23 Molecular breast imaging -MBI

The two types of MBI include breast-specific gamma imaging (BSGI), which tracks the blood flow during the uptake of the radiotracer sestamibi. The process involves a single 1-D image captured per view and is similar to mammography as it uses a small field-of-view gamma camera. The second technique involves high-resolution positron emission mammography (PEM), which uses the PET tracer ^{18}F-FDG to track glucose activity. MBI is applied when the mammogram results are questionable. The primary objective of mammography is to obtain information regarding the anatomical nature of the breast, which is in contrast to MBI, which detects cancers via metabolic activity in the breast.

In some cases, BSGI is used to assist mammography by distinguishing between scar tissue and cancer recurrence. In addition, BSGI is used to complement MRI

investigations regarding the type of breast cancer involved. Moreover, PEM can be applied in pre-surgical staging and planning, including neoadjuvant chemotherapy response monitoring. The reported study of MBI in its effectiveness in detecting breast cancers is concluded in a group of 1,696 women. These patients had dense breasts and gave negative mammography results when screened using MBI. The study concluded that a total of 13 cancers were detected, and 11 were invasive. The cancers ranged in size from 0.6 to 2.4 cm.

31.2.24 Artificial intelligence (AI) systems

The patient's diagnosis is dependent on who interprets the imaging scans relating to breast cancer. These scans can be very complicated and time-consuming for radiologists. However, to speed up the diagnostic outcome of these scans, AI companies like Google Health and DeepMind have developed AI systems to analyse radiological scans which detect breast cancer. The AI system was able to decrease false positives by 5.7% in women by analysing mammograms for breast cancer. To teach the AI system about reading mammograms, the data was collected from 76,000 scans involving UK and USA women. The collective data was used to evaluate X-rays from 25,000 UK women and 3,000 US women. The scans, which indicated that the women had cancer, required verification by obtaining a biopsy. This AI system demonstrated that it was more superior to a single radiologist reading the mammograms and did not require any other medical data to base its outcome. Also, AI reduced the false negatives by 9.4%, and patients were able to undergo a suitable breast cancer treatment plan.

31.3 Conclusion

At present, there is a shortage of senior radiologists in the UK, and this is having an adverse effect on cancer patients. Furthermore, the radiologist's workload of reading and interpreting scans has increased by 30% between 2012 and 2017. Consequently, artificial intelligence (AI) systems in the future will be able to assist in the rapid diagnosis of breast cancer with patients able to receive the correct treatment plan.

Screening programmes involving mammography aim to identify breast cancer before symptoms appear. Hence, facilitating earlier therapy increases a more favourable treatment outcome. The problem with screening programmes is how to interpret the vast data generated from the images. Radiologists must be careful not to give false positives or false negatives regarding the conclusions drawn from the images.

The Google Health AI system was able to show it was better at reading scans than an individual radiologist to locate breast cancer. Clinical data derived from reading mammograms from the US and UK was used to analyse scans. It found that the AI system reduced false positives by 5.7% (US) and 1.2% (UK) compared to false positives being 9.4% (US) and 2.7% (UK).

To further demonstrate the power of the AI system, researchers showed that the AI system was able to outperform six radiologists. These early assessments of the AI system initiated future clinical trials to improve the accuracy and efficiency of breast cancer screening programmes.

However, in the UK, it is a requirement that two radiologists have to review X-rays, and it was concluded that the AI system did not perform better than the two radiologists combined. AI systems will revolutionise diagnostic medicine by reducing waiting times and increasing patient output leading to improved patient treatment plans.

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32 Radiometals for diagnostic imaging and theranostics

Imaging agents can evaluate organ function, detect cancer, measure blood flow, and follow metabolic processes.

32.1 Introduction

The first radiometal molybdenum-99/technetium-99m generator was developed at the Brookhaven National Laboratory in 1959. Then in 1964, technetium-99m radiotracers were established at the Argonne National Laboratory. Currently, 85% of radiopharmaceuticals use technetium-99m based imaging agents. These imaging agents can be used to evaluate organ function, detect cancer, measure blood flow, and follow metabolic processes.

The Imaging Periodic Table below gives an overview of the types of radiation emitted from various radionuclides.

H	The Imaging Periodic Table																He
Li	Be	Alpha emitters α; Beta (electron) emitters β-; Positron emitters β+; Gamma emitters γ; Auger electrons Ae									B	C β+	N β+	O	F β+	Ne
Na	Mg										Al	Si	P β-	S	Cl	Ar
K	Ca	Sc γ β-	Ti	V	Cr	Mn	Fe β+	Co β+	Ni	Cu β- β+ γ	Zn	Ga β- β+ γ	Ge	As β-	Se	Br Ae	Kr
Rb	Sr	Y β-	Zr β+	Nb	Mo	Tc γ	Ru γ β-	Rh γ β-	Pd β-	Ag γ β-	Cd	In γ	Sn	Sb	Te	I γ β- Ae	Xe
Cs	Ba	La	Hf	Ta	W	Re γ β-	Os	Ir	Pt	Au Ae	Hg	TI	Pb β- Ae	Bi α	Po	At α	Rn
Fr	Ra α	Ac α															

Ce	Pr	Nd	Pm	Sm γ β-	Eu	Gd	Tb	Dy β-	Ho β-	Er	Tm	Yb β-	Lu β-
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Imaging Periodic Table showing radiometals

32.2 How do radiopharmaceuticals work?

When a radiopharmaceutical enters the body, it concentrates in organs and tissues and is therefore dependent on the biological or physiological characteristics of the tissue. For example, it may be concentrated at the site of a tumour or infection, or in a particular organ. The patient can then be scanned to image the radioactivity, and this gives an overall picture of what is happening in the body.

An advantage of this method over other imaging techniques is that the dose of the radioactive compound can be given in nanomolar quantities or less. This contrasts with other technologies such as magnetic resonance imaging where gadolinium-containing agents are used to enhance the image by using millimolar amounts of the agent to administer to the patient.

32.3 SPECT imaging

There is a broad range of radiometals that are used for cancer theranostics: these process a different mode of radioactive decay; therefore making them suitable for particular applications. The majority of diagnostic tools use radiometals, which emit gamma rays and are detected using a gamma camera. This captures the rays with a sodium iodide crystal, amplifies the signal and uses it to create an image. The image can be in a single plane parallel to the gamma camera, or a three-dimensional projection which can be built up using a computer-assisted reconstruction technique known as single photon emission computed tomography (SPECT).

SPECT imaging uses radionuclides that emit a single photon of energy, and these include the following gamma-ray emitters.

Commonly used SPECT radiometals

ISOTOPE	DECAY MODE	HALF-LIFE	GAMMA ENERGY
^{99m}Tc	IT	6.01 h	140.5 (87.7)
^{67}Ga	EC	78.3 h	93.3 (37); 184.6 (20.4); 300.2 (16.6)
^{111}In	EC	67.4 h	245.4 (94); 171.3 (90.3)

32.3.1 Molecular Imaging Capabilities of SPECT

- uncovering, staging and monitoring various cancers.
- examining deep venous thrombosis.
- measuring multi-drug resistance to chemotherapy.
- imaging angiogenesis and apoptosis for early diagnoses and measures of therapeutic response.
- diagnosing and evaluating Parkinson's disease and other neurodegenerative conditions.

32.4 PET imaging

A second common imaging technique found in nuclear medicine departments is positron emission tomography (PET). PET imaging uses radionuclides which emit a positron (a positively charged particle with the same mass as an electron) from the nucleus. This positron collides with an electron and both particles are annihilated.

During this process, 511 KeV of energy is released in the form of two gamma rays which travel in opposite directions.

A series of gamma detectors are placed around the patient, allowing both the location and amount of radioactivity in the patient to be calculated: this eventually leads to a processed image. PET uses radionuclides known as positron emitters.

32.4.1 PET radiometals

RADIOMETAL	HALF-LIFE	$E_{\beta+max}$ [MeV]	Production
^{44}Sc	3.9 h	1.474	Cyclotron
^{52g}Mn	5.5 d	0.576	Cyclotron
^{64}Cu	12.7 h	0.653	Cyclotron
^{68}Ga	67.8 min	1.900	Generator
^{82}Rb	1.3 min	3.350	Generator
^{86}Y	14.7 h	1.248	Cyclotron
^{89}Zr	3.3 d	0.897	Cyclotron

32.5 Molecular imaging capabilities of PET

32.5.1 Oncology

- PET imaging can be used to differentiate between malignant and benign tumours.
- It can be used to locate the most appropriate location for a biopsy of the suspected tumour.
- PET can be used to evaluate the effects of therapy from radiation or chemotherapy.
- It can be used to detect the sites of recurrent disease and differentiate from radiation tissue necrosis.
- PET has the ability to detect cancers of the breast, colon, lung etc. compared to conventional imaging tools which are unable to detect cancer.

32.5.2 Cardiology

- PET can be used to assess the extent of cardiovascular disease, especially coronary artery disease (CAD), and is mainly centred on the detection of the myocardium.
- Also, PET helps to identify patients who are likely to benefit from heart bypass surgery.

32.5.3 Neurology

- PET is a useful diagnostic tool in planning treatment and in predicting the outcomes of certain neurological conditions.

32.6 Beta particles

This type of radioactive decay involves the emission of a beta particle (electron) and is generally used for therapy since the beta particle only travels short distances in biological tissues. The resulting biologically damaging collisions between the particle and cellular components close to the radiopharmaceutical limiting damage to healthy surrounding tissues.

Beta particles from different sources contain a variety of ranges as follows:

- Low-range beta sources (mean range <200 μm). Nuclides of this category may provide a superior uniformity of deposit local energy over alpha emitters.
- The medium-range beta sources (200 μm < mean range < 0.2-1.0 mm) include the follow radionuclides: ^{47}Sc, ^{67}Cu, ^{77}As, ^{105}Rh, ^{109}Pd, ^{111}Ag, ^{161}Tb and ^{186}Re.
- This is in comparison to long-range beta sources (mean range > 1 mm) such as ^{32}P, ^{90}Y and ^{188}Re.

32.7 Alpha particles

Alpha particles (helium nucleus) are used in therapy to destroy a variety of tumours and have the following associated properties: short-range in tissue (50-90 μm), irreparable DNA damage, potent single cell, cluster kill with high linear energy transfer (LET) of about 80 keV/μm. For example, an alpha particle transversing a diameter of a 10 μm cell nucleus will deposit energy of about 800 keV, which is equivalent to an absorbed dose of about 0.25 Gy.

However, 3-6 hits of alpha particles per cell nucleus are required to kill a fraction of 63% population. Potential alpha-emitters for radioimmunotherapy (RIT) are ^{211}At and ^{212}Bi: the latter being produced from ^{212}Pb. Bismuth-212 has too short a half-life (60.6 min) to be used alone. Nevertheless, if a lead MoAb conjugation can be formed, ^{212}Pb will continuously generate ^{212}Bi acting on the tumour cells.

32.8 Electron capture

The process of Electron Capture (EC) and Internal Conversion (IC) decaying sources produce gamma rays and flux of Auger electrons. The majority of the emitted Auger electrons have a very short range (<1 μm). In this case, the source is attached or localised very close to the target DNA.

However, during the internal conversion (IC), the released electron is in a high-energy state. EC or IC sources for radiolabelling of monoclonal antibodies with metal chelates – being the dominating bifunctional chelating agents – derivatives of DTPA, especially bicyclic anhydride of DTPA, have been widely used in labelling different proteins. These metal radionuclides include: ^{111}In and to a lesser extent, ^{99}mTc, ^{90}Y, ^{67}Ga, ^{68}Ga, ^{109}Pd, ^{46}Sc, ^{186}Re, ^{212}Bi, and ^{169}Yb.

32.9 Therapy radiometals

Radiometal	Type	Half-Life	E_{max}[MeV]	Mean Range (mm)	Imageable
^{90}Y	beta	2.7 d	2.3	2.76	No
^{177}Lu	beta, gamma	6.7 d	0.50	0.28	Yes
^{153}Sm	beta, gamma	2.0 d	0.80	0.53	Yes
^{186}Re	beta, gamma	3.8 d	1.1	0.92	Yes
^{188}Re	beta, gamma	17.0 h	2.1	2.43	Yes
^{67}Cu	beta, gamma	2.6 d	0.57	0.6	Yes
^{225}Ac	alpha, beta	10 d	5.83	0.04-0.1	Yes
^{213}Bi	alpha	45.7 min	5.87	0.04-0.1	Yes
^{212}Bi	alpha	1.0 h	6.09	0.04-0.1	Yes
^{211}At	alpha	7.2 h	5.87	0.04-0.1	Yes
^{212}Pb	beta	10.6 h	0.57	0.6	Yes
^{67}Ga	Auger, beta, gamma	3.3 d	0.18	0.001-0.02	Yes
^{195m}Pt	Auger	4.0 d	0.13	0.001-0.02	No

32.10 Criteria for the ideal radiometal

For a radiometal to be useful in medical applications, it must be in a stable coordination complex. This is usually achieved by binding the metal to a chelating ligand. To bind the metal effectively, the ligand needs specific properties. The most important are high thermodynamic stability and selectivity for the particular radionuclide. Other factors to be considered are the rate and method by which the complex is taken up and eliminated by the body, its ability to pass through membranes, and its toxicity. If the metal-ligand complex is not stable then the metal is released into the body.

For radiopharmaceutical use, the targeting agent has to be linked to the radiometal chelate complex. The chelate is described as bifunctional because of its ability to bind to the targeting moiety and also to complex the radiometal. The selection of the radiometal to tag onto an antibody via a macrocycle or BFC (bifunctional chelate) can act in two ways:

A bifunctional chelating agent possesses the following functionalities:

- The chelator acts like a ‘crab’ to bind the radiometal.
- The other part contains a chemically reactive functional group and binds to the N-terminal and ε-amines of lysines on the antibody.
- The radiometal if possible, should be added last in the sequence before purification of the final product.

32.10.1 Radiometal chelate properties

- The physical half-life of the radiometal must be between 6-200 hours (^{99m}Tc to ^{111}In): It should be sufficiently long enough to allow for imaging at the time when the tumour to normal tissue ratio reaches a maximum. The time needed for the tumour to uptake the labelled monoclonal antibody is generally much longer 24-76 hours than that for normal organs to uptake common radiopharmaceuticals in nuclear medicine. If the half-life is too long, the radiometal creates an excess of unnecessary radiation dose to the patient.
- For imaging, the radiometal must have a gamma energy range of about 100-300 keV: The gamma-ray energy should match the scintigraph device (SPECT). In conventional nuclear medicine, a range of 100-300 keV is most appropriate for external scanning.
- High single energy gamma abundance per decay: A high photon density is desired for achieving high imaging resolution.
- No emission of particles, or low abundance of low-energy particle radiation. Any accompanying beta-particle will contribute to a considerable dose for the patient.
- The stable daughter product of the radiometal. The daughter nuclide will not only deliver an additional dose but also obscure the image.
- Production in carrier-free form (high specific activity). Since the number of binding sites of the protein or protein conjugating chelate molecule for the radionuclide is limited, only a carrier-free radionuclide can yield a labelled antibody of high specific activity, which is necessary to yield a clear image.
- Satisfactory in vivo chemical stability of the label or radiometal-protein complex. The in vivo chemical stability depends upon the following variables: bond energy of radiometal-protein or radiometal-chelate- protein, thermodynamic properties and pharmacokinetics

The metal is linked to the biomolecule via a bifunctional chelating agent (BFC). The BFC comprises two parts: it contains one or more functional groups that tightly complex the radiometal and an additional functional group that attaches to the biomolecule. Chelators most commonly used are the DTPA, DOTA & TETA derivatives.

- Radiometals require chelation chemistry or bifunctional chelators for linkage to antibodies
- Cyclic dianhydride derivatives
- 1B4M-DTPA (MX-DTPA, tiuxetan)
- CHX-A'DTPA: [effective chelator for ^{111}In(γ), ^{90}Y(β-), ^{177}Lu(β-), ^{99}mTc(γ)]
- DTPA derivatives can form a stable complex with bismuth radiometals conjugated to mAbs or peptides in vivo
- Resulting in radioimmunology conjugates (RIC's) that have been used effectively in clinical trials

DOTA (indium, yttrium, lanthanides, and actinides) and DTPA are suitable BFC for 3+ metals. DTPA is an effective chelating ligand for ^{90}Y, ^{153}Sm, ^{111}In and ^{212}Bi coordination

through 3 amino nitrogens and five carboxylic oxygens atoms; hence, having a spare carboxylic acid group to link to the antibody. The best BFC for ^{177}Lu is DOTA and its analogues.

A single carboxylic acid group is used to link to a biomolecule (peptide, antibody or drug): this includes the DOTA, DTPA and TETA derivatives. The remaining carboxylic acid groups in the DOTA, DTPA and TETA derivatives and the amine residues are used to bind the radiometal.

32.11 Antibodies

Radiolabelled antibodies have been used for detecting cancer since the early 1970s. This marked the beginning of the use of radiolabelled proteins and peptides for targeting receptors on tumours. Initially, antibodies were labelled with iodine radionuclides whereas today the use of radiometal-BFC-antibody conjugates are becoming more common, for example, Zevalin a radiolabelled monoclonal antibody ^{90}Y-ibritumomab tiuxetan.

The Zevalin antibody is first labelled with the radiometal ^{111}In – a gamma-emitter – and imaged using SPECT to verify that the antibody properly distributes within the body.

In about 1% of cases, the distribution of the drug is altered (e.g. from excessive uptake in the bone marrow or kidney).

If drug biodistribution is satisfactory, treatment is continued using a version of the Zevalin antibody labelled with the radiometal ^{90}Y, a beta-emitter.

The radioactive Yttrium can supply a lethal dose of radiation directly to the bound B-cells, and indirectly to neighbouring B-cells.

32.12 Peptides

Peptide precision involving the hormone somatostatin is a peptide containing 14 amino acids. In a large number of human tumours, somatostatin receptors (SSRs) are found in larger numbers than they are in normal tissue. These are known as SSR-positive tumours. Targeting the SSRs with a radionuclide-labelled somatostatin molecule could therefore help image and treat tumours. Unfortunately, somatostatin has a very short biological half-life, so longer-lasting analogues have been developed to rectify this.

Octreotide, which contains eight amino acids, is a cyclic analogue of somatostatin. When conjugated to DTPA and labelled with ^{111}In, it forms the drug pentetreotide, the first peptide-based tumour imaging agent approved for human use in the US and Europe.

Octreotide and other somatostatin analogues (such as RC-160 and several others developed by Diatide) have been labelled with various metal radionuclides via a number of different BFCs. The resulting complexes have been used both in imaging and therapy.

For example, octreotide has been labelled with ^{67}Ga and ^{68}Ga using the BFC desferrioxamine-B (DFO): this is a well-known chelate ligand with a high affinity for Fe(III).

32.13 Imaging and therapy radiometal table

Chelate Derivative	Radiometal	Imaging	Therapy	Notes
DTPA	Tc-99m (g)	SPECT	NO	
DMSA	Tc-99m (g)	SPECT	NO	
MAG-3	Tc-99m (g)	SPECT	NO	
ECD	Tc-99m (g)	SPECT	NO	
DTPA	In-111 (EC)	SPECT	YES	antibodies, peptides
DOTA	In-111 (EC)	SPECT	YES	Peptides, antibodies
DOTA	Y-90 (b-, g)	NO	YES	Very stable for 3+ ions
DTPA	Y-90 (b-, g)	NO	YES	Poor chelate for yittrium
DTPA	Y-86 (EC)	PET	NO	
DOTA	Y-86 (EC)	PET	NO	peptides
DOTA	Cu-64 (EC)	PET/SPECT	Potential	MAb, peptides
DTPA	Ga-67 (EC)	SPECT	NO	antibodies
DOTA	Ga-66			peptides
DTPA	Ga-68 (b+)	PET	NO	
DTPA	Bi-212	NO	YES	
DTPA	Bi-213	NO	YES	
DOTA	Lu-177	NO	YES	
TETA	Cu-64	PET/SPECT	YES	peptides
TETA	Cu-67	NO	YES	peptides
HYNIC	Tc-99m (g)	SPECT		
DOTA	Bi-213 (a)	NO	YES	Conjugated to antibodies
DOTA	Ac-225 (a)	NO	YES	antibodies
DTPA	**Re-186 (b-)**	**NO**	**YES**	

32.13 Conclusion

SPECT and PET imaging will continue to play a vital role in cancer theranostics; for example, monoclonal antibodies have been labelled with several radiometals such as ^{111}In, ^{89}Zr, ^{90}Y and ^{177}Lu. The overall aim is to provide diagnostic information with the therapeutic effect of the pharmaceutical to deliver the most effective approach towards the patient's cancer treatment plan. Advancements in nuclear medicine allow for the ability to perform non-invasive methods to visualise drug target expression across primary and metastatic sites. Also, to evaluate the pharmacokinetics and efficacy of the therapeutic agents used. Currently, ^{68}Ga has become a standard PET radiometal in the clinical setting because of the use of ^{68}Ge/^{68}Ga-generators. Investigations are continuing with the radiometals ^{64}Cu and ^{89}Zr to establish PET imaging applications, especially in combination with theranostic approaches.

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33 Radiopharmaceuticals used in nuclear medicine

Radiopharmaceuticals are used in nuclear medicine for the application of medical imaging and therapy.

33.1 Introduction

Radiopharmaceuticals primarily consist of a radioisotope which is incorporated into a pharmaceutical with the ability to evaluate a disease state inside the human body. The pharmaceutical is used to transport the radioisotope to a certain organ, tissues or particular cells within the body. In some instances, radioisotopes can be used in their ionic or inert form without attachment to an organic molecule. In addition, biomolecules can be attached to radionuclides such as technetium-99m, rhenium-188, lutetium-177 and yttrium-90. When the radiopharmaceutical (imaging agent) is administered to a patient it is continually monitored by a specific imaging device such as a gamma camera for diagnosis and therapeutic purposes. These systems include SPECT and PET imaging.

Incidentally, radiopharmaceuticals possess the intrinsic property of radionuclides (radioisotopes) which is the natural process of decay. This provides routes to theranostic (therapy + diagnosis) applications. In effect, this fundamental property results from the excess energy produced due to nuclear instability since radioactive decay is the product of an unstable nucleus. In order, for the radionuclide to become more stable it must emit particles (e.g. alpha and beta) or rays such as gamma radiation from the nucleus.

Cancer theranostic treatments include 177lutetium PSMA therapy: this is a treatment for advanced prostate cancer and 177lutetium octreotate therapy for the treatment of neuroendocrine tumours (NETs) including head and neck cancers and gastrointestinal tumours.

Accordingly, radiopharmaceuticals are primarily used in the area of nuclear medicine for the application of medical imaging and/or therapy in the diagnosis and treatment of many disease states: for example, brachytherapy is used to treat prostate cancer. There are numerous radiopharmaceuticals that use technetium-99m and possess many useful properties as a gamma-emitting radionuclide in diagnostic imaging.

Nuclear medicine departments are responsible for the administration of radioisotopes and radiation in the diagnosis of the disease state and potential radiotherapy treatments. The objective of nuclear medicine is to provide information about the

functioning of the human body and allow healthcare professionals to diagnosis the disease state of the patient. For example, the heart, liver, thyroid and skeleton can be imaged to detect disease.

Nuclear Medicine uses radiopharmaceuticals to gain insight into the intricate workings of the human body's organs and biological processes. Currently, diagnostic procedures using radiotracers are routinely used in various healthcare organisations.

The advancement of radiotherapy systems incorporating proton therapy and image-guided applications are used to treat several medical oncological conditions. For example, using radiation to target cancer cells in any part of the human body.

- Currently, over 40 million nuclear medicine procedures are performed every year with the demand for radioisotopes is increasing at an annual rate of 5%.
- There are over 10,000 hospitals in the world use medical radioisotopes and approximately about 90% of all procedures are for diagnostic medical imaging. The most popularly used radioisotope in diagnosis is technetium-99m, with over 40 million procedures per year. This radioisotope accounts for approximately 80% of all nuclear medicine procedures.
- In 2015, the global radioisotope market was worth $9.61 billion, with 80% of this figure accounting for medical radioisotopes. It is projected that the worldwide market for radioisotopes will be in the order of $17.28 billion by 2021. The North America market for diagnostic radioisotopes considers approximately 50% of the market share compared to Europe, which accounts for 20% of the market share.

Nuclear medicine departments began to appear in hospitals in the 1950s using iodine-131 to investigate and treat thyroid related diseases. Nuclear medicine continues to expand with the advancement of technologies, which include the hybrid scanner positron emission tomography/computed tomography (PET/CT). This was only achievable through the expansion of accelerators in radioisotope production. For example, the main radioisotope technetium-99m is better quality from nuclear reactors in comparison to the lower quality and higher cost obtained from accelerators.

The radiopharmaceuticals which are used for diagnostic purposes are short-lived radiotracers that emit gamma rays inside the body to produce a 2-D picture: alternatively by the application of tomography to generate a 3-D image. These radiotracers can be introduced into the body either by injection, inhalation or orally.

Consequently, radiation is emitted from various points within the body and gamma cameras are subsequently used for detection and to locate the disease state in order to construct a diagnostic image. The image is then further processed using a computer platform and evaluated by radiologists to locate any abnormalities.

The scanning machine – single photon emission computed tomography (SPECT) is used to diagnose and monitor a broad range of medical conditions. Another scanner

used in nuclear medicine imaging is called positron emission tomography (PET) and uses radioisotopes which are produced in a cyclotron.

The majority of positron-emitting radiopharmaceuticals are injected into the bloodstream of the patient which then accumulates in the target tissue. During the decaying process, a positron is emitted which interacts with the nearby electron resulting in the simultaneous emission of two gamma rays (511 keV) in opposite directions. These gamma rays are detectable by a PET camera in order to construct the relevant images.

The most important clinical role of PET imaging is in the area of oncology, and this involves the radiotracer fluorine-18 (half-life 109.8 mins). These radiotracers have proven to be beneficial in the detection and evaluation of most cancers. PET imaging is also used for cardiac and brain imaging.

In addition, PET imaging can be combined with computed X-ray tomography (CT) scans to superimpose the two images (PET + CT) to provide information on a range of diseases from dementia to cancer. The advantage of these hybrid machines is that they enable a 30% increase in diagnosis compared to using standard gamma camera techniques.

The principle behind nuclear medicine is to have a radiation source emitting inside the human body so that it can be detected outside the body by using gamma cameras. This is in contrast to external imaging techniques such as the usage of planer X-ray machines. Also, the advantage of nuclear imaging over X-ray techniques is that both the bone and soft tissue can be imaged at the same time.

Gamma imaging can be used to determine the location and concentration of the radioisotope within the body. For example, if a particular organ is not functioning correctly, this would result in the accumulation of the radiotracer. During the uptake of the radiotracer, several images can be obtained to investigate the rate of radioisotope movement, which can be correlated to the function of the organ.

33.2 Diagnostic radiopharmaceuticals

The organs in the human body are able to absorb chemicals. For example, the thyroid takes up iodine and the brain consumes glucose. These observations are the basis to the development of a range of radiopharmaceuticals which include attaching radioisotopes to biomolecules. When a radiotracer enters the body, it is incorporated into its biological pathways, metabolised, and then excreted. These radiopharmaceuticals can be used to investigate the flow of blood in the brain, amongst other organs such as the liver, lungs, heart, kidneys and including investigations into bone growth.

However, the amount of radiopharmaceutical given to a patient can range from a small dose of 5 microcuries to 35 millicuries. To put this into context, the radiation received from these dosages is about the same amount of radiation received from an X-ray study of that particular organ

33.2.1 Radiopharmaceuticals used in the diagnosis of the disease state

Disease State	Radiotracer
Brain diseases and tumours	2-deoxy-2-[^{18}F]fluoro-glucose, indium-111 pentetreotide, iofetamine (^{123}I), sodium pertechnetate (^{99m}Tc), technetium-99m exametazime, technetium-99m gluceptate, technetium-99m pentetate
Cancer and tumours	2-deoxy-2-[^{18}F}fluoro-glucose, gallium-67 citrate, indium-111 pentetreotide, methionine (^{11}C), radioiodinated iobenguane, sodium fluoride (^{18}F), technetium-99m arcitumomab, technetium-99m nofetumomab merpentan
Colorectal disease	technetium-99m arcitumomab
Disorders of iron metabolism and absorption	ferrous citrate (^{59}Fe)
Heart disease	ammonia-13, 2-deoxy-2-[^{18}F]fluoro-glucose, rubidium-82, sodium pertechnetate (^{99m}Tc), technetium-99m albumin, technetium-99m sestamibi, technetium-99m teboroxime, technetium-99m tetrofosmin, thallous-201 chloride
Heart muscle damage	ammonia-13, fludeoxyglucose18F), rubidium-82, technetium-99m pyrophosphate, technetium-99m (pyro- and trimeta-)phosphates, technetium-99m sestamibi, technetium-99m teboroxime, technetium-99m tetrofosmin, thallous-201 chloride
Impaired flow of cerebrospinal fluid in the brain	indium-111 pentetate
Kidney diseases	iodohippurate sodium (^{123}I), iodohippurate sodium (^{131}I), iothalamate sodium (^{125}I), technetium-99m gluceptate, technetium-99m mertiatide, technetium-99m pentetate, technetium-99m succime
Liver diseases	ammonia-13, 2-deoxy-2-[^{18}F]fluoro-glucose, technetium-99m albumin colloid, technetium-99m disofenin, technetium-99m lidofenin, technetium-99m mebrofenin, technetium-99m sulfur colloid
Lung diseases	krypton-81m, technetium-99m albumin aggregated, technetium-99m pentetate, xenon-127, xenon-133
Parathyroid diseases including cancer	technetium-99m sestamibi, thallous-201 chloride
Pernicious anaemia and problems in absorbing vitamin B12 from intestines	cyanocobalamin (^{57}Co)

Red blood cell diseases	sodium chromate (^{51}Cr)
Salivary gland diseases	sodium pertechnetate (^{99m}Tc)
Spleen diseases	sodium chromate (^{51}Cr), technetium-99m albumin colloid, technetium-99m sulfur colloid
Stomach and intestinal bleeding	sodium chromate (^{51}Cr), sodium pertechnetate (^{99m}Tc) technetium-99m (pyro- and trimeta-)phosphates, technetium-99m sulfur colloid
Stomach problems	technetium-99m sulfur colloid
Tear duct blockage	Sodium Pertechnetate (^{99m}Tc)
Thyroid diseases and cancer	2-deoxy-2-[^{18}F]fluoro-glucose, indium-111 pentetreotide, radioiodinated iobenguane, sodium Iodide (^{123}I), sodium iodide (^{131}I), sodium pertechnetate (^{99m}Tc), technetium-99m sestamibi
Urinary bladder diseases	sodium pertechnetate (^{99m}Tc)

The diagnostic radioisotope must be able to emit gamma rays and contain enough energy to escape from the body. Ideally, the rate of decay of the radioisotope must be completed quite soon after the imaging.

Technetium-99m is the most extensively used radioisotope in medicine being involved in about 80% of all nuclear medicine procedures. Technetium-99m contains the following characteristics:

- The half-life of technetium-99m is 6 hours which facilitates the investigation of metabolic processes
- The half-life is short enough to minimise the radiation dose to the patient
- The decay process involves an 'isomeric' process by emitting both gamma rays and low energy electrons
- No high-energy beta emission is associated with technetium-99m which results in a low radiation dose to the patient
- The low-energy gamma rays emitted from inside the body are easily detectable by a gamma camera positioned outside the body
- The chemistry of technetium allows for the incorporation of this radiotracer in a range of biomolecules
- Technetium-99m is produced using the molybdenum-99 generator, which is portable

33.3 Radionuclide generators

The nuclear reactor which produces molybdenum-99 has a half-life of 66 hours and decays to technetium-99m. Drytec™ is a technetium-99m generator: each eluent of the generator should not exceed more than 0.0056 MBq of molybdenum-99 per 37 MBq

of technetium-99m for a single administered dose. Also, the RadioGenix® System is a technetium-99m generator used to produce sodium pertechnetate 99mTc injection.

The new TechneLite generator, which is the first technetium-99m generator in the United States containing molybdenum-99 (99Mo) which is produced from at least 95 per cent low-enriched uranium. This new type of generator aims to eliminate the use of highly enriched uranium, which is sourced from 99Mo. Technetium-99m; is used in SPECT imaging; for example, myocardial perfusion imaging to detect coronary artery disease.

In diagnostic medicine, there is a tendency towards using more cyclotron-produced isotopes such as fluorine-18 because PET and PET-CT have become more widely available. For PET imaging, the imaging agent 2-deoxy-2-[^{18}F]fluoro-glucose with a half-life of approximately two hours is the primary radiotracer used in nuclear medicine procedures. FDG can be incorporated into the cell without being broken down and is, therefore, a good indicator of cell metabolism.

However, the procedure needs to be completed within two hours reach of a cyclotron, which limits its utility compared with 99Mo/99m generators. For PET imaging, strontium-82, which has a half-life of 25 days, can be used to generate rubidium-82, making it more accessible.

33.4 FDA-approved radiopharmaceuticals

Radiopharmaceutical / Application
Carbon-11 choline Carbon-11 choline is a PET imaging agent used to evaluate prostate cancer recurrence in patients based on elevated blood prostate-specific antigen (PSA) levels. This imaging agent is used in conjunction with bone scintigraphy, computerised tomography (CT) and/or magnetic resonance imaging to identify potential sites of prostate cancer recurrence.
Carbon-14 urea (Pytest) This radiotracer is used to help in the diagnosis of Helicobacter pylori infection in the stomach by detecting levels of gastric urease.
Fluorine-18 florbetaben (Neuraceq™) The PET imaging agent fluorine-18 florbetaben is used to evaluate β-amyloid neuritic plaque density in the brain to aid in the diagnosis of Alzheimer's disease.
Fluorine-18 florbetapir (Amyvid™)
Fluorine-18 flucicovine (Axumin™) This diagnostic PET imaging agent is used to evaluate suspected prostate cancer recurrence based on elevated blood prostate-specific antigen (PSA) levels following treatment.
Fluorine-18 sodium fluoride Used in PET bone imaging to determine osteogenesis imperfecta (OI) known as brittle bone disease.

2-deoxy-2-[^{18}F]fluoro-glucose (FDG) The PET imaging agent 2-deoxy-2-[^{18}F]fluoro-glucose is used to evaluate abnormal glucose metabolism in oncology and myocardial hibernation. Also, used to indicate abnormal glucose metabolism regions in the body, for example, epileptic seizures.
Fluorine-18 flutemetamol (Vizamyl™) Fluorine-18 flutemetamol is a PET imaging agent used to estimate the level of β amyloid neuritic plaque density in the brain, especially for Alzheimer's disease (AD).
Gallium-67 citrate The half-life of Gallium-67 is 78 hours. This radioisotope is administered intravenously to patients as Ga-citrate. It is used to evaluate Hodgkin's disease, Lymphoma and Bronchogenic carcinoma.
Gallium-68 dotatate (NETSPOT™) Gallium-68 dotatate is a PET imaging agent used to identify somatostatin receptor-positive neuroendocrine tumours (NETs) in patients.
Indium-111 chloride Indium-111 chloride is contained in the imaging agents OncoScint (satumomab pendetide) and ProstaScint (capromab pendetide) for in vivo diagnostic imaging. Also, used in the radiolabelling of Zevalin (ibritumomab tiuxetan).
Indium-111 pentetate Used in cisternography imaging.
Indium-111 oxyquinoline Used for radiolabelling autologous leukocytes to detect inflammatory processes associated with abscesses or other infections.
Indium-111 pentetreotide (Octreoscan™) Octreoscan is used to detect primary and metastatic neuroendocrine tumours with associated somatostatin receptors.
Iodine I-123 iobenguane (AdreView™) Iodine I-123 iobenguane is used as a diagnostic test for primary or metastatic pheochromocytoma or neuroblastoma.
Iodine-123 ioflupane (DaTscan™) This SPECT imaging agent is used to visualise patients with suspected Parkinson's disease. It can also be used to differentiate essential tremor due to Parkinson's disease.
Iodine-123 sodium iodide capsules These capsules are used to evaluate thyroid function.
Iodine-125 human serum albumin (Jeanatope) Radiolabelled albumin is used to evaluate blood and plasma volume.
Iodine-125 iothalamate (Glofil-125) Used to investigate glomerular filtration.
Iodine-131 human serum albumin (Megatope) Megatope is used to evaluate the blood and plasma volumes, including cardiac and pulmonary blood volumes and circulation times. Also used to study protein turnover and the heart, including vessel delineation.

Iodine-131 iobenguane (AZEDRA®) Iodine-131 obenguane is used to image locally advanced or metastatic pheochromocytoma or paraganglioma that require anticancer therapy.
Iodine-131 sodium iodide (HICON™) Diagnostic agent iodine-131 sodium iodide is used to evaluate thyroid function such as hyperthyroidism and treatment of cancer of the thyroid.
Lutetium Lu-177 dotatate (LUTATHERA®) Used in the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs).
Molybdenum Mo-99 generator (UltraTechneKow V4, DRYTEC™, Technelite®, RadioGenix™ System The molybdenum-99 generator is used to produce ^{99m}Tc-sodium pertechnetate for preparation of the radiopharmaceutical. These ^{99m}Tc-SPECT imaging agents can be used to image salivary glands and the Lacrimal Drainage System including the thyroid.
Nitrogen-13 ammonia Nitrogen-13 ammonia is used in PET imaging to investigate the myocardium under rest of pharmacologic stress conditions. Also, to study myocardial perfusion and coronary artery disease.
Radium-223 dichloride (Xofigo®) Radium-223 dichloride is used for the treatment of castration-resistant prostate cancer and bone metastases.
Rubidium-82 chloride (Cardiogen-82®, Ruby-Fill®) Rubidium-82 chloride is a PET myocardial perfusion agent used to investigate myocardial infarction.
Samarium-153 lexidronam (Quadramet®) Samarium-153 lexidronam is used for pain relief in patients suffering from osteoblastic metastatic bone lesions.
Strontium-89 chloride (Metastron™) Used to relieve bone pain in patients suffering from skeletal metastases.
Technetium-99m bicisate (Neurolite®) The SPECT imaging agent technetium-99m bicisate is used after a stroke diagnosis.
Technetium-99m disofenin (Hepatolite®) Technetium-99m disofenin is used to diagnose acute cholecystitis.
Technetium-99m exametazine (Ceretec™) Technetium-99m exametazine is used to detect changes in the regional cerebral perfusion of a stroke patient. Also, used to investigate internal abdominal infection and inflammatory bowel disease.
Technetium-99m macroaggregated albumin Used in the evaluation of pulmonary perfusion.
Technetium-99m mebrofenin (Choletec®) This SPECT imaging agent is used to image the liver and gallbladder.
Technetium-99m medronate (MDP-25, MDP Multidose) A bone imaging agent to investigate osteogenesis.

Technetium-99m mertiatide (Technescan MAG3™) This renal SPECT imaging agent is used for the diagnose of renal failure, congenital abnormalities and urinary tract obstruction.
Technetium-99m oxidronate (Technescan™, HDP) A bone imaging agent to evaluate osteogenesis.
Technetium-99m pentetate Technetium-99m pentetate is used in brain and kidney imaging.
Technetium-99m pyrophosphate (Technescan™, PYP™) This SPECT imaging agent is used to investigate areas of altered osteogenesis in the bone. Also, used as a cardiac imaging agent to diagnose myocardial infarction.
Technetium-99m red blood cells (UltraTag™) Technetium-99m can be used to radiolabel red blood cells to study blood pool imaging including cardiac and gastrointestinal bleeding.
Technetium-99m sestamibi (Cardiolite®) Technetium-99m sestamibi is a SPECT imaging agent to investigate myocardial perfusion, especially in the detection of coronary artery disease.
Technetium-99m sodium pertechnetate Technetium-99m sodium pertechnetate is used in SPECT imaging of the brain including thyroid and salivary gland imaging. Also, used in angiography and urinary bladder imaging.
Technetium-99m succimer Used to evaluate renal parenchymal disorders.
Technetium-99m sulfur colloid Technetium-99m sulfur colloid is used in SPECT imaging of the reticuloendothelial cells in the liver, spleen and bone marrow. It can also be used in oesophageal and gastroesophageal reflux scintigraphy. In addition to the detection of pulmonary aspiration of gastric contents and in the assessment of breast cancer or malignant melanoma.
Technetium-99m tetrofosmin (Myoview™) Myoview is used in SPECT imaging of myocardial perfusion for detecting coronary artery disease by localising myocardial ischemia and infarction. Also, used in the assessment of left ventricular function.
Technetium-99m tilmanocept (Lymphoseek®) Technetium-99m tilmanoceptis used to map the lymphatic system for tumour sites.
Thallium-201 chloride Thallium-201 chloride is a myocardial perfusion SPECT imaging agent used for the diagnosis and localization of myocardial infarction.
Xenon-133 gas Xenon-133 gas is used to investigate the pulmonary function and for imaging the lungs including the assessment of cerebral flow.
Yttrium-90 chloride Zevalin is used for radioimmunotherapy procedures. Yttrium-90 ibritumomab tiuxetan (Zevalin®) Yttrium-90 ibritumomab tiuxetan is used for the treatment of relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL).

33.5 Future of radiopharmaceuticals

Technetium-99m and 2-deoxy-2-[^{18}F]fluoro-glucose (FDG) remain the workhorse radiopharmaceuticals for SPECT and PET imaging accounting for 80 per cent of all nuclear medicine procedures. However, several new radiopharmaceuticals are driving molecular imaging in the clinical setting, and these include the PET imaging agents flutemetamol and florbetapir which are used in the early diagnosis of neurodegenerative diseases such as Alzheimer's. The technetium-99m radiopharmaceutical ubiquicidin is used to detect bacterial infections on the sites of orthopaedic implants extending to ^{68}Ga-NOTA-ubiquicidin for PET imaging of infection.

Incidentally, there are some new cardiovascular PET imaging applications towards myocardial perfusion imaging such as ammonia-13 and flurpiridaz. Also, the recent approval of RUBY-FILL (generator containing strontium-82) and the elution system to produce CardioGen-82: these systems lead to the formation of rubidium-82. This radionuclide is used in the clinical setting in the form of ^{82}RbCl to mimic the potassium ions (K^+) for the imaging of myocardial perfusion. However, due to its short half-life of 1.3 min rubidium-82 poses several challenges for routine applications. However, the benefit of using rubidium-82 is that it provides a higher resolution PET scan in comparison to the SPECT tracer 99mTc-MIBI.

A novel class of PET radiopharmaceuticals using ^{68}Ga-FAPI was able to identify at least 30 types of malignant tumours. This radiotracer targets cancer-associated fibroblasts, which can contribute up to 90 per cent of a tumour's mass.

Advancements of radiopharmaceuticals in oncology have included axumin (^{18}F-fluciclovine) used for the detection of recurrent prostate cancer. The FDA has given approval for the PET imaging agent ^{68}Ga-dotatate known as NETSPOT™ to locate somostatin receptor positive neuroendocrine tumours in both adult and paediatric patients.

Subsequently, the PET radiotracer, ^{18}F-TZ3504 has been used to image neuroinflammation due to multiple sclerosis by quantitative assessment of S1P1 expression in the body.

The generation of technetium-99m introduces problems to the SPECT-CT market and therefore requires an alternative approach. The non-reactor manufacture of technetium-99m in the future will allow SPECT radiopharmaceuticals to effectively compete with cardiac PET.

Theranostics is a hot topic in the radiopharmaceutical market, especially due to the latest FDA approval of lutetium-177 dotatate (lutathera) to image and treat gastroenteropancreatic neuroendocrine tumours. This theranostic agent is a combination of a diagnostic agent and a therapeutic agent, such as ^{68}Ga- and ^{177}Lu-dotatate.

Another promising prostate cancer theranostic pairing are the bombesin analogues, ^{68}Ga and ^{177}Lu-RM2. Also, ^{86}Y (β^+) forms a theranostic isotopic pair with the pure $\beta-$ emitter of ^{90}Y. Currently, the PET radiometal ^{44}Sc which can be obtained from a ^{44}Ti/^{44}Sc generator possesses similar decay characteristics to ^{68}Ga but a longer half-life of 3.97 hours. It has been demonstrated that ^{44}Sc-DOTATOC is compatible with standard radiolabelling techniques and produces a comparable imaging quality to that of the ^{68}Ga-DOTATOC.

In addition, the calcium mimic, Xofigo (radium-223) was approved by the FDA in 2013 for the treatment of bone metastases in prostate cancer. However, a future radiopharmaceutical [^{225}Ac]-FPI-1434 is in development to target solid tumours, which include non-small cell lung, prostate, and breast cancers.

Interestingly, pentixafor can be labelled with ^{99m}Tc for SPECT imaging and ^{68}Ga for PET imaging. This imaging agent binds to CXC chemokine type 4 receptors which are up regulated in several cancers, for example, multiple myeloma.

In January 2019, the diagnostic radiopharmaceutical, ^{64}Cu-dotatate, received fast track designation from the FDA. ^{64}Cu-dotatate is a PET diagnostic agent developed to detect neuroendocrine tumours. Also, the radiotherapy drug Azedra (iobenguane iodine-131) is used to treat rare tumours of the adrenal gland called pheochromocytomas.

On the SPECT horizon, the radiotracer AdreView (iobenguane iodine-123) is the first imaging agent to establish a link between nerve function in the heart and the patient's mortality risk. Also, AdreView has been given FDA approval for the scintigraphic assessment of myocardial sympathetic innervation, known as cardiac nerve activity.

Currently, a new generation of hybrid scanners is entering the clinical setting which combines PET and MRI imaging. This will allow for the development of a new class of imaging agents that incorporate the radionuclide into superparamagnetic iron oxide nanoparticles (SPION) to allow hybrids of PET/MRI and SPECT/MRI.

An alternative approach is to use paramagnetic manganese instead of the MRI contrast agents based on gadolinium. It can be envisaged that the use of paramagnetic manganese and the PET radiometal ^{52g}Mn can be used to produce hybrid PET/MRI images. These scanners will enable radiopharmaceuticals to be developed to evaluate traumatic brain injury and post-traumatic stress disorder amongst other disease states.

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34 EXPLORER PET-CT scanner: a total body experience

EXPLORER, the world's first medical imaging scanner to produce a 3-D picture of the whole human body.

34.1 Introduction

The EXPLORER Whole Body Scanner and its capabilities reminded me about the 'Fantastic Voyage'. The Fantastic Voyage was a 1966 American science fiction film about a submarine crew who were shrunk to a microscopic size. Subsequently, they ventured into the human body of an injured scientist to repair damage to his brain. The synergy is the ability of the EXPLORER to track a radiopharmaceutical through the human body and locate the disease state in real-time.

However, future PET/CT hybrid scanners must be able to use most of the 'PET signal'. At present, all PET scanners are limited by low numbers of detected photons and high dosages of radiation. Nevertheless, some of these challenges have been addressed by the EXPLORER.

The EXPLORER, the world's first medical imaging scanner can produce a 3-D picture of the whole human body in one session and since its development 13 years ago has recently produced its first scans. This next-generation hybrid machine was created by project leaders Simon Cherry and Ramsey Badawi in partnership with United Imaging Healthcare (UIH) and other organisations at a cost of over $15 m. The EXPLORER combines the imaging modalities of PET Imaging (PET) with X-ray computed tomography (CT).

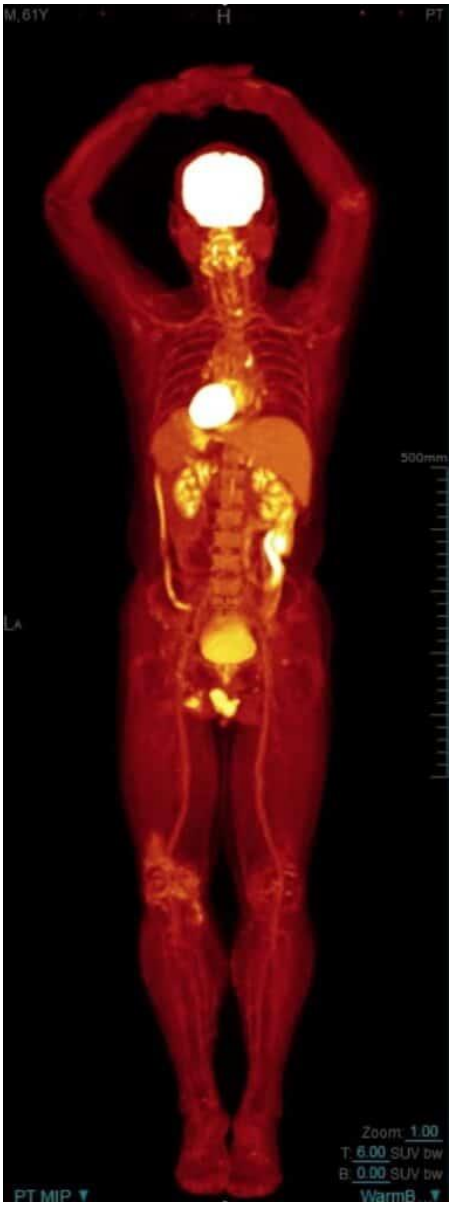
This revolutionary scanner can generate a whole-body image within one second and is equipped with advanced video technology to track radiopharmaceuticals as they have a Fantastic Voyage through the entire body!

34.2 EXPLORER PET/CT scanner design and features

Design	Feature
Cylindrical Total-Body Scanner	The EXPLORER combines positron emission tomography (PET) and X-ray computed tomography (CT) imaging to produce images with high temporal resolution.
Rings and Detectors	40 Rings are present in the EXPLORER scanner including 48 modular block detectors. The ring diameter is approximately 80 cm giving a spatial resolution of 4 mm with an acceptance angle of 46°.
Axial Field of View	The axial field of view (FOV) is 194 cm, and the scanner produces PET images from 500,000 detectors.
Scanning	The EXPLORER scanner can perform a whole-body PET scan up to 40 times better than existing commercial scanners. It can perform 3-D scans of the whole body within 30 seconds. Therefore, rapid scanning.
Solid State	The EXPLORER uses modern solid-state silicon photomultiplier light sensors to provide high-resolution images.

34.3 Video radiotracing

Video technology can be used to show the distribution of the positron emission radiotracer FDG (2-deoxy-2-[^{18}F]fluoro-D-glucose) upon in vivo administration into the patient's vein and captured in real-time by the EXPLORER scanner. These detailed 3-D images produced from the dynamic sequence are not shown on standard PET scanners.



EXPLORER PET image showing glucose metabolism throughout the human body

(Courtesy of Simon Cherry)

- The PET radiotracer is injected into the patient's vein, and after a short time, it travels to the heart. At this point, the radiotracer is dispersed throughout the arteries to all organs of the body.
- At approximately 3 minutes, a percentage of the radiotracer is excreted from the kidneys into the bladder.
- Accumulation of the FDG can be detected in the brain and heart including the liver over this interval.
- The EXPLORER scanner is capable of investigating the metabolism and excretion of a radiolabelled version of the drug throughout the entire human body.
- There is a fine balance between image quality, acquisition time and injected radiation dose. This combination will vary between different applications: in the

majority of instances, the EXPLORER can scan faster and obtain images at a much lower radiation dose.

In essence, the EXPLORER project team have accomplished the ability of a medical imaging scanner to capture a 3-D image of the whole human body which has never been achieved before. This achievement will drive applications towards the improvement of diagnostic medical imaging and develop specific radiopharmaceuticals to track the progression of the disease state.

Future PET/CT scanners will benefit a patient's treatment plans because these EXPLORER machines will provide higher-quality diagnostic PET scans which are not currently available. The EXPLORER is able to scan up to 40 times faster than current PET scanners and deliver a diagnostic scan of the whole body within 30 seconds.

The primary benefit of the EXPLORER is that it can scan a patient using a radiation dose that is 40 times less than what is used in conventional PET scanners. This significant reduction in the dose will allow for repeat scans, especially for children where the cumulative radiation dose is an important factor to be considered.

For the first time, the EXPLORER can evaluate what is happening in all organs and tissues of the body. For example, it has the scope to quantitatively measure blood flow and investigate the mechanism of how the body takes up glucose in the human body. The EXPLORER will be the apex imaging modality in the study of cancer, causes of inflammation and infection as well as immunological and metabolic disorders of the disease state.

The substantial increase in the EXPLORER sensitivity will enable it to:

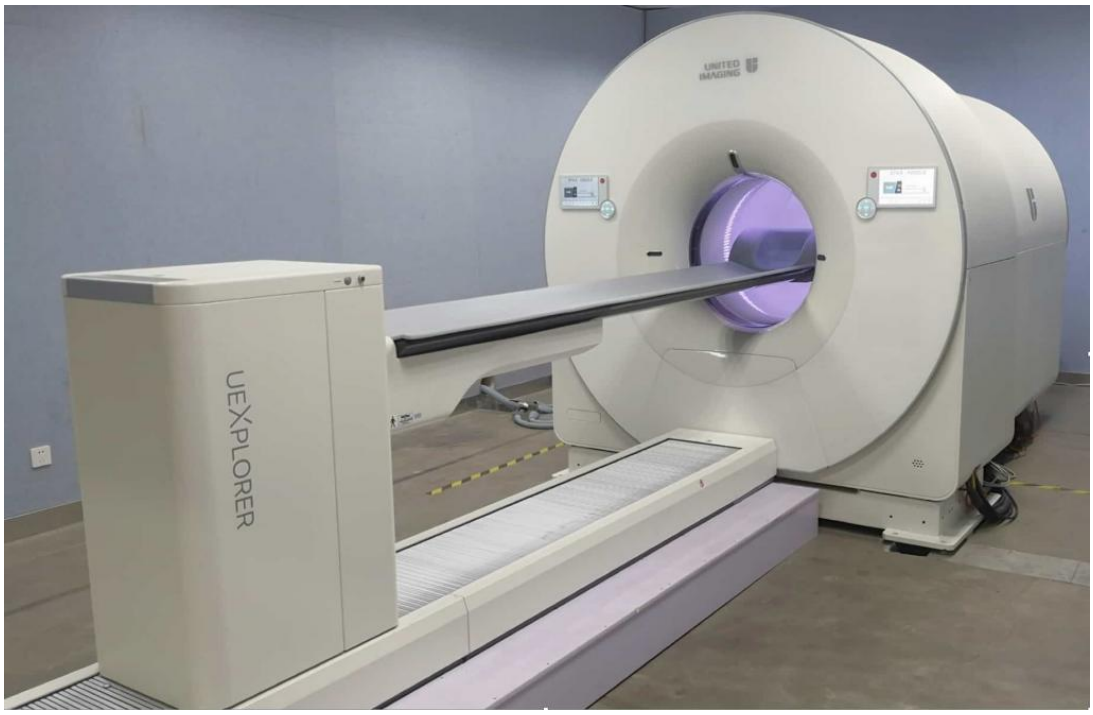
- produce more reliable images
- obtain images by scanning at very low radiation dosages
- rapidly scan within 1 minute
- evaluate the PET radiopharmaceutical after a more significant time interval from an injection of the radiotracer

The EXPLORER total-body imaging applications include:

- fast scanning which requires no anaesthesia
- detection of infections and chronic diseases such as cancer
- investigation of cell-based therapies
- evaluation of drug pharmacokinetics in all organs of the body
- study of metabolic disorders and autoimmune diseases
- toxicological research
- generation of coronal, sagittal and axial slices of the human body.
- research into the endocrine and immunological signalling implicated in a range of disorders including irritable bowel syndrome
- identify the pharmacokinetics (pk) of new medicines in all organs of the body at lower mass and radiation dosages of 100 μSv.
- used in drug development and toxicology studies

EXPLORER is a scanner that is capable of generating 3-D images of the whole human body. The data produced by the whole-body scanner will be used to extract detailed information regarding metabolism, radiopharmaceuticals, and drug-receptor interactions.

34.4 The EXPLORER PET/CT Scanner



Photograph of the EXPLORER Total-Body PET/CT scanner (Courtesy of Simon Cherry)

34.5 The EXPLORER PET/CT scanner specifications

Axial Field of View (FOV)	194.0 cm
Trans-axial Field of View (FOV)	68.6 cm
Bore Diameter of Detector Ring	78.6 cm
Patient Bore Opening	76.0 cm
PET Detector Crystals	Lutetium (yttrium) oxyorthosilicate (LYSO) crystal volume measures 2.76 x 2.76 x 18.1 mm
Number of Crystals	564,480
Crystal Arrangement	Crystals are arranged in 7 x 6 arrays with a crystal pitch of 2.85 mm

Detector Configuration	80-row,160 slice CT scanner
Photomultipliers	Four silicon photomultipliers (6 x 6 mm^2)
Axial units	8 Axial units and each with an axial field of view of 24 cm with a 2.5 mm gap between the units
Total-body PET	30s
Dynamic Range	Image 5 more half-lives: carbon-11 (3 hours); fluorine-18 (> 16 hours); zirconium-89 (> 30 days)
Image with Low Dose	40-Fold reduction in dose (whole-body PET at ~0.15 mSv)
Time-of-Flight (TOF)	Timing resolution ~430 secs
Energy Resolution	11.7%
Reconstructed Spatial Resolution	1 cm from the centre of the field of view, using the NEMA NU-2 2018 protocol
Filtered Back-Projection Reconstruction	~2.9 mm
Energy Window	The majority of the images were collected using a 430-645 keV energy window. The tolerance of the coincidences from the detector pairs was +/-4 which corresponded to an axial acceptance angle of ~+/-57°
Coincidence Time Window	The coincidence time window varies due to the different path lengths through the body and ranges from 4.5-6.9 ns
Image Reconstruction	Reconstruction was carried out using time-of-flight (TOF) and point-spread-function (PSF) with ordered-subset expectation maximisation (OSEM)

34.6 The future

The anatometabolic imaging modalities combined SPECT/CT, PET/CT, and PET/MR imaging are available for clinical use. These hybrid imaging scanners are able to provide advanced information on the disease state by making use of big data using computer-based models for disease and therapy including response prediction. The EXPLORER has set the benchmark for the next generation of PET/CT scanners.

Future developments will have to address clinical applications regarding ultra-fast paediatric scans and limit anaesthesia use. The EXPLORER also allows for low-dose follow-up scanning, especially in paediatric oncology. The next generation of whole-body scanners must be able to produce rapid higher resolution images using low-dose radiation and machines to generate total-body dynamic images with high temporal resolution.

Suggested reading

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35 Medical X-ray imaging using computed tomography

Conventional X-ray systems are based on an immovable X-ray tube, whereas the CT scanner uses a rotational X-ray source.

35.1 Introduction

The computed tomography (CT) Scanner was invented in 1972 by Godfrey Hounsfield, a British engineer at EMI Laboratories, England and the physicist Allan Cormack of Tufts University, Massachusetts.

How can you determine what's in a closed box?

This question was proposed in 1967 when the British electrical engineer Sir Godfrey Hounsfield (1919-2004) was walking in the countryside. Initially, this thought had nothing to do with medicine but was merely an idea that you could determine what was in a box by taking X-ray readings at all angles around the object. In order to develop the concept further, he assembled a computer to obtain position points by focusing X-rays at various angles to create an image of the hidden object.

Subsequently, the prototype head scanner emerged and was first tested on a preserved human brain, followed by a cow brain and Hounsfield himself. However, the first clinical computed tomography (CT) scan on a patient occurred on 1st October 1971, at Atkinson Morley's Hospital (part of St George's Hospital) in London, England. The patient had a suspected frontal lobe tumour and was scanned with the prototype scanner, which produced an image. This 80 x 80 matrix image was obtained by scanning the patient every 5 minutes and generating the image.

In 1975, Hounsfield built a whole-body scanner which became available a year later. Currently, an entire chest scan can be taken in 5 to 10 seconds using the most advanced multi-slice system. These achievements were recognised by both pioneers winning the 1979 Nobel Prize for Physiology and Medicine for developing the diagnostic techniques of X-ray computed tomography.

Computed tomography scanners have improved patient comfort since a scan can be performed quickly. Improvements have led to higher-resolution images, which assist the doctor in making a diagnosis. For example, the computed tomography scan can help doctors visualise small nodules or tumours, which they cannot see with a film X-ray.

It is a fact that in 2017 the NHS of England carried out 42.1 million imaging tests. These consisted of plain radiography (X-ray), of which there were 22.9 million procedures, diagnostic ultrasonography (ultrasound, 9.37 million); computerised axial tomography (CAT scan, 4.82 million) and magnetic resonance imaging (MRI, 3.36 million). In comparison, in 2018, it was estimated that approximately 82 million CT procedures were performed in the U.S.

35.2 How do CT scanners work?

Computed tomography uses X-rays (photons) that travel through the body, absorbing a certain amount of energy. The amount of X-ray energy absorbed is related to the slice thickness and proportional to the tissue density. Therefore, by changing the angle of the X-ray, the tissue densities can be correlated into a cross-sectional image using a computer. In these cases, the processed images are in a greyscale format. These shades of grey can correlate to the tissue density to create the image. The greyscale can be correlated to the Hounsfield scale, which allows a quantitative measure for describing radiodensity in the CT image and is able to calculate an accurate density for a particular type of tissue.

35.3 Hounsfield units (HU)

The CT attenuation values are expressed in Hounsfield units (HU) and are related to the linear density. In the Hounsfield scale, water is assigned a value of 0 HU, and all other CT values are formulated according to the following expression:

$$\text{CT number (HU)} = 1000 \times (\mu_{material} - \mu_{water}) / (\mu_{water})$$

μ is the CT linear attenuation coefficient

Therefore,

$HU_{water} = 0$ as $(\mu_{material} = \mu_{water})$

$HU_{air} = -1000$ as $(\mu_{material} = 0)$

HU=1 is associated with 0.1% of the linear attenuation coefficient of water.

The HU values for each pixel represent the electron density of the imaged tissue at a particular location. These pixels are transformed into a digital image by assigning a greyscale intensity to each value. Therefore, higher HU values will produce a greater pixel intensity (brightness). For example, fat is less dense than water, and the associated HU value is in the −30 to −70 range thus, fat will appear darker than water in the computed tomography images. The table below shows several HU values for the various constituents which are found on head CT scans:

Hounsfield Units (HU)	Material
>1000	Bone, calcium, metal
100 to 600	Iodinated CT contrast
30 to 500	Punctate calcifications
60 to 100	Intracranial haemorrhage
35	Grey matter
25	White matter
20 to 40	Muscle, soft tissue
0	Water
-30 to -70	Fat
< -1000	Air

For example, on the Hounsfield scale:

- air is assigned a value of <−1000 (black on the greyscale)
- the bone between +700 (cancellous bone) to +3000 (dense bone) (white on the greyscale)

The bones are much denser than the surrounding soft tissues and appear very clearly on computed tomography images. Therefore, this makes computed tomography a vital imaging modality when investigating skeletal anatomy. Similarly, the density difference between soft tissues and the air is very good, allowing, for example, the nasal airways to be clearly seen. However, organs and soft tissues produce small Hounsfield value ranges and are therefore become difficult to identify adjacent structures. For example, there is a difference between fat and muscle when viewing a segment of CT data. Artificial contrast agents that absorb X-ray energy may be introduced into the body, which makes some structures stand out more vividly in computed tomography images.

Conventional X-ray systems are based on an immovable X-ray tube: whereas the CT scanner uses a rotational X-ray source that revolves in an unclosed gantry. During the CT scanning process, the patient lies on a moveable bed which transports through the gantry allowing the narrow beams of X-rays to pass through the body at various angles during the rotation. Consequently, the X-ray detectors – located directly opposite the X-ray source – transmit to a computer to generate digital images.

Nevertheless, each time the X-ray source completes one full rotation, the CT computer constructs a 2-D image slice of the patient's anatomy. The thickness of the tissue represents an image slice which varies depending on the type of computed tomography machine used but usually ranges from 1-10 mm. Completing a full slice generates the image data; the motorised bed supporting the patient slowly moves forward into the gantry. The X-ray scanning process is repeated to produce another image slice. This process is repeated several times to accumulate enough slices. The benefit of this imaging process is the ability to rotate the 3D image in space. In addition, to be able to view slices in succession, which can make it simpler to locate the exact position of the abnormality within the body.

Currently, computed tomography scanners include technological developments that enable customers to improve patient care management. This includes lung cancer screening, dose guidance and regulation, including spectral and multi-energy imaging. In addition to cardiac and brain imaging. These CT scanners also provide new levels of information to help clinicians make a more confident diagnosis at a low dose without increasing complexity in their routines.

- Optimising the dose including standardising protocols will contribute to improvements in healthcare systems and ensure operational efficiency and most importantly patient well-being.
- The US computed tomography market has shown consistent growth over the last three years: this has been primarily driven by Big Data and population health management systems.
- Apart from dose reduction there is an important emphasis on workflow and efficiency to create improvements in the imaging experience for both patients and healthcare professionals.
- Trends are being created in the area of preventative screening such as lung cancer.

35.4 Computed tomography advancements

The computed tomography system is capable of dual-energy and spectral imaging to obtain functional information from the same computed tomography scanner. The benefits of this approach are that patients will not be exposed to an additional radiation dose, and valuable functional information is obtained regarding the disease state: for example, the detection of lesions formed earlier in the disease process and also to assist in a personalised treatment plan. These concepts can be extended to structural heart imaging.

The advancements in CT technology are focused on three areas:

- The capability to obtain vital clinical information from the CT investigation. The aim is to produce a more confident diagnosis resulting in less follow-up testing and improved disease management.
- To develop methods to extract clinical information at lower radiation doses. This would enable broader use of CT for high-risk populations and early disease detection, such as lung cancer screening.
- The integration of clinical information across various diagnostic systems to benefit the individual patient treatment plan.

However, to enable clinical excellence for patients with complex disease states, computed tomography systems must be able to develop advanced modalities in spectral imaging technology for the diagnosis and characterisation of disease states.

Furthermore, CT is mostly used to gain anatomical information and is expressed in tissue density (HU). This is compared to GE Healthcare – Gemstone Spectral Imaging (GSI), which can introduce additional contrast to the image to aid the diagnosis of complex disease patterns in the CT images. The GSI system overcomes the

limitations of conventional CT, which adopts a single-parameter imaging mode. GSI will enable the acquisition of polychromatic images, optimal monochromatic images, iodine (water)-based images, and spectral characterisation diagrams. Therefore, GSI achieves high-resolution imaging and material decomposition by qualitative and quantitative analysis, significantly improving diagnostic accuracy and patient safety.

The Gemstone Spectral Imaging (GSI) process improves image quality compared to conventional imaging techniques. This is due to the higher contrast to noise ratio (CNR) and reduced beam hardening artefacts. In addition to enhanced material separation and quantitative material information, all performed at a full 50 cm field of view.

GSI can provide vital information regarding the chemical composition of body materials. For example, to distinguish between calcium, iodine and water in helping in the characterisation of pathology. The GSI approach can be applied across several areas of clinical diagnosis, including:

- Enhancing contrast quality with the monochromatic spectral image
- Beam hardening reduced myocardial perfusion assessment
- Improved coronary visualisation in the presence of calcification
- Quantitative lesion characterisation

GSI is a dual-energy technique that uses fast kV switching, including gemstone detector technology, to generate material density data. It simultaneously acquires high and low-energy data sets to produce excellent anatomical information throughout the full 50 cm field of view. However, GSI decreases the costs by reducing the requirement for other tests, primarily in the area of cancer, vascular disease and kidney stones.

By 2022, the computed tomography scanner market is estimated to be worth $6.5 billion. This has also been attributed to advancements in the area of 3D printing. In the future, the new CT scanners will incorporate the stereolithography file format, which will be used in 3D-printed structures as a standard for CT and MR applications of the technology. Therefore, 3D printers connected to CT scanners can print 3D models of human organs, such as the heart, to assist in preparing for complex surgery and training. The CT scanning takes hundreds of X-ray images of the affected region as it is rotated inside the scanner. The 2D images are combined to produce a 3D point cloud, and the computed tomography image can then be compared to the CAD file to measure the accuracy of the print.

35.5 CT systems

Manufacturer	CT Scanner	Description
Toshiba	Aquilion Lightning	The Aquilion Lightning is a 16-row helical CT scanner containing the smallest detector of 0.5 mm for routine isotropic imaging.
Toshiba	FIRST System	The Toshiba FIRST system produces improvements to image quality by using noise reduction to decrease the radiation dose. It also reduces the time for model-based CT image reconstruction.
Philips	IQon Spectral CT	The Philips IQon Spectral CT scanner produces improvements to tissue characterisation and visualisation for the disease state.
Siemens	SOMATOM Force	The Siemens SOMATOM Force is a dual-source scanner. It uses two X-ray sources and two detectors at the same time. This configuration is capable of imaging paediatric and adult patients within one second.

The Siemens portfolio of CT scanners ranges from the 16-slice SOMATOM Scope up to the SOMATOM Force, which is capable of dual-energy imaging and is NEMA XR-29 compliant.

NEMA XR-29 specifies four attributes of CT scanners to optimise and manage a radiation dose to deliver the diagnostic image quality the clinician needs.

The four criteria specified by NEMA XR-29 are:

- Dose check features
- Referencing adult and paediatric protocols
- Automatic exposure control
- DICOM-compliant radiation dose structured reporting

The equipment advancements continue with GE Healthcare by developing Hepatic VCAR, which enables whole organ segmentation within a minute compared to a standard CT scanner which would be 10 minutes. This system will streamline the workflow and improve patients' CT scanning output.

Furthermore, the TAVI (transcatheter aortic valve implantation) analysis assists physicians in treating sick patients with an intuitive, non-invasive planning tool for interventional surgical teams. Also, the Gemstone Clarity detector platform can have anatomical coverage in a single rotation, reducing the radiation dose required to obtain quality images.

35.6 CT Scanners: 4-,8-, 32-, 40-, 64-, 128-, 256-, 320-, 640

The Toshiba Aquilion One Vision system is amongst the new generation of CT systems currently on the market. This scanner has the ability to offer several dose-lowering technologies, including advancements in hardware and software to enhance image quality over previous CT scanners. Consequently, healthcare institutions have begun to replace the first-generation 64-slice CT scanners with this consideration to be taken into account:

Do more slices make for a better CT scanner?

The answer is that the overall costs versus the benefits must be understood when purchasing high-slice CT systems. Accordingly, the CT scanner must be able to perform for that particular healthcare institution. For example, if it was to be used for cardiovascular imaging. In this case, the technical aspects of CT must have high image quality and resolution.

4-8 Slice CT:

GE BrightSpeed Edge-8, GE LightSpeed Ultra-8, GE BrightSpeed Excel-4, GE LightSpeed Plus-4, GE LightSpeed QX/I-4, Siemens Emotion-6, Toshiba Aquilion-8, Toshiba Aquilion-4 and Toshiba Asteion-4.

- The 4-8 slice CT systems are a cost-efficient solution when only necessary CT imaging is required.
- The CT scanner can be used to perform a wide variety of examinations and take longer to obtain the images. This is because they only scan and detect a small part of the body.

16-slice CT:

GE Optima 540-16, GE Optima 520-16, GE BrightSpeed-16, GE LightSpeed-16, Philips Brilliance-16, Philips MX 8000 IDT-16, Philips MX-16, Siemens Emotion-16, Siemens Scope-16, Siemens Sensation-16 and Toshiba Aquilion-16.

- The 16-slice CT scanners have 16 rows of CT detectors inside the gantry to produce the images.
- Therefore, the scanner can cover a larger area in a single rotation around the patient's body.
- The advantages are the reduced thickness of the body area scanned and therefore an improvement in the resolution compared to a 2-slice CT machine. This results in faster scanning and is able to cover a specific area of the body compared to 2 slices. The total scan time using a 16-slice is much shorter than a 2-slice scanner.

32 to 40-slice CT:

GE LightSpeed VCT-32, Philips Brilliance-40, Siemens Sensation-40, Siemens Definition AS-40 and Toshiba Aquilion-32.

- The 32 to 40-slice CT machines provide a more extended coverage per gantry rotation than 16-slice scanners.
- This results in shorter examination times and a reduction of motion artefacts.

64-Slice CT:

GE Optima 660-64, Discovery 750 HD-64, GE LightSpeed VCT-64, Philips Ingenuity-64, Philips Brilliance-64, Siemens Sensation-64, Siemens Definition AS-64 and Toshiba Aquilion-64.

- The 64-slice CT scanners are the primary workhorse of cardiac and trauma within high-volume critical care units.
- The speed and sensitivity of 64-slice CT scanners allow for freeze-frame imaging. This will reduce the adverse effects that heart and muscle motion have on image quality.

128-slice CT:

GE Optima 660-128, Discovery 750 HD-128, Philips Ict-128, Philips Ingenuity-128, Siemens Definition (AS+)-128 and Toshiba CX-128.

- This 128-slice CT scanner is mostly used in cardiac or research institutions.
- It is the latest generation of CT scanners that have contributed to transforming non-invasive diagnosis.
- This CT machine is capable of scanning the whole body in seconds and provides exceptional sharp 3D images of any organ.

256-slice CT:

GE Revolution-256, Philips Brilliance iCT- 256, Siemens Somatom, Definition Flash-256 and Toshiba Aquilion beta-256.

- The Philips 256-slice Brilliance iCT scanner provides 8 cm of coverage. For example, it can image the entire heart in two scans and includes a rotation speed of 0.27 seconds with 120 kW of power.
- The Brilliance iCT scanner is four times more powerful than a 64-slice CT. Therefore, it allows healthcare professionals to produce high-quality images with excellent acquisition speed.
- This Philips technology is able to reduce radiation doses by up to 80%.
- The GE Revolution 256 CT scanner includes a 16 cm whole organ coverage and spatial resolution through the Gemstone Clarity Detector.
- Also, the gantry can image at a 0.28-second rotation speed.
- The Siemens Somatom Definition Flash 256 CT scanner provides quality imaging and data on many cardiac and vascular conditions, including Aortic

aneurysm, pulmonary emboli or deep vein thrombosis, carotid artery disease, chest pain, coronary artery disease and peripheral artery disease.

- The Toshiba Aquilion beta 256 is equipped with more detectors than the 64-slice CT and in a single scan, it can cover four times the area.
- This CT scanner is capable of a single rotation of the X-ray-emitting gantry and can image a diameter of 12.8 cm.
- This scanner can capture most individual organs in one swoop including the brain, heart, entire joints and most of the lungs and liver.

320-slice CT:

Toshiba Aquilion ONE-320

- The 320-slice CT scanners are at the high end of the market and possess excellent image quality. They are especially outstanding for cardiac examinations because they can image the heart in one rotation.
- Therefore, the patient does not require sedation or other medications to decrease the heart rate. This scanner also reduces artefacts due to heart and lung movements.

640-Slice CT:

Toshiba Aquilion ONE-640

- The 640-slice CT scanner provides superior diagnostic power and enables clinicians to make a diagnosis with confidence in the shortest time.
- The 640-slice CT scanner uses 80% less radiation than conventional scanners.
- The 640-slice CT scanner can image the entire heart in 0.275 seconds.
- The scanner possesses fast rotation with considerable detector coverage.
- The Aquilion ONE has the lowest radiation exposure of any CT scanner on the market. For example, a CT coronary angiogram is less than 0.5 mSv.
- For comparison, a 64-slice scan is approximately 5-8 mSv, and an invasive angiogram is around 10 mSv equivalent to 160 chest X-rays.
- The 640-slice CT scanner is able to image the heart in a single rotation.
- Also, this CT scanner has improved the accuracy in imaging of cholesterol-rich coronary artery plaques that cause heart attacks.
- The only CT scanner that can image the heart in patients with irregular heart rhythm.
- The scanner is capable of real-time 4D imaging of moving joints.
- The 640-slice CT scanner has an increased spatial resolution of 0.3mm versus >0.5mm for 64-slice scanners, therefore producing increased image quality.
- Also, the CT scanner can show the real-time function of organs such as blood flow including the ability to visualise lung nodules as small as 1-2 mm.
- #The scanner can also quantify visceral fat deposition which is a significant contribution to CVD risk.

35.7 Coverage area versus slices

Among healthcare professionals, there is confusion that more slices on a CT scanner mean improved images. Evaluating a CT scanner should involve questioning the detector area coverage – primarily measuring how much of the anatomy is being imaged simultaneously. This is an essential fact that the greater imaging area covered will determine the amount of stitching of the images of a particular organ. The less stitching of images will lead to a reduction of artefacts that otherwise would require more time to reconstruct and review images. This is a problem in the movement of the heart and lungs.

The detector area coverage can vary between scanners with the same number of slices because the size of the detectors varies in size on each machine.

For example, the 64-slice systems can range between 19.5 to 40 mm for detector area coverage. However, a system is considered a wide-area detector with an 8 cm coverage or greater. The wide detector systems tend to produce higher sensitivity associated with iterative reconstruction software. This computer software can improve both contrast and spatial resolutions through more powerful workstations.

One reason why healthcare professionals think more slices in better is because they do not have sound knowledge of physics or the technology that is involved in CT scanning. However, there is another consideration when carrying out high-end CT imaging. For example:

Rotation speed

An important factor of CT scanners is the rotation speed of gantry. A good rotation speed will produce faster temporal resolution accompanied by a reduction in motion blur which is essential within the vicinity of the heart and lungs.

The most recent CT scanners have a rotational speed under 300 milliseconds compared to the older models which are in the region of 400-500 milliseconds.

Consequently, the first generation 320 slice CT scanner had a rotation speed of 500 milliseconds. These early machines produce blurred images due to the motion artefacts.

Patient output and cardiac CT considerations

The ultimate aim of a CT scanner is to produce good quality anatomical images with a rapid and efficient workflow to contribute to the diagnosis of the disease state of the patient.

The 64-slice CT scanner is the minimum standard to perform a coronary computed tomography angiogram.

It is essential to consider the patient flow when evaluating particular CT scanner needs. Will a standard 64-slice CT scanner be suitable?

If the demand for CT scanning is high in a particular hospital, then the management may consider a wider area detector such as a 256-, 320-, 640-slice scanner. These machines will have a higher patient output.

Another factor to consider is the cost of purchasing a CT scanner with a wider area detector to deliver faster patient output versus the cost of maintenance etc.

For example, if the hospital is planning to carry out limited cardiac CT scans, then a 64-slice CT scanner with the latest technology will be satisfactory.

The aim is to create an efficient workflow and complete CT scanning of the patient within 15 minutes.

CT Scanner technology to reduce the dose

Today, medical imaging technology has reduced the CT dose that patients receive during the scanning procedure. The objective of the manufacturer is to produce a CT scanner to provide high-quality images at a lower radiation dose.

For example, the cardiac CT scan used to have an average dose of 15 millisieverts (mSv) or higher. However, the latest CT scanners can perform with doses of less than 1 mSv.

It is important not to compromise a patient with cardiac disease by doing a CT scan with a low dose and therefore produce low-quality images. Consequently, an average dose of 5 mSv or below could be used.

A target dose range for cardiac CT scanning may be considered at around 3 mSv or below.

Also, it is vital to understand patient safety by applying low-dose imaging techniques.

Hospitals should invest in advanced CT scanners to help to lower the radiation dose that patients receive.

Improvements in image resolution

The detailed images of smaller anatomical structures are reliant on the spatial resolution of the CT scanner used.

The majority of CT scanners have a spatial resolution of about 0.50. This could be further reduced by developing improvements in detector and software.

For example, Toshiba has been developing a CT scanner with a spatial resolution of 0.25.

However, at a 0.50 resolution, the radiologists can tell whether there is a stent in a vessel, but it is often a blurry image. At a 0.25 resolution, the images can definitely confirm a stent.

Also, the latest model-based iterative reconstruction software can help improve spatial resolution and contrast.

Miscellaneous

Other considerations regarding CT scanners are the sensitivity of the detectors in capturing photons.

A lower radiation dose can be used with more efficient detectors to produce diagnostic-quality images.

Also, post-processed image data is essential. Therefore, iterative reconstruction software is also important for lowering dosages and improving image quality.

Healthcare professionals who evaluate new scanners must have a greater understanding of how the software functions especially the type of iterative software the new CT scanner uses.

Also, powerful workstations must be available to process thousands of images in a reasonable time.

These image datasets could be processed on-site or off-site but may depend on the speed that the data can be transmitted.

35.8 Mars scanner

Phil Butler and Anthony Butler invented the MARS spectral X-ray scanner at the Universities of Canterbury and Otago, New Zealand. It was used to scan a patient and to produce 3-D colour medical images. The MARS spectral X-ray scanner can potentially revolutionise medical imaging by diagnosing and treating many disease states, such as cancer and heart disease.

This computed tomography system provides greater detail of the chemical components within the human body. It is planned for a clinical trial to use the machine to scan orthopaedic and rheumatology patients. The technology to develop the MARS CT scanner was based on the applications used by CERN to locate the Higgs boson particle.

The MARS CT scanner measures the X-ray spectrum to produce colour images instead of black-and-white ones. It is able to distinguish between various components within the body, such as fat, water, calcium and disease markers.

However, conventional black-and-white X-rays only allow measurement of the density and shape of an object.

A small version of the MARS scanner has been used to study cancer, bone and joint health, including vascular diseases that can cause heart attacks and strokes. The promising early results have indicated that spectral imaging will enable more accurate diagnosis and provide personalised treatment.

35.9 How much does a CT scanner cost?

CT prices for scanners vary considerably, including 16-slices, 64-slices, 128-slices and 256-slices. The price ranges are based on new and refurbished CT scanners across the major manufacturers.

16-slice CT Scanners

Popular 16-slice models include GE BrightSpeed-16, GE LightSpeed-16, GE Optima-540, Siemens Somatom Sensation-16 and Siemens Somatom Emotion-16.

- New 16-slice CT scanner from $285K to $360K.
- Refurbished 16-slice CT scanner vary from $90K to $205K.

64-slice CT Scanners

Popular 64-slice models include: GE LightSpeed VCT-64, GE Optima 660-64, GE Revolution, Siemens SomatomDefinitions AS and Toshiba Aquilion Prime.

- New 64-slice CT scanner from $500K to $700K.
- Refurbished 64-slice CT scanner from $175K to $390K.

128+ Slice CT Scanners

Popular 128 + slice models include: GE Optima 660, GE Revolution CT: ES, GE Revolution CT: EX, Siemens Somatom Drive, Siemens Somatom Edge and Siemens Somatom Force.

- New 128-slice CT scanner from $675K to $1M.
- Refurbished 128-slice CT scanners from $225K to $650K.
- New 256+ slice / dual energy scanners cost from $1.350M-$.1M.

Software and Hardware Features

- CT scanners are categorised by their slice count capabilities are depends on a combination of hardware and software.
- Features and upgrades can have an impact on the price of a CT machine. For example, cardiac software can vary between $35K-$100K compared to lung application which may add an extra $15.5K-$35K.

X-Ray Tube

- The price of an X-ray tube can range from $40K-$200K in speciality scanners.

Service and Support

- The price of a CT scanner is only a fraction of the total cost of ownership. Also, you have to consider maintenance, electricity, site planning and operation costs are other components.
- As a benchmark, full parts and labour service contract is typically 10%-14% of the purchase price of the CT scanner.

35.10 The Future

The next generation of computed tomography scanners will be faster, fully automated and easier to use. This technology platform will depend on transitioning from standard CT machines to more advanced systems, improving quantification and quicker diagnosis. The overall emphasis is to assist medical imaging professionals in

limiting the patient's length of stay, thereby reducing cost and improving efficiency. These future CT scanners will be able to consistently deliver anatomical information and contain the ability to characterise anatomical structures within a single scan. Hence, future systems will contribute to clinical pathways providing individual personalised treatment plans. Nevertheless, these future CT advancements require Big Data, and therefore cloud computing will be used to process the considerable amount of data generated by a single CT scan.

Currently, the GE Health Cloud has enormous potential to analyse data from a CT scan, enabling clinicians to formulate a more accurate response to the treatment of the disease state.

The future of CT scanning will be about how to manage massive data sets during image processing.

Another CT growth area will be in chest pain management. In these cases, it is paramount for the patient to undergo evaluation quickly to reduce the time spent in the emergency department and to facilitate a safe discharge. The healthcare sector currently produces vast amounts of diagnostic imaging data but does not have the resources to process it all.

Future healthcare professionals must be able to understand CT technology fully. Also, they must be confident in quantifying and making sense of the generated data. Furthermore and most importantly, to transfer the results to the patient meaningfully, producing more comprehensive treatment plans and reducing overall costs.

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36 Targeting tumours with proton beam therapy

These cancer-destroying machines are capable of providing proton beam therapy via pencil beam scanning.

36.1 Introduction

In July 2018, Simon Hardacre was the first person in the UK to receive high-energy proton beam therapy to treat an aggressive form of prostate cancer at the Rutherford Cancer Centre in Newport, South Wales. This is the only clinic in the UK where high-energy proton beam therapy is available.

Proton beam therapy in the UK has joined the radiotherapy revolution to fight cancer. This new approach is an advanced form of external radiation therapy which uses high-energy protons rather than photons. The Rutherford Cancer Centre operates proton beam therapy delivered by the IBA Proteus®ONE machine in the UK.

The Proteus®ONE is IBA's (Ion Beam Applications S.A.) compact single-room proton therapy solution that can be integrated into the healthcare setting. It is smaller and more affordable than conventional multi-room proton systems, which makes it more accessible to clinical institutions worldwide for the treatment of cancer patients. It uses Pencil Beam Scanning technology to minimise radiation exposure to healthy tissue.

Pencil Beam Scanning Proton Therapy is capable of enhancing accuracy by using an ultra-narrow proton radiation beam.

Therefore, it reduces radiation exposure to the organs and healthy surrounding tissue and lowers the associated risk of side effects.

Also, it increases the types of tumours which can be treated with proton therapy including irregularly shaped tumours which are intertwined with critical tissue and organs.

These cancer-destroying machines can provide proton beam therapy via pencil beam scanning. Consequently, these advances in technology allow the radiation dose to be given to the exact shape of the tumour target volume. During the targeting of the tumour, the patient is positioned on a couch with the most up-to-date imaging capability, which includes cone beam computed tomography allowing the delivery of precise proton beam treatments.

Proton beam therapy is changing the way we manage tumours without causing damage to organs through the technological revolution in radiotherapy, guided imaging systems and treatment planning.

The patient in receipt of proton beam therapy will have a personalised treatment plan according to their own particular needs.

36.2 How does proton therapy work?

Conventional radiotherapy uses high-energy X-rays, which damage DNA within the cancer cells. This process causes the cancer cells to undergo apoptosis leading to cell death. Proton beam therapy can also be used following surgery or after chemotherapy, hormone therapy and targeted drug therapy. The advantage of proton beam therapy is that the proton beams can be targeted to the tumour site and, therefore, limit damage to healthy surrounding tissues: this compares more favourably to conventional radiotherapy. The proton beams can be used to treat complex tumours, which are difficult to remove by surgery due to their proximity to sensitive healthy tissues.

The protons are accelerated to 60% of the speed of light – with a kinetic energy of 250 MeV using cyclotrons and synchrotrons – to penetrate approximately 38 cm into the body. During their journey towards the cancer site, small amounts of energy are transferred to the molecular electron clouds causing a low degree of ionisation.

This process slows the mono-energetic ions down, generating a greater linear energy transfer which results in the braking effect of the proton. At this point, there forms an energy burst known as the Bragg peak towards the end of the proton path. In contrast to X-rays, the proton radiation is deposited at a lower dose in front of the tumour. Consequently, the tissue mass behind the tumour is not exposed to radiation. Therefore, this physical phenomenon makes it possible to determine the depth of the Bragg peak, which considers the modulation of the particle velocity and can focus the radiation within the tumour volume. This process is conducted with absolute precision and therefore improves the ratio of therapeutic radiation to the effects of harmful radiation.

The spreading and shaping are achieved electro-mechanically to treat patients with passively scattered proton therapy. However, a technique that uses magnetic scanning with thin beamlets of protons contains a sequence of energies. Furthermore, the most powerful proton modality is the magnetic scanning technique to treat patients with optimised intensity modulated proton therapy (IMPT).

Applying proton beams instead of X-rays allows medical physicists to increase the therapeutic dose while controlling the dose deposited in healthy tissue. This approach has reduced the radiation deposited in healthy tissue from 43% to 78%, depending on the tumour's shape.

It is planned for the next three years that the UK will have at least six proton beam centres. However, the UK National Health Service will operate two proton centres, and Proton Partners International will control the remainder. This proton beam therapy revolution will enable first-time cancer patients to be treated in the UK. Before this significant revolution, these same patients would have had to travel to clinics in the US and Europe.

It has been predicted that Proton Partners International will reach approximately 6% of cancer patients who receive radiotherapy every year in the UK.

It is also planned to open more proton therapy centres in Northumberland, Reading, Liverpool and London. The aim is to build eight centres in the UK to be branded as 'Rutherford Cancer Centres'.

By the end of 2020, the NHS will operate higher capacity proton beam centres at the Christie Hospital in Manchester and University College London Hospital.

36.3 Proton beam therapy systems used in the clinical setting

Manufacture	Model	Description
Sumitomo	HM SERIES Proton Therapy Cyclotron plus a robotic positioning table including an integrated CT scanner.	This system uses proton beam therapy which contributes to the quality of life of the patient during the treatment of cancer. The treatment method is performed without any incisions. During proton beam therapy, the radiation dosage is concentrated and targeted on the cancer cells. This approach reduces the radiation dose on the surrounding healthy tissues and organs. Therefore, the right amount of radiation reaches the tumour site which may be difficult to achieve with more conventional radiotherapy techniques.
Varian	PROBEAM 360° Proton Therapy Cyclotron plus a robotic positioning table including an integrated CT scanner.	The ProBeam 360° System contains a smaller footprint and is designed for next-generation proton therapy. It can transpose ultra-high radiation dose rates by utilising a 360° gantry with exceptional precision to treat complex cancer sites. Today, the most advanced radiotherapy technology proton therapy plays a vital role in the fight against cancer.
Varian	PROBEAM® COMPACT Proton Therapy Cyclotron plus a robotic positioning table	The ProBeam® Compact single-room solution aims to make proton therapy more accessible. The advantages of the system include a cylindrical treatment room, dynamic peak imaging, patient positioning system, superconducting cyclotron, beam transport system and a 360° Rotating Gantry.

	including an integrated CT scanner.	
Varian	**PROBEAM® MULTI-ROOM** Proton Therapy Cyclotron plus a robotic positioning table including an integrated CT scanner.	The ProBeam® Multi-Room Proton Therapy Solution is capable of delivering the most sophisticated type of proton therapy known as intensity-modulated proton therapy (IMPT), performed by pencil beam scanning. This set up consists of a Patient Treatment Room, 360° Rotating Gantry, Beam Transport System and the isochronous superconducting cyclotron which uses electromagnetic waves to accelerate proton beams.
IBA	**PROTEUS® ONE** Proton Therapy Synchrocyclotron plus a robotic positioning table including an integrated CT scanner.	The IBA's single-room solution known as Proteus®ONE is a compact proton therapy technology. It is the only compact solution that offers Pencil Beam Scanning and minimises radiation exposure to healthy tissue.
IBA	**PROTEUS® PLUS** Proton Therapy Cyclotron plus a robotic positioning table including an integrated CT scanner.	The PROTEUS® PLUS is an IMPT solution which is scalable. It is a personalised approach to image-guided, intensity-modulated, proton beam technology. This enables the centre to treat much more patients suffering from a range of complex cancer conditions.
MEVION ProNova	**MEVION S250** Proton Therapy Synchrocyclotron plus a robotic positioning table including an integrated CT scanner. **SC360** Proton Therapy Cyclotron plus a robotic positioning table	The MEVION S250™ provides the next generation of proton therapy in the clinical setting. This system is built on a gantry-mounted proton accelerator and is capable of delivering a stable uniform proton beam. The ProNova system is capable of delivering proton beam radiation in a lower-cost clinical setting to treat cancer. In the US, over 1.6 million people are diagnosed every year with cancer, and approximately 20% are potential candidates for proton therapy. This system has several features including a 360° treatment angle and

	including an integrated CT and PET scanner	3D anatomical and functional imaging at the isocenter to provide the most advanced Image-Guided Proton Therapy (IGPT) capability. Also, it includes a standard with cone beam CT and PET imaging capabilities. The SMART Pencil Beam Scanning is able to generate rapid IMPT

36.4 Brief History of Proton Beam Therapy

Proton beam therapy has been driven by cyclotron technology since it was first used in 1932 by Ernest Lawrence at the University of California, Berkeley. This was followed in 1937 by the European cyclotron at the Radium Institute, Leningrad and developed by George Gamow and Lev Mysovskii. However, the largest cyclotron is located at the RIKEN laboratory in Japan and is known as the Superconducting Ring Cyclotron (SRC). The SRC weighs about 8,300 tonnes and accelerates uranium ions to 345 MeV per atomic mass unit. The TRIUMF cyclotron based in Canada can produce a field of 0.46 T while a 23 MHz 94 kV electric field accelerates the 300 μA beam.

Proton beam therapy can trace its progress back to the cyclotron physicist Robert Wilson who in 1946 predicted the use of energetic protons in radiotherapy. In the past two decades, proton therapy has become an emerging treatment option for patients with certain types of cancer as there are advantages over conventional X-ray therapy.

In 1985, at the Fermilab conference, James Slater, Leon Lederman, and Philip Livdahl presented the viability of building a hospital-based proton cyclotron. This was endorsed by the interest of Robert Wilson in the medical use of protons for cancer treatment.

Proton beam therapy uses a beam of energetic protons, while x-rays use a photon to irradiate diseased tissue. The protons and photons must travel through the patient's skin and surrounding tissues to reach the tumour volume. Photons have no associated mass or charge and can deliver a dose of radiation by penetrating the tissue. This radiation is delivered to a depth of 0.5 cm to 3 cm from the patient's skin and depends on the initial energy. The energy of the photons diminishes at the tumour target because the radiation ionises the surrounding healthy tissues and the tumour site. Also, the photons leave the patient's body and continue to emit radiation, known as the exit dose.

However, the proton is heavy (equivalent to ~2000 electrons), and as a charged particle, it gradually loses its speed as it interacts with human tissue. This property gives an element of control and delivers a maximum dose at a precise depth: this is associated with the amount of energy obtained from the cyclotron and is capable of a penetration depth of 38 cm. The advantage of using protons over photons is that protons are very fast at the point of entry into the body and therefore deposit only a small dose on the surrounding tissues.

The beam of protons allows the absorbed dose to increase gradually with greater depth and lower speed. This then produces a peak when the proton comes to rest,

known as the Bragg peak. Proton therapy aims to control the proton beam by directing the Bragg peak inside the tumour volume, followed by a burst of energy when the proton suddenly rests during irradiation. The advantage of proton therapy is that it is possible to target tumours within the body and precisely localise the radiation dose with limited damage to the surrounding healthy tissue.

In 1954, the first proton therapy clinic opened at Berkeley treating 30 patients: since 1990, over 17500 patients have been treated. During the development of proton therapy, new guided imaging systems and treatment planning approaches had to be discovered and implemented.

Since the 1970s, proton therapy has been part of the clinical setting in the USA, receiving U.S. Food and Drug Administration approval in 1988. About 100,000 people have received proton therapy at centres throughout Europe, Asia, and the USA.

36.5 Type of Cancer USA Cancer Statistics for 2018

Type of Cancer	USA Cancer Statistics for 2018
Bladder cancer	81,190 new cases of bladder cancer 17,240 US citizens will die from bladder cancer
Brain cancer	23,880 new cases of brain and other nervous system cancers 16,830 US citizens will die from brain cancer
Breast cancer	About 12% of women will be diagnosed with invasive breast cancer during their lifetime 266,120 women and 2,550 men are expected to be diagnosed with invasive breast cancer Breast cancer will claim the lives of 40,920 women and 480 men US citizens
Oesophageal cancer	17,290 new cases of oesophagal cancer are expected to be diagnosed in the US 15,850 US citizens will die from oesophagal cancer
Head, neck and skull base cancer	51,540 people are expected to be diagnosed with oral cavity/pharynx cancer Head and neck cancers result in 3% of US cancer cases 75% of cases of head and neck cancers linked to tobacco and alcohol
Lymphoma	8,500 US citizens will be diagnosed with Hodgkin lymphoma resulting in 1,050 deaths
Liver cancer	40,710 new cases of liver cancer are expected to be diagnosed

	28,920 people are expected to die from liver cancer in the US In the World Liver cancer is a leading cause of cancer-related deaths Liver cancer incidence and death rates are on the rise, with the incidence more than tripling since 1980
Lung and thorax cancer	234,030 people will be diagnosed with lung cancer 154,050 deaths are expected in the US About 80% of all lung cancer deaths are the result of smoking Smoking accounts for approximately 25% of all cancer deaths Men and women who smoke are 25 times more likely to develop lung cancer Up to 20% of Americans that die from lung cancer have never smoked
Pancreatic cancer	Pancreatic cancer ranks as the third deadliest cancer in the US after cancers of the lung and colon 55,440 people will be diagnosed with pancreatic cancer The death of 44,330 US citizens are expected
Paediatric cancer	10,590 US children under age 15 are expected to be diagnosed with cancer in 2018 More than 50% of childhood cancers are leukaemias (30%) or brain and central nervous system cancers (26%)
Prostate Cancer	11% of men will be diagnosed with prostate cancer in their lifetime 2% of men will die from the disease, making it the second most common cause of cancer death in men 164,690 new cases of prostate cancer will be diagnosed in the US Resulting in 29,430 deaths
Sarcoma	Sarcomas account for about 1% of adult cancers and about 20% of childhood cancers. 13,040 new cases of soft tissue sarcoma are expected to be diagnosed in 2018, resulting in approximately 5,150 deaths

	3,450 new cases of bone and joint cancer are supposed to be diagnosed in 2018, with nearly 1,590 deaths

A breakthrough in cancer diagnosis was the development of X-ray computed tomography (CT) in 1970. These imaging machines could generate 3-D scans to provide tumour volume location and the assignment of CT Hounsfield numbers. This information was beneficial for calculating the electron-density distribution required to perform 3-D dose calculations. The development of CT scanning provides the way forward to CT-based radiation technologies in the treatment planning of cancer patients. Subsequently, in the 1980s, the diagnostic tool magnetic resonance imaging (MRI) arrived, which was central to evaluating the disease states in patients.

The primary emphasis of developing diagnostic imaging tools is finding a relationship between a tumour and surrounding healthy tissue. The advantage of MRI over CT is that there is a generation of images with higher spatial resolution and contrast.

During the 1990s, positron emission tomography (PET) imaging joined the diagnostic toolbox in the treatment planning of cancer patients. Then further advancements led to hybrid scanning machines such as PET-CT, which could visualise tumours and provide more detailed images. PET imaging focuses on distinguishing between tumours and normal tissue sites due to their different metabolism rates.

These modern imaging modalities – in conjunction with proton beam therapy – are used to detect the geometric contours of tumours and to ensure that the correct radiation dose is delivered accurately to the tumour site. Also, further advancements in imaging-guided therapy have produced 4-D computed tomography imaging as the basis for respiratory-gated proton beam therapy to limit motion artefacts.

Today, the apex of medical imaging has combined X-ray radiation techniques with proton beam therapy to treat a broad range of cancers and eradicate them. Cancer treatment depends on the physicist's ability to conform the irradiation outline to the tumour volume.

The problem arises when conventional radiotherapy techniques introduce a high risk of damaging surrounding healthy tissues. Therefore, treatment planning is important to reduce radiation dosage, limit damage to the surrounding healthy tissues, and limit other side effects.

36.6 Prostate cancer

According to Cancer Research UK, there are about 14.1 million new cancer cases globally. The top four cancers are lung, breast, bowel, and prostate. Prostate cancer is caused by the uncontrollable growth of cells in the prostate gland. The prostate neoplasm is the most common form of non-skin cancer in men. Nearly 3% of individuals affected die from this disease due to many medical interventions offered to treat prostate cancer.

The application of proton therapy to treat patients with prostate cancer has increased more than 2-fold from 2004 to 2012. Various studies have shown that the rate of proton beam therapy use has risen from 2.3% in 2004 to 5.2% in 2011 and 4.8% in 2012.

36.6.1 Comparison of treatments for prostate cancer

Type of Treatment	Impotence	Infertility	Urinary Incontinence	Bowel Problems
Proton Beam Therapy	Very Low	Very Low	Very Low	Low
Hormone Treatment	High	High	None	None
Radical Prostatectomy	High	High	High	Low
Radiotherapy	Medium	Medium	Low	Medium
Brachytherapy	Medium	Medium	Low	Medium

The overall advantage of proton beam therapy over conventional radiotherapy is the ability to use protons at a higher radiation dosage.

Medical physicists use the emerging concept of theranostics (therapy + diagnostics) to control and manage cancer with the aim of reducing damage to healthy tissue and surrounding organs. Proton beam therapy offers a personalised approach to using radiotherapy to treat cancer.

Advantages of PBT

- Proton beam therapy can precisely target tumours and reduce the exit dose.
- The overall radiation dose in the patient can be lowered.
- The proton beam reduces the side effects of radiation on the surrounding healthy tissues and organs.
- Proton beam therapy is able to deliver an optimal radiation dose to the tumour volume.
- Also, proton beam therapy can be used to treat recurring tumours.
- The quality of life after treatment is significant.
- The long-term and survival rates of using proton beam therapy benefit many tumours.

36.7 Other PBT centres

Proton beam therapy systems are available in at least 24 sites across the United States; this includes a new proton therapy centre at the Miami Cancer Institute. These facilities can cost over $225 million each and have been called the single most expensive medical device ever built. Consequently, treatment costs exceed those of traditional photon external-beam radiotherapy (EBRT) modalities.

The conventional linear accelerator (LINAC) produces radiation by accelerating electrons down a long, straight tube. However, protons require much more energy to cause them to move this can only be achieved using a cyclotron. Cyclotrons can cost up to £100m, and since the advancement of cyclotron technology can be purchased for £25m compared to a conventional radiotherapy machine which costs about £2.5m.

Nevertheless, proton beam therapy is more expensive than conventional LINAC-based radiotherapy and is currently mostly channelled towards paediatric cancers of the brain and spinal cord. In addition, proton beam therapy treatment for the lung and prostate reduces long-term side effects. Also, in patients where the anatomy of a tumour contains critical normal tissues, a dose distribution with protons is the favourable option.

Presently, two proton beam therapy machines are installed at University College Hospital in London and Christie Hospital in Manchester. These will be equipped with large machines which can cost about £80m and require up to 80 staff to manage each machine.

However, the compact models installed by private sector providers for NHS use cost less than £25m and require only 20 staff. That means the cost per single treatment will be far more expensive in the NHS installations.

Therefore, the UCLH/Christie true cost per treatment will approach £5,000, whereas the cost of the compact model will be less than £1,500.

Radiotherapy in the UK urgently requires upgrades since routine radiation machines are over 10 years old. Replacing these machines with modern versions involves an injection of capital, and by 2020 the NHS may produce a £20bn deficit.

Due to an ever-ageing population, there is a requirement for more effective means of delivering the radiation dose to destroy cancer. Therefore, partnerships with the private sector can help the NHS in the area of proton beam therapy. This is by creating advanced radiotherapy networks throughout the UK which use high-energy beams of protons rather than high-energy X-rays to deliver radiotherapy.

The national proton beam therapy service was integral to the Government's Cancer Strategy Improving Outcomes: A Strategy for Cancer (2011).

36.7.1 Particle beam therapy facilities in clinical operation (since February 2019)

Country	City	Institution
Canada	Vancouver	TRIUMF
China	Zibo	Wanjie Proton Bean Therapy
China	Shanghai	SPHIC
Czech Republic	Prague	Proton Beam Therapy Center Czech
France	Caen	Centre Cyclhad / Centre Francois Baclesse
France	Nice	Centre Lacassagne
France	Orsay	Centre de Protontherpie de l'Institut Curie
Germany	Berlin	HMI
Germany	Heidelberg	Heidelberg Ion Therapy Center
Germany	Munich	Rinecker
Germany	Dresden	Universitatsklinikum Carl Gustav Carus
Germany	Essen	Westdeutsches
Italy	Catania	Laboratori Nazionali del Sud
Italy	Pavia	CNAO Pavia
Italy	Trento	Agenzia Provinciale Per la Protonterapia (ATreP)
Japan	Chiba	HIMAC (NIRS)
Japan	Hyogo	HIBMC
Japan	Kashiwa	Japanese National Cancer
Japan	Shizuoka	Shizuoka
Japan	Tsukuba	PMRC
Japan	Fukui	Fukui Proton Cancer
Japan	Matsumoto	Aizawa hospital
Japan	Nagoya	Nagoya University
Japan	Tokyo	Tokyo University
Japan	Sapporo	Hokkaido University Hospital
Japan	Ibusuki	Mediapolis Medical Research Institute
Japan	Koriyama	Southern Tohoku Proton Beam Therapy Center
South Korea	Ilsan	Korean National Cancer
South Korea	Seoul	Samsung Hospital
Netherlands	Groningen	University Medical Groningen (UMCG)
Poland	Krakow	Instytut Fizyki Jądrowej PAN
Russia	St Petersburg	Center of Nuclear Medicine
Russia	Moscow	Institute for Theoretical and Experimental Physics
Russia	Dubna	Joint Institute for Nuclear Research
South Africa	Cape Town	iThemba
Sweden	Uppsala	Skandion Kliniken
Switzerland	Villigen	Paul Scherrer Institut
Taiwan	Tapei	Chang Gung Memorial Hospital (CGMH)
United Kingdom	Newport	The Rutherford Cancer Centre, South Wales
United Kingdom	Clatterbridge	The Clatterbridge Cancer Centre

USA	Baltimore	University of Maryland Medical
USA	Boston	The Massachusetts General Hospital
USA	Chicago	Northwestern Medicine Chicago Proton Center
USA	Cincinnati	Cincinnati Children's
USA	Hampton	Hampton University Proton Therapy Institute
USA	Houston	MD Anderson Cancer
USA	Irving	Texas for Proton Beam Therapy
USA	Jacksonville	The University of Florida Proton Beam Therapy Institute
USA	Jacksonville	Ackerman Cancer Center
USA	Knoxville	Provision Center for Proton Beam Therapy
USA	Loma Linda	Loma Linda University Medical
USA	Miami	Baptist Health South Florida, Inc.
USA	Miami	Baptist Health South Florida, Inc.
USA	Memphis	St. Jude Children s Research Hospital
USA	New Jersey	University Orthopaedic Associates, Inc.
USA	New Brunswick	The Laurie Proton Therapy Center at Robert Wood Johnson
USA	Orlando	Orlando Health UF Health Cancer Center
USA	Philadelphia	The University of Pennsylvania Proton Therapy Center
USA	Royal Oak	Beaumont Hospital
USA	Rochester	Mayo Clinic Hospital Rochester
USA	San Fransisco	UCSF (UC Davis)
USA	Scottsdale	Mayo Clinic Hospital Scottsdale
USA	Somerset	ProCure Proton Therapy Center
USA	Seattle	Seattle Cancer Care Alliance Proton Therapy
USA	Shreveport	Willis-Knighton Cancer Center
USA	St. Louis	Barnes-Jewish Hospital (Washington University)
USA	Washington DC	MedStar Georgetown University Hospital

36.7.2 Particle beam therapy facilities under construction (January 2019)

COUNTRY	LOCATION	START OF TREATMENT PLANNED<
Belgium	ParTICLe, Leuven	2019
China	HITFil at IMP, Lanzhou, Gansu	2019
China	Heavy Ion Cancer Treatment Wuwei Gansu	2019
China	Ruijin Hospital, Jiao Tong University, Shanghai	2019
China	Zhuozhou Proton Beam Therapy Center	2019
China	Guangdong Hen Ju Medical Technologies Co., Guangzhou	2019

China	Qingdao Zhong Jia Lian He Healthcare, Shandong	2019
China	Beijing Roton Center, Beijing	2019?
China	HIMC Center, Hefei, Anhui	2019?
China	Guangzhou Concord Cancer Hospital, SSGKC, Guangdong	2020
Emirate of Abu Dhabi	Proton Partners International, Abu Dhabi	2019
France	ARCHADE, Caen	2023
India	Tata Memorial Centre, Mumbai	2019
India	Health Care Global	2020
Japan	Social Medical Corporation Kouseikai Takai Hospital, Tenri City, Nara Pref.	2018
Japan	Teishinkai Hospital, Sapporo, Hokkaido	2018
Japan	Hokkaido Ohno Memorial Hospital, Sapporo	2018?
Japan	Nagamori Memorial Center of Innovative Cancer Therapy, Kyoto Univ. of Medicine	2019
Japan	Yamagata University Hospital, Yamagata	2020
Japan	Shonan Kamakura Advanced Medical Center	2020
Russia	PMHPTC, Protvino	?
Russia	Federal HighTech Center of FMBA, Dimitrovgrad	2019
Saudi Arabia	King Fahad Medical City PTC, Riyadh	2019
Singapore	National Cancer Center Singapore (NCCS)	2021
Singapore	Singapore Institute of Advanced Medicine Ptc	2020
Slovak Rep	CMHPTC, Ruzomberok	?
South Korea	KIRAMS, Busan	2021?
Spain	Quironsalud Hospital, Madrid	2019
Spain	CUN, Madrid	2020
Thailand	Her Royal Highness Princess Chakri Sirindhorn PTC, Bangkok	2020?
Taiwan	National Taiwan University CC, Taipei	2019
Taiwan	Kaohsiung Chang Gung Memorial Hospital, Kaohsiung	2019
United Kingdom	PTC UCLH, London	2019
United Kingdom	Proton Partners International, Northumbria	2019
United Kingdom	Partners International, Reading	2019
United Kingdom	Partners International, Imperial, West, London	2019
USA	McLaren PTC, Flint, MI	2019
USA	MGH, Boston, MA	2019

USA	UFHPTI, Jacksonville, FL	2019
USA	The New York Proton Center, East Harlem, New York, NY	2019
USA	Sibley Memorial Hospital, Washington DC	2019
USA	Inova Schar Cancer Institute, Capital Beltway, Washington DC	2019
USA	University of Alabama PTC, Birmingham	2020
USA	UM Sylvester Comprehensive Cancer Center, Miami, FL	2020
USA	Delray Medical Center Delray Beach, FL	2020

According to the Particle Therapy Co-Operative Group (PTCOG), at the end of 2017, nearly 200,000 patients were treated globally using particle radiotherapy. This includes 170,500 using protons, 25,700 with carbon-ion radiotherapy, and 3,500 helium ion beams, pions and other particles.

36.8 Conclusion

Currently, proton beam therapy is becoming a more accessible radiotherapy treatment. This is mainly due to the ability of protons to deposit a high radiation dose at the cancer site and limit damage to surrounding healthy tissue. The efficacy of using different radiation modalities to create biological effects in cells by targeting with photons (X-rays) and charged particles (protons) is the radiation weighting factor used to calculate the relative biological effectiveness (RBE).

This is defined as the rate of the doses required by two different radiations to cause the same effect level. When calculating the radiation dose, it is essential that the proton RBE generic value is given a more realistic value regarding the conversion of photon dose to proton dose and is dependent on several factors.

Incidentally, the generic value of 1.1 is used in the clinical setting for protons. Currently, there is uncertainty on this dose-weighting factor which is why there is an unfortunate contribution to normal tissue toxicity.

It has been suggested that the proton RBE should be greater than 1.1 and also that it may vary depending on the position relative to the Bragg peak and the increased linear energy transfer. The uncertainty surrounding the proton RBE value may lead to an undesired increase in the radiation dose: for example, to organs most at risk, such as the brainstem, temporal lobe and optic chiasm, if within the vicinity of the tumour volume. Therefore, to reduce the risk of potential radiation toxicity during proton beam therapy, a more rational approach to assigning RBE values is required. These values must consider the dose per fraction and include an assessment of the tissue type and radiobiological tumour characteristics.

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37 A bright future for robotic surgery

The da Vinci Surgery System is a universal robot used in robotic surgery systems.

37.1 Introduction

Robotic surgery involves minimally invasive surgical procedures that allow doctors to perform complex operations with greater precision and control compared to conventional techniques. The concepts of Cybernetics and Artificial Intelligence are different in many ways. For example, the idea of Artificial Intelligence is to make computers smart compared to Cybernetics which is to understand and build systems that can achieve goals. Therefore, smart computers versus goal-directed systems have developed concepts applicable to robots.

These robotic technology platforms allow for creative interaction between humans and machines. This process, called cybernetics, will deliver innovation through efficient, sustainable and cost-effective products, services and work environments.

Consequently, the robotics and automation revolution is transforming industries such as manufacturing, agriculture, healthcare and transport. For example, just imagine going into the hospital for cardiac surgery done by robotics with no human intervention. In most cases, robotic operations are carried out using the da Vinci Surgical System. However, this is no longer regarded as current news within the healthcare sector.

This is in comparison to robots which are driven by Artificial Intelligence networks with the advancement of nanorobotic surgery, which will produce blockbuster medical devices in the robotics market and definitely make the news! For example, in 2017, a Chinese robot called Xiao Yi, had passed China's National Medical Licensing Examination and scored the first position with 456 points.

The robot's ability to automatically capture and analyse patient information was able to formulate an initial diagnosis. However, the question is as to whether the robot will replace human doctors possibly in the future; at present, the aim is to help improve efficiency. Xiao Yi is part of China's effort to make Artificial Intelligence central to healthcare and fundamental to the national plan to build a 1 trillion-yuan AI-based industry by 2030.

The word 'robot' was first coined by the Czech writer Karl Capek for his 1920 science fiction play R.U.R (Rossum's Universal Robots). However, Karl Capek did not invent the word robot, although his brother, the cubist painter Josef Capek suggested using the

word ‘robot’. Also, the robotic theme was presented by Isaac Asimov in his 1941 story Liar and Runaround.

Runaround was first published in the March 1942 issue of Astounding Science Fiction and appeared in the following works: I, Robot (1950), The Complete Robot (1982), and Robot Visions (1990). Runaround featured Isaac Asimov’s – The Three Laws of Robotics:

1. A robot must not be in danger to a human being and prevent a human being from coming to harm.
2. A robot must carry out orders given by human beings only if it does not conflict with the First Law.
3. A robot must defend its own existence only if it does not conflict with the First or Second Law.

The economic benefits of robots are enormous, especially in the reduction of waiting lists for patients undergoing operations. The opinion is that robotic surgery is safer than open surgery. Also, the hospital stay is shorter, and therefore the potential risk of infection is reduced. Another benefit of robotic operations is that it limits blood loss, and therefore, there is a reduction in transfusions and also faster patient recovery.

These robots can work without rest and evaluate the disease state of patients more effectively than their human counterparts. Wireless medical imaging data can be transferred to the robotic doctor to generate a potential diagnosis for the patient. These robotic surgeons are also able to perform various minimally invasive procedures.

Today, robotic surgery is not entirely automated and consists of miniaturised surgical instruments mounted on the robotic arm operated by surgeons. The surgeons control these instruments remotely by using cameras located in the operating room. In 2017, the robotic surgery statistics released by iData Research stated that 693,000 robotic-assisted procedures were performed in the US.

These precision technologies have boosted the surgical robotics market and are expected to reach $98.7 billion by the end of 2024. The most used robotic system is the da Vinci Surgical System, and since 2000 has been used in more than 1.5 million surgeries.

The overall market for 2017 for robotic surgical systems was valued at over $2.4 billion. This market value included minimally invasive surgery such as laparoscopy, gynaecological, digestive tract, urological, cardiac surgeries and colorectal. In addition to radiosurgery, orthopaedic robotic-assisted systems, robotic surgery equipment for spinal surgery and neurosurgery.

The idea of using remote surgery can be traced back to the 1970s when NASA was experimenting with the concept by applying it to astronauts in orbit. The premise was that a surgical machine located on a space station could be operated by a surgeon on

Earth. Other programmes included DARPA (Defence Advanced Research Projects Agency), which was involved in developing concepts of remote surgery on the battlefield.

In 1985, the first robot-assisted surgical procedure was performed on a patient using the PUMA 560 robotic surgical arm to carry out a neurosurgical biopsy. This procedure demonstrated the potential for greater precision when used in minimally invasive surgeries, such as laparoscopies which typically utilise flexible fibre-optic cameras. Consequently, this procedure was completed with greater accuracy – free from hand tremors – during the needle insertion.

In 1987, the first cholecystectomy was also carried out using the same system and, in the following year, robotic surgery transurethral resection. Then in 1990, the AESOP system was approved by the Food and Drug Administration (FDA) for its endoscopic surgical procedure.

In 1988, PROBOT was developed at Imperial College London to perform transurethral prostate surgery. This led to other robotic systems, and in 1992, ROBODOC was jointly developed by Integrated Surgical Systems and IBM for hip replacement in human patients.

The advancement in robotic telesurgical concepts and in telecommunication technologies enabled the 2001 Lindbergh Operation. The French physician Jacques Marescaux and surgeon Michel Gagner performed a remote removal of the gallbladder while based in New York City to a patient in Strasbourg, France. This was a significant breakthrough; however, telesurgery failed to gain widespread popularity.

In 2000, the FDA gave approval for the da Vinci Surgery System to become the first robotic to perform general laparoscopic surgery.

37.2 Da Vinci surgery system

Leonardo da Vinci studied the anatomy of the human body under the direction of Andrea del Verrocchio. As an artist, he quickly became a master of topographic anatomy, drawing many studies of muscles, tendons and other visible anatomical features. The da Vinci robot is named after Leonardo da Vinci, who envisaged the future of tetrapod robots.

The da Vinci Surgery System is the most universal robot used in robotic surgery systems: since 2017, there have been approximately 4,271 installed within the healthcare sectors. Moreover, this included 2,770 in the United States, 719 in Europe, 561 in Asia, and 221 in the rest of the world. The da Vinci system used worldwide is designed to perform various minimally invasive surgeries and has been the subject of more than 7,000 peer-reviewed publications and studies. The number of procedures performed throughout the world using the da Vinci robotic system are 1998 (127); 1999 (321); 2000 (1,031); 2001 (2,478); 2002 (5,075); 2003 (9,500); 2004 (16,288); 2005 (26,809); 2006 (49,038); 2007 (85,447); 2008 (132,454).

The da Vinci Surgery System consists of three main parts: the surgeon console, instruments that mimic the human wrists and a viewing system. The principle of the da Vinci Surgery System was that it behaved like a 'slave' system. This is because the surgeon operates from the remote console, which contains the 'master controllers.' The objective of these controllers was to provide direct movements of the binocular camera and to initiate the wrist-mimicking instruments. Several surgical instruments are attached to a cart which is positioned alongside the patient. These instruments are placed in the surgical field by the surgeon before initiating the procedure.

The 3-D surgical view is transported at a monitor to enable spatial relationships of the instruments while a surgeon is at the console. These included: remote console and surgeon, the elimination of unwanted motion and minimally invasive access.

Hence, the removal of unwanted tremors by the action of the robotic arms, which mimic the movements of the human hand. This approach produced a high degree of skill in tight spaces and is capable of generating 3-D visualisation using the binocular camera system.

At the beginning of 2018, a patient had pioneering robotic heart surgery and was recovering at home just 2 days later. The patient was one of the first to benefit from the UK's only robotic heart and lung surgery programme at Liverpool's Heart and Chest Hospital. The robot was used to repair a damaged mitral valve. The team of robotic surgeons were able to perform up to 300 heart and lung procedures in their first year.

A Robotic Surgeon is routinely used to perform prostate cancer surgery. In addition, these robots can be used in cardiothoracic surgery to perform endoscopic coronary artery bypass grafting, mitral valve and atrial septal defect repairs. They have also been used for liver resection, pancreatectomy and liver transplantation. Further robotic applications include bariatric surgery, bowel resection, oesophageal fundoplication and cholecystectomy. In gynaecology, robotic surgery has been utilised in hysterectomy and fibroid removal. Other robotic procedures include sleep apnea surgery, paediatric surgeries, and renal cancer procedures, including kidney transplants.

The use of robotic surgical systems – in conjunction with image guidance – such as magnetic resonance imaging (MRI) will lead to minimally invasive surgery, especially in sectors where visualisation would be problematic such as neurosurgery. Also, systems that use infrared or ultraviolet light sources will aid precise movement during surgical operations. In addition, fibre-optically delivered lasers and ultrasonic vibratory devices will enable further interaction with multiple tissue types and allow for selective destruction while not damaging healthy tissues.

The advancement of digital cameras will transform the next generation of small robotic systems to enable surgery to be performed in deep tissue. Also, the development of haptics, which is an area of tactile feedback technology, will improve precision movements in robotic surgical systems and therefore give less stress to the patient.

There are several FDA-approved devices and platforms for robotic surgery, and these include the da Vinci Surgical System, Sensei X Robotic Catheter System, FreeHand 1.2 and the invendoscopy E200 system. Also approved are Flex® Robotic System, Senhance, ARES, the Single-Port Instrument Delivery Extended Research (SPIDER) and the NeoGuide Colonoscope. Other technology platforms waiting for FDA approval include MiroSurge, ViaCath System, Miniature In Vivo Robot, Master and Slave Transluminal Endoscopic Robot, SPORT™ Surgical System, Einstein Surgical Robot, Verb Surgical, SurgiBot and the Versius Robotic System.

37.3 Robotic surgery timeline

Surgical System		Developer	Applications
1961	UNIMATE	Unimation, Inc., USA	First industrial robot in the USA
1967	Versatron	American Machine and Foundry	First industrial robot in Japan
1978	Unimate	Unimation, Inc., USA	Electric motor based programmable miniaturised version of Unimate
1979	Definition of "Robot" established	Robot Institute of America	Reprogrammable, multifunctional manipulator which is designed to move materials, parts and tools. Also, specialised devices through various programmed motions for the performance of a variety of tasks
1980s	Telepresence surgical systems	Stanford Research Institute (SRI) & National Aeronautics and Space Administration (NASA) Ames Research	Anastomosis of femoral arteries
1980s	SRI Green Telepresence Surgical System	SRI & US Department of Defence	Open surgery - military applications
1980s	SRI Green Telepresence Surgical System	Bowersox and Cornum	Nephrectomy, cystotomy closure, ureteral anastomosis
1988	PUMA	Imperial College, London, UK	Transurethral prostate resection

Late 1980s	SARP (Surgeon Assistant Robot for Prostatectomy)	Imperial College, London, UK	Transurethral prostate resection
1991-1997	PROBOT (Robot for prostatectomies)	Harris	Transurethral prostate resection (TURP)
1990s	ARTEMIS system	Schurr	Procedures in animal models
1993	HERMES	Computer Motion, Goieta, CA	Voice-controlled integration of operative room components
1993	AESOP (Automated Endoscopic System for Optimal Positioning)	Computer Motion, Goieta, CA	Laparoscopic abdominal surgery
1997	Prototype of da Vinci surgical system	Intuitive Surgical, Sunnyvale, CA (founded 1995)	Laparoscopic surgery
Late 1990s-2001	URobot	Nanyang Technological University (NTU - Singapore)	TURP, prostate biopsy, brachytherapy seed placement
1997-2002	PAKY (Percutaneous access to the kidney)	Johns Hopkins University & Medical Centre	Percutaneous access to kidney
1998	Surgeon programmable urological device (SPUD)	NTU & Dornier Asia medical	TURP, prostate biopsy, brachytherapy seed placement
2000	da Vinci Surgery System	Intuitive Surgical	Da Vinci robotic system FDA approved
2000	da Vinci Surgical System	Intuitive Surgical, Sunnyvale, CA	Laparoscopic surgery
2000	da Vinci Surgery System	Intuitive Surgical	Used for hysterectomies and prostate removals
2001	Zeus Surgical System	Computer Motion, Goleta, CA	Laparoscopic surgery
2001	Socrates Robotic Telecollaboration System	Computer Vision	Used for sharing control of AESOP 3000 from different locations

2003			Merger of Intuitive Surgical & Computer Motion
2004	Robotic system	Johns Hopkins University	Trans-rectal ultrasound-guided biopsy of the prostate
2005	The Raven I	University Of Washington	Used for open-surgery and MIS
2006	Robotic system for TRUS guided brachytherapy	Johns Hopkins University	Trans-rectal ultrasound-guided brachytherapy
2006	Type S da Vinci robotic system	Intuitive Surgical, Sunnyvale, CA	Laparoscopic surgery
2007	NeuroArm	University of Calgary and MacDonald Dettwiler Associates	Used in neurosurgery for both biopsy and microsurgery
2009	Type Si da Vinci robotic system	Intuitive Surgical, Sunnyvale, CA	Laparoscopic surgery
2009	Robotic Doppler Micro Probe	Vascular Technology, Nashua, NH	Doppler for vascular identification during robotic microsurgical procedures
2009	Robotic Doppler MicroProbe	Vascular Technology	Used for vascular identification in robotic microsurgical procedures
2009	iDrive Intelligent Power Unit	Power Medical Interventions	Used for resecting and transecting tissue as well as for creating anastomoses between structures
2010	SOFIE "Surgeon's Operating Eindhoven" Surgical Robot	Eindhoven University of Technology	1st surgical robot based on force feedback
2012	The Raven II	University Of Washington and UC Santa Cruz	Open-Source surgery robot
2012	Amadeus Robotic Surgical System	Titan Medical	Used for laparoscopic surgery
2018	Versius surgical robotic system	CMR Surgical, England	Laparoscopic surgery

37.4 The robotic revolution

The healthcare sector is booming with surgical robots, and the top 7 companies include:

Company	Developments
Intuitive Surgical	Da Vinci Surgical System, which uses the 3-D HD vision system to function.
Hansen Medical	Developed two medical robots called the Magellan and Sensei X robotic systems, which can perform cardiac and vascular surgeries.
Medrobotics	Launched a robot-assisted platform called Flex Robotics System. This system was to support surgeons in their operations by reaching out to anatomical parts of the human body.
Verb Surgical	Aims to build a digital surgery platform implementing AI, including data analytics. Also, using advanced visualisation and instrumentation.
Microbot Medical	Developing new technologies for surgeries.
Titan Medical	Developing the SPORT Surgical systems to cover areas that have not been explored, like abdominal, gynaecological and urologic operations.
CyberKnife System	The Cyberknife System is a fully robotic radiation delivery platform. It works on treating cancerous and non-cancerous tumours.

37.5 Advantages of robots

- The application of robotics in medicine allows the advancement of new medical techniques.
- Robots offer precision, reliability, performance and speed during surgical operations.
- Robotic technology is able to be exposed to
- The surgical robot systems do not experience fatigue or tremor.
- Video cameras can be incorporated into the robotic equipment to record the operation.
- Surgical operations can be carried out from different parts of the world.

37.6 Disadvantages of robots

- The main problem with robotic technology is the high cost of equipment and
- Surgical robot systems and equipment require advanced software.
- Technological equipment, machines and robotic systems will become obsolete due to the advancement of robotic and Artificial Intelligence platforms.

37.7 Conclusion

At present, the robotic surgery platform is dominated by the da Vinci system, which has been in operation in the UK since 2001. The da Vinci system is mostly used to perform prostate, bladder and gynaecological surgeries. In 2016, the essential patents for the da Vinci system expired, and this will encourage other companies to enter the field of surgical robotics. Alphabet has partnered with Johnson & Johnson to form the start-up Verb Surgical. This new venture aims to develop robotics and machine learning tools for surgery. Also, Verb Surgical aims to have robots connected to the internet by 2020 so they can learn from each other.

However, Medtronic, the world's largest medical device company, also has a surgical robot due for release in 2019. All of these developments will make robots an essential feature in the operating theatre. The present generation of robots is more versatile, compact and cost-effective. This means they can deliver robotic surgery locally, meaning surgery is not required to take place in large hospitals.

British scientists have developed the world's smallest surgical robot, which can transform everyday operations for tens of thousands of patients. The robot, called Versius, mimics the human arm and can be used to carry out a wide range of laparoscopic procedures. These include hernia repairs, colorectal operations and prostate, including ear, nose and throat surgery. The Versius robot will be the first made-in-Britain surgical robot and is expected to receive a European health and safety approval mark by 2019.

In the future, robotic surgeons will be more involved in the healthcare requirements of individuals. Robots require a communication link and applications that connect the robots to their clients or users. These communication links are usually supported through client/server network connections. Therefore, the networking system is vulnerable to cyber-attacks, and consequently, the security and privacy of the robotic platforms is paramount.

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38 Targeted radionuclide therapy towards precision cancer treatment

Targeted radionuclide therapy was first used to treat cancer for an 'over-active' thyroid using radioactive iodine-131 seeds.

38.1 Introduction

Targeted radionuclide therapy, such as targeted alpha therapy, is a new approach to the treatment of cancer, and this blog article will provide a general overview of the current status. This kind of therapy was first used to treat cancer for an 'over-active' thyroid using radioactive iodine-131 seeds. These seeds concentrate in the thyroid gland and emit strong gamma and beta particle radiation to kill the cancer cells leaving the healthy cells mostly intact.

Over the past decade, there has been considerable interest in developing targeted radionuclide therapy to treat lymphoma and liver cancers. The radioactive source can be tagged to biological peptides, drug substrates and monoclonal antibodies. The activity is transported to the cancer site, and the cancer cells are then killed.

Monoclonal antibodies have been used in the treatment of lymphomas but are proving unsuccessful in the treatment of solid tumours. To circumvent these issues, low molecular weight drug molecules have been designed to deliver high doses of radiation via emitting radiometals and also to recognise certain receptors on the surface of solid tumours. This has been successfully demonstrated with the use of somatostatin analogues to treat neuron-endocrine tumours and metastatic liver cancers where surgery is not viable.

38.2 Alpha particles

The therapeutic potential of several alpha particle-emitting radionuclides has been assessed to treat a range of cancers. Alpha particles are positively charged and have a mass of four units and a charge equal to that of the helium nucleus. The energy range for alpha particles is between 5 and 9 MeV. These highly charged particles can travel between 5 and 10 cell widths in living tissues. They travel in straight lines and leave energy of about 80 to 100 keV/μm in their path. The maximum rate of energy increases to approximately 300 keV/μm at the end of each track.

When considering the use of alpha particles for cancer treatment, it is important to consider the molecular distance from the point source (the radionuclide) – during the decay of the radionuclide – from the nucleus of the tumour cell. The other factor is the interaction of the alpha particle when bound to the DNA in cancer cells.

Hence, when radionuclides decay, they emit a quantity of energy and accumulation in the tumour – which can result in the death of cancer cells – leaving the healthy cells with minimum damage. Therefore, to destroy a cancer cell, the high-energy alpha-emitting particle must be contained within the volume of the tumour.

38.3 Linear energy transfer

In 1927, the researchers Regoud and Lacassagne used alpha-emitting radionuclides to target tumours due to their high linear energy transfer properties. When these alpha-emitting radionuclides are conjugated to carrier molecules such as drug substrates, peptides or monoclonal antibodies, they are capable of delivering a radiation dose to tumour cells. The accumulation of the radiation dose inside the tumour causes the cancer cells to die, leaving the majority of normal cells to function properly.

Various studies have shown that the ideal radionuclides for targeted radiotherapy must have all these basic characteristics:

- The energy emitted from the electrons of the radionuclide should be lower than 40keV
- The photon-to-electron emission ratio should be within 2 units
- For practical and treatment purposes, the half-life of the radionuclide must be within the range of 30 minutes to 10 days
- To generate 'medical' radionuclides, the daughter radionuclide must be stable with a half-life higher than 60 days
- The radiochemical transformations must be able to incorporate the radionuclide into the carrier substrate in an efficient and timely manner.

The critical factors which make an excellent radionuclide to kill cancer cells selectively are the linear energy transfer (LET) and relative biologic effectiveness (RBE) of the emitted particles. The property LET is a measure of the number of ionisation taking place when a charged particle passes through a number of cell widths.

These doubly charged alpha particles have a high LET value of approximately 100 keV/μm compared to beta particles which have a low LET value of 0.2 keV/μm. The other property RBE refers to is a measure of dose relating to x-rays and is called reference radiation; this is closely related to LET.

The extent of damage to cells varies between low and high LET radiation values. At high LET levels, double-stranded DNA tends to break down compared to low LET levels. It has been calculated that LET ranges are of the order of 100–200 keV/μm, causing maximum breaks in tumour DNA. This is because the ionisations equate to the distance between the double-stranded DNA.

Therefore, the advantage of using alpha emitters is that they do not destroy all the healthy cells in the vicinity of the cancer cells. For example, the alpha emitter bismuth-213 – coupled with the anti-CD33 monoclonal antibody – has been used to treat myeloid leukaemia.

38.4 Targeted alpha therapy

To develop targeted alpha therapy into a viable treatment for cancer, there is a need to supply the alpha emitter radionuclides at the site where the radioactive drugs are to be prepared and delivered. The most popular radionuclide generator over the last twenty years uses the actinium-225/bismuth-213 radionuclide combination.

Hence, bismuth-213 emits both alpha and beta particles and mostly decays to give the alpha emitter polonium-213. Pre-clinical trials using bismuth-213 with an associated half-life of 46 minutes and actinium-225 with a half-life of 10 days have been successful in the treatment of a variety of cancers, including leukaemia, melanoma, and lymphoma.

In various nuclear medicine departments, in excess of 130 patients have received this novel treatment targeted alpha therapy by using the alpha emitter's bismuth-213 or actinium-225 coupled to peptides and monoclonal conjugates.

A new radionuclide generator is capable of producing 100 mCi of bismuth-213 from the parent actinium-225 for the synthesis of radionuclide-antibody conjugates. The set-up of the generator contains a prefilled syringe of hydrochloric acid connected to an organic resin containing another syringe filled with actinium-225 and a hydrochloric acid mixture. This mixture produces the alpha emitter bismuth-213 under negative pressure and is able to generate six doses of bismuth-213 every 24 hours.

To be able to prepare radioimmuno-pharmaceuticals a source of the radiometal must be generated and have a realistic half-life. One of the best radiometals which fit this criterion is the use of bismuth-213, which has a half-life of 46 minutes. This alpha-emitting radiometal is central to targeted alpha therapy and has been used in human clinical trials to kill leukaemia cells when conjugated with the monoclonal antibody HuM195.

These alpha-emitting particles possess cytotoxic properties and 'selectively' kill tumour cells due to their short-range and high LET value. Most importantly, they tend not to damage many of the surrounding normal functional cells. The generation of bismuth-213 and the preparation of the radiopharmaceutical are completed within 30 minutes (using an automated radiochemical synthesis set-up). During the synthesis of the radiopharmaceutical, the activity of bismuth-213 can be reduced by one third.

To circumvent these large activity losses, a process has been developed where the activity is eluted off directly into the actinium-225/bismuth-213 generator and the 'naked' bismuth-213 is eluted off directly into the buffered antibody solution. The addition of the chelator DTPA is then mixed with both the bismuth-213 and the antibody. The whole process can take about 10 minutes, and after anion exchange purification, the radiopharmaceutical drug can be injected into the patient.

38.5 Metastatic melanoma

Targeted alpha therapy is used in the treatment of metastatic melanoma by using the monoclonal antibody 9.2.27. This monoclonal antibody is tagged to the chelator DTPA containing the alpha emitter bismuth-213. The resultant immuno-conjugate is then

used to carry out an assessment of the patient by using tumour imaging-specific biomarkers to look at the changes in tumour growth.

A study of 22 patients with stage IV melanoma metastatic cancer was treated with a range of activities ranging from 55 MBq to 947 MBq. The cancers were assessed using the RECIST criteria (Response Evaluation Criteria in Solid Tumours). The outcome of this therapy showed 14% of the patient group gave a partial response with 30% leading to progressive disease.

However, the usage of tumour marker melanoma inhibitory activity protein (MIA) showed a reduction over a period of two months in most of the patients. This group of patients showed no toxic side effects, demonstrating that targeted alpha therapy could be a safe and effective treatment for metastatic melanoma.

Alpha emitting immuno-conjugate bismuth-213-DTPA-9.2.27 was assessed for its application in targeted alpha therapy to kill melanoma cancer cells. The radioconjugate, bismuth-213-DTPA-9.2.27 used in vitro and in vivo biological systems have been employed in a number of small clinical trials to study pharmacokinetics and toxicology profiles in the treatment of melanoma.

A melanoma in its metastatic cancer state has to develop through a number of stages. During the advanced stages of tumour development, cancer cells are diffused out of the tumour site into the lymphatic circulation system. These free-flowing cancer cells can then group together and infiltrate the body's vital organs. On mass, they can then impede the functions of that particular organ and eventually lead to organ failure.

The key to understanding metastatic cancer is to work out the bio-mechanism of how antigens help the spread of cancer cells. Consequently, future radiopharmaceuticals can be designed to treat and target melanomas.

38.6 Targeting gliomas

Gliomas are associated with 'adult' brain tumours and stem from the glial part of the brain. They become malignant due to the high concentration of neurokinin type 1 receptors on the tumour. Brachytherapy is used to treat these gliomas by inserting radioactive iodine-125 seeds into the tumour site. This approach is very effective for low-grade gliomas. Unfortunately, for the treatment of high-grade gliomas, a therapy is required that diffuses the activity onto the surface of the tumour. In order to circumvent these problems, it is necessary to design selective cytotoxic radiopharmaceuticals which can find and latch onto the neurokinin type 1 receptors.

Therefore, it was necessary to use the radionuclide bismuth-213 with a half-life of 46 minutes. This alpha emitter was chelated and attached to a low molecular weight drug, which was able to transport the activity to the surface of the tumour, where it is able to spread out over the entire tumour volume in order to kill it. The radiopharmaceutical drug which was used in the study was [DOTAD-Phe-Tyr]-octreotide.

Previous studies have shown that the DOTAD moiety was able to chelate the radionuclides yttrium-90 and indium-111 and target somatostatin type 2 receptors on gliomas. This approach was taken further to design a novel peptide that can specifically target the neurokinin type-1 receptor in malignant gliomas.

The ligand used in this case was substance-P and is based on a tachykinin neuropeptide. Interestingly, neurokinin type-1 receptors have also been located in the central nervous system and appear in lesions of patients with multiple sclerosis.

Consequently, the chelator (DOTAGA) was conjugated to the arginine amino acid residue of the eleven-unit peptide Substance-P to generate the (DOTAGA-Arg-Substance-P). This radiopharmaceutical peptide was then administered to 20 patients in a pre-clinical study to assess its effects on gliomas.

The study concluded that 13 patients showed tumour shrinkage and further clinical trials were needed to evaluate the targeted alpha therapy approach for the treatment of advanced brain gliomas.

38.7 Conclusion

The incorporation of alpha particles into the design of the drug has many advantages, including short-range, high LET and high energy leading to high radiobiological effectiveness (RBE). Therefore, bismuth-213, which has a 46-minute half-life, can be incorporated into radiopharmaceuticals due to its easy generation from the actinium-225/bismuth-213 generator, with a 10-day half-life. This allows actinium-225 to be transported to hospitals and research laboratories to allow radiochemists to design effective targeted alpha therapy drugs to kill melanoma and other types of cancer.

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39 What is myocardial perfusion imaging of the heart?

The most commonly used medical radioisotope in diagnostic procedures is technetium-99m

39.1 Introduction

The most commonly used medical radioisotope, especially in myocardial perfusion, is the metastable nuclear isomer of technetium-99 and is known as technetium-99m (Tc-99m). This radioisotope was discovered in the 1950s by Walter Tucker and Margaret Greene at the Brookhaven National Laboratory. The first article on the use of technetium as a medical tracer was presented by Powell Richards at the 7th International Electronic and Nuclear Symposium in Rome in June of 1960. Paul Harper was the first person to purchase a technetium-99m generator from the Brookhaven National Laboratory to investigate blood flow measurements in patients. During these experiments, he observed the rapid uptake of technetium-99m in the thyroid gland, especially in brain tumours. In 1976, Powell Richards developed the first kit for labelling red blood cells, and the subsequent development was made between 1963 and 1966 in the area of diagnostic imaging.

Currently, technetium-99m is the major workhorse in Nuclear Medicine departments throughout the world. This is because of its gamma-ray energy of about 140 keV, which makes it suitable for detection. Also, both its physical half-life and its biological half-life are very short, which leads to rapid removal from the human body after an imaging scan. Technetium-99m only emits gamma radiation in the imaging process. There is no beta emission which allows for a more precise alignment of imaging detectors.

Technetium-99m is produced by bombarding molybdenum-98 with neutrons. The resultant molybdenum-99 decays with a half-life of 66 hours to the metastable state of technetium. This process permits the production of technetium-99m for medical purposes. Since molybdenum-99 is a fission product of uranium-235 fission, it can be separated from other fission products and then used to generate technetium-99m. For medical purposes, the technetium-99m is used in the form of pertechnetate (chemical formula $TcO4–$).

Technetium-99m has a half-life of 6.03 hours – gamma emission – which is longer for an electromagnetic decay compared to 10-16 seconds. This emission leads to a long half-life for the excited state and decays to a metastable state assigned by 99m. The dominant decay mode generates a gamma ray at 140.5 keV.

The isotope of choice for routine labelling of kits for diagnostic work is technetium-99m. This radionuclide has a gamma photon emission that can be used with the gamma camera with no associated beta emission, therefore minimising the radiation exposure to the patient. The chemical properties of technetium-99m also mean that it binds well to the tracers contained in the kits. Other radioisotopes are also used, for example, indium-111, iodine-123, selenium-75, fluorine-18.

39.2 Cardiac nuclear medicine imaging

Myocardial Perfusion is a nuclear medicine examination of the heart – the myocardium. This technique can be used to evaluate coronary artery disease (CAD) and cardiac stress. Technetium-99m tetrofosmin (Myoview™) is a radiopharmaceutical with many applications in nuclear medicine to generate cardiac images. These myocardial perfusion scans play an essential part in the non-intrusive evaluation of coronary artery disease, thereby providing prognostic information regarding potential cardiac events for the patient. New radionuclides are being investigated for myocardial perfusion: particularly the use of rubidium-82. The aim is to reduce radiation exposure to the patient of technetium-99m. A complete myocardial perfusion examination can be accomplished under a radiation dose of 3 mSv.

39.3 SPECT imaging

SPECT imaging (single-photon emission computed tomography) is a nuclear medicine tomographic technique which detects gamma radiation through a gamma camera. It is used to generate 3-D images from the distribution of a gamma-emitting radionuclide which is administered via the bloodstream. SPECT emits a gamma array which is in contrast to the positron emitters (fluorine-18) employed by PET (positron emission tomography). These SPECT radiotracers include the technetium-99m. This is a metastable nuclear isomer of technetium-99 compared to indium-111, iodine-123 and thallium-201.

In addition, gaseous xenon-133 has been used in diagnostic inhalation with the usage of a gamma camera. These cameras include the scintillation detector, collimator, sodium iodide crystals and several photomultipliers. Also, imaging of cerebral blood flow is of interest, and several studies are using SPECT radiopharmaceuticals, but these are mostly technetium-99m agents.

These technetium-99m agents contain technetium-99m pertechnetate, technetium-99m DTPA (diethylene-triamine-pentaacetate) used in renal imaging, technetium-99m gluceptate (Tc-GH), technetium-99m exametazime (Tc-HMPAO) and technetium-99m bicisate (Tc-ECD). All gamma radiation emitted from SPECT imaging agents are detected by rotating a gamma camera around the patient to produce 3-D imaging. The generated images undergo several electronic transformations in relation to the distribution of the radiotracer by the application of tomographic techniques.

The radioisotopes used in SPECT imaging have a relatively long half-life; for instance, technetium-99m (t½ = 6 hours), iodine-123 (t½ = 13.22 hours), indium-111 (t½ = 2.8

days), and thallium-201 (t½ = 73 hours). The radionuclide technetium-99m is prepared from molybdenum-99 by using a generator.

These technetium-99m radiopharmaceuticals are relatively cheap compared to PET and fMRI imaging. The main issue with SPECT imaging is reduced spatial resolution. However, the increase in radioactivity of the radiopharmaceutical may contain some safety issues concerning the preparation and dispensing of the radioisotopes.

In some cases, the radionuclide is attached to a specific ligand to produce a radioligand complex. This complex allows the radiopharmaceutical to be transported and localised in a particular part of the body. At the location, the radiopharmaceutical will emit radiation which will be detected by a gamma camera to generate 3-D images.

39.4 Hybrid scanners

The diagnostic modalities employed to study the brain include computerised tomography (CT) and fMRI (functional magnetic resonance imaging). This includes the radiopharmaceuticals used for SPECT and PET. Also for hybrids of PET-CT, SPECT-CT and PET-MRI scanning systems. These hybrid scanning machines are able to identify anatomical construction and contain the diagnostic power to recognise a particular disease pattern. This allows a personalised treatment plan for the patient.

The Brain imaging arsenal contains SPECT and PET radiopharmaceuticals. Recent developments in PET imaging aim to design selective agents for different types of tumours, related cognitive diseases and motor indisposition.

Accordingly, SPECT and SPECT-CT imaging of the brain plays a primary role in patient diagnosis. These brain imaging modalities contain photon-emitting agents to evaluate epilepsy as well as different cerebrovascular states.

The scanner spatial resolution for clinical SPECT is between 8-12 mm compared to clinical PET 4-6 mm. However, preclinical SPECT ≤ 1 mm compared to preclinical PET 1-2 mm. The clinical gamma cameras have a tomographic spatial decision of approximately 10 mm.

Furthermore, certain preclinical SPECT scanners can provide a submillimetre spatial resolution. Subsequently, further modifications using several pinhole systems can exhibit a spatial analysis below 1 mm. In addition, the clinical and preclinical PET scanners have a spatial separation of 1-2 mm and 4-6 mm relatively.

Developments in PET scanners have generated an amended spatial resolution of approximately 2.5 mm and continuing research is providing a spatial resolution of less than 1 mm. This is achieved by using lutetium orthosilicate (LSO) crystals with applications in the concept of micro-SPECT as a diagnostic screening tool.

39.5 Diagnostic imaging kits

Diagnostic imaging kits containing technetium-99m labelled exametazime (Ceretec™) are used to evaluate blood flow within the brain, especially after a stroke, epilepsy, Alzheimer's disease and migraine. This radiopharmaceutical is not charged and is lipophilic with a low molecular weight which enables the passage through the blood-

brain barrier. Therefore, the maximum uptake of technetium-99m labelled exametazime into the brain occurs within one minute after the in vivo administration, and about 7% of the injected dose reaches the brain.

Diagnostic imaging of the heart is made possible using the technetium-99m labelled tetrofosmin (Myoview) and sestamibi (Cardiolite). Both these cardiac imaging agents are used to evaluate patients with myocardial infarction, especially locating reversible ischemia and infarcted tissue in the heart.

The digital images are generated when a patient is at rest and in a cardiac stress state from running on a treadmill. During the diagnostic study, the injected dose of technetium-99m is taken up by myocardial tissue and reaches its maximum level in about 5 minutes. After the diagnostic procedure, about 66% of the total injected dose is excreted within 2 days

The patient will receive a dose of Myoview up to 33 mCi followed by a two-dose stress/rest dosing. The standard protocol is usually a 10 mCi dose, then after 4 hours a dose of 30 mCi resulting in Imaging after 15 minutes following injection.

During a ventilation scan, the patient inhales an aerosol of technetium-99m labelled DTPA or radioactive krypton gas. The resulting image shows where air circulates in the lungs. Aerosols of radiolabelled DTPA tend to be used more commonly because aerosol generation devices produce a consistent particle size, and technetium-99m is readily available in most radiopharmacy departments.

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40 Understanding optic nerve imaging towards glaucoma

Since the 1800s, optic disc photography has been considered the gold standard for optic nerve evaluation.

40.1 Introduction

The head, neck and torso of the human body are connected to the brain via the brainstem through a network of 12 cranial nerves. For example, the cranial optic nerve (II) is 50 mm in length and myelinated by oligodendrocytes and passes through the optic foramen and travels to the eye. The primary function of the optic nerve is to transmit visual impulses from the retina to the visual cortex of the brain. The visual cortex is a part of the cerebral cortex and is located in the occipital lobe. Hence, the visual nerves run straight from the eye to the primary visual cortex to the visual association cortex. The area where the ganglion cell axons leave the retina does not have any photoreceptors, and therefore, no visual information is detected in this region. This results in a blind spot in the visual field.

This information channel can be disruptive due to abnormalities of the optic nerve and brain function. The inner nuclear layer of the retina contains the first sensory bipolar cell body, which is a ganglion cell layer that transforms the bipolar cell synapses into the optic nerve. Hence, the axons leave the globe at the optic disc to form the optic nerves. The gold standard used to investigate the optic nerve is called optic disc photography and has been used since the 1800s.

40.2 The basic anatomy of the optic nerve

The imaging of the optic nerve is vital to the diagnosis of glaucoma, where the optic nerve is damaged by pressure due to the fluid inside the eye. In the United States, more than three million Americans are living with glaucoma, and 2.7 million are aged 40 and over. By 2020 it is predicted that 80 million people in the world will develop glaucoma.

- The intraocular is about 1 mm in diameter and emerges through the scleral opening.
- The Intraorbital is a 25 mm long segment, and its function is to communicate between the subarachnoid space around the optic nerve.
- Intracanalicular is 9 mm long and passes through the bony optic canal along with the ophthalmic artery.
- Finally, the prechiasmatic is 16 mm in length and is the intracranial segment in the suprasellar cistern region.

The optic nerve is composed of approximately 1.5 million axons that connect the retina to the visual parts of the brain. Most of the axons are about 1 μm in diameter; about 10% of them are 2-10 μm in diameter altogether a nerve fibre is about 3-4 μm thick. In comparison to 120 million photoreceptors in the retina, the signal becomes immensely intensified. Consequently, these axons are like a bundle of fibre optic cables and are extensions of the retinal ganglion cells.

During the stages of glaucoma, the retinal ganglion cells and axons suffer damage which creates a loss of function of the optic nerve that can result in visual field deficits.

The technology platform of optic nerve imaging has undergone several advancements over the last decade, especially in the area of glaucoma diagnosis. For example, the application of optic nerve photographs, including stereo disc-photography. This technique acquires imaging data regarding the state of the optic nerves and can be used in conjunction with high-resolution photographs. The technique of stereo disc-photography allows the health professional to detect any changes from the last photographs.

Currently, more advanced optic nerve imaging techniques have allowed the quantification of specific parameters related to the optic nerves and retina. The disadvantage of optic nerve photographs is that it does not provide quantitative information. The advantage of the advanced techniques allows for quantitative data. The goal of these techniques is to measure the thickness of the nerve fibre layer, which is part of the retina that contains the axons of the retinal ganglion cells. This approach is used to determine if the patient has glaucoma due to the reduction of the retinal nerve fibre layer.

40.3 Advanced imaging techniques

40.3.1 Optical coherence tomography – OCT

This technique measures the reflection of laser light to generate a 3-D reconstruction of the optic nerve. The most recent advances in OCT include optical coherence tomography angiography (OCT-Angiography), which is used to measure the blood flow to vessels surrounding the optic nerve and the macula. This research indicates that the optic nerves are vulnerable to changes in optic nerve blood flow, and this measurement can be used to help in the diagnosis of the disease state of the eye.

40.3.2 Heidelberg retina tomography -HRT

HRT is used to produce a 3-D representation of the optic nerve. This diagnostic procedure is used for precise observation and documentation of the optic nerve head, which is paramount in the diagnosis and management of glaucoma. The laser is focused on the surface of the optic nerve to generate the image. During this process, the eye is not damaged by the laser, and HRT is able to produce images in the deeper layers of the optic nerve. The type of damage that glaucoma causes in the optic nerve is called cupping. When the cells die in the optic nerve, they leave a small cup in the nerve. Therefore, the imaging information will be able to calculate the dimensions of

the cup. Also, HRT can be used to calculate the change in the area of the optic disc, including the volume of the cup, over a period of time.

40.3.3 Nerve fibre analyser – GDx

The imaging modality uses laser light to measure the thickness of the nerve fibre layer to detect glaucoma. The earlier glaucoma tests centred on measuring eye pressure or measuring the effect that glaucoma has on your overall visual field. During the test, the thickness of the nerve fibre layer is compared with the nerve fibre layer of normal eyes. The GDx maps the nerve fibres and compares them to a database of healthy glaucoma-free patients. A thinning of the fibres indicates glaucoma. The GDx provides good results about the optic nerve status: having more advanced instruments available, such as Optical Coherence Tomography (OCT).

40.3.4 Scanning laser ophthalmoscopy – SLO

This technology uses the principle of confocal, which is based on the near-infrared diode laser (675 nm) beam to scan the posterior pole. This imaging platform works by detecting the reflected light by using the confocal photodiode, which is conjugated to the retinal plane. During this process, the confocal filter only records the light reflected from the narrow spot, which is illuminated by the laser to generate stereoscopic high-contrast digital images of the optic nerve. These images can be produced with fluorescein: changing the laser wavelength will enable a selective examination of different tissue depths.

The advantage of using SLO is that it generates high magnification of fine structures within the eye. It also gives a high frame rate to allow a more accurate diagnosis of the retinal structures.

40.3.5 Tomography

Furthermore, a 3-D tomograph can be produced of the retina to provide information on the thickness. These optical slices are created in the digital mode by obtaining 32 consecutive and equidistant optical section images. The primary use of SLO in the clinical setting has been for the assessment of the surface contour of the optic nerve head, especially in glaucoma.

Diagnostic imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), X-ray and ultrasound look at the structure or anatomy in the region of interest.

40.3.6 Optoacoustic imaging

The technique evaluates the structure by fusing information about functionality around its location. This approach works by the combination of anatomic and functional diagnostic imaging, which is facilitated by the use of laser optics and conventional ultrasound in real-time in order to generate high-resolution contrast images.

Optoacoustic imaging can be used to evaluate the presence of tumour neoangiogenesis by detecting new blood vessels produced by malignant tumours. These blood vessels are used by a tumour to supply nutrients and remove waste

products. However, these malignant masses cannot grow larger than 2-3 mm without generating neovessels.

The parameters of the laser wavelength are set to enable the visualisation of relative amounts of oxygenated and deoxygenated haemoglobin within the vasculature and surrounding tissues.

Inside the tumour, there are vessels that supply and drain from a malignant tumour: the haemoglobin gives up its oxygen to the rapidly growing cells and becomes deoxygenated. The combination of haemoglobin concentration and its relative oxygenation has been shown to provide good diagnostic accuracy. Malignant tumours have increased blood (haemoglobin) concentration with relatively decreased oxygen content. Benign growths have variable blood (haemoglobin) concentrations with relatively more oxygenation.

Functional information has direct significance to tumour pathophysiology and contributes to the treatment plan of the patient. This is dependent on the nature of the malignancy and whether biopsies are needed to be obtained for further study.

Optoacoustic imaging has the ability to detect 3 mm tumours, and early detection is essential because biologically advanced tumours are more capable of metastasis.

40.4 Conclusion

All these advanced optical imaging techniques are able to quantitatively analyse the nerve fibre layer, especially its depth, including the optic nerve head and macula. They are all used in the diagnosis and monitoring of glaucoma in the clinical setting.

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41 Recent advances in ultrasound imaging technology

The magic of ultrasound imaging enables healthcare professionals to look inside the human body without being invasive.

41.1 Introduction

The National Health Service in England carried out 42.1 million imaging tests in the year to March 2017 compared with 40.7 million in the previous year. Plain X-ray radiography was the most common, with 22.9 million procedures followed by 9.37 million ultrasound scans. In addition, the total of computed tomography scans was 4.82 million compared to 3.36 million magnetic resonance imaging scans.

These imaging modalities demonstrate that ultrasound is more available across a broad spectrum of healthcare services. Ultrasound imaging offers a more cost-effective diagnostic procedure to contribute to the overall diagnosis of the disease state in the patient.

The incorporation of ultrasound imaging in the clinical point-of-care pathway of the patient is to enable the delivery of healthcare products and services in a safe and economical approach compared to traditional X-ray imaging, which is not really recommended to be over-used for radiation dosage considerations.

In the last 5 years, many healthcare organisations have made substantial investments in medical ultrasound imaging. This commitment is driven by the advancement of software technology to be able to produce greater accuracy in analysing ultrasound images, thereby delivering the best treatment plan for the patient.

The magic of ultrasound imaging enables healthcare professionals to look inside the human body without being invasive. These high-tech ultrasound machines can diagnose and screen for abnormalities to allow a course of treatment and monitoring.

Since the 1960s, ultrasound imaging systems have been widely distributed and used throughout the world, amounting to a yearly use of over a billion scans. These portable ultrasound medical devices have been available since the early start of 2000 and, after a decade, have given way to wireless ultrasound imaging transducers in the form of handheld computers.

41.2 Ultrasound machines

During these past two decades, medical ultrasound imaging has contributed to the advancement of theranostics. For example, in the development of ultrasound

machines to be used in elastography, contrast agents, resolution imaging and the application of 2-D array transducers. The imaging modality elastography maps the elastic properties and stiffness of soft tissue.

Elastography aims to determine if the tissue mass is hard or soft and will generate information towards a possible cancer diagnosis of certain fibrous tumours. Other applications would include the evaluation of plaque in an artery during stent implantation. However, elastic characteristics cannot be clearly visualised in general ultrasound images.

To circumvent these issues, the quantitative measure of elasticity can be assisted by using an acoustic radiation force which is a physical phenomenon resulting from the interaction of an acoustic wave with an obstacle placed along with its projection. The force exerted on the obstacle is calculated by the integration of the acoustic radiation pressure over its surface. This radiation force provides controlled deformation of the target tissue.

This action is implemented by an ultrasound imaging transducer via an algorithm to the local tissue position, which is accurate to tens of micrometres. These technologies – combined with a high-frame ultrasound imaging system – can have a frame rate of 10,000/s, providing high-resolution quantitative elastography.

41.3 Microbubbles

Other ultrasound technologies use super-resolution imaging by tracking microbubbles in a blood vessel with a high frame system. However, a single microbubble is classed as a scatterer due to the resolution being more elevated than the point spread function of the ultrasound system. The resultant images can provide excellent vasculature networks in the organ. In order to expand ultrasound 3-D imaging, a 2-D array transducer is required, which has led to the development of micro-machined sensors.

These 2-D phased array transducers operate in high-intensity focussed ultrasound (HIFU) and can facilitate a response to implement abdominal cancer treatment. Also, this approach can be used to treat brain diseases without craniotomy or burr hole trephination.

Furthermore, MRI guidance systems for brain treatment can be used in conjunction with ultrasound technology to apply a non-invasive selective treatment towards brain-related diseases. This technology platform can deliver results in targeted drug delivery aided by ultrasound and microbubbles.

These microbubbles are generated in the time-variable acoustic pressure field and will undergo oscillation resulting in the collapse of the bubbles. This process is called acoustic cavitation and occurs close to the biological boundary, which is temporarily disturbed.

Research has demonstrated that ultrasound-mediated drug delivery through the blood-brain barrier has been most successful in animal model experiments and

consequently extended to targeted brain cancer treatments as well as other parts of the human body.

41.4 Histotripsy

A new ultrasound imaging technique is called histotripsy, where the tissue structure is subjected to short, high-intensity ultrasound pulses. This mechanical fractionation uses an ultrasound intensity of several orders higher than conventional diagnostic imaging. The applied pulse sequence is similar to lithotripsy and is used to break down kidney stones.

The action of histotripsy at the fluid-tissue interface will result in localised tissue removal with appropriate sharp boundaries. This approach has been used to remove cardiac tissue in the treatment of congenital heart disease. However, when applied to bulk tissue, histotripsy results in mechanical fragmentation of the tissue site leading to liquefication.

Histotripsy has several clinical applications, for example, causing defined tissue ablation in the removal of the tumour. This technique provides clear-cut lines between treated tissue and surrounding tissue, unlike HIFU, which uses a thermal effect and produces an irregular boundary. Therefore, histotripsy can be a selective tool for cancer treatment.

41.5 Conclusion

Since ultrasound imaging does not involve radiation compared to CT scanning: these new developments in ultrasound technology will, in the future, become more prevalent in the clinical arena, especially in emergency medicine. The ultrasound imaging platform will be the chosen diagnostic tool for cardiology, critical care, and anaesthesiology.

Ultrasound imaging has become more mobile amongst healthcare professionals by providing a broad range of diagnostic imaging capabilities at the patient's location. This proven technology offers a fast, high-quality ultrasound examination at the patient's point of care. These ultrasound technologies bring many advantages towards patient treatment programmes, especially with an increase in patient safety and the improvement of clinician efficiency. This can be clearly demonstrated by using the Edge II, which can enhance to accelerate image acquisition to enable the clinicians to make the correct diagnosis of the disease state of the patient.

Future developments in ultrasound medical imaging will be to provide cost-effective solutions that do not compromise image quality. The next generation of ultrasound machines will be automated and mobile to enable effective patient diagnosis and treatment planning.

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42 Artificial intelligence in cancer imaging

Artificial Intelligence will play a vital role in the analysis of vast amounts of medical imaging data

42.1 Introduction

Radiology can trace its roots back to the Nobel Laureate Wilhelm Conrad Röntgen, who discovered X-rays in 1895. Consequently, this discovery led to the imaging of the human body, which contributes to assisting with the diagnosis of various disease states.

Today, X-ray planer imaging is still being used, for example, in mammography or chest X-rays in the clinical setting. However, the next generation of diagnostic imaging tools, such as computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US) and Nuclear Medicine (NM), are now being used to produce 3-D anatomical and functional images of the human body.

Accordingly, Nuclear Medicine departments make use of gamma emitters for single photon emission computed tomography (SPECT) and positron emitters for positron emission tomography (PET).

At present, X-ray scans account for 60% of all medical imaging in the Healthcare sector, although 25% are rejected due to poor image quality. The objective is to decrease these X-ray rejection rates and facilitate resources to improve the quality of patient treatment through Artificial Intelligence.

The phrase Artificial Intelligence was first coined in 1956 by computer scientists at IBM and refers to a machine or computer that demonstrates intelligence in performing a task.

The market for Artificial Intelligence tools to process and analyse medical imaging studies is considered to push past $2 billion by 2023. The future of healthcare will depend on deep learning machines to provide solutions for the diagnosis of disease states, especially in larger ageing populations. The advancement of algorithms will drive clinical support towards patients with the assistance of radiologists and pathologists to implement theranostics. Artificial Intelligence will create data-driven platforms for decision-making in the diagnosis of disease states.

The relationship between the physician and patient will change through various Artificial Intelligence platforms, which will take time to implement in the healthcare system. The existing workflow will contain hidden changes regarding the patient

experience, provider productivity and diagnostic accuracy of medical imaging modalities.

42.2 Medical imaging neural networks

Artificial Intelligence will complement the vast number of digital images generated in hospitals which are the product of the next generation of imaging scanners, especially the hybrids, which include: MRI, CT, PET and SPECT. Advancements in the technology of CT and MRI scanners are making it possible to utilise even thinner slices of the human body to create more detailed 3-D and 4-D images.

These powerful images require vast amounts of digital data to help in the diagnosis of the patient. This has led to some hospitals exceeding 50 petabytes of data per year. To put this data into context, 50 petabytes could store the entire written works of mankind! Medical imaging accounts for 90% of all healthcare data, and astonishingly 97% of the acquired data will never be analysed.

Consequently, Artificial Intelligence will play a vital role in the analysis of medical imaging data, and this will only be viable if Artificial Intelligence and healthcare professionals interact to embrace deep thinking platforms such as automation in the diagnosis of the disease state of the patient.

Artificial Intelligence will help radiologists to analyse medical images with regard to current trends and design treatment programmes which are personalised to the patient. This approach aims to provide the best care and treatment in the most cost-effective manner.

The Artificial Intelligence revolution in medical imaging will only work with the cooperation of healthcare providers and especially equipment manufacturers to incorporate the necessary software to advance the initiatives: these will include the development of data analytics tools to help consolidate vast amounts of generated digital images from complex algorithms in the clinical setting.

Several imaging providers are developing the next generation of imaging technology with the objective of transforming hospitals to become more efficient in the management of patient treatment plans. This will be achieved by producing faster imaging and reducing radiation dosages through the PET and SPECT imaging modalities. This will allow medical imaging professionals to evaluate the anatomical images at a faster rate. The data cluster from these images can be translated into small data packages that can be accessed by healthcare departments to give the professional a real-time insight into patient care and the required intervention.

42.3 Conclusion

Artificial Intelligence requires barriers to be broken down for it to become widely accepted and trusted in the mainstream medical imaging setting. For example, the regulatory process remains challenging for new instrumentation regarding Artificial Intelligence products. This is because validation studies are required to demonstrate the performance of deep learning algorithms in the clinical setting.

However, the main obstacle is to ensure the confidence of the radiologist in using Artificial Intelligence. It is paramount that algorithm developers' partner with imaging technologists to provide solutions that are integrated with the workflow of the radiologists. In other situations, Healthcare providers are hesitant to purchase Artificial Intelligence tools from various software developers. This is because of vendor-specific integration and implementation, which bring many challenges for hospitals and healthcare professionals. To circumvent these issues, the developers need to form Artificial Intelligence platforms to address the algorithms already used by Healthcare organisations to allow the costs to be kept in perspective.

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43 Exploring brain function with magnetic resonance imaging

A useful brain imaging technique uses functional magnetic resonance imaging to analyse metabolic changes such as blood oxygenation

43.1 Introduction

Advancements in brain imaging using non-invasive technologies such as functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and electroencephalography (EEG) have allowed neuroscientists to obtain a greater understanding of how the brain functions with its environment.

Understanding neuro-networks will assist in the development of treatments for neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. In order to complement brain imaging, various animal models have been developed to investigate the genetic nature of disease states, especially concentrating on neurophysiological processes.

A useful brain imaging technique uses functional magnetic resonance imaging (fMRI) by analysing metabolic changes such as blood oxygenation. The advantage of using fMRI is that it produces good spatial resolution. The disadvantage of fMRI is its poor time resolution of approximately six seconds and is therefore too slow for tracking single or clusters of neurons in real-time. This is because the change in blood flow takes several seconds to catch up with neural activity. However, fMRI has good spatial specificity in the areas of localised brain function compared to EEG, which uses electrical signals and magnetic signals derived from MEG.

Consequently, both EEG and MEG have excellent temporal resolution but very poor spatial precision. This is even though these imaging techniques can track neuron population activity within several hundred milliseconds. During these processes, both imaging modalities cannot distinguish which set of neurons is being used.

In order to circumvent these issues, fMRI is sometimes used in conjunction with EEG to obtain paramount temporal and spatial precision.

Brain imaging can contribute to the patient through personalised medicine in the treatment and management of neurological diseases by creating 3-D individual images in real-time. Both MRI and computed tomography (CT) hybrid scanners can be used to generate 3-D images of the brain at a specific moment.

These 3-D images of brain volume are made up of voxels.

The spatial resolution of the MRI scanner determines how the small voxels can be measured during brain imaging of the neural networks. Therefore, the stronger magnetic field strength will increase the spatial resolution and will enable better resolution of brain structure.

Image-guided systems controlled by advanced brain navigation software will assist neurosurgeons in precise locations to perform the operation on the patient. These systems are based on the Talairach coordinates (x, y and z).

43.2 Comparison of neuroimaging modalities

IMAGING MODALITY	RESOLUTION	APPLICATION	ADVANTAGES	DISADVANTAGES
EEG	S - LOW T- HIGH	Study various rhythms, epilepsy, preoperative mapping, degenerative disorders.	Non-invasive, no ionising radiation, widely used, low cost	Low spatial resolution
MEG	S - MEDIUM T - HIGH	Study epilepsy	Non-invasive, no ionising radiation can identify epileptic foci	Low spatial resolution
fMRI	S - LOW T - HIGH	Preoperative mapping, functional mapping	Non-invasive, no ionising radiation	High cost

S = Spatial Resolution; T = Temporal Resolution

43.3 Conclusion

Brain imaging assists neurosurgeons to remove disease-causing agents and preserve the function of the surrounding tissues. These imaging modalities include MRI and CT, which generates a 3-D brain map in real-time and is essential to understanding functional measurements using EEG, MEG, fMRI, including deep brain recording and the ability to understand brain structure and function.

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44 Hyperpolarized carbon-13 pyruvate magnetic resonance imaging

These non-radioactive labels can be incorporated into small molecules to study in vivo metabolic pathways in real-time.

44.1 Introduction

Hyperpolarization results from the nuclear spin polarization of the material when subjected to a magnetic field determined by the Boltzmann distribution. The signal-to-noise ratio (SNR) in magnetic resonance can be made more prominent by hyperpolarization. Currently, hyperpolarization is being used in clinical studies labelling drug candidates with carbon-13.

These non-radioactive labels can be incorporated into small molecules and can then be used to study in vivo metabolic pathways in real-time. For example, carbon-13 labelled pyruvate is becoming the gold standard when it comes to the development of hyperpolarized probes. Several preclinical models have demonstrated that hyperpolarized probes can be used in the areas of neurology and oncology. Therefore, these probes can be used in conjunction with magnetic resonance imaging (MRI) and consequently have great potential towards diagnosing a disease state in personalised medicine.

The output signals generated by MRI are weak compared to other imaging modalities. These include imaging techniques based on acoustics, optics and emission. However, several factors can be used to increase the SNR, especially by applying more powerful magnetic fields, high concentrations of spins and longer acquisition times. MRI works on the human body because of its high concentration of water and, therefore an abundance of protons. These protons have a relatively higher gyromagnetic ratio.

Hyperpolarization increases the signal response in magnetic resonance by increasing spin polarisation. Hyperpolarization aims to use the fundamental ability of nuclear magnetic resonance spectroscopy to identify chemical environments by chemical shift and characterise their dynamic properties in vivo.

44.2 NMR-active nucleus

The most abundant isotope of hydrogen is the proton which has a spin of ½ a nucleus and therefore produces observable NMR signals. Consequently, the carbon-13 isotope of carbon possesses a spin of ½ a nucleus with an associated 1.1% natural abundance. To obtain a favourable NMR signal, it would be necessary to enrich the target molecule to increase SNR further isotopically.

The degree of hyperpolarization of the molecule will be the result of the location of the NMR-active nucleus. Therefore, the position of isotopic enrichment is a factor in the properties of the hyperpolarized molecule. For example, [1-^{13}C] pyruvate molecules contain an enriched carbon-13 in position 1 of the molecule. Accordingly, this carbon-13 label would be the target of the hyperpolarization process through the nuclear spin.

The hyperpolarized carbon-13 atom will be transformed during the in vivo metabolic pathways, and each metabolite would produce a different signal. This approach offers great potential in ADME human studies because the hyperpolarized molecules can be used in vivo studies to determine the fate of the drug substance. The drug can be administered to the patient at physiological concentrations without harmful effects.

44.3 Conclusion

The imaging properties of hyperpolarized molecules are a function of their relaxation properties and ease of hyperpolarization. Other factors include the safety profile in addition to biological availability and metabolism profile. Several molecules including carbon-13 labelled pyruvate have been subjected to hyperpolarization, and their associated metabolism was imaged. These hyperpolarized probes include [1,4-$^{13}C_2$]fumarate used to evaluate cell necrosis and [U-^{2}H, U-^{13}C]glucose for assessment of the glycolytic and pentose phosphate pathway activities and for detecting early treatment response. In addition to ^{13}C-labelled bicarbonate for in vivo mapping of pH, including ^{13}C-labelled urea as a marker of perfusion.

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45 The role of positron emission mammography in breast cancer imaging

The diagnostic breast imaging tool Positron Emission Mammography uses short-lived positron isotopes to detect breast cancer

45.1 Introduction

The diagnostic breast imaging tool Positron Emission Mammography (PEM) uses short-lived positron-emitting isotopes to generate high-resolution tomographic images of cancer within the breast.

PEM works by using an intravenous injection of the radiopharmaceutical 2-deoxy-2-(^{18}F)fluoro-D-glucose abbreviated as ^{18}F-FDG. Thereby, the radiopharmaceutical is based on the design of the radioisotope fluorine-18 (half-life = 109.8 mins), which is attached to the delivery compound deoxyglucose to produce ^{18}F-FDG. This modified radiolabelled glucose is then absorbed by the cancer cells via the glucose transporter 1 system. The fundamental principle of PEM technology works on the premise that cancer cells display a high uptake of glucose. This imaging agent is effective in patients with dense breast tissue that may present with multiple lesions.

The radiopharmaceutical (^{18}F-FDG) enters the cancer cell undergoing phosphorylation and therefore cannot be transported back out of the cell. This process then leads to the accumulation of the imaging agent, and because the fluorine-18 nucleus is unstable, it undergoes a decay process continually emitting positrons. The positron collides with an electron in the tumour tissue, which results in annihilation to produce two 511 keV gamma rays emitted in opposite directions. During the PEM scan, the gamma rays are detected when they strike a pair of detectors that are placed between the breasts. The detected gamma rays are then amplified by photon-sensitive photomultipliers, which translate into an electrical signal that then becomes an image.

45.2 PEM breast imaging

Positron Emission Mammography is currently part of the diagnostic toolkit to help assess patients that had detectable abnormalities in their mammogram. Both PEM and PET (positron emission tomography) are able to provide functional imaging by using the radiotracer ^{18}F-FDG. However, PEM is primarily used for small body parts and utilises gentle immobilisation of the breast to attain higher spatial resolution: 1-2 mm for PEM and 4-6 mm for PET. The crystal detectors in PEM are constructed to provide this improved spatial resolution, including 1.5 mm in-plane and 5 mm between planes. Also, the combination of PET and CT (computed tomography) scanners using ^{18}F-FDG are beneficial for the staging and restaging of advanced breast carcinoma.

In addition, PEM was approved by the US Food and Drug Administration and has been introduced into the clinical setting as a diagnostic aid to mammography and breast ultrasonography. Furthermore, PEM is currently under clinical investigation to improve the sensitivity of breast cancer screening programmes. The indications for PEM include:

- The initial staging evaluation of patients with diagnosed cancer.
- Distinguishing recurrent carcinoma from scar tissue.
- Monitoring response to chemotherapy treatment.

45.3 Conclusion

PEM has high imaging sensitivity for breast lesions. However, its clinical utility requires further investigation. Nevertheless, PEM cannot provide the anatomical detail that is provided by magnetic resonance imaging (MRI).

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46 Brachytherapy – delivering radiation from the inside

Brachytherapy techniques have been a powerhouse in the treatment of cancer since the beginning of the twentieth century.

46.1 Introduction

Brachytherapy techniques have been a powerhouse in the treatment of cancer since the beginning of the twentieth century. The advancement of other theranostic treatments has not removed internal radiotherapy entirely from the clinician's armoury war in the ongoing quest to destroy cancer.

Currently, one century forward, brachytherapy, although in some cases not always an effective radiotherapy treatment, continues to play a fundamental role in cancer therapy. Brachytherapy treatment for prostate cancer, gynaecological, skin and breast cancer treatments is believed to will offer continuing treatment possibilities through technological developments in the future.

The definition of brachytherapy is merely short therapy, and it is used in radiotherapy by applying a sealed radiation source inside the human body. The radiation source is usually placed near where the treatment is required. This type of therapy aims to damage the DNA of cancer cells and ultimately kill them. In the treatment of prostate cancer, brachytherapy can be used in the following modes: low dose rate and high dose rate.

46.2 Types of Brachytherapy

A low Dose Rate uses a smaller strength radioactive source and is associated with longer treatment times, especially for one-off treatment. The primary use of low-dose-rate treatment is the prostate. This involves inserting tiny radioactive seeds inside the prostate tissue. This low dose rate approach has been used in the treatment of head and neck tumours, during which low activity sealed sources are temporarily placed at the cancer source for several days and then removed.

High Dose Rate applies a higher strength of radioactive source contained within the after-loader device. The aim of the after-loader is to deliver the radioactive source in the vicinity of the tumour for a brief period of time. This is usually facilitated by the use of catheters and needles, which are inserted into the tumour site.

High-dose-rate treatment is a much shorter procedure – minutes compared to several days of low-dose-rate treatments. However, high-dose rate treatment requires multiple

sessions and has become the more favourable option to replace low-dose rate techniques for most body sites.

In addition, other internal radiotherapy radiation techniques include pulse dose rate and image-guided brachytherapy.

Pulsed dose rate brachytherapy treatment combines the physical advantages of high-dose-rate technology with the radiobiological advantages of low-dose-rate brachytherapy. Pulsed brachytherapy consists of using a stronger radiation source than low-dose-rate brachytherapy and produces a series of short exposures of up to 30 minutes every hour to approximately the same total dose in the same overall time as with the low-dose-rate brachytherapy.

The advancements in afterloading equipment provide several advantages over the intracavitary insertion of separate tubes, wires, needles and seeds. The internal radioactive source is removed from the patient using an automated approach to reduce radiation exposure. The radiation exposure is also reduced for the staff who formerly loaded and unloaded a multiplicity of radioactive sources into the catheters and tubes.

Image-guided brachytherapy involves the use of advanced imaging techniques to make brachytherapy more accurate, safe, and effective. Internal radiotherapy consists of four phases: Placement of hollow catheters or hollow carriers; Computed tomography or magnetic resonance imaging of the site; computer calculations of the dose distribution (dosimetry) and robotic radiation treatment delivery with a tiny radiation source. The imaging techniques used for interventional radiology may be used to guide the placement of internal radiotherapy catheters.

46.3 Conclusion

The advantages of image-guided brachytherapy include more accurate treatment distribution throughout the targeted area and the reduced risk of injury to healthy tissues. Also, this type of internal radiotherapy has the ability to treat a wide variety of cancer lesions, such as those that are deep within the body or adjacent to blood vessels which would ordinarily be more dangerous to remove.

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47 Unlocking the Central Nervous System: Anatomy, Functions, and Pathologies in Daily Life

The central nervous system is a complex network that manages sensory processing, motor functions, and cognitive abilities.

47.1 Introduction

The Central Nervous System (CNS) is a complex network that regulates our daily lives. Its primary components, the brain and spinal cord, collaborate to process and transmit information throughout the body, ensuring communication with the peripheral nervous system (PNS). This article briefly explores the central nervous system's anatomy, functions, and pathology.

The CNS comprises two primary structures – the brain and the spinal cord. The brain is divided into the cerebrum, cerebellum, and brainstem and contains billions of neurons organised into specialised regions responsible for various functions. The spinal cord, a long bundle of nerve fibres, is the primary channel for information exchange between the brain and the remainder of the human body. Together, these structures form the core of the CNS.

The CNS is responsible for various functions that govern our everyday experiences. For example, it processes sensory information, allowing us to perceive and interpret our surroundings. The CNS also controls motor functions, coordinating voluntary and involuntary movements. Additionally, it is responsible for higher cognitive functions such as reasoning, learning, and memory. The complicated organisation and connectivity within the CNS make these diverse functions possible.

Numerous pathologies can affect the CNS, leading to various symptoms and impairments. Neurodegenerative diseases, such as Alzheimer's and Parkinson's, result from the progressive loss of neurons and their functions. TBIs and strokes can cause acute disruptions in brain function, leading to significant neurological deficits. Autoimmune disorders, for example, multiple sclerosis (MS), can damage the protective myelin sheaths of neurons, impairing their ability to transmit signals efficiently.

47.2 Anatomy of the Central Nervous System

The brain, as the primary organ of the CNS, is a highly specialised structure containing billions of neurons. These neurons are arranged into distinct regions carrying a broad range of functions. The brain falls into three major parts: the cerebrum, the cerebellum, and the brainstem, each contributing to various aspects of human cognition and behaviour.

The cerebrum is the most significant part of the cerebral and accounts for approximately 85% of its total weight. It comprises two hemispheres connected by the corpus callosum, a bundle of nerve fibres facilitating communication between the left and right hemispheres. The cerebrum is further divided into four lobes, each responsible for specific functions:

The Frontal Lobe is positioned at the front of the brain and plays a crucial role in various higher cognitive processes. For example, it is responsible for motor control, enabling the execution of voluntary movements. Moreover, the frontal lobe is involved in decision-making, problem-solving, and language processing, allowing the navigation of complex social environments.

The parietal lobe is mainly responsible for sensory information from various sources, including touch, temperature, and pain. Additionally, it is involved in spatial awareness, enabling one to perceive and interact with the surroundings.

However, the Temporal lobe is located near the temples and is vital for auditory processing, ensuring we can interpret and respond to auditory stimuli. The temporal lobes also play a significant role in memory formation and emotional regulation, allowing us to remember past experiences and react appropriately to various situations.

The occipital lobe at the back of the brain processes visual information. It interprets and integrates visual information to perceive and make sense of the world.

47.3 The Cerebellum: A Key Component in Motor Coordination and Balance

The cerebellum at the back of the brain below the cerebrum is an essential structure within the CNS. It is responsible for coordinating motor function and maintaining balance. Although smaller in size compared to the cerebrum, the cerebellum contains more neurons and is crucial for the proper execution of voluntary and involuntary movements.

The cerebellum receives sensory input from the spinal cord and other regions of the brain, such as the motor cortex, and processes this information for movement and posture. It is essential for coordinating and adjusting muscle contractions' timing, force, and sequence, ensuring smooth and precise motor control.

In addition to its role in motor coordination, the cerebellum is involved in retaining balance and equilibrium. It receives and processes information from the vestibular apparatus, which detects changes in head position and movement, and from the proprioceptive system, which provides feedback on the position and movement of limbs and joints. By integrating this sensory input, the cerebellum allows the body to maintain a stable posture and adapt to environmental changes or unexpected perturbations.

Recent research has also suggested that the cerebellum may contribute to specific cognitive functions, such as attention, language processing, and emotion regulation. These findings indicate that the cerebellum's role may extend beyond motor

coordination and balance, although the extent of its involvement in these non-motor functions is still being investigated.

Damage to the cerebellum can result in various movement and balance disorders. Common symptoms include ataxia (a lack of muscle coordination), dysmetria (difficulty judging distances), and tremors. Individuals with cerebellar dysfunction may also experience difficulty maintaining balance and adjusting their posture, leading to an unsteady gait.

47.4 The Brainstem: A Vital Bridge Between the Brain and Spinal Cord

The brainstem is a critical component of the CNS that serves as a bridge connecting the cerebrum and cerebellum to the spinal cord. Consisting of three structures – the midbrain, the pons, and the medulla oblongata – the brainstem controls numerous essential functions, including respiration, heart rate, and blood pressure. Moreover, it acts as a relay centre for sensory and motor signals between the brain and spinal cord.

The midbrain is the top portion of the brainstem and controls eye movement and visual and auditory information processing. It contains structures such as the superior and inferior colliculi, which coordinate visual and auditory reflexes. Additionally, the midbrain houses the substantia nigra and the ventral tegmental area, which are associated with the production and modulation of dopamine, a neurotransmitter essential for movement control and reward processing.

The pons is situated between the midbrain and the medulla oblongata. The pons is a relay centre for transmitting signals between the cerebrum, cerebellum, and spinal cord. It also contains nuclei regulating sleep, respiration, and facial movements. The pons is vital in coordinating movements between the two sides of the body and maintaining overall balance.

The Medulla Oblongata is in the lower region of the brainstem and controls several involuntary and life-sustaining functions. It contains the cardiovascular centre, which regulates heart rate and blood pressure, and the respiratory centre, which controls the rate and depth of breathing. The medulla also houses the vomiting, coughing, and swallowing centres, which manage reflex actions essential for survival.

The brainstem is indispensable for maintaining essential bodily functions and facilitating communication between the brain and the spinal cord. Damage to the brainstem can have severe consequences, such as impaired motor and sensory function, difficulty swallowing, and disruptions in vital functions such as breathing and heart rate regulation. Understanding the intricate workings of the brainstem and its interactions with other components of the CNS is crucial for the continued advancement of neuroscience and the development of targeted therapies for brainstem-related disorders.

47.5 The Spinal Cord: A Crucial Pathway for Communication Between the Brain and Body

The spinal cord, a cylindrical bundle of nerve fibres, extends from the base of the brainstem down the vertebral column and serves as the primary pathway for

information exchange between the brain and the rest of the body. Its vital role in facilitating communication between the CNS and PNS is essential for both motor and sensory functions.

The spinal cord is organised into 31 segments, each causing a pair of spinal nerves. These spinal nerves, in turn, connect to the PNS, enabling the CNS to communicate with peripheral tissues and organs. The spinal nerves are divided into five groups based on their location along the vertebral column: 8 cervical, 12 thoracics, 5 lumbar, 5 sacral, and 1 coccygeal pair. Each spinal nerve carries sensory (afferent) and motor (efferent) fibres, allowing bidirectional communication between the CNS and the PNS.

The spinal cord is divided into two main regions: the white matter and the grey matter. The white matter consists of myelinated nerve fibres, forming ascending and descending tracts responsible for transmitting sensory and motor signals, respectively. The grey matter, conversely, contains neuron cell bodies, dendrites, and unmyelinated axons. It is organised into a butterfly-shaped structure, with a pair of dorsal (posterior) and ventral (anterior) horns. The dorsal horns receive sensory information from the PNS, while the ventral horns contain motor neurons that send signals to control muscle movements.

The spinal cord coordinates many essential reflexes, which are rapid, involuntary responses to specific stimuli. Reflexes are mediated by neural circuits called reflex arcs, bypassing the brain and allowing faster responses. This ensures that crucial protective actions, for example, withdrawing a hand from a hot surface, can be carried out quickly and efficiently.

47.6 The CNS and Sensory Information Processing: Perceiving Our World

The CNS is crucial in receiving and processing sensory information from various external and internal sources. This information lets us perceive and interact with our environment and regulate our internal states. Sensory neurons within the PNS transmit information to the CNS, processing and integrating it, ultimately resulting in perception or sensation.

Specialised sensory receptors are located throughout the body to detect external stimuli, for example, light, sound, and touch. These receptors convert the physical stimuli into electrical signals transmitted via sensory neurons to the CNS. For example, photoreceptors in the retina detect light and send signals to the brain for visual processing. In comparison, the mechanoreceptors in the skin respond to touch, pressure, and vibration.

Internal signals, such as pain and temperature, are crucial for maintaining our body's homeostasis and alerting us to potential harm. For example, nociceptors, specialised sensory neurons, detect noxious stimuli, such as extreme heat or pressure, and transmit this information to the CNS, resulting in pain perception. Similarly, thermoreceptors detect temperature changes, allowing us to maintain our body's internal temperature within a narrow range.

Once sensory information reaches the CNS, it is processed and integrated into various brain regions. For instance, visual information is primarily processed in the occipital lobe, while auditory information is processed in the temporal lobe. In addition, sensory information from the body is relayed to the parietal lobe, which is responsible for processing touch, pain, and temperature sensations, as well as proprioceptive information about the position of our limbs and joints.

The integration of sensory information in the CNS allows us to form perceptions and sensations, which are the basis of our conscious experience. This process enables us to navigate our surroundings, avoid danger, and interact with our environment meaningfully. Understanding how the CNS receives, and processes sensory information is vital for gaining insights into the neural mechanisms underlying perception and sensation and developing therapeutic interventions for sensory disorders and impairments.

47.7 The CNS and Motor Control: Orchestrating Voluntary and Involuntary Movements

The CNS plays a pivotal role in controlling voluntary and involuntary movements, allowing us to perform complex actions, maintain balance, and react to unexpected stimuli. Motor neurons in the spinal cord transmit signals from the brain to muscles, enabling precise movement control. In addition, the CNS regulates involuntary movements, such as reflexes and postural adjustments.

Voluntary movements are controlled by the motor cortex, a region in the brain's frontal lobe. The motor cortex sends signals to the brainstem and spinal cord, transmitting these signals to the appropriate muscles via motor neurons. The cerebellum and basal ganglia, two other vital structures within the CNS, also contribute to voluntary movement control by providing feedback and modulating the activity of the motor cortex. The cerebellum is essential for coordinating and fine-tuning movements, ensuring they are smooth and accurate. On the other hand, the basal ganglia participate in the initiation and termination of movements and the control of muscle tone.

Involuntary movements, such as reflexes and postural adjustments, are also under the purview of the CNS. Reflexes are rapid, automatic responses to specific stimuli that help protect the body from harm. They are mediated by neural circuits called reflex arcs, bypassing the brain and allowing faster responses. Postural adjustments are essential for maintaining balance and stability and are regulated by a complex interplay of sensory input and motor output. The cerebellum and brainstem both play crucial roles in maintaining posture by integrating sensory information from the vestibular, proprioceptive, and visual systems and generating appropriate motor responses.

47.8 The CNS and Higher Cognitive Functions: Facilitating Learning, Memory, and Reasoning

The CNS is responsible for basic motor and sensory functions and is crucial in higher cognitive functions, such as learning, memory, and reasoning. These higher-order

processes are essential for navigating our complex world, allowing us to adapt, solve problems, and make informed decisions.

The CNS enables complex reasoning by integrating information from various sources and processing it to generate appropriate responses. Reasoning encompasses many cognitive processes, including problem-solving, decision-making, planning, and abstract thinking. The prefrontal cortex, situated in the frontal lobe of the cerebrum, is primarily responsible for these executive functions.

Learning and memory are interconnected processes that allow us to acquire, store, and retrieve information over time. The CNS is involved in various forms of learning, such as habituation, sensitisation, classical conditioning, and operant conditioning. Memory can be broadly divided into short-term and long-term, each with distinct neural substrates. Short-term memory, also called working memory, is supported by the prefrontal cortex and involves the temporary storage and manipulation of information. Long-term memory, which can last from hours to a lifetime, is mediated by various brain structures. For example, the hippocampus plays a fundamental role in consolidating and retrieving declarative memories.

Reasoning and problem-solving abilities depend on integrating information from multiple cognitive domains, such as perception, attention, memory, and language. The prefrontal cortex is essential for coordinating these processes and enabling flexible, goal-directed behaviour. It involves tasks requiring planning, organising, and executing complex actions, inhibiting inappropriate responses and adapting to changing circumstances.

47.9 Neurons: The Primary Functional Units of the Central Nervous System

Neurons are the main functional units of the CNS. These specialised cells transmit electrical and chemical signals, facilitating communication within the CNS and between the CNS and the PNS. Neurons have three main components: the cell body (soma), dendrites, and an axon, each with its distinct function.

- The Cell Body (Soma) houses the nucleus and other essential organelles for the neuron's metabolic functions. It serves as the control centre of the neuron, orchestrating the synthesis and degradation of proteins, lipids, and other cellular components.
- Dendrites are branch-like extensions that radiate from the cell body, receiving incoming signals from other neurons and transmitting them to the cell. Dendrites contain numerous synapses, allowing them to integrate information from multiple sources and contribute to the neuron's overall activity.
- Axons are long, slender projections extending from the cell body and carrying electrical signals, known as action potentials, away from the cell body and towards other neurons or target cells. Axons can vary in length, with some extending over a meter in the human body.

Neurons communicate with one another at specialised junctions called synapses. When an action potential reaches the end of the axons, it triggers the release of

neurotransmitters from small, membrane-bound vesicles. These chemical messengers diffuse across the synaptic cleft, a narrow space separating the presynaptic and postsynaptic neurons, and bind to receptors on the postsynaptic nerve cell. Depending on the type of neurotransmitter and receptor, the binding can either excite or inhibit, generating a new action potential for postsynaptic neurons.

47.10 Glial Cells: Essential Support and Protection for Neurons in the CNS

Glial cells, or neuroglia, are non-neuronal cells in the CNS that support and protect neurons. These cells are critical for maintaining the proper functioning of the nervous system, and they outnumber neurons by a ratio of approximately 10:1. There are several types of glial cells, these include astrocytes, oligodendrocytes, and microglia, each with unique functions.

- Astrocytes are star-shaped cells that provide structural support for neurons, helping to anchor them in place and maintain the organisation of neural networks. Astrocytes are also responsible for maintaining the blood-brain barrier, a selective barrier that protects the CNS from toxins and pathogens in the bloodstream. In addition, they regulate the extracellular environment by controlling ion concentrations, neurotransmitter levels, and nutrient availability. Astrocytes also play a role in the formation and maintenance of synapses, contributing to the plasticity and adaptability of the nervous system.
- Oligodendrocytes produce myelin, a fatty substance that insulates axons and speeds up electrical signal transmission. By wrapping around axons in multiple layers, oligodendrocytes form a myelin sheath that allows faster and more efficient communication between neurons. This increased signal transmission speed is essential for the proper functioning of the nerves and contributes to the remarkable computational capabilities of the CNS.
- Microglia cells protect the CNS by removing cellular debris, damaged cells, and pathogens. As the primary immune system cells of the CNS, microglia continuously survey their environment, detecting and responding to potential threats. They can become activated in response to injury or infection, undergoing morphological and functional changes to engulf and eliminate harmful agents. Microglia also play a role in synaptic pruning, which refines neural connections during development and learning.

47.11 Pathologies of the Central Nervous System

The CNS is susceptible to various pathologies, including neurodegenerative diseases, infections, autoimmune disorders, and traumatic injuries. Conditions such as Alzheimer's disease, Parkinson's disease, and MS involve the dysfunction or loss of specific neuronal populations or the disruption of normal glial cell function. Understanding the complex interactions between neurons and glial cells and the underlying mechanisms of CNS pathologies is crucial for developing targeted therapies and interventions to treat these devastating disorders.

47.11.1 Neurodegenerative Diseases: Progressive Neuronal Loss and Functional Decline

Neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS), are characterised by the progressive loss of neurons and their functions. As a result, these diseases often lead to cognitive decline, motor impairments, and other debilitating symptoms that significantly impact the quality of life of affected individuals and pose a significant challenge for healthcare systems worldwide.

- Alzheimer's disease is the foremost cause of dementia which affects millions globally. It is characterised by the accumulation of amyloid-beta plaques and tau protein tangles in the brain, leading to the death of neurons and subsequent cognitive decline. Early symptoms of Alzheimer's disease include memory loss, confusion, and difficulty with problem-solving. As the disease progresses, individuals may experience severe cognitive decline, disorientation, and impaired ability to perform daily tasks. Currently, there is no treatment for Alzheimer's disease, but some treatments can help manage symptoms and slow the progression of the disease.
- Parkinson's disease is a neurological disorder that primarily affects the motor system. It is triggered by the degeneration of dopamine-producing neurons in the substantia nigra, a region of the brain which is involved in controlling movement. The loss of dopamine leads to the characteristic symptoms of Parkinson's disease, including tremors, rigidity, bradykinesia (slowed movement), and postural instability. Although there is no cure for Parkinson's, medications and therapies such as deep brain stimulation can manage symptoms and improve the quality of life for individuals with the condition.
- Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a rare neurodegenerative disease affecting motor neurons in the brain and spine. The progressive degeneration of these neurons leads to muscle weakness, atrophy, and eventually paralysis. As a result, individuals with ALS may initially experience difficulty with tasks such as walking, speaking, or swallowing. Individuals cannot move, speak, or even breathe as the disease progresses without assistance. At present, no treatment for ALS, and treatments primarily focus on managing symptoms, improving quality of life, and prolonging survival.

47.11.2 Traumatic Brain Injury (TBI): Causes, Symptoms, and Consequences

Traumatic Brain Injury (TBI) occurs when external forces, such as a blow to the head, disrupt normal brain function. TBIs can result from various causes, including falls, car accidents, sports injuries, and violence. Depending on the severity and location of the injury, TBI can cause a range of symptoms, from mild (e.g., headache, dizziness) to severe (e.g., unconsciousness, memory loss, seizures).

TBIs can be classified into two main categories: closed and penetrating. In closed TBIs, the skull remains intact. The injury results from the sudden acceleration and deceleration of the brain within the skull, causing it to collide with the inner surface. Penetrating TBIs involve a breach of the skull and dura mater, typically caused by a foreign object, such as a bullet or sharp instrument, penetrating the brain tissue.

The severity of TBI is often categorised as mild, moderate, or serious based on the Glasgow Coma Scale (GCS) score, which assesses the patient's level of consciousness, eye response, and motor response. Mild TBI, generally known as a concussion, is the most prevalent form of TBI and usually results in short-lived symptoms that resolve within days or weeks. However, moderate and severe TBIs can cause more significant neurological impairments and long-lasting or permanent disabilities.

Symptoms of TBI can vary widely depending on the severity and location of the injury. Some common symptoms include:

• Headache • Dizziness or balance problems • Nausea or vomiting • Blurred vision or sensitivity to light • Tinnitus • Confusion or disorientation • Memory loss or amnesia • Sleep disturbances • Mood changes or irritability

In more severe cases, individuals may experience unconsciousness, seizures, difficulty with speech or motor function, weakness or numbness in the extremities, and loss of coordination. Additionally, TBIs can have long-term consequences, such as an increased risk of developing neurodegenerative diseases such as Alzheimer's or Parkinson's, chronic pain, cognitive deficits, and emotional and behavioural changes.

Treatment for TBI will vary depending on the severity of the injury and the specific symptoms experienced. For example, rest and symptom management may be sufficient for mild TBIs, while more severe cases may require surgery, rehabilitation, and ongoing medical care. Therefore, early intervention and appropriate management of TBI are crucial for minimising long-term consequences and promoting optimal recovery.

47.11.3 Stroke: Types, Symptoms, and Consequences

A stroke occurs when blood flow to part of the brain is interrupted by a blood clot (ischemic stroke) or a ruptured blood vessel (haemorrhagic stroke). This deprives brain tissue of oxygen and nutrients, leading to the rapid death of affected neurons. Strokes are a leading cause of mortality and disability worldwide. They can cause a variety of symptoms, such as paralysis, speech difficulties, and cognitive impairments, depending on the affected brain region.

Ischemic strokes, which account for approximately 85% of all strokes, occur when a blood clot blocks blood flow to part of the brain. The clot may form in a small blood vessel within the brain (thrombotic stroke) or travel from another part of the body and become lodged in a brain artery (embolic stroke). Ischemic strokes often result from underlying conditions such as atherosclerosis, which is the buildup of fatty deposits on the inside walls of blood vessels.

Alternatively, haemorrhagic strokes occur when blood vessels rupture, causing bleeding in the surrounding brain tissue. However, this type of stroke is less common but often more severe than ischemic. Haemorrhagic strokes can also be caused by high blood pressure, aneurysms (a weakened, bulging area in a blood vessel), or arteriovenous malformations (abnormal tangles of blood vessels).

The symptoms of a stroke can differ depending on the affected brain region and the extent of neuronal damage. Some common symptoms include:

• Sudden weakness or insensitivity on one side of the body • Difficulty speaking or understanding speech • Blurred or lost sight in one or both eyes • Dizziness, loss of balance, or difficulty walking • Severe, sudden headache with no known cause

Strokes can have long-lasting consequences, such as paralysis or muscle weakness, speech and language difficulties, memory and cognitive impairments, and emotional and behavioural changes. Recovery from a stroke depends on the severity of the injury, the affected brain region, and the individual's overall health. Recovery, including physical, occupational, and speech therapy, is crucial in helping stroke survivors regain lost function and adapt to any remaining disabilities.

47.11.4 Multiple Sclerosis (MS): Overview, Symptoms, and Progression

MS is a long-term autoimmune disease that affects the CNS, causing inflammation and damage to the protective myelin sheaths produced by oligodendrocytes. The myelin sheaths insulate the axons of nerve cells and facilitate the efficient transmission of electrical signals. As the myelin is damaged or destroyed, the normal flow of electrical signals along the axons is disrupted, leading to a wide range of neurological symptoms. The severity and progression of MS can vary significantly between individuals, and the underlying cause of the autoimmune attack remains unclear.

Common symptoms of MS include:

• Muscle weakness or stiffness • Difficulty with coordination and balance • Vision problems, such as blurred or double vision • Cognitive impairments, including memory problems and difficulty concentrating • Fatigue • Numbness or tingling sensations in the limbs • Speech difficulties • Bladder and bowel dysfunction • Emotional changes, such as depression or mood swings

The progression of MS is highly variable and can be categorised into four main types:

- Relapsing-Remitting MS (RRMS) is characterised by periods of acute symptom flare-ups (relapses) followed by periods of partial or complete recovery (remissions). The majority of MS patients are initially diagnosed with RRMS.
- Secondary Progressive MS (SPMS) forms over time, and in some cases, individuals with RRMS transition to SPMS, where the disease progresses more steadily and leads to worsening disability. Relapses may still occur but become less frequent.

- In Primary Progressive MS (PPMS), the symptoms gradually worsen from the onset without distinct relapses or remissions. PPMS accounts for about 10-15% of MS cases.
- Progressive-Relapsing MS (PRMS) is a rare MS characterised by a steady disease progression from the beginning, with occasional acute relapses. There are no periods of remission in PRMS.

However, MS has no cure; various treatments are available to manage symptoms, reduce inflammation, and slow disease progression. These treatments include disease-modifying therapies, corticosteroids, physical therapy, and medications to manage specific symptoms, such as muscle spasms or fatigue. Therefore, early diagnosis and treatment are essential for improving the quality of life for individuals living with MS.

47.12 Conclusion

The CNS is a highly intricate and organised structure that plays a crucial role in nearly every aspect of human life. Comprising the brain and spinal cord, the CNS is responsible for processing sensory information, coordinating motor function, and enabling higher cognitive processes such as reasoning, learning, and memory. Neurons and glial cells work in tandem to facilitate communication and maintain the overall health and function of the CNS.

Various pathologies can impact the CNS, leading to a wide array of diverse and often debilitating symptoms. These pathologies include neurodegenerative diseases, TBIs, strokes, and autoimmune disorders, for example, multiple sclerosis. As a result, understanding the complexities of the CNS is a central focus of neuroscience research.

By delving deeper into the intricacies of the CNS, scientists hope to unlock the mysteries of human cognition and develop innovative treatments for neurological disorders. Continued research is essential for improving our understanding of the brain's function and dysfunction, leading to advances in diagnostic techniques and therapeutic interventions and, ultimately, enhancing the quality of life for individuals affected by neurological conditions.

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48 The Impact of PET Scans in Medical Imaging and Diagnostics

Positrons, alpha particles, beta particles, and electron capture contribute to nuclear medicine, diagnostics, and diverse scientific applications.

48.1 Introduction

The role of positrons in nuclear medicine began with its discovery in 1932 by Carl David Anderson. It opened up numerous opportunities for their application in various fields, including medical imaging. This article will discuss the role of positrons in medical imaging, specifically focusing on their use in Positron Emission Tomography (PET) scans, the associated benefits and limitations, and future developments in the field.

PET is a non-invasive diagnostic imaging technique that visualises the metabolic activity of tissues within the body. It is primarily used for detecting cancer, evaluating the response to therapy, and monitoring the progression of neurological disorders such as Alzheimer's disease and Parkinson's disease.

The PET scan procedure involves injecting a small amount of a radioactive tracer, usually a biologically active molecule labelled with a positron-emitting radionuclide, into the patient's bloodstream. The radionuclide decays as the tracer accumulates in the target tissues, emitting positrons. Upon encountering an electron in the tissue, the positron undergoes annihilation, producing two gamma photons with energies of 511 keV, which travel in opposite directions.

These gamma photons are detected by a ring of detectors surrounding the patient. Their coincident detection allows for accurately determining the location of the tracer's uptake within the body. This information is then used to generate a three-dimensional image, providing insights into the metabolic activity of the tissues.

48.2 Positrons in Nuclear Medicine

Several positron-emitting radionuclides are used in PET imaging, each with different characteristics that make them suitable for specific applications. The most commonly used radionuclide is fluorine-18 (F-18), which has a half-life of approximately 110 minutes. F-18 is often used to label fluorodeoxyglucose (FDG), a glucose analogue that is taken up by cells with high metabolic activity, such as cancer cells.

Other positron-emitting radionuclides include carbon-11 (C-11), nitrogen-13 (N-13), and oxygen-15 (O-15), which have shorter half-lives and are used for specialised imaging applications.

PET scans offer a high degree of sensitivity and specificity for detecting and localising cancerous lesions, making them an invaluable tool in diagnosing and staging various types of cancer. This high accuracy is due to the ability of PET scans to detect changes in the metabolic activity of tissues, which often precedes anatomical changes observed in other imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI).

In addition to providing information on the body's anatomy, PET scans can reveal functional and molecular processes occurring within tissues. This allows for assessing various physiological parameters, such as blood flow, oxygen consumption, and glucose metabolism, providing insights into the underlying disease processes and monitoring treatment response.

Combination with Other Imaging Modalities PET scans is often combined with CT or MRI scans in a single examination, known as PET/CT or PET/MRI, respectively. This combination provides functional and anatomical information in a single image, enabling more accurate localisation of lesions and improving diagnostic confidence.

PET scans are crucial in monitoring the response to treatment in patients undergoing cancer therapy. By evaluating changes in metabolic activity, PET scans can help determine the effectiveness of a given treatment, allowing clinicians to make informed decisions about continuing, modifying, or stopping a particular therapy. This helps in personalising treatment plans and optimising patient outcomes.

One of the primary concerns associated with PET scans is exposure to ionising radiation, which can potentially increase the risk of cancer over time. However, the radiation dose from a single PET scan is relatively low and is considered acceptable when balanced against the significant diagnostic benefits provided.

PET scans are generally more expensive than other imaging modalities such as CT and MRI, making them less accessible to some patients. Additionally, the availability of PET scanners is limited in certain geographic areas, potentially requiring patients to travel long distances to access this technology.

While PET scans offer high sensitivity for detecting metabolic changes in tissues, their spatial resolution is lower than CT and MRI scans. This can make it challenging to precisely localise small lesions or abnormalities, particularly in areas with complex anatomy.

PET scans can occasionally produce false-positive results, where areas of increased tracer uptake are incorrectly identified as cancerous lesions. This can be due to inflammation, infection, or other benign processes that increase metabolic activity. Conversely, false-negative results can occur when cancerous lesions have low metabolic activity or are too small to be detected.

Research is ongoing to develop new tracers and radionuclides that target specific molecular markers, improving the specificity and sensitivity of PET imaging. These

novel tracers will detect a more comprehensive range of diseases and provide a more detailed understanding of the underlying molecular processes.

Time-of-Flight (TOF) PET is an advanced PET imaging technique that measures the difference in arrival times of the two gamma photons produced during positron annihilation. This additional timing information improves the image quality and spatial resolution, allowing for more accurate localisation of tracer uptake within the body.

Integrating artificial intelligence and machine learning in PET imaging can revolutionise the field by automating the analysis and interpretation of PET images, improving the accuracy of diagnosis, and providing predictive insights into disease progression and treatment response.

The table below shows some radioisotopes used in medical imaging, along with their half-lives and typical applications:

Radioisotope	Half-Life	Application
Technetium-99m	6 hours	Single Photon Emission Computed Tomography (SPECT) for various applications, including bone, heart and brain imaging
Iodine-123	13.2 hours	Thyroid imaging, cerebral blood flow and neuroendocrine tumour imaging
Iodine-131	8.02 days	Thyroid imaging and therapy, whole-body scans in thyroid cancer patients
Fluorine-18	109.8 minutes	Positron Emission Tomography (PET) for cancer, brain and cardiac imaging
Gallium-67	3.26 days	Infection and inflammation imaging, tumour location
Thallium-201	73 hours	Myocardial perfusion imaging (MPI) for cardiac evaluation
Indium-111	2.83 days	Infection imaging, tumour imaging, white blood cell imaging
Carbon-11	20.4 minutes	PET imaging for brain metabolism, neurotransmitter imaging, and tumour imaging
Nitrogen-13	9.97 minutes	PET imaging for myocardial perfusion and blood flow
Oxygen-15	2.03 minutes	PET imaging for cerebral blood flow and oxygen metabolism
Rubidium-82	1.27 minutes	PET imaging for myocardial perfusion imaging (MPI)
Gallium-68	67.71 minutes	PET imaging for neuroendocrine tumour imaging and prostate-specific membrane antigen (PSMA) imaging
Copper-64	12.7 hours	PET imaging for cancer imaging and therapy, cell trafficking and hypoxia imaging
Zirconium-89	78.4 hours	PET imaging for immuno-PET applications and tracking of labelled antibodies

- A positron, a positively charged subatomic particle (the antiparticle of an electron), is emitted by a radionuclide, typically used in medical imaging procedures like PET scans.
- The positron travels a short distance within the tissue (usually a few millimetres) before encountering an electron, a negatively charged subatomic particle.
- When the positron meets the electron, they undergo a process called annihilation. In this process, both particles are destroyed, and their combined mass is converted into energy.
- The annihilation event generates two gamma photons, each with an energy of 511 keV (kilo-electron volts). These photons are emitted in opposite directions (approximately 180 degrees apart) due to the conservation of momentum.
- The gamma photons travel through the tissue and are detected by the PET scanner's ring of detectors. The PET scanner uses the information from these detected photons to determine the location of the original positron emission, ultimately generating a three-dimensional image of the tracer's distribution in the body.

The table below shows some radiopharmaceuticals used in medical imaging and their applications:

Radiopharmaceutical	Application
F-18 Fluorodeoxyglucose (FDG)	PET imaging for cancer, brain and cardiac imaging, as well as inflammation and infection imaging
Tc-99m Methylene Diphosphonate (MDP)	SPECT imaging for bone scans (e.g. detecting fractures, infections and metastases)
Tc-99m Sestamibi (MIBI)	SPECT imaging for myocardial perfusion imaging (MPI) and parathyroid imaging
Tc-99m Tetrofosmin	SPECT imaging for myocardial perfusion imaging (MPI)
I-123 Sodium iodide	SPECT imaging for thyroid function and morphology and thyroid cancer imaging
I-131 Sodium iodide	SPECT imaging and therapy for thyroid cancer and hyperthyroidism
In-111 Pentetreotide (Octreoscan)	SPECT imaging for neuroendocrine tumour imaging
Ga-68 DOTATATE / DOTATOC / DOTANOC	PET imaging for neuroendocrine tumour imaging
Ga-68 PSMA-HBED-CC	PET imaging for prostate cancer imaging
C-11 Choline	PET imaging for prostate cancer and brain tumour imaging
C-11 PIB (Pittsburgh Compound B)	PET imaging for Alzheimer's disease, assessing amyloid-beta plaques in the brain
N-11 Ammonia	PET imaging for myocardial perfusion and blood flow
O-15 Water	PET imaging for cerebral blood flow and oxygen metabolism

Rb-82 Rubidium chloride	PET imaging for myocardial perfusion imaging (MPI)
Zr-89 Labelled antibodies	PET imaging for immuno-PET applications, tracking labelled antibodies for cancer imaging

48.3 Alpha Particles

Alpha particles, consisting of two protons and two neutrons, are ionising radiation emitted during the decay of certain radioactive isotopes. While their use in medical imaging is limited due to their short range and high linear energy transfer, they have found valuable applications in targeted alpha therapy (TAT) for cancer treatment. This essay will discuss the role of alpha particles in medical imaging and therapy, focusing on their properties, therapeutic applications, and potential future developments.

Alpha particles are heavy, positively charged particles with a high linear energy transfer (LET), meaning they deposit a large amount of energy over a relatively short distance. In tissue, alpha particles typically have a range of only a few tens of micrometres. Depending on the application, this short-range results in a significant dose deposition in a small volume, which can be both advantageous and disadvantageous.

Due to their high LET, alpha particles can cause significant damage to biological tissues, particularly the DNA within cells. This makes them potentially effective for cancer treatment but also poses risks to healthy tissues if not accurately targeted.

Alpha particles have limited direct applications in medical imaging due to their short range and high LET. In addition, the short range of alpha particles prevents them from effectively penetrating tissues and reaching detectors outside the body, making them unsuitable for traditional imaging techniques like PET and SPECT.

However, alpha-emitting isotopes can play a role in specialised imaging techniques, such as autoradiography and single-cell imaging. Autoradiography involves using alpha-emitting isotopes in histological studies to visualise the distribution of radiolabelled compounds in tissue samples. This technique can help researchers understand the uptake and distribution of therapeutic agents or other molecules in biological systems.

48.4 Alpha Particles in Targeted Alpha Therapy for Cancer Treatment

Alpha particles are used in targeted alpha therapy (TAT), an emerging cancer treatment modality. TAT involves using alpha-emitting isotopes conjugated to cancer-targeting molecules, such as antibodies, peptides, or small molecules. These alpha-emitting radiopharmaceutical conjugates can selectively bind to cancer cells, delivering a highly localised dose of ionising radiation.

The high LET and short range of alpha particles offer several advantages for TAT:

- The ionising radiation emitted by alpha particles is highly effective at inducing irreparable DNA damage in cancer cells, leading to cell death. This makes alpha-emitting radiopharmaceuticals highly potent, even against radioresistant or hypoxic tumours.

- Due to their short range, alpha particles deposit most of their energy within a small volume, reducing the risk of damage to surrounding healthy tissues. This property allows for delivering a high therapeutic dose to cancer cells while minimising side effects.
- The unique DNA damage caused by alpha particles is challenging for cancer cells to repair, reducing the risk of developing resistance to the therapy.

Several alpha-emitting radiopharmaceuticals are currently under investigation for TAT applications: Radium-223 dichloride (Ra-223): Radium-223 is an alpha-emitting isotope for treating bone metastases in patients with castration-resistant prostate cancer. It selectively targets areas of bone remodelling, delivering a high dose of alpha radiation to the metastatic lesions. Actinium-225 (Ac-225) and Bismuth-213 (Bi-213) conjugates: Actinium-225 and Bismuth-213 are alpha-emitting isotopes that can be conjugated to cancer-targeting molecules, such as antibodies or peptides. These conjugates can selectively deliver alpha radiation to specific cancer cells, sparing healthy tissues. Some examples of Ac-225 and Bi-213 conjugates under investigation include:

- Ac-225-PSMA-617, this radiopharmaceutical, targets the prostate-specific membrane antigen (PSMA), which is overexpressed in prostate cancer cells. Ac-225-PSMA-617 has shown promising results in early clinical trials to treat metastatic castration-resistant prostate cancer.
- Ac-225-DOTATOC/DOTATATE, these radiopharmaceuticals target somatostatin receptors, which are overexpressed in neuroendocrine tumours. Preclinical studies and early clinical trials have demonstrated the potential of Ac-225-DOTATOC/DOTATATE for treating patients with advanced neuroendocrine tumours.
- Bi-213-Lintuzumab, this radiopharmaceutical, is an anti-CD33 monoclonal antibody conjugated to Bismuth-213. It targets the CD33 antigen, which is overexpressed on the surface of acute myeloid leukaemia (AML) cells. Bi-213-Lintuzumab is currently under investigation as a potential targeted therapy for patients with AML.

48.4 Challenges and Future Perspectives

While targeted alpha therapy has shown promise in preclinical studies and early clinical trials, several challenges must be addressed to realise its potential fully:

The production of alpha-emitting isotopes, such as Ac-225 and Bi-213, is complex and often limited by the availability of suitable reactors and targets. As a result, efforts are underway to develop new production methods and improve isotope availability for research and clinical use.

Developing effective and safe alpha-emitting radiopharmaceuticals requires optimisation of the targeting molecule, chelator, and radionuclide to ensure selective delivery and minimal off-target effects. This involves extensive preclinical research and testing.

Accurate dosimetry is essential for determining the optimal therapeutic dose while minimising the risk of radiation-induced side effects. Improved dosimetry models and methods are needed to predict better alpha-emitting radiopharmaceuticals' biodistribution, radiation dose, and potential toxicities.

As with any novel therapeutic modality, targeted alpha therapy must navigate complex regulatory pathways and commercialisation challenges to reach patients. Close collaboration between researchers, clinicians, regulatory agencies, and industry partners will translate TAT from the bench to the bedside.

In summary, alpha particles have limited direct applications in medical imaging, but their unique properties have opened new avenues for cancer therapy through targeted alpha therapy. The development of alpha-emitting radiopharmaceuticals has shown promising results in preclinical and early clinical studies, offering the potential for improved outcomes for patients with hard-to-treat cancers. Continued research, development, and collaboration across disciplines will be essential to overcome the challenges associated with TAT and bring this promising therapeutic modality to routine clinical practice.

48.5 Beta Particles in Medicine: Illuminating the Path for Imaging and Radionuclide Therapy

Beta particles are high-energy, charged particles emitted during the decay of certain radioactive isotopes. They play a significant role in medical imaging and therapy, particularly in single-photon emission computed tomography (SPECT) and positron emission tomography (PET). This essay will discuss the role of beta particles in medical imaging and therapy, focusing on their properties, applications in imaging and radionuclide therapy, and potential future developments.

Beta particles are subatomic particles emitted during beta decay, which can be of two types: beta-minus (β-) decay and beta-plus (β+) decay. Beta-minus particles are electrons, while beta-plus particles are positrons (the antimatter counterpart of electrons). Both types of beta particles have a negative or positive charge and a relatively low mass, and they can travel several millimetres to centimetres in biological tissues.

The range of beta particles depends on their energy, with higher-energy particles travelling greater distances. As ionising radiation, beta particles can interact with and damage biological molecules, such as DNA, which can be exploited for therapeutic purposes.

48.6 Applications in Medical Imaging

Beta particles, particularly positrons (β+), play a significant role in medical imaging through positron emission tomography (PET). PET imaging relies on detecting gamma rays produced when a positron emitted by a radiotracer annihilates with an electron in the surrounding tissue.

Radiotracers used in PET imaging are typically labelled with positron-emitting isotopes, such as fluorine-18 (F-18), carbon-11 (C-11), or oxygen-15 (O-15). These tracers can target specific biological processes or molecules, allowing for functional imaging of various physiological and pathological conditions.

Some typical applications of PET imaging using beta-emitting radiotracers include:

- PET scans using F-18 fluorodeoxyglucose (FDG) are widely used for cancer diagnosis, staging, and monitoring treatment response. FDG is a glucose analogue that accumulates in cells with high glucose metabolism, such as cancer cells.
- In neurology, PET imaging with beta-emitting radiotracers, such as C-11 PiB for Alzheimer's disease or F-18 fluorodopa for Parkinson's disease, enables the visualisation of specific neurotransmitter systems and pathological processes in the brain.
- Beta-emitting radiotracers, such as N-13 ammonia or rubidium-82, are used in PET imaging to assess myocardial perfusion and evaluate blood flow in the heart.

48.7 Applications in Radionuclide Therapy

Beta particles are also used in radionuclide therapy, delivering a targeted dose of ionising radiation to cancer cells or other pathological tissues. Beta-emitting radionuclides, such as iodine-131 (I-131), lutetium-177 (Lu-177), and yttrium-90 (Y-90), can be attached to cancer-targeting molecules, like antibodies or peptides, to form radiopharmaceuticals.

Examples of beta-emitting radiopharmaceuticals in therapy include:

- I-131 for thyroid cancer and hyperthyroidism: Iodine-131 is a beta-emitting isotope used to treat differentiated thyroid cancer and hyperthyroidism. After oral administration, I-131 accumulates in the thyroid gland, delivering a localised dose of beta radiation to destroy cancerous or overactive thyroid cells.
- Lu-177-DOTATATE for neuroendocrine tumours: Lutetium-177 is a beta-emitting isotope conjugated to the peptide DOTATATE, which targets somatostatin receptors overexpressed on the surface of neuroendocrine tumour cells. This radiopharmaceutical, known as Lutathera, selectively delivers beta radiation to neuroendocrine tumours, causing DNA damage and cell death. Lu-177-DOTATATE has been approved for treating gastroenteropancreatic neuroendocrine tumours (GEP-NETs) and has shown promising results in clinical trials, with improved progression-free survival and reduced tumour burden in many patients.
- Y-90 microspheres for liver cancer: Yttrium-90 is a beta-emitting isotope that can be incorporated into microspheres (tiny beads) to treat liver cancer. The Y-90 microspheres are delivered via a catheter directly into the hepatic artery, which supplies blood to the liver tumours. The microspheres become lodged in the tumour's blood vessels, providing a high dose of localised beta radiation

that destroys cancer cells while sparing healthy liver tissue. This treatment, known as selective internal radiation therapy (SIRT) or radioembolisation, has been used to treat primary liver cancer (hepatocellular carcinoma) and liver metastases from other cancers.

48.8 Challenges and Future Perspectives

The role of beta particles in medical imaging and therapy, there are several challenges and areas for improvement:

- Developing effective and safe beta-emitting radiopharmaceuticals requires optimisation of the targeting molecule, chelator, and radionuclide to ensure selective delivery and minimal off-target effects. This involves extensive preclinical research and testing.
- Accurate dosimetry is crucial for determining the optimal therapeutic dose while minimising the risk of radiation-induced side effects. Improved dosimetry models and methods are needed to predict better beta-emitting radiopharmaceuticals' biodistribution, radiation dose, and potential toxicities.
- Combining beta-emitting radionuclide therapy with other treatment modalities, such as chemotherapy, immunotherapy, or targeted therapies, may enhance treatment efficacy and overcome resistance mechanisms. However, these therapies' optimal combination, sequencing, and timing must be investigated in preclinical and clinical studies.
- As with any cancer therapy, there is a need for personalised medicine approaches in beta-emitting radionuclide therapy to identify patients who are most likely to benefit from the treatment. Biomarkers and imaging techniques that can predict treatment response and monitor treatment effects are critical for the optimal selection and management of patients.

In summary, beta particles play a crucial role in medical imaging and therapy, with applications in PET imaging and radionuclide therapy for various cancer types and other diseases. Developing novel beta-emitting radiopharmaceuticals, optimisation of dosimetry, and integrating combination therapies and personalised medicine approaches can potentially improve patient outcomes and expand the applications of beta particles in medicine. Continued research, development, and collaboration across disciplines will be essential to realise the full potential of beta particles in medical imaging and therapy.

48.9 The Role of Electron Capture in Medical Imaging

Electron capture is a nuclear decay process in which a proton-rich nuclide captures one of its atomic electrons, converting a proton into a neutron and emitting a neutrino. This process can produce gamma rays, which can be utilised in medical imaging techniques like single-photon emission computed tomography (SPECT). This essay will discuss the role of electron capture in medical imaging, focusing on its

implications for radiotracer design, applications in SPECT imaging, and potential future developments.

The electron capture process can play a role in the design of radiotracers for medical imaging. For example, isotopes that undergo electron capture can emit gamma rays, which can be detected using gamma cameras to create a functional image of the distribution of the radiotracer in the body.

The choice of an isotope is critical when designing a radiotracer for medical imaging. Isotopes that undergo electron capture typically have relatively long half-lives, making them suitable for imaging studies requiring extended tracer distribution and uptake periods. Additionally, the energy of the emitted gamma rays should be optimal for detection and imaging while minimising the radiation dose to the patient.

48.10 Applications in SPECT Imaging

Single-photon emission computed tomography (SPECT) is a nuclear medicine imaging technique that relies on detecting gamma rays emitted by radiotracers. SPECT has been widely used for various clinical applications, including oncology, cardiology, and neurology.

Radiotracers used in SPECT imaging can be designed with isotopes that undergo electron capture, emitting gamma rays that the gamma camera can detect. Some common electron capture isotopes used in SPECT imaging include:

- Thallium-201 (Tl-201) is an isotope that undergoes electron capture, emitting gamma rays with energies of 69 and 81 keV. Tl-201 has been used as a radiotracer in SPECT imaging for myocardial perfusion, helping to diagnose coronary artery disease and assess the viability of heart tissue after a heart attack.
- Gallium-67 (Ga-67) is another isotope that undergoes electron capture, emitting gamma rays with energies ranging from 93 to 300 keV. Ga-67 citrate has been used as a radiotracer in SPECT imaging for infection, inflammation, and tumour imaging in certain types of cancers, such as lymphoma.
- Indium-111 (In-111) is an isotope that undergoes electron capture, emitting gamma rays with energies of 171 and 245 keV. In-111 can be conjugated to various targeting molecules, such as antibodies or peptides, to create radiotracers for SPECT imaging of specific biological targets. Some examples include In-111-labeled octreotide for neuroendocrine tumour imaging and In-111-labeled leukocytes for infection imaging.

48.11 Challenges and Future Perspectives

While electron capture plays a role in medical imaging through the design and application of SPECT radiotracers, there are several challenges and areas for improvement:

- Developing effective and safe electron capture-based radiotracers requires optimisation of the targeting molecule, chelator, and radionuclide to ensure

selective delivery and minimal off-target effects. This involves extensive preclinical research and testing.

- The energy of gamma rays emitted by electron capture isotopes can affect image quality and sensitivity. High-energy gamma rays may increase scatter and attenuation, while low-energy gamma rays may be more susceptible to absorption in the patient's body.
- Optimising the energy of the emitted gamma rays is essential for achieving high-quality images and maximising sensitivity in SPECT imaging. Therefore, radiotracers designed with electron capture isotopes should be carefully selected and evaluated based on the energy of their emitted gamma rays to minimise the adverse effects on image quality and sensitivity.

48.12 Advancements in Detector Technology and Image Reconstruction Algorithms

Technological advancements in gamma camera detectors and image reconstruction algorithms can help address the challenges associated with the energy of gamma rays emitted by electron capture isotopes. For example, new detector materials with higher energy resolution and improved efficiency can reduce scatter and attenuation effects, resulting in better image quality and sensitivity.

Similarly, advancements in image reconstruction algorithms, such as iterative reconstruction methods and scatter correction techniques, can help compensate for the effects of high-energy gamma rays on image quality and sensitivity. These improvements can lead to more accurate and reliable SPECT images, enabling better diagnosis and monitoring of diseases.

While electron capture-based SPECT imaging offers unique advantages, it is essential to consider its strengths and limitations compared to other imaging techniques, such as PET imaging. For example, PET imaging, which relies on detecting annihilation photons resulting from positron-electron interactions, often provides higher sensitivity and spatial resolution than SPECT imaging. Moreover, the development of PET tracers labelled with positron-emitting isotopes has expanded rapidly, enabling the imaging of a broader range of biological targets and processes.

However, SPECT imaging using electron capture isotopes offers some advantages over PET imaging, such as the availability of a broader range of gamma-ray energies and the possibility of using multiple tracers in a single imaging session. Additionally, SPECT imaging is often more accessible and affordable than PET imaging, making it a valuable alternative or complementary tool in medical imaging.

In summary, Electron capture plays a significant role in medical imaging by designing and applying radiotracers for SPECT imaging. However, the energy of gamma rays emitted by electron capture isotopes can affect image quality and sensitivity, highlighting the importance of optimising radiotracer design and utilising advancements in detector technology and image reconstruction algorithms.

The challenges and limitations associated with electron capture-based SPECT imaging, it remains a valuable tool in medical imaging for various clinical applications,

including oncology, cardiology, and neurology. Continued research and development in radiotracer design, detector technology, and image reconstruction methods will be essential for maximising the potential of electron capture in medical imaging and expanding its applications in disease diagnosis and management.

48.13 Harnessing Subatomic Particles: Transforming Nuclear Medicine and Medical Imaging for the Future

In conclusion, positrons, alpha particles, beta particles, and electron capture contribute significantly to the advancements and diverse applications in nuclear medicine and medical imaging. Understanding their distinct properties and functions is essential for researchers and clinicians to harness their potential for diagnosing and treating various diseases. The ongoing development of novel radiotracers, imaging techniques, and therapeutic applications based on these subatomic particles and nuclear decay processes continues to revolutionise the field, offering new possibilities for patient care and the advancement of personalised medicine. As technology and our understanding of these particles and processes evolve, the future of nuclear medicine and medical imaging holds immense promise for improving disease diagnosis, management, and therapy outcomes.

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49 Mastering Dosimetry: Pivotal Science for Radiological Protection, Nuclear Medicine, and Radiotherapy Applications

Dosimetry measures radiation dose, ensuring safety in radiological protection, nuclear medicine, and occupational environments through calculations.

49.1 Introduction

Dosimetry, the science of measuring and calculating the radiation dose absorbed by matter, plays a pivotal role in radiological protection, nuclear medicine, and radiotherapy. This field is a cornerstone for accurate radiation dose estimation, minimising potential health hazards, particularly in medical treatment and occupational settings. The mathematics of dosimetry enables accurate and consistent dose calculation by integrating various aspects, such as the physical properties of radiation, interaction with matter, and biological effects.

Radiation can be ionising or non-ionising, depending on its energy level. Ionising radiation, such as alpha, beta, gamma, and X-rays, possesses enough energy to ionise atoms and molecules in the matter it interacts with, causing biological damage. Non-ionising radiation, such as ultraviolet, visible light, and radio waves typically does not cause ionisation but can still cause harm at high intensities. Dosimetry primarily focuses on ionising radiation due to its potential risks and in various applications, including medical diagnosis and treatment, industrial processes, and research.

The interaction of ionising radiation with matter leads to energy deposition, which can cause localised damage to biological tissues. To quantify this damage, dosimetry employs several dose units, such as the Gray (Gy) for absorbed dose, Sievert (Sv) for equivalent and effective dose, and Becquerel (Bq) for activity. These units provide a standardised means of comparing radiation exposure and evaluating risks across different scenarios.

Dosimetry calculations often rely on mathematical models and simulations to account for the complex behaviour of radiation within matter. Monte Carlo simulations, for example, use random sampling techniques to model radiation transport and interaction, providing a statistically accurate representation of dose distribution in a given medium. In addition, these models can be customised to consider various factors, such as radiation type, energy spectrum, and the geometrical arrangement of the source, medium, and detectors.

In medical applications, dosimetry is critical in determining the optimal radiation dose for diagnostic and therapeutic procedures. For example, in diagnostic imaging, such as computed tomography (CT) scans and X-ray examinations, dosimetry helps balance image quality and patient dose to ensure accurate diagnosis with minimal risk. In radiotherapy, dosimetry helps plan the radiation dose distribution to deliver the maximum dose to the tumour while sparing healthy tissues, improving the likelihood of successful treatment.

Occupational dosimetry monitors and controls radiation exposure in workplaces such as nuclear power plants, research facilities, and hospitals. Tracking radiation dose using personal dosimeters ensures compliance with regulatory limits, minimising health risks and promoting a safety culture.

49.2 Basic Concepts and Units in Dosimetry

Radiation can be classified into two main categories: ionising and non-ionising. Ionising radiation carries enough energy to remove tightly bound electrons from atoms and molecules, forming charged particles or ions. Non-ionising radiation, on the other hand, does not possess sufficient energy to cause ionisation but can still produce thermal and photochemical effects.

Ionising radiation is further divided into directly ionising and indirectly ionising radiation. Directly ionising radiation consists of charged particles, such as alpha and beta particles, which can ionise atoms and molecules in their path due to their inherent electric charge. Alpha particles are heavy, positively charged particles emitted from the nucleus of heavy elements during radioactive decay. They have low penetration power and can be stopped by a sheet of paper or a few centimetres of air. Beta particles are lighter, negatively charged particles (electrons) or positively charged particles (positrons) also emitted during radioactive decay. Their penetration power is higher than alpha particles but can be stopped by thin plastic, glass, or aluminium, directly ionising radiation, including photons, gamma and X-rays, and neutrons.

Gamma rays are high-energy electromagnetic radiation emitted during nuclear reactions or radioactive decay. They are highly penetrating and require dense materials, like lead or concrete, for effective shielding. X-rays are similar to gamma rays in nature but are produced through different mechanisms, such as the interaction between high-energy electrons and matter. Neutrons are uncharged particles that can cause ionisation indirectly by interacting with atomic nuclei, causing the emission of charged particles. Neutrons can be highly penetrating, and their shielding requires materials rich in hydrogen, like water or polyethene.

These various types of radiation possess different energies and interaction properties with matter. Understanding their characteristics is essential for effective radiation protection, dosimetry, and the development of radiation-based technologies in medicine, industry, and research. Knowing the energy levels and properties of each radiation type makes it possible to design appropriate shielding, monitoring, and control strategies to minimise potential health risks and optimise the beneficial applications of radiation in numerous fields.

49.3 Dosimetric Quantities

In dosimetry, two key quantities are essential for understanding and assessing the impact of ionising radiation on matter and living organisms: the absorbed dose (D) and the equivalent dose (H). These quantities provide a standardised way to quantify the potential biological effects of different types of radiation, allowing for informed decision-making in medical, industrial, and research settings.

The absorbed dose (D) represents the mean energy imparted by ionising radiation per unit mass of matter. It is typically expressed in Gray (Gy) units, where 1 Gy equals the absorption of 1 joule of radiation energy per kilogram of matter. The absorbed dose indicates the amount of energy deposited in a material or tissue, which can cause ionisation and potential biological damage in the case of living organisms. However, the absorbed dose does not account for the varying effectiveness of different radiation types in causing harm.

The equivalent dose (H) considers the biological effectiveness of the radiation by accounting for the type and energy of the radiation. The absorbed dose is multiplied by a radiation weighting factor (wR) to calculate the equivalent dose, reflecting the specific radiation type's relative biological effectiveness (RBE). The unit for equivalent dose is the sievert (Sv), and 1 Sv equals 1 Gy multiplied by the radiation weighting factor.

$$\text{Equivalent dose (H)} = \text{Absorbed dose (D)} \times \text{Radiation weighting factor (wR)}$$

The radiation weighting factors account for the differences in the ionising potential and the density of ionisation events caused by various types of radiation. For example, alpha particles have a higher radiation weighting factor than beta particles, gamma rays, or X-rays because of their greater ability to cause biological damage.

Creating a comprehensive table of dosimetry values for the human body is challenging due to the factors involved, such as the type of radiation, energy, and individual tissue sensitivities. However, I can provide a simplified table illustrating the organ and tissue weighting factors (wT) used for calculating the effective dose (E) from the equivalent dose (H) in radiation protection:

Organ/Tissue	Weighting Factor (wT)
Gonads (Testes, Ovaries	0.20
Red Bone Marrow	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Oesophagus	0.05
Thyroid	0.05
Skin	0.01
Bone Surface	0.01
The Remainder (Other Organs/Tissues)	0.12

Note that these values are based on the International Commission on Radiological Protection (ICRP) Publication 103 recommendations and are subject to change with updated recommendations.

The effective dose (E) can be calculated by summing the product of the equivalent dose (H) and the weighting factor (wT) for each organ or tissue:

$$E = \Sigma [wT * H(T)]$$

This calculation allows for the comparison of radiation exposure across different organs, tissues, and radiation types, accounting for the varying sensitivities of different organs to ionising radiation.

49.4 Interaction of Radiation with Matter

Attenuation is a critical concept in understanding the behaviour of radiation as it interacts with and passes through matter. As radiation traverses a medium, it loses intensity due to attenuation, including absorption (energy transfer to the medium) and scattering (deflection of radiation in different directions). Understanding attenuation is vital for designing effective shielding, radiation protection, and dosimetry strategies in various applications, including medicine, industry, and research.

The intensity of the radiation (I) after passing through a given thickness (x) of material can be determined using the Beer-Lambert law:

$$I(x) = I0 * e^{-\mu x}$$

Where I0 is the initial intensity, μ is the linear attenuation coefficient, and x is the thickness of the material. The linear attenuation coefficient (μ) is a property of the material and the type and energy of the radiation. It quantifies the likelihood of interaction between the radiation and the material, with higher values indicating greater attenuation.

The linear attenuation coefficient (μ) varies depending on the type and energy of radiation and the composition of the specific tissue in the human body. Here is a simplified list of approximate linear attenuation coefficients for some common tissues and materials in the human body at a photon energy of 100 keV.

Tissue / Material	Linear Attenuation Coefficient (μ) (cm^{-1})
Air	0.0002
Water	0.17
Fat	0.19
Muscle	0,20
Lung Tissue	0.23
Blood	0.21
Bone	**0.35 – 0.6**

Note that these values are approximate and specific to the given photon energy of 100 keV. The linear attenuation coefficients for other energies or types of radiation, such as alpha or beta particles, will be different. Additionally, the values may vary for specific tissues or materials, even within the same general category.

For a more detailed and accurate list of linear attenuation coefficients, refer to the National Institute of Standards and Technology (NIST) XCOM database, which provides values for various materials and energies.

Attenuation is a significant factor when designing radiation shielding, as it determines the thickness and material properties required to reduce radiation exposure to acceptable levels. Different materials have varying attenuation characteristics for specific types of radiation. For instance, dense materials like lead or concrete effectively attenuate gamma rays, while materials rich in hydrogen, such as water or polyethene, are suitable for shielding against neutrons.

Understanding attenuation is essential for optimising image quality and radiation dose in medical imaging and radiotherapy. By knowing how radiation interacts with different tissues and materials, medical professionals can adjust imaging parameters and plan therapeutic interventions to minimise the radiation dose to patients while maximising diagnostic or therapeutic outcomes.

49.5 Linear Energy Transfer (LET)

Linear energy transfer (LET) is critical in radiation physics and dosimetry. It quantifies the energy a charged particle deposits per unit length of its path through a medium. It is typically expressed in units of keV/μm (kilo-electron volts per micrometre) or MeV/cm (mega-electron volts per centimetre). The LET of radiation significantly impacts its biological effects and interaction properties with matter.

High LET radiation, such as alpha particles, is characterised by a dense ionisation pattern along the particle's track, causing more ionisations and excitations per unit length than low LET radiation, such as gamma rays or X-rays. Due to the high ionisation

density, high LET radiation has a greater probability of causing severe and clustered DNA damage in living cells, which is less likely to be accurately repaired by cellular repair mechanisms. Consequently, high LET radiation is generally considered more biologically effective than low LET radiation of the same absorbed dose.

Low LET radiation, such as gamma rays and X-rays, has a sparse ionisation pattern and deposits its energy over a longer distance in the medium. This type of radiation typically causes less severe and more isolated DNA damage, which is more likely to be repaired by cellular mechanisms. However, low LET radiation can still cause significant biological effects, especially at high doses or dose rates.

Below is a table summarising the properties of alpha, beta, and gamma radiation, including their LET values and other relevant information:

Radiation Type	Symbol	Particle/Photon	Charge	Mass (amu)	LET (keV/μm)	Penetrating Power	Shielding Material
Alpha	α	Helium nucleus	+2	4	50-200	Low	Paper, clothing
Beta	β	Electron	-1	~0	0.1-10	Moderate	Plastic, glass
Gamma	γ	Photon	0	0	<0.1	High	Lead, concrete

-
- Alpha (α) radiation consists of helium nuclei (2 protons and 2 neutrons) and has a high LET value, which means it causes many ionisations and excitations per unit length. Due to its high LET, alpha radiation has low penetrating power and can be stopped by paper or clothing.
- Beta (β) radiation consists of electrons, which are much lighter and have a negative charge. Beta particles have a lower LET value than alpha particles, indicating fewer ionisations and excitations per unit length. Beta radiation has moderate penetrating power and can penetrate materials like plastic or glass but can be shielded by denser materials.
- Gamma (γ) radiation is a type of electromagnetic radiation consisting of photons with no charge or mass. Gamma rays have the lowest LET values, implying minimal ionisations and excitations per unit length. However, they have high penetrating power and can pass through many materials, requiring lead or concrete to provide effective shielding.

It is important to note that these values are approximate and may change on the specific radionuclide and energy of the radiation.

Understanding the LET of radiation is essential for various applications, including radiation protection, medical imaging, and radiotherapy. Knowing the LET can guide

the choice of appropriate shielding materials and designs to minimise exposure to radiation protection. In medical imaging, the knowledge of LET can help balance image quality and patient dose by optimising imaging parameters. In radiotherapy, considering the LET can help design treatment plans that maximise the radiation dose to tumours while minimising the dose to healthy tissues.

49.6 Mathematical Models in Dosimetry

The point-source model is the simplest dosimetric model used to estimate the radiation dose from a source, assuming that the radiation source is an infinitesimally small point. This assumption simplifies the mathematical calculations and provides a good approximation when the source dimensions are much smaller than the distance to the point of interest or when the dose is calculated far from the source.

In this model, the dose at any point in space can be calculated using the inverse square law:

$$D(r) = K * (1/r^2)$$

D(r) is the dose at a distance r from the source, and K is a constant representing the source strength. The inverse square law demonstrates that the dose decreases rapidly as the distance from the source increases. This relationship is valid for isotropic sources that emit radiation uniformly in all directions.

The point-source model is widely used in basic dosimetry calculations, particularly for initial estimates and simple geometries. However, it has limitations when applied to more complex situations or when the source dimensions cannot be ignored. In such cases, more advanced models like line-source or volumetric-source models may be required, which account for the spatial distribution of the radiation source.

Despite its simplicity, the point-source model provides valuable insight into the fundamental behaviour of radiation in space and serves as a basis for more complex dosimetric models. By understanding the relationship between dose and distance from the source, radiation protection professionals can design effective shielding, develop safe work practices, and estimate potential radiation exposures. In medical applications, the point-source model can be used as a starting point for treatment planning in radiotherapy, allowing clinicians to estimate dose distributions around tumours and minimise the dose to healthy tissues.

49.7 Line-Source Model

The line-source model is an extension of the point-source model, addressing the limitations of the point-source model by considering a one-dimensional linear radiation source instead of an infinitesimally small point. This model is useful when the radiation source has a significant length, or the source geometry is more complex than a single point.

To calculate the dose at a point in space, the line-source model integrates the contribution of the infinitesimal point sources along the line:

The line-source model equation you provided calculates the dose at a point in space by integrating the contribution of the infinitesimal point sources along the line:

$$D(r, \theta) = \int K(x) * 1 / [(r^2 + x^2) - 2rx*\cos(\theta)]^{3/2} dx$$

Where:

D(r, θ) is the dose at a distance r from the source and an angle θ from the line,

K(x) is the source strength per unit length (e.g., radiation intensity),

r is the radial distance from the centre of the line source,

x is the position along the line,

θ is the angle between the point of interest and the line source.

The line-source model is particularly useful in situations where the geometry of the radiation source is long and thin, such as in brachytherapy or when analysing radiation from transmission lines. It is important to note that the line-source model is still a simplification and might not fully account for all factors in real-world situations.

The line-source model is more versatile than the point-source model, as it can account for the spatial distribution of the radiation source and provide a more accurate estimation of the dose distribution around the source. This model is particularly relevant when the radiation source is linear or elongated, such as radioactive wires used in brachytherapy or linear accelerator beams used in external beam radiotherapy.

Although it increased complexity compared to the point-source model, the line-source model still relies on simplifying assumptions, such as the one-dimensional nature of the source. In cases where the source geometry is more complex, other models, such as the volumetric-source model, may be required for accurate dose estimation.

49.8 Volume-Source Model

The volume-source model is a more advanced dosimetric model that accounts for a three-dimensional radiation source, such as a solid radioactive material or an irradiated volume within a patient. This model offers a higher level of accuracy in dose estimation, particularly when the radiation source has a complex geometry or when the dose distribution needs to be determined within a three-dimensional volume.

The volume-source model integrates the contribution of infinitesimal point sources within the volume to calculate the dose at a point in space. For example, the dose at a point (r, θ, φ) in a spherical coordinate system can be expressed as:

$$D(r, \theta, \varphi) = \iiint K(r', \theta', \varphi') * 1/[(r^2 + r'^2) - 2rr'\cos(\theta)\sin(\theta')\cos(\varphi-\varphi')]^{3/2} * r'^2 \sin(\theta') dr' d\theta' d\varphi'$$

Where D(r, θ, φ) is the dose at a distance r from the source, K(r', θ', φ') is the source strength per unit volume at a point (r', θ', φ') within the source, and r', θ', and φ' are the spherical coordinates of the infinitesimal point sources within the volume.

The volume-source model is especially relevant in medical applications, such as brachytherapy and external beam radiotherapy, where the radiation source or target volume has a complex three-dimensional shape. By accurately modelling the spatial distribution of the source, this model allows for more precise treatment planning and dose optimisation.

In radiation protection, the volume-source model can help design effective shielding and containment for radioactive materials and estimate potential exposure doses in various scenarios.

49.9 Calculation of Equivalent Dose

Estimating the equivalent dose (H) is crucial in radiation protection and dosimetry, as it considers not only the absorbed dose (D) but also the relative biological effectiveness (RBE) of the radiation, which varies depending on the type and energy of the radiation. The equivalent dose is calculated by multiplying the absorbed dose by a radiation weighting factor (wR):

$$H = wR * D$$

Here is a table with some example values of absorbed dose (D), radiation weighting factor (wR), and the resulting equivalent dose (H). Please note that these values are for illustrative purposes only and may not represent real-life situations.

Radiation Type	Absorbed Dose (D) (mGy)	Radiation Weighting Factor (wR)	Equivalent Dose (H) (mSv)
X-rays	100	1	100
Gamma Rays	50	1	50
Electrons	200	1	200
Neutrons	30	5 (for 1 MeV neutron)	150
Alpha Particles	10	20	200

Remember that the radiation weighting factor (wR) depends on the radiation's type and energy, and the values provided in the table are examples based on general recommendations by the International Commission on Radiological Protection (ICRP). In practice, the absorbed dose (D) and equivalent dose (H) values will vary depending on the specific radiation source, energy, and exposure conditions.

Radiation weighting factors (wR) account for the differences in biological damage caused by different types of radiation. These factors depend on the radiation type and energy. They represent the ratio of the biological effectiveness of a specific type of radiation to that of a reference radiation (usually X-rays or gamma rays).

For example, wR values for photons (X-rays and gamma rays) and electrons are 1, indicating that these low-LET radiations have similar biological effects to the reference radiation. On the other hand, alpha particles have a wR value of 20, reflecting their higher LET and greater capacity to cause biological damage.

For neutrons, wR values vary with energy, ranging from 2 for low-energy neutrons to 20 for high-energy neutrons. This variation reflects the complex energy-dependent interactions of neutrons with matter and their wide range of biological effectiveness.

In radiation protection, an equivalent dose is used to compare the potential biological effects of exposure to different radiation types and establish dose limits for occupational and public exposure. An equivalent dose is essential for treatment planning and evaluating the risks associated with radiation-based diagnostics and therapies in medical applications.

49.10 Dosimetry in Radiation Therapy

In radiation therapy, dosimetric calculations are essential for developing an effective treatment plan that delivers an optimal radiation dose to the tumour while minimising the dose to surrounding healthy tissues. Accurate dosimetry is crucial for maximising the likelihood of tumour control and reducing the risk of complications in normal tissues. The mathematical models used in radiation therapy planning include the following:

The dose-volume histogram (DVH): A DVH is a graphical representation of the dose distribution within a target volume (e.g., tumour) and critical structures (e.g., organs at risk). It displays the volume of the target or structure receiving a specific dose or higher. DVHs allow clinicians to evaluate the treatment plan's effectiveness in terms of tumour coverage and dose homogeneity, as well as the potential toxicity to nearby healthy tissues. By comparing different treatment plans using DVHs, clinicians can choose the optimal plan to maximise tumour control while minimising the risk of side effects.

The linear-quadratic (LQ) model: The LQ model is used to describe the cell survival probability (S) after exposure to radiation as a function of dose (D) and two radiosensitivity parameters, α and β:

$$S = \exp(-\alpha D - \beta D^2)$$

The LQ model is widely used in radiation therapy to estimate the tumour control probability (TCP) and normal tissue complication probability (NTCP). TCP represents the likelihood of eradicating all tumour cells and achieving local control, while NTCP quantifies the risk of complications in healthy tissues. In addition, the LQ model guides the optimisation of fractionation schemes, which involves dividing the total radiation dose into smaller doses (fractions) delivered over several sessions, and dose escalation strategies to improve treatment outcomes.

Dosimetry calculations are essential for estimating the radiation dose received by an individual or a material. Here's an example of a simple dosimetry calculation for an external radiation source

Assumptions:

- The source is a point source of gamma radiation.
- The individual is at a fixed distance from the source.

- The source emits radiation isotropically.
- The radiation dose rate is constant during the exposure time.
- No shielding is present between the source and the individual.

Parameters:

- The activity of the source (A) in Becquerels (Bq)
- Distance from the source to the individual (d) in meters (m)
- Exposure time (t) in hours (h)
- Dose rate constant (Γ) in microsieverts per hour per becquerel (μSv/h/Bq)

Step 1: Determine the dose rate at the distance d. The dose rate (Drate) can be calculated using the inverse square law and the dose rate constant:

$$D_{rate} = (\Gamma \times A) / (4 \times \pi \times d^2)$$

Step 2: Calculate the total dose. To calculate the total dose (Dtotal) received by the individual during the exposure time, multiply the dose rate by the exposure time:

$$D_{total} = D_{rate} * t$$

Example: Suppose a source with an activity of 1,000 Bq emits gamma radiation. The individual is located 2 meters away from the source and is exposed for 1 hour. The dose rate constant for the particular gamma radiation is 0.2 μSv/h/Bq.

Step 1: Calculate the dose rate. D_{rate} = (0.2 μSv/h/Bq × 1,000 Bq) / (4 × π × 2² m²) D_{rate} ≈ 7.96 μSv/h

Step 2: Calculate the total dose. D_{total} = 7.96 μSv/h × 1 h D_{total} ≈ 7.96 μSv

In this example, the individual would receive a total dose of approximately 7.96 μSv from the gamma radiation source.

49.11 Conclusion

The mathematics of dosimetry is fundamental in understanding and quantifying the interaction of radiation with matter. Accurate dosimetry is essential in various applications, such as radiation protection, nuclear medicine, and radiotherapy, to minimise potential health risks and ensure effective treatment. Mathematical models, including point-source, line-source, and volume-source models, facilitate the calculation of the absorbed dose and equivalent dose for different radiation types and source geometries.

In radiation therapy, dosimetric calculations are vital for treatment planning, ensuring that an optimal radiation dose is delivered to the tumour while minimising the dose to surrounding healthy tissues. Mathematical models, such as the dose-volume

histogram (DVH) and the linear-quadratic (LQ) model, are employed to evaluate treatment efficacy and potential toxicity. DVHs offer a graphical representation of dose distribution within the target volume and critical structures, allowing clinicians to assess the treatment plan's effectiveness and compare alternative plans. The LQ model helps estimate the tumour control probability (TCP) and normal tissue complication probability (NTCP), guiding the optimisation of fractionation schemes and dose escalation strategies.

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50 Microscopic Odyssey: The Timeless Allure and Influence of ‘Fantastic Voyage’ in Science Fiction

Navigating the human body unveils intricate systems, astounding complexity, interconnected processes, and breathtaking biological phenomena within.

50.1 Introduction

A Journey Through the Human Body starts with the state-of-the-art submarine at the centre of our fantastic voyage is a marvel of modern engineering and technology. Designed specifically for navigating the human body’s delicate and complex structures, this microscopic vessel is equipped with advanced features that allow it to adapt to its environment’s unique challenges seamlessly.

The submarine’s exterior is crafted from cutting-edge materials, providing unmatched durability and flexibility to withstand the dynamic pressures and forces it encounters while journeying through the circulatory system. Its propulsion system, powered by innovative energy sources, allows it to traverse the body’s intricate pathways with precision and efficiency.

An array of sophisticated sensors and monitoring systems inside the submarine enables the exploration team to continuously collect and analyse data on the body’s myriad processes. These tools offer invaluable insights into the human body’s inner workings, unlocking the secrets of cellular functions, molecular interactions, and physiological responses.

The submarine’s advanced communication system ensures that the exploration team remains in constant contact with the outside world, allowing for real-time updates and collaboration with researchers and scientists who eagerly await the discoveries made during this unprecedented journey.

The fantastic voyage submarine represents the pinnacle of human ingenuity, bridging the gap between our understanding of the human body and the tantalising mysteries that remain within.

50.2 Embarkation and Entering the Circulatory System

Embarking on this incredible journey, our microscopic submarine deftly manoeuvres through the body’s circulatory system, revealing the awe-inspiring complexity of life-sustaining processes. As the vessel glides through the veins, we witness the vital roles played by red blood cells, white blood cells, and platelets in maintaining our health and well-being.

The circulatory system, a vast and intricate network, showcases the delicate balance within the human body. The submarine's advanced sensors and monitoring equipment provide an unparalleled view of the various cellular components that work harmoniously to ensure our body functions optimally. The breathtaking sights and newfound understanding of these biological wonders inspire a profound appreciation for the intricate systems that make up the human body.

As we immerse ourselves further into the circulatory system, we access the concealed realm of cellular interaction and collaboration. The myriad processes within our veins, arteries, and capillaries are a testament to the incredible resilience and adaptability of the human body. Observing these complex interactions, we are reminded of the importance of maintaining our health, as it is the foundation upon which our body's harmonious symphony is built.

Our fantastic journey through the circulatory system is just the beginning of a remarkable journey that will take us through the depths of the human body, unveiling the wonders and mysteries within.

50.3 The Heart – The Pump House of Life

As our submarine ventures further into the heart, we are struck by the intricate choreography and synchronisation required for this vital organ to function efficiently. With its rhythmic contractions and relaxations, the heart acts as the body's central pump, ensuring that oxygen-rich blood reaches every corner of the body. This incredible organ, working day and night tirelessly, is the very essence of life itself.

Upon entering the right atrium, we witness deoxygenated blood returning from the body, preparing for its rejuvenating journey to the lungs. The heart's intricate architecture and design are a marvel as the right ventricle contracts to send blood coursing towards the lungs for reoxygenation.

In the lungs, the exchange of gases occurs with remarkable efficiency, as oxygen binds to red blood cells and carbon dioxide is expelled. This delicate dance of molecular interactions is critical to maintaining the body's delicate balance.

As our submarine follows the oxygen-rich blood back to the heart, we observe the left atrium and ventricle working in unison, propelling the revitalised blood into the aorta and throughout the arterial network. This complex system of blood vessels, fuelled by the relentless power of the heart, serves as the body's life-sustaining highway, delivering the essential oxygen and nutrients needed to maintain our health and vitality.

50.4 Journey Through the Arteries

As our submarine traverses the arterial network, we marvel at the beautifully efficient design of arteries, arterioles, and capillaries. These thick-walled vessels transport life-giving oxygenated blood and serve as the body's distribution system for vital nutrients. The remarkable organisation of these blood vessels reveals the intricate and intelligent design of the human body.

As we explore the capillary beds, we witness the essential exchanges between the blood and the body's tissues. Nutrients and oxygen are delivered to cells, while waste products and carbon dioxide are removed, highlighting the seamless cooperation of the circulatory and cellular systems.

Our voyage leads us to the brain, where we encounter the blood-brain barrier, an ingenious and selective filter that safeguards the delicate neural tissue from potential harm. This vital protective mechanism ensures the brain's proper functioning, allowing us to think, feel, and perceive the world around us.

Continuing our journey, we arrive at the kidneys, a pair of remarkable organs that perform essential functions such as filtering waste products, regulating blood pressure, maintaining electrolyte balance, and stimulating red blood cell production. The incredible efficiency and adaptability of these organs underscore the resilience and complexity of the human body, offering yet another example of the miraculous and harmonious processes that sustain life.

50.5 Venturing into the Capillaries and Veins

As our submarine navigates the delicate network of capillaries, we are immersed in the bustling microcosm of cellular exchange. The capillary walls, thin and permeable, facilitate the passage of oxygen, nutrients, and waste products between the blood and the surrounding tissues. This vital exchange sustains the cells, fuelling their activities and ensuring the proper functioning of our bodies.

We enter the venous system from the capillary beds, a vast and intricate vessel network that returns deoxygenated blood to the heart. The veins, with their distinctive blue hue, serve as the body's recycling system, ensuring that every drop of blood is replenished and ready for its next journey.

As we travel through the veins, we encounter an ingenious design feature: valves that prevent blood from flowing backwards. These one-way gates ensure that blood moves efficiently and continuously towards the heart, despite the pull of gravity. We marvel at the elegant simplicity of these valves, yet another example of the body's remarkable engineering.

Our journey through the venous system offers a fascinating glimpse into the human body's inner workings. From the delicate exchanges within the capillaries to the efficient return of blood to the heart, we are left with a profound appreciation for the intricate and harmonious processes that sustain life.

50.6 The Lymphatic System – The Unsung Hero

Our exploration of the lymphatic system unveils an intricate and vital network that plays a critical role in maintaining our body's overall health. As we navigate the lymphatic capillaries, we observe the transport of lymph, a fluid derived from the interstitial fluid that bathes our cells, serving as the system's lifeblood.

The lymphatic system's primary function is to gather and return surplus fluid to the circulatory system while simultaneously serving as the body's protective barrier

against detrimental pathogens and cellular waste. We witness the presence of lymph nodes, small yet powerful structures that act as checkpoints, filtering the lymph and providing a battleground for the immune cells, known as lymphocytes, to eliminate foreign invaders and cancerous cells.

As we proceed further into the lymphatic system, our submarine arrives at the spleen, the largest lymphatic organ in the body. This critical organ serves multiple functions, including filtering the blood, removing old or damaged red blood cells, and acting as a reservoir for immune cells. The spleen's role in maintaining our body's defences and overall health is a testament to the intricate and interconnected systems that work together to ensure our well-being.

Our voyage through the lymphatic system offers a unique perspective on the body's defence mechanisms and fluid balance, further deepening our appreciation for the incredible complexity and harmony of the human body.

50.7 The Respiratory System – The Breath of Life

Our journey through the respiratory system offers a fascinating glimpse into the body's intricate airway, a vital conduit for life-giving oxygen and eliminating waste carbon dioxide. As we navigate the trachea, we are struck by the remarkable design of the cilia lining its walls. These tiny hairs tirelessly clean our airways, ensuring our breaths are free from harmful debris.

Our submarine continues to the bronchi, the two main branches that extend from the trachea into the lungs. The bronchi's delicate branching structure is reminiscent of an inverted tree, its branches further dividing into smaller bronchioles. This intricate network of airways allows for the efficient distribution of oxygen throughout the lungs.

As we approach the alveoli, tiny air sacs at the terminal ends of the bronchioles, we witness the miraculous gas exchange process. The thin walls of the alveoli facilitate the diffusion of oxygen molecules into the bloodstream while simultaneously allowing carbon dioxide to exit the blood and be expelled from the body. This delicate balance of inhalation and exhalation is a constant reminder of the human body's incredible design and adaptability.

Our exploration of the respiratory system leaves us with a profound appreciation for the body's ability to take in the oxygen we need to survive and to eliminate the waste products that result from our cellular processes.

50.8 The Digestive System – The Powerhouse of Nutrition

As our submarine embarks on a journey through the digestive system, we delve into the complex world of food processing, nutrient absorption, and waste elimination. Our exploration begins in the mouth, where the combined forces of teeth, saliva, and enzymes initiate food's mechanical and chemical breakdown, preparing it for its journey through the alimentary canal.

As we navigate the oesophagus, stomach, and intestines, we observe the astonishing interplay of enzymes, acids, and muscular contractions that collaborate to transform

food into essential nutrients. These complex and synchronised processes highlight the body's remarkable ability to extract and utilise the vital components of our diet.

Our voyage continues through the small intestine, a winding and intricately folded structure that serves as the primary site for nutrient absorption. The minute villi that line the small intestine's walls significantly increase its surface area, allowing maximum nutrient uptake.

Finally, we enter the large intestine or colon, a crucial organ responsible for absorbing water and electrolytes, forming solid waste, and hosting a diverse community of beneficial bacteria. This rich and complex microbiome plays a vital role in maintaining our overall health, showcasing the intricate balance within our bodies.

Our journey through the digestive system offers a captivating glimpse into the body's extraordinary ability to process, absorb, and eliminate the food we consume, emphasising the importance of a balanced and healthy diet for optimal well-being.

50.9 The Nervous System – The Command Centre

Our fantastic voyage through the human body continues as we delve into the mysterious and complex world of the nervous system. This intricate network of neurons, glial cells, and blood vessels control our every thought, movement, and sensation. As our submarine enters the brain, we are struck by the remarkable architecture of this extraordinary organ, which enables us to navigate and understand the world around us.

We witness the intricate dance of electrical impulses and chemical signals that facilitate communication between neurons, which underlies our every thought, feeling, and perception. This delicate interplay of signalling is a testament to the incredible complexity and adaptability of the human brain, which has evolved to meet the challenges of an ever-changing environment.

Our journey through the brain takes us on a tour of its various structures, each of which plays a unique and essential role in our daily lives. Initially, we investigate the cerebrum, the most prominent region of the brain, accountable for advanced cognitive processes such as critical thinking, decision-making, and conscious awareness. This remarkable structure allows us to create, innovate, and solve complex problems, setting us apart from other species on our planet.

We continue our voyage to the cerebellum, a smaller structure located at the base of the brain. This crucial region coordinates movement and maintains balance, ensuring we can walk, run, and perform countless other physical activities gracefully and precisely.

As we descend further into the brain, we encounter the brainstem, a vital structure that links the brain to the spinal cord. The brainstem regulates essential functions such as heart rate, respiration, and digestion, allowing our bodies to function seamlessly and efficiently.

Exiting the brain, we follow the spinal cord and peripheral nerves, the crucial conduits that transmit information between the brain and the rest of the body. We marvel at the precision and speed at which these signals travel, allowing us to experience and interact with our environment in real-time. This unique communication system is essential for our survival, enabling us to respond rapidly and effectively to the challenges we face every day.

Our investigation of the nervous system would be incomplete without delving into the sensory organs that enable us to perceive and make sense of our surroundings. We explore the eyes, extraordinary organs that convert light into electrical impulses, which the brain can interpret, enabling us to observe and admire the splendour of our environment.

We also explore the ears, which convert sound waves into neural signals that enable us to hear and process the myriad sounds that fill our lives. These incredible organs allow us to communicate with others and play a vital role in our ability to navigate and understand our environment.

Our journey through the nervous system would not be complete without a visit to the skin, the body's largest organ, which serves as a protective barrier and sensory interface with the outside world. The skin is replete with nerve endings that detect touch, temperature, and pain, allowing us to react and adapt to the countless stimuli we encounter every day.

As we continue our fantastic voyage, we are struck by the incredible resilience and adaptability of the nervous system, which has evolved to meet the myriad challenges of our ever-changing world. We marvel at the brain's remarkable plasticity, which allows us to learn, grow, and adapt throughout our lives. This extraordinary organ, with its vast and intricate network of connections, is a testament to the boundless potential of the human mind.

As we venture further into the nervous system, we appreciate the complex and often subtle interplay of hormones and neurotransmitters that influence our emotions, moods, and overall well-being.

50.10 Harmony of Hormones: Unlocking the Secrets of the Endocrine System

Finally, we explore the fascinating world of the endocrine system, a collection of glands that produce and secrete hormones that act as chemical messengers regulating various bodily functions. This intricate system is critical in maintaining our body's homeostasis, ensuring everything runs smoothly and efficiently.

The endocrine system comprises several key glands, including the pituitary, thyroid, adrenal, pineal glands, pancreas, ovaries, and testes. Each gland secretes specific hormones that target certain organs or tissues, eliciting precise responses to maintain balance within the body.

For example, the pituitary gland, often called the "master gland," produces and releases several essential hormones. These hormones control growth, reproduction,

and the stress response, among other critical functions. The thyroid gland in the neck generates hormones that control metabolism, growth, and development. The adrenal glands, positioned atop the kidneys, release hormones that aid the body in coping with stress, regulating blood pressure, and maintaining the equilibrium of salt and water.

The endocrine system is crucial for growth and development, reproduction, and the body's ability to handle stress. Additionally, it is engaged in sustaining energy levels, managing metabolism, and guaranteeing the appropriate operation of the immune system.

As we journey through the endocrine system, we gain a deeper understanding of the intricate dance of hormones that guide and regulate the countless processes occurring within our bodies. The endocrine system exemplifies the body's remarkable ability to communicate and coordinate functions, ensuring that we remain healthy and balanced.

50.11 Neurological Symphony: Awe-Inspiring Discoveries in the Nervous System's Wonders

As we conclude our exploration of the nervous system, we are left with a profound sense of awe at this intricate network's extraordinary complexity and elegance. The nervous system is an unparalleled marvel of nature, a testament to the incredible adaptability and resilience of the human body. From the highest levels of conscious thought to the most basic reflexes that ensure survival, the nervous system is the foundation upon which our every experience, memory, and interaction is built.

Throughout our fantastic voyage, we have witnessed firsthand the remarkable symphony of biological processes underlying our existence. From the circulatory system's continuous delivery of oxygen and nutrients to the delicate dance of neurons that enables us to perceive and understand the world, the human body is a testament to life's incredible power and potential.

As we exit the human body and reflect upon our journey, we are left with a deepened appreciation for the intricacies and interconnections that make up the miracle of life. Exploring the human body has afforded us a unique perspective on the world, a reminder of the incredible beauty and complexity within each of us. Our fantastic voyage has been a journey of discovery, a celebration of the boundless potential of the human spirit, and an affirmation of the wonders that await us as we continue to explore the mysteries of the universe.

50.12 A Journey Through the Human Body Enduring Legacy of 'Fantastic Voyage' and its Impact on Science Fiction Cinema

"Fantastic Voyage," released in 1966, is a groundbreaking science fiction film that captured the imagination of audiences worldwide. Under the direction of Richard Fleischer and featuring Stephen Boyd, Raquel Welch, Edmond O'Brien, and Donald Pleasence, the film presents an exhilarating and visually captivating expedition into the undiscovered realm of the human body. The film's plot revolves around a secret government organisation, the Combined Miniature Defense Force (CMDF), which has

developed an incredibly shrinking technology. A brilliant scientist, Dr Jan Benes, is the only person who can create a new, stable form of miniaturisation technology capable of revolutionising warfare and medicine. However, Benes suffers a critical injury from an assassination attempt, leaving him unconscious with a blood clot in his brain. To save his life and crucial knowledge, the CMDF assembles a team of experts to be miniaturised, along with a state-of-the-art submarine, the Proteus, to remove the clot from Benes' brain.

The movie showcases the adventures of this diverse team, which includes a skilled pilot, a medical specialist, a surgeon, a technician, and a security officer, as they journey through the scientist's body to complete their life-saving mission. They face multiple hurdles and difficulties throughout their journey, like traversing the bloodstream, evading the body's immune system, and enduring the hazards of the human body's inner landscape.

"Fantastic Voyage" was a remarkable achievement for its time, utilising cutting-edge special effects to bring the microscopic world to life. The film's iconic visual style and creative set design won it two Academy Awards, one for Best Art Direction and the other for Best Visual Effects. In addition, the movie's influence on popular culture cannot be overstated, as it inspired countless stories, television shows, and films that explored the microscopic realm.

The film's success also led to the development of a short-lived animated television series in 1968 and a novelisation by famed science fiction writer Isaac Asimov. While Asimov's novelisation was published shortly before the film's release, it expanded on the movie's plot and explored various scientific concepts in greater detail.

"Fantastic Voyage" remains an enduring classic of science fiction cinema, with its captivating premise, innovative special effects, and compelling narrative. The film's ability to blend scientific speculation with thrilling adventure makes it a must-watch for fans. Moreover, the movie's exploration of the human body's inner workings has resonated with audiences for decades, inspiring generations to ponder the mysteries and marvels of biology.

50.13 Conclusion

Fantastic Voyage is an innovative movie that has enthralled viewers since its debut in 1966. Its innovative special effects, engaging storyline, and intriguing scientific concepts continue to inspire and entertain viewers today. By taking audiences on an unforgettable journey into the human body, "Fantastic Voyage" opened up a world of wonder and imagination, leaving a lasting impact on the science fiction genre and popular culture.

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51 Unveiling the Hidden Depths of Alzheimer's Disease

Alzheimer's disease, an age-related neurodegenerative disorder, impacts brain structure and function, requiring advanced imaging techniques for improved understanding and diagnosis.

51.1 Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder affecting more than 55 million people worldwide, causing significant cognitive decline, memory loss, and impairments in daily functioning. In addition, as the global population ages, the incidence of AD is expected to rise, increasing the need for early diagnosis and effective treatments. As a result, brain imaging has emerged as a critical tool in understanding, diagnosing, and monitoring Alzheimer's disease.

Structural imaging techniques offer in-depth insights into the brain's anatomy, enabling the detection of brain atrophy, a characteristic sign of Alzheimer's disease. The primary structural imaging methods are magnetic resonance imaging (MRI) and computed tomography (CT).

MRI employs a strong magnet and radio waves to produce intricate brain images. It is especially valuable in Alzheimer's disease research, as it can identify minor alterations in the brain's structure, such as the contraction of the hippocampus and entorhinal cortex – early warning signs of Alzheimer's. High-resolution MRI can also visualise the accumulation of amyloid-beta plaques, a critical pathological feature of the disease.

CT scans, on the other hand, use X-rays to generate cross-sectional brain images. Though they are less sensitive than MRI in detecting initial brain changes related to Alzheimer's, CT scans can still uncover significant atrophy and help exclude other potential dementia causes.

Functional imaging methods assess brain activity by observing alterations in blood flow, glucose metabolism, or oxygen usage. Techniques in this category encompass functional MRI (fMRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT).

fMRI evaluates brain activity by identifying changes in blood flow linked to neuronal activation. In the context of Alzheimer's disease, fMRI can unveil modifications in brain connectivity and activation patterns, especially within the default mode network, which is impacted during the disease's early phases.

PET employs minimal quantities of radioactive tracers to create images of particular molecules within the brain. In the study of Alzheimer's, PET tracers help detect amyloid-beta plaques, tau tangles, and shifts in glucose metabolism, all indicative of the disease. Amyloid PET imaging has gained significance in Alzheimer's research, enabling real-time observation of amyloid-beta accumulation within living organisms.

Single-Photon Emission Computed Tomography (SPECT) shares similarities with PET but employs distinct radioactive tracers and detectors. Although SPECT has a lower spatial resolution than PET, it remains valuable in Alzheimer's research. This technique is particularly beneficial for gauging regional cerebral blood flow and evaluating the cholinergic system's integrity.

51.2 Recent Advancements in Brain Imaging for Alzheimer's Disease

Sophisticated MRI methods, such as diffusion tensor imaging (DTI) and resting-state fMRI, have shed light on the early pathological changes and functional alterations related to Alzheimer's disease. For example, DTI evaluates water molecule diffusion in brain tissue, enabling the visualisation of white matter tracts and the identification of microstructural abnormalities linked to Alzheimer's. Resting-state fMRI investigates functional connectivity between brain regions while the brain is at rest, unveiling alterations in brain networks associated with the disease.

Tracers have been designed to target specific biomarkers in Alzheimer's, enhancing the precision and specificity of PET imaging. Some of the most promising tracers include those that bind to tau proteins, facilitating the visualisation of tau tangles, another characteristic of Alzheimer's. Moreover, new tracers have been developed to target neuroinflammation and synaptic density, offering a complete perspective on the pathological changes in Alzheimer's disease.

Multimodal imaging, combining various imaging techniques, has become a potent instrument in Alzheimer's research. By consolidating structural, functional, and molecular data, multimodal imaging can better understand the disease's progression and the intricate interplay between distinct pathological factors. For instance, integrating MRI and PET imaging enables researchers to associate brain atrophy with amyloid-beta and tau accumulation, illuminating the underlying mechanisms of Alzheimer's disease.

51.3 Challenges in Brain Imaging for Alzheimer's Disease

A primary challenge in utilising brain imaging for Alzheimer's disease lies in the accessibility and cost of cutting-edge imaging techniques. MRI, PET, and SPECT scans can be costly, and operating and interpreting them necessitates specialised equipment and expertise. These factors limit the widespread adoption of these techniques in routine clinical practice and settings with limited resources.

Standardising imaging protocols and validating innovative imaging techniques and biomarkers are crucial hurdles in the field. The absence of standardised protocols can result in variability in the collection and analysis of imaging data, complicating comparisons across different studies and populations. Furthermore, validating new

biomarkers and imaging techniques demands extensive, longitudinal studies to determine their sensitivity, specificity, and prognostic value concerning Alzheimer's disease.

Employing brain imaging in Alzheimer's disease presents several ethical concerns, especially in terms of early diagnosis and preclinical stages. Sharing imaging results with patients and their families may have significant emotional and psychological implications, particularly when effective Alzheimer's treatments remain limited. Additionally, it is vital to carefully address issues related to patient privacy and the potential for discrimination based on imaging findings.

51.4 Future Directions and Potential Applications

Brain imaging methods can potentially transform the early diagnosis of Alzheimer's disease by detecting pathological changes before substantial clinical symptoms appear. This could facilitate earlier intervention and the creation of disease-modifying therapies targeting Alzheimer's underlying pathology, possibly slowing or halting the disease's progression.

Brain imaging research has already substantially enhanced our understanding of the pathological mechanisms underlying Alzheimer's disease. As imaging techniques progress, they will undoubtedly yield further insights into the intricate interplay among genetic, molecular, and environmental factors contributing to Alzheimer's. This knowledge will be crucial for identifying novel therapeutic targets and devising more effective treatments for the disease.

51.5 Imaging Agents for Alzheimer's Disease: Visualising Molecules and Processes in the Brain

Imaging agents, also known as radiotracers or contrast agents, are used in various brain imaging techniques to visualise specific molecules or processes in the brain associated with Alzheimer's disease. Some commonly used imaging agents for Alzheimer's disease include:

Pittsburgh Compound-B (PiB) is a radiolabelled compound employed as a radiotracer in positron emission tomography (PET) scans for visualising amyloid-beta plaques in the brain. Amyloid-beta plaques are a pathological characteristic of Alzheimer's disease, and their accumulation in the brain is believed to contribute to neurodegeneration. PiB, the first amyloid imaging agent developed, has significantly impacted our understanding of Alzheimer's disease.

PiB is a derivative of thioflavin-T, a dye that binds explicitly to amyloid-beta plaques. The compound is labelled with carbon-11 (^{11}C), a radioactive isotope, enabling its detection and visualisation in PET scans. When administered into the bloodstream, PiB crosses the blood-brain barrier and attaches to amyloid-beta plaques present in the brain. The PET scanner identifies the radioactive decay of ^{11}C, and the resulting images represent the distribution and density of amyloid-beta plaques.

The development and application of PiB have had several significant implications for Alzheimer's disease research. In vivo visualisation of amyloid-beta plaques: Before

PiB's development, amyloid-beta plaques could only be confirmed through post-mortem brain tissue examination. PiB-PET enables in vivo visualisation of plaques, allowing researchers to investigate their role in Alzheimer's disease progression.

Early detection and diagnosis: PiB-PET has shown the capacity to identify amyloid-beta plaque accumulation in individuals with mild cognitive impairment or before cognitive symptoms appear, potentially enabling earlier diagnosis and intervention.

Evaluation of therapeutic interventions: PiB-PET can be employed to track the efficacy of treatments targeting amyloid-beta plaques, offering valuable insights for developing novel therapies.

However, it is crucial to acknowledge PiB's limitations, including carbon-11 short half-life of around 20 minutes, necessitating an on-site cyclotron for production. This has prompted the development of alternative amyloid imaging agents labelled with fluorine-18, a longer-lived isotope, such as florbetapir, florbetaben, and flutemetamol, which are more practical for clinical use.

51.6 The Role of Florbetapir, Florbetaben, and Flutemetamol-PET Scans in Early Detection of Alzheimer's Disease

Florbetapir, marketed as Amyvid, is a radiotracer utilised in positron emission tomography (PET) scans to visualise amyloid-beta plaques in the brain. Amyloid-beta plaques are a key pathological characteristic of Alzheimer's disease, and their accumulation in the brain is associated with the disorder's development and progression. Florbetapir has been authorised by the US Food and Drug Administration (FDA) and other regulatory bodies for imaging amyloid-beta plaques in the brain.

Florbetapir is labelled with fluorine-18, a radioactive isotope with a longer half-life (about 110 minutes) compared to carbon-11, used in Pittsburgh Compound-B (PiB). This longer half-life renders Florbetapir more practical for clinical use, as it does not necessitate an on-site cyclotron for its production.

Improved diagnosis: Florbetapir-PET scans can help differentiate Alzheimer's disease from other forms of dementia by providing in vivo evidence of amyloid-beta plaque accumulation in the brain. This can enhance diagnostic accuracy and support appropriate patient management.

Early detection: Florbetapir-PET scans can detect amyloid-beta plaque accumulation in individuals with mild cognitive impairment or before the onset of cognitive symptoms, potentially enabling earlier diagnosis and intervention.

Monitoring treatment efficacy: Florbetapir-PET scans can assess the effectiveness of treatments targeting amyloid-beta plaques, offering valuable insights for developing and evaluating novel therapies.

Research applications: Various studies have used Florbetapir-PET scans to investigate the relationship between amyloid-beta plaque accumulation and Alzheimer's disease pathology, progression, and cognitive decline.

It is crucial to note that a positive Florbetapir-PET scan indicates the presence of amyloid-beta plaques in the brain but does not necessarily confirm an Alzheimer's diagnosis, as amyloid-beta plaques can also be present in other conditions or cognitively normal older individuals. Therefore, Florbetapir-PET scans should be combined with other clinical assessments and diagnostic tests to evaluate patients suspected of having Alzheimer's disease.

51.7 Beta-Amyloid Imaging with Florbetaben

Neuraceq, commercially known as Florbetaben, is a radiotracer used in PET scans to visualise amyloid-beta plaques in the brain, characteristic pathological features of Alzheimer's disease. The US FDA and other regulatory agencies have approved Florbetaben for imaging amyloid-beta plaques in the brain.

Florbetaben is labelled with fluorine-18, a radioactive isotope with a longer half-life than carbon-11 used in Pittsburgh Compound-B (PiB), making it more suitable for clinical use since it does not require an on-site cyclotron for its production.

The use of Florbetaben-PET scans in Alzheimer's disease research and clinical practice has significant implications, including improved diagnosis and differentiation of Alzheimer's disease from other forms of dementia. Florbetaben-PET scans can also detect amyloid-beta plaque accumulation in individuals with mild cognitive impairment or before the onset of cognitive symptoms, potentially allowing for earlier diagnosis and intervention.

Additionally, Florbetaben-PET scans can be used to evaluate the effectiveness of treatments targeting amyloid-beta plaques, providing valuable information for developing and assessing novel therapies. Finally, Florbetaben-PET scans have been used in various research studies to investigate the relationship between amyloid-beta plaque accumulation and Alzheimer's disease pathology, progression, and cognitive decline.

51.8 Flutemetamol: A β-Amyloid PET Imaging Agent for Diagnosing Alzheimer's Disease and Dementia

Vizamyl, commercially known as Flutemetamol, is a radiotracer utilised in PET scans to visualise amyloid-beta plaques in the brain, a hallmark pathological feature of Alzheimer's disease. The US FDA and other regulatory agencies have approved Flutemetamol for imaging amyloid-beta plaques in the brain.

Flutemetamol, similar to Florbetapir and Florbetaben, is labelled with fluorine-18, a radioactive isotope with a longer half-life of approximately 110 minutes compared to carbon-11 used in Pittsburgh Compound-B (PiB). This longer half-life makes Flutemetamol more convenient for clinical use since it does not require an on-site cyclotron for its production.

Using Flutemetamol-PET scans in Alzheimer's disease research and clinical practice has several important implications, including improved diagnosis and differentiation of Alzheimer's disease from other forms of dementia. Flutemetamol-PET scans can also detect amyloid-beta plaque accumulation in individuals with mild cognitive

impairment or before the onset of cognitive symptoms, potentially allowing for earlier diagnosis and intervention.

Additionally, Flutemetamol-PET scans can be used to evaluate the effectiveness of treatments targeting amyloid-beta plaques, providing valuable information for developing and assessing novel therapies. Finally, Flutemetamol-PET scans have been used in various research studies to investigate the relationship between amyloid-beta plaque accumulation and Alzheimer's disease pathology, progression, and cognitive decline.

These agents bind to amyloid-beta plaques, a key pathological feature of Alzheimer's disease, and are used in PET scans to visualise their distribution in the brain.

51.9 Advancing Understanding of Tau Pathology in Alzheimer's Disease through PET Imaging

A radiotracer known as Flortaucipir, or Avid-1451/AV-1451, is used in PET scans to visualise tau protein accumulation in the brain. Tau proteins, which form neurofibrillary tangles, are a key pathological feature of Alzheimer's disease, contributing to neuronal dysfunction and degeneration. The development of tau-specific radiotracers like Flortaucipir has significantly advanced our understanding of the role of tau pathology in Alzheimer's disease.

Flortaucipir is labelled with fluorine-18, a radioactive isotope with a longer half-life of approximately 110 minutes compared to carbon-11 used in Pittsburgh Compound-B (PiB) for amyloid-beta imaging. This longer half-life makes Flortaucipir more suitable for clinical use, as it does not require an on-site cyclotron for its production.

Using Flortaucipir-PET scans in Alzheimer's disease research and clinical practice has several important implications, including an improved understanding of tau pathology and the in vivo visualisation of tau tangles in the brain. This provides insights into their distribution and relationship with Alzheimer's disease progression.

51.10 Flortaucipir-PET Scans: Enhancing Alzheimer's Diagnosis and Treatment Through Tau Pathology Detection

Flortaucipir-PET scans can also help differentiate Alzheimer's disease from other forms of dementia by providing evidence of tau pathology in the brain, improving diagnostic accuracy and facilitating appropriate patient management. Additionally, Flortaucipir-PET scans can potentially detect tau protein accumulation in individuals with mild cognitive impairment or even before the onset of cognitive symptoms, allowing for earlier diagnosis and intervention.

Flortaucipir-PET scans can be used to evaluate the effectiveness of treatments targeting tau pathology, providing valuable information for developing and accessing novel therapies. Finally, Flortaucipir-PET scans have been used in various research studies to investigate the relationship between tau protein accumulation and Alzheimer's disease pathology, progression, and cognitive decline.

51.11 MK-6240: Advancing Understanding of Tau Pathology in Alzheimer's Disease Through PET Imaging

MK-6240 is a radiotracer utilised in PET scans to visualise tau protein accumulation in the brain, a crucial pathological feature of Alzheimer's disease contributing to neuronal dysfunction and degeneration. The development of tau-specific radiotracers like MK-6240 has significantly advanced our understanding of the role of tau pathology in Alzheimer's disease.

The imaging agent, MK-6240, is labelled with fluorine-18, a radioactive isotope with a longer half-life of approximately 110 minutes compared to carbon-11 (20 minutes) used in Pittsburgh Compound-B (PiB) for amyloid-beta imaging. This longer half-life makes MK-6240 more suitable for clinical use, as it does not require an on-site cyclotron for production.

The use of MK-6240-PET scans in Alzheimer's disease research and clinical practice has several important implications, including an improved understanding of tau pathology and the in vivo visualisation of tau tangles in the brain, providing insights into their distribution and their relationship with Alzheimer's disease progression.

MK-6240-PET scans can also help differentiate Alzheimer's disease from other forms of dementia by providing evidence of tau pathology in the brain, improving diagnostic accuracy and facilitating appropriate patient management. Additionally, MK-6240-PET scans can potentially detect tau protein accumulation in individuals with mild cognitive impairment or even before the onset of cognitive symptoms, allowing for earlier diagnosis and intervention.

Furthermore, MK-6240-PET scans can be used to evaluate the effectiveness of treatments targeting tau pathology, providing valuable information for developing and assessing novel therapies. Furthermore, MK-6240-PET scans have been used in various research studies to investigate the relationship between tau protein accumulation and Alzheimer's disease pathology, progression, and cognitive decline.

It is important to note that a positive MK-6240-PET scan indicates the presence of tau tangles in the brain but does not necessarily confirm a diagnosis of Alzheimer's disease, as tau pathology can also be present in other conditions. Therefore, MK-6240-PET scans should be used with other clinical assessments and diagnostic tests to evaluate patients with suspected Alzheimer's disease.

51.12 RO-948 Radiotracer in PET Scans Through Tau Protein Visualisation

The radiotracer RO-948 is utilised in PET scans to visualise tau protein accumulation in the brain, which is a central pathological feature of Alzheimer's disease and contributes to neuronal dysfunction and degeneration. The development of tau-specific radiotracers like RO-948 has considerably advanced our understanding of the role of tau pathology in Alzheimer's disease.

RO-948 is labelled with fluorine-18, a radioactive isotope with a longer half-life of approximately 110 minutes compared to carbon-11 used in Pittsburgh Compound-B

(PiB) for amyloid-beta imaging. This longer half-life makes RO-948 more suitable for clinical use, as it does not require an on-site cyclotron for production.

However, RO-948-PET scans in Alzheimer's disease research and clinical practice have several important implications, including an improved understanding of tau pathology and the in vivo visualisation of tau tangles in the brain, providing insights into their distribution and their relationship with Alzheimer's disease progression. Also, RO-948-PET scans can also help differentiate Alzheimer's disease from other forms of dementia by providing evidence of tau pathology in the brain, improving diagnostic accuracy and facilitating appropriate patient management. Additionally, RO-948-PET scans can potentially detect tau protein accumulation in individuals with mild cognitive impairment or even before the onset of cognitive symptoms, allowing for earlier diagnosis and intervention.

Furthermore, RO-948-PET scans can be used to evaluate the effectiveness of treatments targeting tau pathology, providing valuable information for developing and assessing novel therapies. Furthermore, RO-948-PET scans have been used in various research studies to investigate the relationship between tau protein accumulation and Alzheimer's disease pathology, progression, and cognitive decline.

51.13 PI-2620 Radiotracer in PET Scans: Enhancing Alzheimer's Disease through In Vivo Tau Protein Imaging

PI-2620 is a radiotracer utilised in PET scans to visualise tau protein accumulation in the brain, a critical pathological feature of Alzheimer's disease that contributes to neuronal dysfunction and degeneration. The development of tau-specific radiotracers like PI-2620 has greatly advanced our understanding of the role of tau pathology in Alzheimer's disease.

PI-2620 is labelled with fluorine-18, a radioactive isotope with a longer half-life of approximately 110 minutes compared to carbon-11 used in Pittsburgh Compound-B (PiB) for amyloid-beta imaging. This longer half-life makes PI-2620 more suitable for clinical use, as it does not require an on-site cyclotron for production.

However, PI-2620-PET scans in Alzheimer's disease research and clinical practice have several important implications, including an improved understanding of tau pathology and the in vivo visualisation of tau tangles in the brain. This approach would provide insight into the progression of Alzheimer's disease.

Furthermore, these PI-2620-PET scans can also help differentiate Alzheimer's disease from other forms of dementia by providing evidence of tau pathology in the brain, improving diagnostic accuracy and facilitating appropriate patient management.

Additionally, PI-2620-PET scans can potentially detect tau protein accumulation in individuals with mild cognitive impairment or even before the onset of cognitive symptoms, allowing for earlier diagnosis and intervention.

Therefore, Tau imaging agents are designed to bind to tau tangles, another hallmark of Alzheimer's disease. PET imaging visualises the brain's accumulation and distribution of tau tangles.

51.14 Fluorine-^{18}FDG-PET Scans: A Valuable Tool for Measuring Glucose Metabolism in Alzheimer's Disease

FDG, a radiotracer labelled with fluorine-18, is utilised in PET scans to measure glucose metabolism in the brain. This technique allows for the measurement of glucose utilisation, which is critical for the functioning of brain cells and neural networks.

In the case of Alzheimer's disease, reduced glucose metabolism is observed in specific brain regions, such as the temporoparietal and posterior cingulate cortices, and can be detected using FDG-PET scans.

Compared to carbon-11, used in Pittsburgh Compound-B (PiB) for amyloid-beta imaging, FDG has a longer half-life (approximately 110 minutes) and does not require an on-site cyclotron for production, making it more suitable for clinical use.

51.15 Advancements in Neuroimaging for Alzheimer's Disease: Radiotracers, Brain Metabolism, and Neuroinflammation

First, it provides a better understanding of brain metabolism, which is essential for identifying affected brain cells and neural networks.

Second, it can help differentiate Alzheimer's disease from other forms of dementia by detecting altered glucose metabolism in specific brain regions, thereby improving diagnostic accuracy and patient management.

Third, FDG-PET scans can detect changes in glucose metabolism in individuals with mild cognitive impairment or even before the onset of cognitive symptoms, allowing for earlier diagnosis and intervention.

Fourth, it can be used to evaluate the effectiveness of treatments targeting brain metabolism or other aspects of Alzheimer's disease, providing valuable information for developing and assessing novel therapies.

Finally, FDG-PET scans have been used in various research studies to investigate the relationship between glucose metabolism and Alzheimer's disease pathology, progression, and cognitive decline.

51.16 Tc-99m HMPAO and Tc-99m ECD Radiotracers in SPECT Scans: Assessing Regional Cerebral Blood Flow for Alzheimer's Disease

The radiotracers Technetium-99m hexamethylpropylene amine oxime (Tc-99m HMPAO) and Technetium-99m ethyl cysteinate dimer (Tc-99m ECD) are used in single-photon emission computed tomography (SPECT) scans to measure regional cerebral blood flow (rCBF), providing valuable insights into brain function and allowing for the differentiation of Alzheimer's disease from other types of dementia.

Both Tc-99m HMPAO and Tc-99m ECD are labelled with technetium-99m (Tc-99m), a radioactive isotope with a relatively short half-life (approximately 6 hours) that is

suitable for SPECT imaging. These imaging agents cross the blood-brain barrier and accumulate in brain cells, facilitating the measurement of rCBF.

Also, Tc-99m HMPAO and Tc-99m ECD SPECT scans in Alzheimer's disease enable the in vivo measurement of rCBF. These radiotracers provide insights into the functioning of brain regions affected by Alzheimer's disease. In addition, they can help distinguish Alzheimer's disease from other forms of dementia by detecting altered blood flow patterns in specific brain regions.

51.17 Neuroinflammation Imaging Agent: PK-11195

PK-11195 is a radiotracer used in PET scans to visualise neuroinflammation, which is believed to be involved in Alzheimer's disease pathology. This imaging agent binds to the translocator protein (TSPO), a marker of activated microglia, allowing for assessing neuroinflammatory processes in the brain.

The radiotracer PK-11195 is labelled with carbon-11, a radioactive isotope with a short half-life (approximately 20 minutes) that requires an on-site cyclotron for production.

Despite this limitation, PK-11195 has been used in research settings to study neuroinflammation in Alzheimer's disease and other neurodegenerative conditions.

Newer TSPO radiotracers with improved characteristics, such as longer half-lives labelled with fluorine-18 and higher specific binding, have been developed to overcome some limitations of PK-11195.

These newer agents may provide better imaging of neuroinflammation and contribute to a better understanding of the role of neuroinflammation in Alzheimer's disease and other neurodegenerative conditions.

51.18 The Future of Alzheimer's Disease Research: Innovations in Medical Imaging, Biomarkers, and Multimodal Approaches

The future of medical imaging in Alzheimer's disease research will be propelled by advancements in imaging technology, novel biomarkers, and the integration of multimodal imaging techniques, leading to a better understanding of the disease, improved early detection and diagnosis, and more effective treatments.

Developing new imaging biomarkers that can accurately detect early pathological changes in Alzheimer's disease, such as tau protein, synaptic dysfunction, and other proteins involved in the disease's pathogenesis, will be a critical area of focus. In addition, creating novel radiotracers targeting various aspects of the disease will play a vital role in achieving this goal.

Integrating different imaging modalities, such as MRI, PET, and SPECT, can provide complementary information about the brain's structural, functional, and molecular changes associated with Alzheimer's disease. In addition, advanced imaging techniques, including high-field MRI, diffusion tensor imaging (DTI), and resting-state functional MRI, can offer more detailed insights into the brain alterations linked to Alzheimer's disease.

Applying AI and machine learning algorithms to medical imaging data can identify subtle patterns and changes in brain structure and function indicative of early Alzheimer's disease and facilitate the identification of at-risk individuals. Longitudinal imaging studies can track the progression of Alzheimer's disease over time, leading to a better understanding of the disease's natural history and treatment effectiveness. Using medical imaging to identify individual variations in Alzheimer's disease pathology can lead to personalised treatment strategies tailored to each patient's specific needs, improving treatment outcomes and minimising potential side effects.

Medical imaging can guide the delivery of targeted therapies, such as gene therapy or stem cell transplantation, to affected brain regions, potentially enhancing treatment efficacy and minimising off-target effects. As imaging technology advances, ethical considerations concerning patient privacy, informed consent, and incidental findings must be addressed.

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52 Molecular Imaging with PET: Radiotracers and Beyond

PET molecular imaging visualises cellular activity, aiding early diagnosis and tailored treatment for patients.

52.1 Introduction

Positron Emission Tomography (PET scanners) are medical imaging machines that use radiotracers to produce 3-D images of the human body's internal structures and functions. These radiotracers can be injected into the patient's bloodstream, inhaled, or swallowed. As the radiotracer travels through the body, it emits positively charged particles (positrons), which collide with negatively charged electrons in the body's tissues. This collision produces gamma rays, detected by the PET scanner and used to create detailed anatomical images.

PET scanners diagnose and monitor various medical conditions, including cancer, heart disease, and brain disorders. They can also assess treatments' effectiveness and guide surgical procedures. In addition, PET scans are often combined with CT (computed tomography) or MRI (magnetic resonance imaging) scans to provide even more detailed information about the body's structures and functions.

The most used radioisotope in PET scanning is fluorine-18 ($t_{1/2}$= 109.77 mins), which creates a tracer molecule called fluorodeoxyglucose (2-deoxy-2-[^{18}F]fluoro-D-glucose) known as FDG.

FDG is a form of glucose modified to include a radioisotope of fluorine. When injected into the body, FDG is taken up by cells that use glucose as an energy source, such as cancer cells. As the FDG accumulates in these cells, it emits positrons, which collide with electrons in the surrounding tissue to produce gamma rays detected by the PET scanner.

Other radioisotopes used in PET scanning include carbon-11 ($t_{1/2}$= 20.34 mins), nitrogen-13 ($t_{1/2}$= 9.965 mins), and oxygen-15 ($t_{1/2}$= 2.03 mins). These radioisotopes are used to create tracers that target specific biochemical processes in the body, such as blood flow or oxygen consumption.

It's important to note that the radioisotopes used in PET scanning have short half-lives, meaning they decay rapidly and lose their radioactivity within a short period of time. This minimises the risk of long-term radiation exposure to the patient.

52.2 Positron Emission Tomography: Principles and Applications

Several advanced PET scanners are currently available, each with unique features and capabilities, for example:

- Digital photon counting (DPC) PET scanners use advanced detectors to detect individual photons emitted by the radioactive tracer. This allows for higher spatial resolution, faster acquisition times, and improved sensitivity compared to traditional PET scanners.
- Time-of-flight (TOF) PET scanners use advanced detectors to measure the time gamma rays travel from the tracer to the detector. By measuring the time of flight, TOF PET scanners can improve the accuracy and quality of the images produced.
- Total-body PET scanners can image the entire body in a single scan, allowing for more comprehensive disease and treatment response assessments.
- Hybrid PET/MRI scanners combine PET and MRI technologies, allowing for the simultaneous acquisition of anatomical and functional information. This provides a complete picture of the anatomical structures and functions.
- Preclinical PET scanners are designed for animal research and drug development. They offer higher spatial resolution and greater sensitivity than clinical PET scanners, allowing researchers to study disease processes at the cellular and molecular levels.

The field of PET scanning is rapidly evolving, and new technologies and advancements are constantly being developed.

52.3 Neuroimaging with PET: Advances in Brain Disorders

PET imaging is an important tool in neurology for assessing brain structure and function. This diagnostic imaging tool can detect the accumulation of amyloid plaques and tau tangles in the brain, characteristic of Alzheimer's disease.

This can help with early diagnosis and monitoring of disease progression. It can also measure dopamine levels in the brain, which are depleted in Parkinson's disease. This can help with the diagnosis and monitoring of disease progression. Furthermore, a PET examination can identify the brain's specific regions responsible for seizures, which can help with surgical planning and treatment decisions. In addition, PET imaging can be used to assess blood flow and metabolic activity in the brain following a stroke.

52.4 Hybrid Imaging: Integrating PET with MRI and CT

PET scanner hybrids are machines that combine PET technology with other imaging modalities, such as CT, MRI, or SPECT (single photon emission computed tomography). These hybrid scanners offer several advantages over conventional PET scanners, including:

- Improved anatomical localisation by combining PET with other imaging modalities; hybrid scanners can provide more precise anatomical localisation of the areas of interest.

- Hybrid scanners can provide complementary information from multiple imaging modalities, improving the accuracy of diagnoses and treatment planning.
- By combining PET with other imaging modalities, hybrid scanners can reduce the total radiation exposure to the patient compared to separate PET and CT scans.
- Hybrid scanners can perform multiple imaging modalities in a single session, reducing the time and cost of separate imaging sessions.

PET scanner hybrids include PET/CT, PET/MRI, and SPECT/CT. PET/CT combines PET and CT technologies to provide functional and anatomical information, making it particularly useful for cancer imaging. PET/MRI combines PET and MRI technologies to provide detailed anatomical and functional information with high soft tissue contrast, making it particularly useful for brain and musculoskeletal imaging. Finally, SPECT/CT combines SPECT and CT technologies to provide functional and anatomical information, making it particularly useful for cardiac imaging and bone scans.

PET scanner hybrids are powerful tools in medical imaging that allow for more precise and accurate diagnoses while reducing radiation exposure and increasing efficiency.

52.5 Milestones in PET Technology: Innovations That Shaped Modern Imaging

The development of PET imaging was a collaborative effort among several pioneers in physics, chemistry, and medicine. Some of the key figures involved in the development of PET imaging include:

- Gordon Brownell, in the 1950s, began researching the use of positron-emitting isotopes for medical imaging.
- Michel Ter-Pogossian collaborated with Brownell to develop the first PET scanner in the 1970s.
- Edward Hoffman helped to refine PET technology and develop new radiopharmaceuticals for use in PET imaging.
- David Kuhl developed new image reconstruction and interpretation techniques in PET imaging.
- Sami Shihab pioneered PET imaging in oncology, particularly in diagnosing and treating lung cancer.

These pioneers and other researchers developed and refined PET imaging technology, paving the way for its widespread use in modern medicine.

52.6 Next-Generation PET Scanners: A Glimpse into the Future of Molecular Imaging

Siemens Biograph PET/CT is a popular model of PET scanner manufactured by Siemens Healthineers, a global medical technology company headquartered in Germany. The Biograph PET/CT combines two imaging technologies, PET and CT (Computed tomography), into one device, allowing for more comprehensive body imaging.

This hybrid scanner is designed to provide high-resolution images with excellent contrast, helping to accurately detect and diagnose various medical conditions, including cancer, neurological disorders, and cardiovascular disease. In addition, the scanner uses a low radiation dose to produce images, making it safe for patients.

The Siemens Biograph PET/CT also has advanced software for efficient image reconstruction, analysis, and image sharing with other medical professionals. This makes it a valuable tool for medical research and clinical studies.

The GE Discovery PET/CT can produce detailed images of the body's function and structure and help to diagnose cancer, heart disease, and neurological disorders.

The Philips Ingenuity TF PET/CT allows healthcare professionals to diagnose and treat various medical conditions, including cancer, heart disease, and neurological disorders. It has several advanced features, including time-of-flight PET technology, which helps improve image quality and reduce scan times, and a large bore, allowing larger patient imaging.

The Toshiba Celesteion PET/CT has several advanced features, including a high-speed CT scanner and a large detector ring for PET imaging, which can help reduce scan times and improve image quality.

The Mediso AnyScan PET/CT is a medical imaging scanner that can produce highly detailed images that provide information about the body's function and structure. It has advanced features, including a high-resolution PET detector, a low-dose CT scanner, and a patient-friendly design that can help improve patient comfort during the scanning process.

Hitachi PET/CT scanners allow for imaging of larger patients, and a 64-slice CT scanner can help reduce scan times and improve image quality.

The NeuroLogica Quantum PET/CT has several advanced features, including a compact design, which allows for easier installation in smaller spaces, and a fast PET detector, which can help reduce scan times and improve image quality.

The Cubresa NuPET™ scanner is a preclinical medical imaging device that can produce highly detailed images that provide information about the body's function and structure. This allows researchers to understand the underlying mechanisms of diseases better and develop new therapies to treat them.

Also, the Cubresa NuPET™ scanner has several advanced features, including a compact design, which allows for easier installation in smaller spaces, and a high-sensitivity PET detector, which can help reduce the amount of radioactive material needed for imaging. The device is used primarily in preclinical research and drug development and is considered a valuable tool in medical research.

The Raycan α-PET scanner uses silicon photomultiplier (SiPM) detectors, which are highly sensitive to light and can detect even very small amounts of radiation. This allows for a higher level of accuracy and sensitivity in PET imaging. The scanner also

has a compact design, which allows for easier installation in smaller spaces and a fast acquisition time, which can help reduce scan times and improve patient comfort. The Raycan α-PET scanner is used primarily in research and clinical settings, particularly in diagnosing and treating cancer, neurological disorders, and cardiovascular disease.

The United Imaging uMI 550 PET/CT scanner has several advanced features, including a large bore, which allows for imaging of larger patients, and a high-definition digital detector, which can help reduce scan times and improve image quality. The device is used in hospitals and imaging centres worldwide and is considered a valuable tool in medical imaging. Additionally, the uMI 550 PET/CT has several advanced software tools for image reconstruction, quantitative analysis, and artificial intelligence-based interpretation, making it a powerful tool for clinical and research applications.

52.7 Total-Body PET/CT Imaging: Enhancing Diagnosis and Treatment Planning

The PET/CT Explorer scanner is a groundbreaking total-body imaging system that combines the functional information of PET with the anatomical details provided by CT. With its extended field of view, the PET/CT Explorer delivers enhanced sensitivity, enabling faster scans, reduced radiation doses, and improved patient diagnostic accuracy.

This innovative technology can transform clinical practice and research by providing a more comprehensive understanding of diseases and their progression. It is particularly beneficial for detecting cancer, monitoring treatment response, and assessing cardiovascular and neurological conditions.

Furthermore, the PET/CT Explorer scanner can open new opportunities for research in pharmacokinetics, immunology, and stem cell therapy. This advanced imaging system paves the way for more personalised medicine and improved patient outcomes by providing a holistic view of the human body.

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53 Machine Learning in Oncology: Advancements in Cancer Identification

Machine learning revolutionises cancer diagnostics, enabling early detection and personalised treatment for improved prognosis.

53.1 Introduction

Cancer is a complicated disease affecting millions worldwide, accounting for 10 million deaths in 2020. Cancer diagnosis, treatment, and prognosis remain challenging despite advances in medicine. Machine Learning (ML), a subgroup of artificial intelligence (AI), has shown immense potential in improving cancer outcomes by analysing large amounts of data and identifying patterns that may be difficult for human experts to detect.

One of ML's most significant applications in cancer is diagnosing the disease. ML algorithms can analyse the big data from medical images such as computed tomography (CT), magnetic resonance imaging (MRI) and mammograms to find cancerous tissues or lesions. This process can be assisted with the application of deep learning algorithms in which ML can analyse vast datasets of medical images and find patterns that are difficult to detect by human experts. This has led to improvements in the accuracy and speed of cancer diagnosis.

For example, researchers at Google have developed an ML algorithm that can detect breast cancer with high accuracy in mammograms. In a study published in Nature, the algorithm was as correct as human radiologists in detecting breast cancer. Similarly, researchers at MIT have developed an ML algorithm that can detect lung cancer in CT scans with a high level of accuracy.

In addition to improving the accuracy of cancer diagnosis, ML algorithms can also aid in interpreting medical images. For instance, an ML algorithm can analyse a medical image and highlight areas suspicious of cancer, making it easier for radiologists to interpret the results. This approach can help reduce the time needed for diagnosis and increase the accuracy of cancer detection.

Furthermore, ML algorithms can also analyse medical images over time to track cancer progression and monitor treatment effectiveness. This can help doctors identify changes in tumours' size, shape, and texture, providing insights into the response to treatment and the need for further intervention.

For instance, researchers have used deep learning algorithms to analyse mammograms and identify breast cancer with an accuracy of over 90%. These

algorithms can also process electronic health records (EHRs) to identify patients with a high risk of developing cancer, allowing for early intervention and prevention.

In addition to diagnosis, ML can also assist oncologists in selecting the most effective treatment for a patient. For example, researchers have used ML to predict which chemotherapy drugs will be most effective for patients based on their medical history and genomic data. This approach, known as precision medicine, tailors treatment to the individual patient, increasing the likelihood of success and reducing side effects.

ML can also predict the likelihood of a patient's cancer returning or progressing after treatment, known as prognosis. These predictions can help doctors determine the most appropriate follow-up care plan for each patient, ensuring they receive the care they need to prevent a recurrence. For example, an ML algorithm developed by researchers at Stanford University can predict the risk of metastasis in breast cancer patients with high accuracy.

53.2 Machine Learning Revolution: Transforming Cancer Detection and Diagnosis

Another significant application of ML in cancer is drug discovery. ML algorithms can identify molecules likely to be effective against a specific type of cancer, accelerating the drug discovery process. Researchers have used ML to design new drug candidates for cancer treatment, such as using reinforcement learning to optimise drug combinations. This approach can potentially reduce the time and cost associated with traditional drug development and improve patient outcomes.

ML algorithms can predict the interactions between drugs and their targets, such as proteins or enzymes involved in cancer progression. This information can help find new drug candidates and optimise existing drugs for improved efficacy and reduced side effects. This approach is used to screen large molecule databases to identify the most effective against a specific type of cancer. Therefore, accelerate the drug discovery process by reducing the number of candidates that must be tested in the laboratory.

Furthermore, ML algorithms can be used to optimise drug combinations for cancer treatment and identify the most effective drug combinations based on patient-specific data, such as genomics and medical history. ML algorithms can also analyse patient data to develop personalised treatment plans for cancer patients. This precision medicine approach tailors treatment to the individual patient, increasing the likelihood of success and reducing side effects.

ML can also be used to find the mechanisms contributing to drug resistance in cancer cells. This information can help find new drug targets and develop strategies to overcome resistance and improve treatment outcomes.

Despite the potential of ML in cancer diagnosis, treatment, and prognosis, it is important to note that these technologies are still in the initial stages of development. Further research is needed to confirm their clinical utility and ensure they are safe, effective, and affordable for all patients. Additionally, using ML in cancer care raises

ethical and regulatory issues that must be addressed to ensure patient privacy, safety, and autonomy.

53.3 Accelerating Cancer Treatment: The Role of Machine Learning in Diagnostic Accuracy

ML has shown immense potential in cancer diagnosis, treatment, and prognosis. One area of focus for ML in cancer care is the development of predictive models. These models can help identify patients at high risk of developing cancer, enabling earlier intervention and preventive measures. For example, a study published in the Journal of the American Medical Association found that an ML algorithm could predict breast cancer up to five years before diagnosis with high accuracy.

Another area where ML could significantly impact is the development of precision medicine. By analysing genomic data, medical history, and other factors, ML algorithms can help tailor cancer treatment to the individual patient, increasing the likelihood of success and reducing side effects. In the future, ML algorithms will likely play an increasingly key role in identifying the most effective treatment for each patient based on their unique characteristics.

53.4 The Future of Oncology: Machine Learning's Impact on Cancer Care

ML can potentially revolutionise how we diagnose, treat, and prevent cancer. By analysing enormous amounts of data and identifying patterns that may be difficult for human experts to detect, ML can improve cancer outcomes and ultimately save lives. While there are still challenges to overcome, the potential benefits of these technologies are significant, and continued investment in R&D is essential to unlocking their full potential.

Furthermore, ML has the potential to revolutionise the drug discovery process and develop more personalised treatments for cancer patients. Additionally, the use of ML in drug discovery and personalised medicine raises ethical and regulatory issues that must be addressed to ensure patient privacy, safety, and autonomy.

Advances in ML algorithms have transformed how medical images are analysed for cancer diagnosis and monitoring. These technologies can potentially improve the accuracy and speed of cancer diagnosis, reduce the need for invasive procedures, and save lives. However, further research is to validate the clinical utility of these technologies and ensure that they are safe and effective for all patients.

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54 From Science Fiction to Reality: The Early Days of Laser Medicine

Medical laser milestones encompass pivotal discoveries, advancing treatment efficacy, and expanding therapeutic applications.

54.1 Introduction

The history of medical lasers dates back to the 1960s when the first lasers were invented. In 1960, Theodore H. Maiman developed the first laser, which used a ruby crystal to produce a beam of red light. Shortly after, other types of lasers, such as gas and semiconductor, were developed, and researchers began exploring their potential applications in medicine.

In 1963, the first medical laser was used in ophthalmology to treat retinal diseases. The ruby laser was used to destroy small blood vessels in the retina, causing vision loss. This procedure, called photocoagulation, was the first of many medical applications for lasers.

Throughout the 1960s and 1970s, researchers and physicians continued exploring lasers in medicine, developing new techniques for surgery, dermatology, dentistry, and other fields. Finally, in 1973, the carbon dioxide laser was developed, which became the first widely used medical laser. Carbon dioxide lasers were used for a variety of procedures, including the removal of skin lesions, the treatment of acne scars, and the removal of tumours.

New lasers were developed in the 1980s and 1990s, including the argon laser, the Nd:YAG laser, and the excimer laser. These lasers were used for a broader range of medical applications, such as treating varicose veins, removing tattoos, and correcting vision problems.

In the 2000s and beyond, medical laser technology continued to advance with the development of new types of lasers and new applications for existing lasers. One of the most significant advances was the free-electron laser (FEL) development, which is capable of generating high-energy, tightly focused beams of light that can be used for precision surgery and radiation therapy.

Medical lasers are used in various applications, from surgery and ophthalmology to dentistry and oncology. Laser technology continues evolving, with researchers exploring new diagnosis, imaging, and treatment techniques. As medical lasers continue to advance, the potential for new and innovative applications in healthcare is virtually limitless.

Medical lasers have revolutionised modern medicine and have become an essential tool for diagnosis, treatment, and surgical procedures. These devices use light energy to cut, vaporise, coagulate, and sterilise tissue, making them incredibly versatile in medicine. This article will discuss the several types of medical lasers, their applications, and their advantages and disadvantages.

54.2 From Ruby to CO_2: The Evolution of Laser Types and Their Medical Uses

Several types of medical lasers are designed for specific medical procedures. The most common types of medical lasers are:

- Carbon dioxide lasers emit a wavelength of 10.6 micrometres, making them useful for surgical procedures requiring tissue removal or cutting.
- Argon lasers emit a blue-green light and are useful for treating skin conditions and in ophthalmology to treat glaucoma and retinal diseases.
- Excimer lasers emit ultraviolet light and are used for corneal surgeries.
- Nd:YAG lasers emit near-infrared light and are useful for treating conditions such as varicose veins, skin lesions, and hair removal.
- Diode lasers emit red or infrared light and are used for hair removal, skin rejuvenation, and treating vascular lesions.
- Er:YAG and Er,Cr:YSGG Lasers: Er:YAG and Er,Cr:YSGG lasers emit a wavelength of 2.94 micrometres and are used for dental procedures, such as cavity preparation and periodontal treatment.

54.3 Unveiling the Power of Extreme Light: An In-Depth Exploration of the ELI Beamlines Laser Facility

The most powerful laser in the world is the Extreme Light Infrastructure (ELI) Beamlines laser, located in the Czech Republic. The ELI Beamlines laser was completed in 2015 and produced pulses of light with a power of up to 10 petawatts (PW), equivalent to 10 quadrillion watts or 10 million billion watts.

The ELI Beamlines laser is a high-power, ultrafast laser that is used for a wide range of applications, including physics research, materials science, and medical research. Its high power and short pulse duration allow researchers to study the behaviour of matter at the atomic and molecular level and generate high-energy particles and X-rays.

The ELI Beamlines laser consists of a series of high-power lasers synchronised to produce ultrafast light pulses. The laser system uses a technique called chirped pulse amplification (CPA) to amplify the power of the laser pulses. In CPA, the laser pulses are stretched out in time, allowing them to be amplified without damaging the laser components. The pulses are then compressed to their original duration, resulting in a high-power, ultrafast laser pulse.

While the ELI Beamlines laser is currently the most powerful globally, other high-power lasers are also under development, including the High-Repetition-Rate Advanced Petawatt Laser System (HAPLS) in the United States and the Shanghai Superintense Ultrafast Laser Facility (SULF) in China. These lasers are expected to produce even

higher powers than the ELI Beamlines laser, further advancing our ability to study and manipulate matter at the atomic and molecular levels.

54.4 Harnessing the Power of Light: Clinical Laser Applications

Medical lasers have a wide range of applications in the medical field, including:

- Medical lasers are used to cut, vaporise, or coagulate tissue in various surgical procedures.
- They are also used in LASIK and PRK surgeries to correct refractive errors.
- Dentistry uses lasers for cavity preparation, periodontal treatment, and tooth whitening.
- Lasers are used in oncology to treat several types of cancer, including skin, breast, and prostate cancer.

54.5 Lasers in Modern Medicine: A Revolution in Healthcare

Medical lasers offer several advantages over traditional surgical methods, including:

- Target specific tissues, minimising damage to surrounding healthy tissue.
- Cauterise blood vessels as they cut, reducing blood loss during surgery.
- Laser surgery can result in less pain, swelling, and scarring than traditional surgical methods.
- Sterilise the tissue as it is cut, reducing the risk of infection.
- Laser surgery can result in a shorter recovery time compared to traditional surgery.

54.6 Lasers in Medicine: Balancing the Promise of Innovation with Patient Safety Concerns

- Medical lasers emit high-energy beams that can cause tissue damage if not used properly. Inexperienced or untrained personnel may accidentally damage surrounding healthy tissue or cause burns.
- Lasers can cause severe eye damage, including blindness, if they are not used correctly or if protective eyewear is not worn.
- Lasers can generate heat, which may increase the risk of infection if the treated area is not adequately sterilised before and after the procedure.
- Medical lasers are expensive to purchase and maintain, which may make them inaccessible to some healthcare facilities.
- While lasers have successfully treated certain medical conditions, they may not be effective in treating all conditions, and traditional treatment methods may be required.
- Several types of lasers have different wavelengths, which can limit their ability to penetrate deep tissues. This can make them less effective for certain types of procedures.
- Some laser treatments may require multiple sessions, which can be time-consuming and inconvenient for patients.

54.7 Lasers in Surgery: Revolutionising Precision and Minimally Invasive Techniques

The use of medical lasers in healthcare has come a long way from their invention in the 1960s. As technology advances, the future of medical lasers looks promising, potentially revolutionising how we diagnose and treat diseases.

One of the most interesting areas of evolution in medical lasers is their use for non-invasive diagnostic techniques. For example, researchers are developing laser-based systems that can quickly and accurately diagnose cancer by analysing the unique molecular signatures of cancer cells. These systems have the potential to significantly improve early detection rates and reduce the need for invasive biopsy procedures.

Similarly, medical lasers are being used to develop non-invasive techniques for imaging internal organs and tissues. These techniques could provide physicians with a better understanding of diseases and improve treatment outcomes.

In the field of surgery, medical lasers are already being used to perform minimally invasive procedures, reducing the need for traditional surgical techniques that require large incisions. Advances in laser technology are expected to make these procedures even more precise and effective, leading to better patient outcomes.

One area of research that shows particular promise is using lasers to stimulate tissue regeneration. Researchers are exploring the use of low-level laser therapy to promote healing and tissue regeneration in various applications, from wound healing to treating chronic pain. While this area of research is still in its preliminary stages, it can potentially transform how we treat a wide range of medical conditions.

Another promising area of development is using lasers for targeted drug delivery. Researchers are exploring using laser-activated nanoparticles to deliver drugs directly to cancer cells, reducing the side effects of traditional chemotherapy treatments. This technique has shown promising results in preclinical studies and could potentially improve the effectiveness of cancer treatments in the future.

As with any modern technology, there are challenges to overcome in developing and using medical lasers. One of the biggest challenges is in ensuring the safety of patients and healthcare professionals. While lasers are generally considered safe when used properly, there is always the risk of accidental injury or damage if misused. As medical laser technology continues to evolve, developing and implementing strict safety guidelines and training programs to ensure their safe and effective use will be essential.

Another challenge is in making medical laser technology more affordable and accessible. While the cost of laser technology has decreased over the years, it is still expensive, which can limit its use in specific healthcare settings. As demand for medical laser technology increases, there will be a need to develop more affordable and accessible systems that healthcare professionals in a wider range of settings can use.

54.8 Unleashing the Power of Light: The Free-Electron Laser (FEL) and its Transformative Impact on Modern Medicine

The most powerful medical laser currently in use is the free-electron laser (FEL). Free-electron lasers generate high-energy, coherent beams of light by accelerating electrons to nearly the speed of light using a linear accelerator, unlike other lasers, which rely on the stimulated emission of photons from excited atoms or molecules. FELs generate light by passing a beam of electrons through a series of magnetic undulators.

FELs are used in various medical applications, including radiation therapy for cancer treatment. The high-energy, tightly focused beams of FELs can be used to precisely target cancerous tissue while minimising damage to healthy surrounding tissue. FELs are also used in ophthalmology to treat retinal diseases and in dermatology to remove skin lesions.

While FELs are the most powerful medical lasers currently in use, they are also the most expensive and technically complex. In addition, FEL systems require a large amount of space and energy to operate, making them inaccessible to many healthcare facilities. As a result, other types of medical lasers, such as diode lasers and carbon dioxide lasers, are more commonly used for medical applications due to their affordability and accessibility.

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55 Nuclear Technologists: Supporting Patients and Healthcare Teams in Diagnosis and Treatment

Nuclear Medicine Technologist is a specialised healthcare professional affiliated with a Nuclear Medicine Department.

55.1 Introduction

A Nuclear Medicine Technologist is a specialised healthcare professional affiliated with a Nuclear Medicine Department or Radiopharmacy. Nuclear medicine encompasses several disciplines, including medical physics, imaging algorithms, radiochemistry, and medical sciences, to help create a treatment plan for each patient. The role of the Nuclear Medicine Technologist is to prepare and formulate a radiopharmaceutical imaging or radiotherapeutic agent and organise the administration of the individual dose to the patient. The aim is to help form a patient treatment plan for the diagnosis of a range of disease states. These disease states include stages of cancers, neurological disorders, heart disease, and endocrine and gastrointestinal conditions, amongst others.

Thinking of a career as a nuclear medicine technologist?

The radiopharmaceutical contains a radionuclide that spontaneously emits radiation via alpha particles, beta particles or gamma rays. The Nuclear Medicine Technologists – in association with the medical physicist – operate SPECT imaging (single photon emission tomography) and PET imaging (positron emission tomography) gamma camera systems to detect the radiation from the radiopharmaceuticals emitting from inside the human body.

This setup enables the generation of images that are analysed to show the regions of the radiopharmaceuticals localised within the organs of the human body. The abnormal areas will retain a level of radioactivity compared to the healthy surrounding tissues. The nuclear medicine technologist and physicians analyse the generated images to diagnose molecular and metabolic processes: Also useful in evaluating physiological, anatomical and pathological conditions.

The duties of the Nuclear Medicine Technologist extend to the operation of computed tomography (SPECT) and magnetic resonance imaging (MRI) scanners. Both these systems can be hybrids of SPECT and PET scanners.

55.2 Nuclear Medicine Imaging: An Overview of PET, SPECT, and CT

Nuclear medicine imaging generates non-invasive images except when a radiopharmaceutical is given intravenously. In most cases, the procedure is pain-free

to help in the diagnosis and evaluation of the disease state of the patient. These SPECT and PET imaging scans utilise radioactive materials called radiopharmaceuticals or radiotracers. The radiotracer can be inhaled as a gas, injected into the bloodstream, or swallowed.

The tracer will then accumulate in the human body during the examination. The radioactive emissions from the radiotracer are detected by a gamma camera or another imaging device that is capable of producing images from inside the human body to generate molecular information. The advantages of these systems are that nuclear medicine images can be combined with computed tomography (CT) or magnetic resonance imaging (MRI) to generate image fusion. This approach enables two scans to be done in one patient sitting, and the information can be correlated with one image combined to produce an accurate diagnosis.

These hybrid scanners extend to single-photon emission computed tomography (SPECT)/computed tomography (CT) systems, including positron emission tomography (PET)/computed tomography (CT) machines. Another technology platform being developed uses a combination of the PET/MRI hybrid scanner.

Nuclear medicine technologist also offers radiotherapeutic procedures, which include radioactive iodine (I-131) therapy using SPECT imaging. This procedure uses a tiny amount of radioactive material to treat cancer and other medical conditions affecting the thyroid gland. Also, Non-Hodgkin's lymphoma patients may undergo radioimmunotherapy (RIT) if they are unresponsive to chemotherapy. The radioimmunotherapy (RIT) approach to cancer treatment combines radiation therapy with the targeting ability of immunotherapy. It is designed to imitate cellular activity in the human body's immune system.

55.3 Radiation Therapy Physics and Brachytherapy: Applications and Innovations

Radiation therapeutic physics (radiotherapy physics or radiation oncology physics) is concerned mostly with linear accelerator (Linac) systems and kilovoltage x-ray treatment units. In addition to more advanced modalities such as cyberknife, tomotherapy, brachytherapy and proton therapy.

Therapeutic physics may include boron neutron capture therapy, sealed source radiotherapy and terahertz radiation systems. Therapeutic physics also involves high-intensity focused ultrasound, optical radiation lasers, ultraviolet and others. Furthermore, extending to photodynamic therapy, including nuclear medicine using unsealed source radiotherapy and photomedicine.

Nuclear Medicine is a discipline that uses radiation to gain information about the functioning of the human body's organs to diagnose diseases and to apply appropriate therapy treatments. The information generated helps physicians to make a reasonable and accurate diagnosis of the patient's disease state.

The organs of the human body which can easily undergo imaging include the thyroid, bones, heart, liver, etc. Another use of radiation is its ability to treat diseased organs and/or tumours. Radiotracers in medicine are widely used throughout the World of

healthcare organisations, extending to mobile facilities. About 10,000+ hospitals worldwide use radioisotopes in medicine for diagnosis and therapy procedures.

The most diverse radioisotope used in diagnosis is technetium-99m. This radionuclide accounts for over 30 million procedures per annum and accounts for 80% of all nuclear medicine procedures. In context, the USA produces some 18 million nuclear medicine procedures per year. In Europe, there is about 10 million procedure from a population of 500 million people. Marketing suggests that the use of radiopharmaceuticals in diagnosis is growing at a rate of 10% per annum.

55.4 The Evolution of Radiopharmaceuticals and Radiotracers in Nuclear Medicine

Nuclear medicine began in the 1950s by physicians investigating the endocrine system using iodine-131 to diagnose and treat thyroid disease. The medical physicist liaises with a radiologist due to the hybrid PET-CT systems, including SPECT scanners. CT scanning and nuclear medicine contribute to over a third of the total radiation exposure. The average total yearly radiation exposure in the USA per person is 6 mSv per year.

The responsibility of the Health Physicist (Radiation Safety or Radiation Protection Officer) is the evaluation and control health hazards associated with the safe handling of radiation sources. Therefore, the supervision and monitoring of radionuclides or ionising radiation in the clinical setting are of paramount importance to regulatory requirements.

The application of more advanced computer systems enables processes to analyse complex driven by the generation of computer algorithms for delineating anatomical structures for the next generation of PET and SPECT scanners. For example, image segmentation is central to various biomedical imaging applications. These include quantification of tissue volumes, diagnosis and localization of pathology.

In addition, to the study of anatomical structure, treatment planning and computer-integrated surgery, the application of a 3-D volume extraction algorithm was suggested for the segmentation of cerebrovascular structure for the brain. Previous knowledge of the cerebrovascular structure and multiple seed voxels is identified on the initial image.

The seed voxels were grown within the cerebrovascular structure area throughout the 3-D volume extraction procedure in light of the preserved voxel connectivity. This algorithm improved the segmentation results compared to other methods, such as the histogram approach. Furthermore, this 3-D volume extraction algorithm is also applicable to segment tree-like organ structures. For example, the renal artery and coronary artery can be derived from these medical imaging modalities.

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56 The Role of Radiotracers in Molecular Imaging Techniques

Nuclear Medicine Technologist is a specialised healthcare professional affiliated with a Nuclear Medicine Department.

56.1 Introduction

Radiotracers and radiopharmaceuticals are substances that follow the behaviour of various biological processes. They are also used for flow visualisation through different medical imaging modalities such as Positron Emission Tomography (PET imaging), Single Photon Emission Computed Tomography (SPECT imaging) and Computed Radioactive Particle Tracking (CARPT) systems.

Radiopharmaceuticals – are used in vitro and in vivo to study drug metabolism profiles. The premise behind radiolabelled drugs is to quantify the amount of drug-related substances in different biological systems. The advantage of radiolabelled isotopes is the ability to apply chromatographic separation and quantify the individual metabolites.

Therefore, radiolabelled drugs are used mostly in ADME (absorption, distribution, metabolism and excretion) studies. Carbon-14 (^{14}C) labelled compounds benefit these investigations because of the higher metabolic stability of this compared to the tritium (^{3H}) tagged version. The radiolabel is inserted into the metabolically stable core group of the compound. The radiolabel may be placed on stable and labile moieties depending on the labelling requirements. Furthermore, double-labelled compounds with different isotopes, for example, $^{13}C/^{14}C$ or $^{3}H/^{14}C$, might be synthesised to aid in metabolite identification and quantification of the individual moieties.

Radiotracers used in the investigation of metabolic pathways fall into two categories:

- Radioisotopes of the parent compound, for example, ^{11}C-palmitate and ^{11}C-glucose, follow the same metabolic fate of the parent compound to evaluate the metabolic pathway quantitatively.
- The analogues of the parent compound, such as [2-^{18}F]-2-fluoro-2-deoxyglucose [FDG] and [^{123}I]-BMIPP (β-methyl-iodophenyl-pentadecanoic acid), provide qualitative assessments of metabolism because they are generally retained by the tissue and make imaging more viable.

56.2 FDG-PET Radiotracers: A Widely Used Tool for Cancer Diagnosis and Staging

The PET radiotracer [1-^{11}C]glucose cannot be biochemically indistinguishable from glucose and, therefore, can follow the exact fate of glucose during metabolism. This

process releases cardiomyocytes as $^{11}CO_2$ and results in the uptake, retention and disappearance of the radiotracer from the heart.

In the other situation, FDG is taken up and phosphorylated by hexokinase and does not undergo further metabolism in the cardiomyocyte because of the modification of the carbohydrate structure from glucose to deoxyglucose.

As a result, FDG becomes trapped in the cell. Kinetic analysis of the time-activity curves for FDG can be used to estimate glucose's initial uptake and phosphorylation. This process provides no information regarding the oxidative fate of glucose, and kinetic analysis demonstrates irreversible trapping compared to the accumulation and disappearance of other radiotracers.

The irreversible 'trapped' radiotracers regarding myocardial substrate utilisation generate:

- Information regarding a part of a given metabolic process.
- differences in the structure of the parent compound and the radiotracer will alter the reliability with which the tracer measures the utilisation of the parent compound.
- the relationship between tracer and detection can vary under different metabolic conditions.

56.3 The Role of Laboratory Radiotracers in Nuclear Medicine Research

Radiotracers can be classified as to whether they are single photon-emitting or positron-emitting nuclides. PET radiotracers require the coincidence detection of the two 511-keV photons produced by positron annihilation combined with the attenuation correction that is needed for the radiopharmaceutical. Also, kinetic analysis can be performed with the positron-emitting metabolic radiotracers to generate quantitative measurements of rates of substrate uptake and metabolism.

However, single photon-emitting metabolic radiotracers can only provide qualitative assessments of metabolic processes. The primary advantage of these radiotracers is that an on-site cyclotron is not required to produce the short-lived carbon-11 and oxygen-15 radiopharmaceuticals. This is a significant advantage and accelerates the newer technetium-99m (Tc-99m) labelled fatty acid analogues for metabolic imaging by building on the established iodine-123 tagged fatty acid analogue platform, namely, BMIPP.

Research into radiolabelled nanoparticles offers several advantages, such as prolonged circulation time, high plasma stability and a high potential for clinical applications in the early diagnosis of cancer and cardiovascular diseases.

This theranostic technology is able to generate single-photon emission computed tomography (SPECT) or positron emission tomography (PET) for targeted in vivo imaging. Both these technologies are highly sensitive, specific and useful for inaccurate quantification compared to in vivo imaging techniques with limited application due to the type of tissue involved.

Radiolabelled monoclonal antibodies (Mab) – which are being developed to target specific antigens, have been safely administered to patients with leukaemia. For example, yttrium-90-anti-CD25 was shown to be active against acute T-cell leukaemia. Also, iodine-131-anti-CD33 was active in the treatment of acute myeloid leukaemia (AML), Myelodysplastic syndrome (MDS), including myeloblastic chronic myeloid/myelogenous leukaemia (CML]). Other indications involving yttrium-90-anti-CD33 and iodine-131-anti-CD45 were effective against AML, ALL (Acute lymphoblastic leukaemia) and MDS. The radiolabelled Mab, rhenium-188-anti-CD66c showed promise against AML, ALL and CML.

Radioconjugates that emit alpha particles, for example, bismuth-213-anti-CD33 and actinium-225-anti-CD33, may be better suited for the treatment of small-volume disease.

In the 1980s, Tc-99m–labelled hepatobiliary-based radiopharmaceuticals became available for 'experimental' treatment plans due to the production of superior images. These imaging agents superseded iodine-123 rose bengal and gave rise to three U.S. Food and Drug Administration (FDA) approved hepatobiliary radiopharmaceuticals for clinical use. This included the first Tc-99m dimethyl iminodiacetic acid (IDA) and has become a generic term for all Tc-99m IDA radiopharmaceuticals. Tc-99m contains the ability to bridge between two IDA ligand molecules and binds to an acetanilide analogue of lidocaine. The whole structure determines the overall radio-pharmacokinetic profile, including modifications to the phenyl ring moiety resulting in the different pharmacokinetics of IDA radiopharmaceuticals.

56.4 Radiopharmaceuticals for the Diagnosis and Treatment of Cancer

Several radiopharmaceuticals, such as Tc-99m-hepatobiliary (HIDA) analogues that possess different chemical substituents on the aromatic ring, have been investigated. This demonstrated to have less uptake, including slower clearance than the approved commercially available agents. In another example, Tc-99m-sestamibi has coordinated with six methoxyisobutylisonitrile (MIBI) ligands. The resultant complex is a cationic SPECT imaging agent that accumulates in cytoplasm and mitochondria by the process of passive diffusion across the polarised cellular/organelle membrane.

Similarly, for thallium-201, Tc-99m-sestamibi is generally excluded from the brain via the blood-brain barrier (BBB), and therefore tumour uptake appears to be mainly related to BBB breakdown. The normal MIBI distribution is in the pituitary gland, scalp and choroid plexus. However, the MIBI radiotracer is not imageable in normal brain parenchyma. Also, normal uptake of MIBI in the choroids can be perplexing and limit the evaluation of deep periventricular tumours.

However, the research using Tc-99m-sestamibi SPECT imaging of glioma recurrence following radiation therapy demonstrated a pooled sensitivity of 90% and specificity of 92%.

Nevertheless, Tc-99m-sestamibi has better imaging properties than thallium-201 producing an energy of 140 KeV and higher allowable injection dosages of up to 30

mCi. However, further research is required to evaluate the benefits of Tc-99m-sestamibi for diagnosis and prognosis, including detecting tumour recurrence over the superiority of thallium-201. Interestingly, studies have suggested that Tc-99m-sestamibi has increased specificity over thallium-201.

Further, investigations using Tc-99m-sestamibi as a prognostic biomarker for patient survival and a predictive biomarker in chemotherapy treatment are promising. Research has shown that quantitative analysis of Tc-99m-sestamibi uptake using SPECT imaging correlates well with survival time in patients following chemoradiotherapy. This modern approach contributes to the patient's overall prognosis by evaluating the chemotherapy response of Tc-99m-sestamibi.

Overall, the collective evidence points towards Tc-99m-sestamibi as an early indicator of treatment success by demonstrating tumour progression on average four months before changes are detected on magnetic resonance imaging. Remarkably, Tc-99m-sestamibi is eliminated from cells by P-glycoprotein, which also acts as an energy-driven efflux pump for several antineoplastic agents. Moreover, multiple drug resistance (MDR)-1 gene expression demonstrated by Tc-99m-sestamibi does not appear to correlate with chemoresistance in gliomas.

56.5 Myoview in Heart SPECT Imaging

Technetium-99m-tetrofosmin, known as Myoview, was approved by the FDA in 1996 and, in some respects, is similar to Tc-99m-sestamibi. My view is rapidly removed from the liver compared to other Tc-99m imaging-based agents. The tetrofosmin ligand is a member of the diphosphine chemical class (6,9-bis [2-ethoxyethyl]-3,12-dioxa-6,9-diphosphatetradecane). This SPECT imaging agent is prepared from a commercial kit (Myoview) and is similar to Tc-99m-sestamibi. This Tc-99m-tetrofosmin is a lipophilic cation that localises near mitochondria in the myocardial cell and remains fixed at that site.

Immediately after intravenous injection, the Tc-99m tetrofosmin is rapidly cleared from the bloodstream, and the myocardial quickly uptakes the radiotracer. However, the first-pass extraction is less than that of sestamibi (50% vs 60%), including 1.2% of the administered dose taken up in the myocardium within 5 minutes after injection. The extraction is proportional to blood flow but underestimated at high flow rates. Furthermore, the heart-to-lung and heart-to-liver ratios improve over time because of physiological clearance through the liver and kidneys.

Studies have found that the heart-to-liver rates are higher for Tc-99m tetrofosmin compared to sestamibi. This is because of faster hepatic clearance, which allows for further imaging. However, after the stress exercise, an imaging interval of 15 minutes is achievable, followed by rest studies that started 30 minutes after the injection.

The dosimetry profile is comparable to that of Tc-99m sestamibi, and the gallbladder is capable of receiving a high dose rate at 5.4 rems/20 mCi, compared to the colon for sestamibi. The reason for the difference may be due to whether the studied subjects

ate and had gallbladder contractions. The whole-body radiation effective dose is 0.8 rem/30 mCi.

56.6 Radiopharmaceuticals in Targeted Radionuclide Therapy: A Promising Approach in Cancer Treatment

Nuclear medicine healthcare involves using specific radiotracer laboratories for administering radiopharmaceuticals to patients, including therapeutic procedures. Therefore, for medical imaging, the radiation emitted from these radiopharmaceuticals must be detected by external detectors to determine its in vivo distribution in the human body.

Furthermore, the emitted radiation must be absorbed by targeted tissues for radiopharmaceutical medicine to achieve the desired effect of killing cancer cells. Therefore, theranostics requires understanding the type of radioactivity, the amount administered, and the radiation emissions and how it interacts with the surrounding healthy tissue in the human body to personalise a treatment plan.

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57 MRI is a non-invasive diagnostic tool

The principles of magnetic resonance imaging (MRI) are based on the fundamentals of nuclear magnetic resonance (NMR).

57.1 Introduction

The 2003 Nobel Prize in medicine was awarded jointly to Sir Peter Mansfield and Paul Lauterbur for their contribution towards the development of magnetic resonance imaging (MRI). However, Raymond Vahan Damadian 1977 was the first to perform a full-body scan of a human being to diagnose cancer.

The principles of magnetic resonance imaging (MRI) are based on the fundamentals of nuclear magnetic resonance (NMR), which is used to obtain structural and physical information on chemical compounds. This magnetic resonance imaging (MRI) spectroscopic technique is based on the absorption and emission of energy from the electromagnetic spectrum in the radiofrequency range (20 kHz to 300 GHz).

Spatial variations in the phase generate the images. These are dependent on the radiofrequency energy, which is absorbed and emitted by the imaged object. Several biologically active nuclei can produce magnetic resonance images, including hydrogen, oxygen-16, oxygen-17, fluorine-19, sodium-23 and phosphorus-31.

The human body contains 63% hydrogen atoms from its fat and water components. Each hydrogen nuclei has a characteristic NMR signal, enabling clinical magnetic resonance imaging to generate pictures.

One way to understand this is to imagine the protons behaving like tiny bar magnets with the associated north and south poles lying within the domain of the magnetic field. However, the magnetic moment of a single proton is tiny and undetectable, whereas the orientation of the protons is random in the setting without an external magnetic field.

In order to produce the magnetic resonance imaging (MRI) signal, an external magnetic field must be applied to allow the protons to become aligned. This results in an increase in a measurable magnetic moment in the direction of the external magnetic field. Therefore, by applying a sequence of radiofrequency pulses, various images can be created based on the change in the signal from the hydrogen atoms in different types of human tissue.

Currently, several MRI systems are used in medical imaging. Regarding whole-body clinical scanners with field strengths of up to 3.0 Tesla, it is important to mention that

most MRI scanners have a 1.5-Tesla superconducting magnet. In order to put this magnetic field strength into context, it is 30,000 times stronger than that of the Earth.

57.2 MRI scans produce detailed images of the body's interior

A complete MRI scan can take up to 75 minutes, depending on the procedure involved. These may include scanning the brain, heart, spine, liver and muscles. MRI data can produce exceptional structural images of the brain and spinal cord.

These images are formed from a series of slices which can be viewed from:

- The front to the back (coronal) and from top to bottom (axial).
- From one side of the body to the other (sagittal).

These images are generated in 3 planes and analysed by the radiologist, who will provide a clinical opinion.

MRI techniques are useful due to their higher soft-tissue contrast resolution, especially in imaging the internal joints and the central nervous system, including conditions that involve inflammatory responses.

57.3 Magnetic Resonance Imaging: Advantages and Limitations in Clinical Diagnosis

- MRI and Ultrasound imaging involve no ionising radiation.
- Resolution of soft tissue using contrast agents.
- High-resolution imaging, including multiplanar imaging abilities.

The duration of an MRI image is regarded as a significant disadvantage which continues to be so even with faster-computed tomography with the usage of multislice CT technology. To circumvent this, newer imaging techniques, such as parallel imaging, have been developed to generate a faster pulse sequence and, therefore, higher field strength systems. The most basic pulse sequences include T1-weighted and T2-weighted sequences to highlight the differences in the signal of various soft tissues.

- T1-weighted sequences are suitable for the evaluation of various anatomic structures.
- Tissues that allow a high signal (bright) and T1-weighted images include fat, blood, proteinaceous fluid, melanin and the contrast agent gadolinium.
- T2-weighted sequences are useful for the identification of pathologic processes.
- Higher T2-weighted images are obtained with joint and cerebrospinal fluids and cysts.
- Pathologic state causes an increase in extracellular fluid resulting from infection or inflammation.

Several advanced medical imaging techniques are based on MRI and include:

- Functional imaging of the brain.
- Diffusion-weighted imaging.

- Magnetic resonance angiography (MRA).
- MR spectroscopy.
- Chemical shift imaging (fat suppression).

Several of the above techniques are especially useful in brain imaging and include:

- MRA in the time-of-flight or phase contrast mode, in addition to diffusion-weighted imaging, is helpful in detecting and characterising ischemic insults in the brain.
- MRS uses the changes in chemical composition in tissues to differentiate necrosis from normal brain matter as a result of a tumour.

In musculoskeletal imaging, MR arthrography is a technique available to facilitate the depiction of internal derangements of joints.

- Indirect arthrography involves the intravenous administration of gadolinium to be diffused into the joint.
- Direct arthrography involves injecting a dilute gadolinium solution into the joint. This allows the enlargement of a joint to evaluate ligaments, cartilage, and synovial proliferation.

57.4 MR Arthrography: Techniques, Applications, and Clinical Outcomes

- The shoulder by contouring the labral-ligamentous abnormalities. This technique can differentiate damage to the rotator cuff and any labral tears in the hip and the collateral ligament of the elbow.
- Meniscectomy of the knee, especially in detecting recurrent or residual meniscal tears.
- Investigate perforations of the ligaments and triangular fibrocartilage in the wrist.
- The stability of osteochondral lesions associated with the articular surface of joints.

MR arthrography uses T1-weighted images to convey the T1 shortening effects of gadolinium resulting from fat saturation. The T2-weighted sequence in at least one plane is also necessary to detect cysts and oedema in other soft tissues and bone marrow.

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58 Cancer Theranostics: Strategies and Applications

The nuclear medicine imaging approach is to use theranostics, for example, Zevalin, to establish tools for specific molecular targeting.

58.1 Introduction

Medical imaging is being revolutionised through personalised medicine to avoid unnecessary and expensive treatments. The nuclear medicine imaging approach is to use theranostics [targeted therapeutic (Rx) + companion diagnostic (DX)], for example, Zevalin, to establish tools for specific molecular targeting.

The aim is to visualise potential biological targets and develop a personalised treatment plan for the patient. The advent of the development of radiopharmaceuticals and diagnostic procedures will drive these theranostic agents (Zevalin) to be utilised in various nuclear medicine departments. This article aims to provide an overview of theranostics, highlighting radioiodine therapy in patients with thyroid cancer and then progressing through multiple approaches for the treatment of advanced cancer by applying targeted therapies.

Theranostics is an emerging field of nuclear medicine with the aim to target disease states by applying a specific targeted therapy based on precise diagnostic tests. This strategy is focused on the patient to produce a favourable outcome from medical imaging by treating the disease state. This approach moves away from a conventional medicine platform to a personalised and precision methodology. The theranostics model involves bridging nanoscience with diagnostic and therapeutic applications to generate a single agent to facilitate diagnosis, drug delivery and treatment response monitoring.

58.2 Therapeutic Bullets for Targeted Cancer Therapy

The premise behind theranostics is to take advantage of specific biological pathways in the human body to enable the acquisition of diagnostic images. The transformation of these digital images will increase the chance that the therapeutic dose will specifically target the disease site and therefore limit the damage to the surrounding tissues. This approach of using a specific diagnostic test identifies a particular molecular target on tumour cells, allowing a therapeutic agent to bind to the receptor sites and specifically target the regions in the tumour volume.

Theranostics nuclear medicine imaging has started to revolutionise medicine in how we diagnose and develop treatment plans for patients, especially in oncology. This is

in contrast to the more orthodox treatment approach based on the “one-medicine-fits-all” concept. The economic benefits are vast because the patient will receive the correct treatment plan, which would include the right amount of dose to produce a favourable pharmacotherapy outcome in the form of theranostics.

Today, theranostics is used in medical and research establishments to focus on the development of personalised treatment plans by using targeted therapies to eliminate specific disease subtypes, and this may include the genetic profiling of patients. The collaborative approach between nuclear medicine imaging and biosciences will enable successful protocols in the optimisation of drug efficacy, including safety profiles. The merit of this approach is to rationalise

the drug development process and reduce costs. The dual diagnostic and therapy tool will form a central part in elucidating the disease subtypes and understanding its progression within a particular patient. All the information obtained will create an overall rationale to progress the treatment plan, including the type of drugs to be administered, dosing schedules and an understanding of how the patient responds to treatment.

Theranostics can trace its roots back to the pioneering work of Glenn Seaborg and John Livingood, who, in 1938, at the University of California, Berkeley, discovered radioactive iodine-131. This radioisotope became the gold standard in diagnosing and treating thyroid cancer in nuclear medicine imaging departments worldwide.

58.3 Hybrid Imaging Systems in Nuclear Medicine: PET/CT and SPECT/CT Integration

During the past decade, a similar model has been developed for neuroendocrine tumours, which use the radionuclide gallium-68. This positron emission tomography (PET) radiotracer is chelated to DOTA-octreotate and is utilised in tumour diagnosis and produces a higher sensitivity compared to Indium-111 octreotide imaging. The disease state in patients can be assessed by targeting the somatostatin receptor volume by using the gallium-68 DOTA-TATE and image with a hybrid scanner such as PET-CT (Positron Emission Tomography-Computer Tomography).

Patients with disease states that respond to gallium-68 DOTA-TATE PET-CT imaging can receive a treatment plan involving lutetium-177 octreotate therapy for the treatment of carcinoid and endocrine pancreatic tumours. In these cases, the patient will receive 4 to 6 hours of intravenous infusion of lutetium-177 octreotate before leaving the hospital on the advice of the medical physicist. The beta-emitting therapeutic radiopharmaceutical is known as Lutetium Octreotate Therapy and is available in five medical centres throughout North America, including several European nuclear medicine departments.

Since the discovery of this radiotherapeutic method by Harvey and Claringbold using a chemo-targeted radiopeptide therapy approach and building on the platform, theranostic technologies are emerging by building on the platform of radio-sensitising chemotherapy.

The theranostics approach to personalised medicine is gaining pace through a series of milestones, including:

- Lutetium PSMA therapy for the treatment of resistant prostate cancer or metastatic cancer
- Yttrium-90 SIRT therapy for liver cancer
- Iodine-131 therapy for thyrotoxicosis and thyroid cancer
- Radium-223 therapy for metastatic prostate cancer in bones
- Yttrium-90 radiosynovectomy therapy for inflammatory synovitis of joints.

Theranostics offers many challenges in the implementation of targeted therapy towards cancer due to tumour heterogeneity between individuals. The application of molecular characteristics contributes to tumour reclassification and the best-targeted therapies to be used to ensure the most promising outcome for each patient.

To understand the targeted approach, functional imaging such as PET and CT scanning or its hybrids have been used with the versatile radiotracer [^{18}F]fluorodeoxyglucose (FDG) to evaluate the glucose metabolism in tumour cells. Building on this platform has identified other radiopharmaceutical targets which are capable of tumour characterisation, microenvironment, angiogenesis, proliferation, apoptosis and receptor expression.

Several studies have explored specific imaging probes to study receptor expression in tumours. These include PET-CT and Single Photon Emission Computed Tomography (SPECT-CT). However, these hybrid scanners have proved to be invaluable by exchanging between diagnosis and therapy functionality using a specific therapeutic radionuclide.

Moreover, these molecular imaging techniques have demonstrated a great potential to link target identification with therapy and personalise it towards the patient's treatment plan. Furthermore, creating the potential for in vivo tissue characterisation and improve prediction, including prognostication. These components lead to a roadmap for biopsy and therapy monitoring.

The unique feature of Zevalin® is that it can target the CD20 antigen on B-cell non-Hodgkin's lymphoma (Zevalin) to allow imaging during radiotherapy. Zevalin works by fixing the radiometal indium-111 into a tiuxetan chelate. The monoclonal antibody ibritumomab can detect B-cells and transport the beta/alpha-emitting radiometal to destroy the lymphoma. SPECT imaging can confirm that the antibody is distributed within the body. The indium-111 is swapped with radionuclide yttrium-90 transporting beta particles to kill the B-cells.

58.4 Theranostic Aspects of Zevalin: Bridging Molecular Imaging and Targeted Radiotherapy

Zevalin® therapy has shown useful indications for B-cell non-Hodgkin's lymphoma, including relapsed or refractory low-grade or follicular forms. Since 2002, Zevalin® has been used for the treatment of this indication, including B-cell non-Hodgkin's

lymphoma and rituximab refractory follicular non-Hodgkin's lymphoma. In 2008, Zevalin® was given FDA approval for follicular lymphoma in the European Union.

The theranostics integration platform enables 'drug' selection to target specific cancers through a personalised medicine approach and is the result of the information processed from a diagnostic test. Targeted therapy strategies are becoming prevalent in oncology (Zevalin) and nuclear medicine imaging by moving towards an ultimate goal of personalised medicine.

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59 Ultrasound in Obstetrics and Gynaecology: A Clinical Approach

Ultrasonography is ultrasound imaging and is used to obtain clinical information regarding a patient.

59.1 Introduction

Ultrasonography is ultrasound imaging and is used to obtain clinical information regarding a patient. This imaging technology creates real-time diagnostic data and has produced several benefits – primarily in the reduction of healthcare costs – due to replacing more expensive investigative procedures. Ultrasonography is used over a broad spectrum in the clinical setting, including obstetrics and gynaecology, orthopaedics and cardiology, emergency medicine, prostate cancer, breast cancer detection etc.

The merits of ultrasonography over other imaging modalities include the speed in obtaining images, cost-effectiveness and the benefit of being a non-invasive procedure. Also, ultrasonography equipment is relatively inexpensive compared to magnetic resonance imaging (MRI) systems.

Today, ultrasound images can be generated on hand-held portable devices to inspect the abdomen, kidney, heart and peripheral vasculature. The advancement of computer imaging software – by applying algorithms – has enabled the enhancement of image reconstruction.

59.2 High-Intensity Focused Ultrasound in Prostate Cancer

The hyperthermia therapy technique using high-intensity focused ultrasound (HIFU) was developed in the 1940s as an imaging tool that uses temperature to treat a variety of diseases. HIFU has been successfully applied in the treatment of cancer to destroy solid tumours of the brain, bone, liver, breast, rectum, pancreas, testes and kidney. In addition, it can be used to treat uterine fibroids, benign thyroid nodules, hypertrophic parathyroid gland ablation and breast fibroadenoma ablation.

Currently, there is an emerging technique called transcranial magnetic resonance-guided focused ultrasound (tcMRgFUS surgery): this is a non-invasive treatment for a variety of brain disorders. In 2015, the FDA gave approval for HIFU in the ablation of prostate tissue. This procedure uses a transrectal probe capable of transferring the heat from the focused ultrasound waves to destroy the cancerous prostate cells.

59.3 Multimodal Brain Imaging: Integrating MRI and Transcranial Sonography for Improved Diagnostics

HIFU has advantages over conventional modalities such as surgery, radiotherapy and chemotherapy because this procedure treats tumours non-invasively, is non-radioactive and has fewer complications after treatment. To date, 100,000+ cases have been treated in clinics with HIFU.

The theory behind HIFU ablation involves the important property of thermal necrosis due to the absorption of ultrasound energy. During transmission, the sound energy intensifies at the tissue site and induces cavitation damage. The focused ultrasound energy applies local heat and destroys the diseased tissue through ablation. This elevation of temperature to 90 degrees means no tissue can survive.

The FDA gave approval to the HIFU system called Sonablate 450 for the treatment of prostate cancer. HIFU is currently used to treat uterine fibroids and relieve pain from bone metastases. Clinical HIFU procedures are typically image-guided to permit treatment planning and targeting before applying a therapeutic or ablative level of ultrasound energy.

59.4 Therapeutic Applications of Magnetic Resonance-Guided Focused Ultrasound

Magnetic resonance-guided focused ultrasound (MRgFUS) aims to deliver focused, high-energy ultrasound waves into the tissue to cause thermal coagulation of the targeted tissue. The ultrasound transducer contains a piezoelectric plate that is capable of producing high-energy sound waves. During this process, the ultrasound field and vibration frequency depend on the shape and size of the organ(s) and/or tissue within the human body.

The ultrasound waves can be focussed using a combination of lenses and/or reflectors. In some cases, the transducer can automatically adjust the sound wave according to the medical scenario. situation. The usage of an ExAblate machine allows for automatic focusing to be performed using phased arrays. These phased arrays permit the generation of a larger focal spot – in addition to controlling the location of the focus by the phase and amplitude of the radiofrequency (RF) signals – driving each component.

59.5 Magnetic Resonance Guided-Focused Ultrasound System

The phased array components can focus the ultrasound waves into a beam and can also produce multiple beams, which can cause intensification at the target. These sound waves can pass through the skin and focus directly on a particular target (e.g., tumour) to deliver the energy. The ExAblate system contains a phased-array transducer with 208 array elements that are individually controlled. Also, there is a computer-controlled positioning system, a multichannel RF amplifier system and a user interface. All of these modules integrate with the MRI (1.5 T to 3 T) system to give guidance to the ultrasound therapy at the disease site.

Ultrasonography has several advantages over other medical imaging modalities, for example, computed tomography (CT) and magnetic resonance imaging (MRI),

because it can produce real-time images of the anatomical structures within the human body. Other imaging technologies, such as positron emission tomography (PET), can measure the body's functional activities compared to ultrasound imaging, which is not used for functional imaging over a longer period of time.

This limitation has started an investigation into the potential of using ultrasound imaging for measuring events as a function of time. For example, what happens to contrast agents over a period of time in the human body and how organs such as the heart respond to the perfusion of a contrast agent.

The key components which can expand ultrasonography to create functional and volume imaging are primarily due to: (1) increased computational power, (2) cost-effective volume imaging and (3) the availability of contrast agents for ultrasound imaging.

Ultrasound systems using real-time 3-D ultrasonography or 4-D ultrasound imaging have several advantages for guiding interventional medical procedures. These systems can visualise real-time tissues and organs in 3-D. Due to its accuracy and efficacy, real-time 3-D ultrasonography is preferred over 2-D ultrasound imaging for surgical tasks and complex procedures. In comparison to volumetric imaging alternatives, such as MRI and CT, real-time ultrasound imaging has a faster imaging acquisition rate of 30 volumes per second, thus enabling excellent image visualisation.

Ultrasonography in 4-D is not often used in clinical procedures, as 2-D ultrasound imaging is still the clinical standard. High-end imaging technology can produce its own individual problems regarding the image resolution relating to voxel size for volumetric imaging, which is less than 1 mm. Another disadvantage encountered is due to the noise and associated artefacts which can make it challenging to differentiate features that are less than a few millimetres. Subsequently, 3-D ultrasound images are produced in a volume-rendered format which can distinguish between the tissues and surrounding fluids. This approach can be applied to the clinical setting of cardiology, gynaecology and obstetrics.

In addition, volume-rendered images can enhance the noise and distortions present in the 3-D images, resulting in irregular surfaces in the picture image. This technique's major disadvantage is the distorted visualisation of the internal features of solid organs such as the liver and kidneys, which can produce raised reflections in the anatomical images.

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60 A Versatile Tool: SPECT Imaging in Myocardial Perfusion and Brain Diagnostics

SPECT imaging is used to obtain a myocardial perfusion scan (SPECT scan) to investigate the function of the heart muscle.

60.1 Introduction

SPECT imaging is used to obtain a myocardial perfusion scan (SPECT scan) to investigate the function of the heart muscle (myocardium). This technique evaluates heart conditions such as coronary artery disease (CAD) and the motion of heart chambers. The main function of the myocardium is evaluated for the heart's left ventricular ejection fraction (LVEF). The scan is usually performed in conjunction with a cardiac stress test. Technetium-99m tetrofosmin (Myoview™) is a radiopharmaceutical used in nuclear medicine for cardiac imaging.

60.2 SPECT Scanning: Bridging the Gap Between Nuclear Medicine and Radiology

The nuclear medicine tomography technique single-photon emission computed tomography (SPECT) uses gamma rays and is similar to conventional planar imaging using a gamma camera. SPECT can produce 3-D scans in the form of cross-sectional slice images of the patient, for example, brain imaging. Computer imaging systems can transform this information to produce the required image. Overall, the technique requires the delivery of a gamma-emitting radionuclide into the patient, normally through injection into the bloodstream. Since the development of computed tomography in the 1970s, the radioisotope in the organ and/or tissue can be mapped by SPECT imaging.

New radionuclides are being developed for myocardial perfusion, and this particularly includes rubidium-82. The aim is to decrease the radiation dose to the patient by a factor of 10 compared to technetium-99m. In the future, a complete myocardial perfusion exam may be achieved while maintaining a patient dose under 3 mSv.

The radiotracers used in SPECT emit gamma rays, whereas positron emitters (fluorine-18) are employed in PET. These SPECT radiotracers include the technetium-99m, a metastable nuclear isomer of technetium-99, indium-111, iodine-123 and thallium-201. Furthermore, gaseous xenon-133 has shown promise for diagnostic inhalation studies in evaluating pulmonary function and imaging for the lung. The detection of the xenon-133 gas is by the usage of a gamma camera. These specialized cameras contain the scintillation detector, collimator, sodium iodide crystals, and several photomultiplier vacuum tubes.

Imaging cerebral blood flow is used to assess brain function. These studies use several SPECT radiopharmaceuticals and mostly are technetium-99m imaging agents. They include technetium-99m pertechnetate, technetium-99m-pentetate (Tc-DTPA), technetium-99m gluceptate (Tc-GH), technetium-99m exametazime (Tc-HMPAO) and technetium-99m bicisate (Tc-ECD).

All gamma radiation emitted from SPECT radiopharmaceuticals is detected by the usage of a rotating gamma camera around the patient to produce 3-D imaging. The images undergo various electronic transformations by considering the distribution of the radiotracer, the process of filtered back projection and other tomographic techniques.

The radioisotopes used in SPECT scanning have relatively long half-lives, for example, technetium-99m (t½ = 6 hours), indium-111 (t½ = 2.8 days), iodine-123 (t½ = 13.22 hours) and thallium-201 (t½ = 73 hours). The radionuclide technetium-99m was prepared from molybdenum-99 using the technetium-99m generator and used for various nuclear medicine diagnostic procedures. These technetium-99m based imaging agents are relatively cheap compared to PET and fMRI imaging. The problem with SPECT scanning is the absence of good spatial resolution.

In addition, the radioactivity of the contrast agent may highlight some safety issues concerning the administration of radioisotopes to the patient. The radionuclide is sometimes attached to a specific ligand to create a radioligand complex. This complex allows the radiopharmaceutical to be transported and localized in a particular part of the body. At this location, the radiopharmaceutical will emit radiation to be detected by a gamma camera to produce 3-D images.

60.3 The Future of Neuroimaging: Exploring Hybrid SPECT Brain Imaging Technique

Brain imaging forms a central part of nuclear medicine by providing physicians with functional diagnostic information about the disease states of the central nervous system. The various imaging modalities employed to study the brain include computerized tomography (CT) and functional magnetic resonance imaging (fMRI). Radiopharmaceuticals are used for planar imaging, single-photon emission computed tomography (SPECT) and positron emission tomography (PET). In addition, to hybrids of PET-CT, SPECT-CT and PET-MRI can be used as suitable scanning systems.

These hybrid imaging scanners provide anatomic structures and functional information, increasing the diagnostic power to identify an appropriate treatment plan for an individual patient. Brain imaging tools have utilized radiopharmaceuticals and/or imaging agents, which utilise SPECT and PET imaging. Overall, there continue to be new developments in PET brain imaging agents for more selective targeting of brain tumours, cognitive disorders and central motor disorders.

SPECT and SPECT-CT imaging studies of the brain play a primary role in patient diagnosis. These brain imaging modalities involve single photon emitting agents to

evaluate brain death, epilepsy, cerebrovascular disease, neuronal function, and cerebrospinal fluid (CSF) dynamics.

60.4 The Battle for Precision: Exploring Spatial Resolution in SPECT and PET Imaging

Spatial resolution and detection sensitivity are both important factors that play a vital role in SPECT scanning and PET radiotracers.

Scanner	Spatial resolution
Clinical SPECT	8-12 mm
Clinical PET	4-6 mm
Preclinical SPECT	≤1 mm
Preclinical PET	1-2 mm

The majority of clinical gamma cameras can produce a tomographic spatial resolution of approximately 10 mm. However, certain preclinical SPECT scanners can provide a submillimetre spatial resolution. Subsequently, further modifications using multi-pinhole systems can produce a spatial resolution below 1 mm. Furthermore, the clinical and preclinical PET scanners have a spatial resolution of 1-2 mm and 4-6 mm, respectively. Developments in brain PET scanners have produced an improved spatial resolution of approximately 2.5 mm in the central field of view.

Several research groups have achieved a spatial resolution of less than 1 mm by using finely segmented lutetium orthosilicate (LSO) crystals leading to the concept of micro-SPECT as a diagnostic imaging tool.

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61 Image-guided Gamma Knife Radiosurgery with MRI and PET-CT for Intracranial Metastases

Stereotactic radiosurgery is a non-surgical procedure that utilises gamma radiation for the management of brain tumours, amongst others.

61.1 Introduction

Stereotactic radiosurgery is a non-surgical procedure that utilises gamma radiation for the management of brain tumours, amongst others. The objective of stereotactic radiosurgery is to deliver a high dose of radiation to the tumour site via a gamma knife in comparison to other radiotherapy treatments. The application of imaging modalities such as computed tomography (CT), positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) assists in the treatment planning stage for a patient undergoing image-guided surgery using a Gamma Knife.

These image-guided surgery techniques (Gamma Knife Radiation) are also employed to limit collateral damage to the surrounding healthy tissues. However, when radiosurgery is used to treat body tumours, the procedure is known as stereotactic body radiotherapy. Both procedures can deliver high-precision radiation within millimetres to destroy the tumour and achieve a permanent accuracy of the radiation delivered.

Both stereotactic radiosurgery and stereotactic body radiotherapy depend on several imaging modalities to generate 3-D scans and computer analysis to determine the exact coordinates of the tumour target within the human body. The patient must be immobilised to enable the highly focused gamma-ray or x-ray beams to converge on the tumour (volume) site. The application of image-guided radiation therapy and additional medical imaging is used to confirm a tumour's location before the administration of a radiation dose. Image-guided radiation therapy improves the precision and accuracy of the treatment.

The imaging modalities CT, fMRI and PET-CT are all capable of producing 3-D imaging to help locate the human body's tumour mass. It is also able to calculate the tumour volume. These scans support the patient's treatment plan to ensure that the radiation beam can converge on the tumour at various angles.

SRS can also be used to deliver a radiation dose to several therapy sessions. These radiotherapy sessions depend on the size of the tumour mass and the nature of the tumour. Suppose larger doses of radiation are required for the treatment plan. In that case, the patient normally will receive these over a number of radiotherapy sessions

to limit damage to the surrounding healthy tissues. Therefore, this fractionating treatment approach allows for high doses to be delivered safely within the target volume. This approach is called fractionated stereotactic radiotherapy and is usually carried out over two to five treatment sessions.

Both stereotactic radiosurgery and stereotactic body radiotherapy are alternatives to invasive surgery, especially for patients who are unable to undergo surgery and also for tumours and other abnormalities. In some of these cases, the surgery would be difficult due to tumours being near

vital organs/anatomic regions and subject to movement within the body. Stereotactic radiosurgery is used to treat numerous types of brain tumours, including benign and malignant, primary and metastatic. In addition to arteriovenous malformations (AVMs), they disrupt normal blood flow in the brain and sometimes bleed. Furthermore, radiosurgery machines can treat other neurological conditions such as trigeminal neuralgia (a nerve disorder in the face) and tremor. The procedure of stereotactic body radiotherapy is utilised in the treatment of malignant or benign small-to-medium size tumours present in the liver, abdomen, lung, prostate, spine, head and neck.

61.2 Stereotactic Radiosurgery: A Brief Introduction to the Technology

Stereotactic radiosurgery works in a similar way to other forms of radiation treatments. The main difference is that the stereotactic radiosurgery procedure does not remove the tumour, but the DNA is damaged to stop replication. After treatment, benign tumours usually shrink within two years, and metastatic tumours can take up to 2-3 months. The treatment of arteriovenous malformations (AVMs) by stereotactic radiosurgery may result in thickening and cutting off the blood over several years. A number of tumours will remain stable and inactive without any degree of change.

The aim of the treatment plan is to prevent tumour growth and, in some cases, acoustic neuromas, which are temporary enlargements and may be observed following stereotactic radiosurgery. This is due to an inflammatory response within the tumour tissue that, over time, either stabilises or a subsequent tumour regression is observed called pseudo-progression.

61.3 Gamma Knife Radiosurgery: A High Precision Radiation Therapy Technique

The Gamma Knife uses 192 or 201 cobalt-60 beams of highly focused gamma rays, all aimed at the target region. The Gamma Knife is perfect for treating small to medium size intracranial lesions.

Linear accelerator (LINAC) machines deliver high-energy photons known as X-rays. The linear accelerator is capable of performing image-guided surgery on larger tumours in a single therapy session, extending to fractionated stereotactic radiotherapy if required by the treatment plan. These machine types are called Novalis Tx™, X-Knife™, Axesse™ and CyberKnife®, respectively.

Several studies have been conducted on Gamma Knife radiosurgery. For example, a study involving 90 patients diagnosed with intracranial meningiomas underwent either

Gamma Knife radiosurgery (59 patients) or microsurgery (31 patients). The conclusion from the study indicated that the Gamma Knife system had a significantly higher rate of tumour control compared with surgery (95% vs 81%, p=0.003). Also, the Gamma Knife approach produced a more extended period of recurrence-free survival (94 months vs 84 months, p=0.04).

The Gamma Knife is a unique system with a frame that allows the neurosurgeon to target a treatment area in the brain with pinpoint accuracy. The advantage of Gamma Knife procedures is that they are non-invasive and can be performed in a single session without general anaesthesia. The Gamma Knife approach is a cost-effective alternative to open brain surgery with superior clinical efficiency. Gamma Knife produces a more effective treatment of smaller lesions of the brain with fewer complications.

Gamma Knife therapy requires a team of dedicated medical professionals, including the medical radiation physicist and oncologist.

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62 Introduction to Proton Therapy: Principles and Advantages

Proton therapy targets tumours precisely, reducing collateral damage to surrounding healthy tissue.

62.1 Introduction

Proton Therapy UK (Proton Beam Therapy) – A technological revolution in image-guided radiotherapy systems and treatment planning is growing fast in the management of tumours without damage to organs at risk (OAR).

In 1946, cyclotron physicist Robert Wilson envisaged the use of energetic protons to be used in radiotherapy. The premise of protons is their inverted dose profile, called the Bragg peak. The major characteristic of the Bragg peak is its ability to position at any depth in the patient and to expand into a larger volume. These events generate zero doses behind the most distal peak position. Essentially, after a rapid build-up in the modified proton beam (250 MeV) region, the conventional radiation photon beam (6 MeV) shows an exponential decrease in energy deposition with increasing depth in tissue. In comparison, protons show an increase in energy deposition leading to a maximum (Bragg peak) near the end of the proton beam range.

The first proton therapy clinic opened in 1954 at Berkeley 184 Institute in California and treated 30 patients. However, the Loma Linda Institute in California has treated over 17500 patients since 1990. The main reason for its delay from the initial conception was poor guided imaging and treatment planning. Today, 58 proton beam therapy facilities are operational worldwide and have performed over 96,537 oncological treatments. These include the treatment of a spectrum of diseases: paranasal sinus tumours, chordoma, chondrosarcoma, meningioma, prostate and lung cancer: in addition to uveal melanomas, sarcomas of the base of a skull, sarcomas of the paravertebral region and medulloblastoma brain tumour. Also, proton radiosurgery can be applied to the treatment of large arterial-venous malformations and intracranial lesions.

The development of X-ray computed tomography (CT) in 1970 was instrumental in producing 3-D scans to provide tumour volume location and the assignment of CT Hounsfield numbers to enable electron-density distribution required to perform 3-D dose calculations. This invention provided the foundation for the development of CT-based radiation technologies in treatment planning. During the 1980s, magnetic resonance imaging (MRI) became a vital diagnostic tool for disease states in patients.

Further, development enabled the discovery of the relationship between a tumour and the surrounding healthy tissue.

The advantage of MRI over CT is the ability to provide images with a higher spatial resolution with contrast. Then in the 1990s, positron emission tomography (PET) imaging became an integral part of treatment planning. Conversely, PET combined with CT became a powerful scanner for imaging tumours. This hybrid can visualise tumours and, in particular, distinguish a tumour from normal tissue due to the different metabolism rates. The application of conformal radiation modalities such as proton therapy is necessary to guide the correct dosage of radiation to the patient.

62.2 Image-Guided Radiotherapy Systems: Techniques for Tumour Localisation and Targeting

Another aspect of image-guided radiotherapy (IGRT) which includes respiratory gating, is becoming apparent in the clinical setting for more advanced instruments/scanners in radiotherapy departments. The reason which gives these modern imaging technologies is to enable the detection of the geometric contours of the tumours to ensure that the radiation dose is delivered accurately to the tumour site. Consequently, further advancements in imaging-guided therapy have produced 4-D computed tomography imaging as the basis for respiratory-gated proton therapy to limit motion artefacts.

Furthermore, X-ray radiation techniques combined with proton beam therapy can control numerous cancers, even destroying them. Problems can arise with the ability of the physicist to conform the irradiation outline to tumour volume. Conventional radiotherapy techniques can damage surrounding healthy tissues. Treatment planning is required to enable a reduced radiation dose which would be useful to avoid damage to the healthy tissues and limit side effects. The overall benefit of proton beam therapy over conventional radiotherapy, i.e. protons vs photons, is the ability to use protons at higher radiation doses with image-guided radiotherapy.

The physicist can control and manage cancer while reducing the damage to healthy tissue and surrounding organs using the concept of theranostics. Proton Beam Therapy is essentially a form of radiation that makes use of the properties of protons. The treatment of tumours involves the clinical proton accelerator cyclotron, generating proton beam energies between 230-250 MeV and giving an associated range in tissues of 35-40 cm in water. There are cyclotrons that generate a maximum proton beam of about 70 MeV, which is only powerful enough to treat ocular tumours. Conversely, the synchrotron circular accelerator ring delivers a pulse beam of protons. Other techniques include beamline and gantry/fixed beams.

62.3 Proton Therapy Centres in the UK

In 2009, the UK Government announced a programme to set up the National Health Service Proton Beam Therapy, with an initial investment of £250 million and a commitment to construct two centres at University College London Hospital (UCLH), the Christie Hospital in Manchester. Each of these centres will offer high-energy proton beam therapy treatment. Since 1989, the UK has been treating patients with

rare eye cancer by the use of low-energy beam therapy. It is expected in the latter part of 2018 that, the new proton therapy centre based in Manchester will be accepting the first patients to be treated with the high-energy proton machine. In 2020, a proton treatment is expected to be extended to London in purpose-built cancer and surgery centre at UCLH, which contains the 90-tonne cyclotron to be part of the Proton Therapy UK network.

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63 PET-CT and PET-MRI in Radiation Therapy Planning

PET imaging (Positron Emission Tomography) is an established diagnostic imaging tool used in Nuclear Medicine.

63.1 Introduction

PET imaging (Positron Emission Tomography) is an established diagnostic imaging tool used in Nuclear Medicine to obtain clinical information from the patient. An extension of this imaging modality is the PET-CT hybrid. This system consists of two scanning machines: PET imaging and an X-ray computed tomography (CT) scanner. These modern medical modalities occupy a central position in the technological apex of Nuclear Medicine and occupy a prominent role in theranostics.

The second hybrid is PET combined with magnetic resonance imaging (MRI). This powerful imaging tool can obtain clinical images and provide corresponding information about the diagnosis of many disease states. These hybrid scanning machines can be used to show the effect of current and new therapies. PET scanning can detect the processes by which certain cancers utilise sugar molecules, while MRI provides structural details of tissues within a tumour or in brain disease. The advantage of using the diagnostic imaging tool PET-MRI over PET-CT is the two-fold reduction in radiation dose given to the patient. PET-MRI is a valuable imaging tool, especially in the areas of oncology, neuropsychiatric and heart diseases.

Consequently, PET-CT has the capability to evaluate diseases through a simultaneous functional approach, including morphostructural analysis. The benefit of PET scanning is the potential for early diagnosis of the disease state, leading to a favourable prognosis and appropriate therapy towards the patient. Today, the most used PET radiotracer is [18F]fluorodeoxyglucose (FDG), which plays a central role in oncology.

Vital information can be acquired using [18F]FDG and several other radiopharmaceuticals. These include fluorine-18 florbetapir (Amyvid), fluorine-18 florbetaben (Neuraceq), fluorine-j18 flutemetamol (Vizamyl), fluorine-18 ethylcholine (FECH), amongst others, with the overall aim to evaluate biological processes. PET imaging is creating vast opportunities in the area of molecular imaging and provides a platform for a potential revolution in clinical diagnostics, especially for oncology, neurology and cardiology.

PET imaging has been the focus of research in the human body since the 1970s. This impressive technological platform has allowed for a prominent clinical role in

diagnosing, staging and monitoring disease in patients by the 1990s. The pioneering work commenced by Brownell and Sweet at Massachusetts General Hospital in 1953 allowed for the first positron detector to study human brain function. Several milestone discoveries in the clinical application of PET scanning have been reached by the following scientists: Kuhl, Pogossian, Wolf, Sokoloff, Phelps, Di Chiro, Alavi and Wagner.

In the 1990s, Wagner demonstrated that the glucose analogue, FDG, could be utilised in various PET studies. Preliminary applications of clinical interest were carried out in the studies of brain disease, cancer and dementia.

In the late 1980s, technological advances permitted a faster and more accurate whole-body examination acquired by PET-FDG, which became an important clinical tool in oncology. The central role of PET-FDG was for diagnosing, staging and re-staging several types of cancer in patients on a daily basis.

An important milestone came in 1997 when the FDA approved the utilisation of PET as an imaging tool in diagnostics. Subsequently, PET-FDG became an established imaging modality in the clinical assessment of many neoplasms, finding a role in non-malignant diseases such as dementia, myocardial ischaemia, inflammation and infection.

63.2 Introduction to PET Imaging: Basic Principles and Physics

Positron emission tomography (PET) imaging works by detecting the radiation inside the body. The radiation is generated by the decay of the radiotracer containing an unstable radionuclide. During decay, a positron (β+) and neutrino are ejected simultaneously. The positron is an anti-matter electron (β-) with an identical mass to an electron having a positive charge. In decay, the ejected positron loses kinetic energy by colliding with the surrounding atoms. This action suddenly causes the positron to lose kinetic energy and come to abrupt rest. These positions have a short range in human tissue with peaking energy of 0.63 MeV.

The positron collides with an electron (β-) which results in an annihilation reaction releasing an amount of energy. This energy takes the form of two 'annihilation' photons (511 keV) resulting from the (β+ – β-) interaction in opposite directions. These annihilated photons are quantified by applying the principles of coincidence PET detection of gamma rays.

The gamma rays leave the patient's body and interact with the scintillation crystals such as BGO (bismuth germinate), LSO (lutetium oxyorthosilicate), GSO (cerium-doped gadolinium silicate), LYSO (cerium-doped lutetium yttrium orthosilicate) and the photomultiplier tubes in the detectors. These crystals act as transducers by converting the gamma rays into 'light' photons.

The energy of the photons is converted into electrical signals and immediately registered by the tomography electronics. The computer then processes the information to generate a complex 3-D real-time image of the brain or a whole-body scan.

63.3 PET Imaging Spatial Resolution: Principles and Limitations

Spatial resolution is a contributing factor towards quantitative PET diagnostic imaging tools. It is defined as the distance between two infinitely small point sources that can be distinguished from each other. Various preclinical PET scanners reveal a spatial resolution in the order of 1.5 – 2.5 mm. This measurement is defined at full-width-half-maximum (FWHM) of the point spread function in the central field of view (cFOV).

The PET diagnostic imaging tool's spatial resolution depends on the PET scanners' radial offset. These tests are usually performed according to the NEMA NU 4-2008 standards (The National Electrical Manufacturers Association standard NU 4-2008 for performance measurements of small-animal tomographs) using a sodium-22 point source.

Several PET scanners have indicated that at a radial offset of 5 mm, the radial spatial resolution was approximately 1.6 mm FWHM. However, at a 25 mm radial offset, the FWHM value was 25 mm, and PET scanners with a more substantial bore size suffer less from radial elongation effects. Further, investigations have found that the spatial resolution improved by reducing the scintillator size from 5 mm (human scanners) to around 1.5 mm. Although all of these observations gave individual improvements, it is still challenging to image small structures such as the architecture of a mouse brain.

This rationale led to the development of scanners with scintillator sizes of less than 1 mm. In addition, reducing the size of the crystals produces fewer counts per crystal, which becomes a factor regarding the noise and signal strength. Furthermore, PET scanners detect the point of annihilation and not the point of positron emission. This is because the positron range in tissue is a function of kinetic energy emitted from the nucleus and is dependent on the specific radionuclide used.

The consequence is that any residual kinetic energy at the time of annihilation creates gamma radiation emitted at less than 180 degrees. This results in non-collinearity and loss of accurate placement, which is also related to the field of view size.

All the above factors may well contribute to the limitation of PET spatial resolution. As for the future, research continues to produce the next generation of PET diagnostic Imaging tool systems.

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64 The Role of Medical Physics in Radiation Oncology: Treatment Planning and Dosimetry

Medical physics applies physics principles to enhance healthcare diagnostics and treatment outcomes.

64.1 Introduction

Medical physics is concerned with radiation and dosimetry in the clinical services of the Nuclear Medicine and Radiology Departments, including technological advancement of new instruments and procedures in using various medical imaging modalities. The medical physicist works in the areas of medical Diagnostic Imaging, Radiation and Dosimetry with the aim of ALARA, which is a radiation safety term that stands for As Low As Reasonably Achievable. It simply means that radiation exposure should be minimal towards medical physics radiation personnel and patients within a reasonable effort by the organisation.

64.2 The Role of Medical Physicists in Radiation Safety

Medical physics plays an integral part in the patient treatment plan, especially in the area of diagnosis and therapy, including dosimetry and the application of radiopharmaceuticals in radiology and radiography. The role of medical physics is to interact with physicians, especially in the oncology setting: their critical role is to devise a safe treatment plan which involves administering the correct radiation dose to the cancer patient, for example, during proton therapy.

Consequently, complex calculations are required for external radiation beams or internal radioactive sources. The most important factor is to derive accurate dosimetry radiation calculations involving the radiation output from the sources employed at the various cancer stages.

64.3 Dosimetry in Radiotherapy: Treatment Planning and Accurate Dose Delivery

According to dosimetry, the reirradiation of spinal metastases requires previous knowledge of the delivered dose to the spinal cord. This information is necessary to minimise further exposure to radiation dose delivery. In most cases, the reirradiation of spinal metastases is performed by stereotactic radiosurgery using the cyberknife or tomotherapy. Cyberknife procedures require the patient to remain still for longer time periods. This can induce stress in the patient.

Therefore, the radiation dose transferred to the patient is performed by the principles of tomotherapy. This approach uses rotational radiation beams, thus limiting damage to the surrounding organs. Furthermore, the application of stereotactic body

radiotherapy is employed for reirradiation. This allows for high radiation doses to the target while sparing the spinal cord and neighbouring organs.

64.4 Medical Physics plays an integral part in the patient treatment plan, especially in the area of radiotherapy and dosimetry

Medical physics is central to nuclear medicine, either in a regulatory capacity or for consultation with other medical colleagues. Nuclear medicine uses radiotracers to delineate organs and to decide the most significant physiological variables. These may include metabolic rates and blood flow analysis.

Another area that involves the physicist is equipment performance, writing standard operating procedures (SOPs), quality control in imaging systems and input into the design of radiation installations. In addition, the physicist has a role in radiological protection and the control of radiation exposure to medical staff and patients. The medical physicist, in most cases, is part of the clinical and scientific advisory board to help solve and analyse problems arising in specialised medical radiation areas.

64.5 Advancing Medical Physics: Innovations in Imaging, Radiotherapy, and Diagnosis

Medical physics radiation has a vital role in the medical research team. They have numerous responsibilities in the fields of oncology, cardiology, and neurology using radiation. In oncology departments, they work mostly with radiation and are interested in the mechanism of biological change after irradiation.

Further technological advances are paving the way for high-energy machines to treat patients and new techniques to determine the exact measurement of radiation. Computer software designed based on more advanced algorithms is used to calculate the correct dose for patient treatment. An active area of research is particle irradiation applied to biological systems compared to photon therapy.

Medical physicists play a significant role in patients with heart disease by measuring the blood flow and levels of oxygenation. In mental health patients, they interpret the evoked potential (EP) tests due to the brain's electrical activity, which is also an application used in multiple sclerosis patients. Medical physicists are also interested in the application of digital computers in medicine and information systems.

In addition to the concept of diagnostic problems, which include processing, data storage and accessing medical images. Furthermore, to measure the amount of radioactivity in the patient and study the behaviour of radioactive substances in the body. Medical physicists are an integral part of the development of instrumentation and technology applied to theranostic medical imaging.

Consequently, this involves the use of magnetic and electro-optical storage devices for the manipulation of X-ray images. Furthermore, the physicist has a role in quantitatively analysing static and dynamic images using digital computer techniques. In addition, radiation methods for the analysis of various tissue characteristics. With the expanding areas of MRI-CT scanners used to generate cross-sectional images of

the human body: medical physicists engage in research and development on imaging procedures, utilising non-radiation infrared and ultrasound sources.

64.6 Quantitative Imaging Phantoms for Radiation Therapy: Dosimetry and Treatment Planning

The IEC Image Quality Phantom conforms with the NEMA 2012 standard and is applied in the simulation of whole-body PET imaging and camera-based coincidence imaging techniques. This quality phantom calculates the coincidence count rate parameters for both brain and cardiac imaging.

Furthermore, the IEC Quality Phantom extends to the evaluation between the true coincidence count rate and radioactivity. Also, to address any errors relating to the address pile up and the evaluation of the count loss in the correction scheme.

Medical imaging physics deals with testing, optimization and quality assurance, especially in diagnostic radiology physics, including radiographic X-rays, fluoroscopy, mammography, angiography and computed tomography. Medical imaging physics is also important in the area of non-ionizing radiation modalities such as ultrasound (US) and magnetic resonance imaging (MRI).

The duties of the medical physicist include radiation protection procedures and radiation monitoring, including dosimetry. The current role of the medical imaging physicist includes the responsibility of PET radiation and SPECT imaging and hybrids with MRI and CT scanners.

Functional magnetic resonance imaging (fMRI) began in the 1990s by Ogawa and Kwong. This technique is used to measure brain activity and works by detecting the changes in the oxygenated blood and response to neural activity. Imaging studies have shown when the brain area becomes more active, and it consumes more oxygen.

Therefore, to keep up with this demand, the blood flow increases in these active regions of the brain. fMRI can be used to produce various activation maps showing which parts of the brain are active. fMRI is part of the medical imaging apex, including positron emission tomography (PET) imaging and near-infrared spectroscopy (NIRS).

These two techniques are involved in the study of blood flow and oxygen metabolism of brain activity. fMRI of the brain has several key benefits, including a non-invasive procedure that does not involve radiation. Both of these provide safety for the patient and medical personnel. Also, it produces excellent spatial and good temporal resolution.

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65 The Future of Radiology and Radiography: X-rays and Radiopharmaceutical Applications

Radiology employs imaging technology for accurate diagnosis, guiding treatment, and monitoring patient progress.

65.1 Introduction

Wilhelm Conrad Röntgen produced the first radiographic images in 1895. Today, the medical speciality of clinical radiology uses an array of imaging techniques to help in the patient's overall diagnosis. The radiologists' toolbox consists of various modern imaging modalities exemplified by computed tomography CT, amongst others. Another technique uses acoustics, creating 3-D images in real-time without the need for radiation: this is called ultrasonography.

Magnetic resonance imaging (MRI), however, makes use of powerful magnetic fields (>3 teslas) and radiofrequency pulses to generate 2-D and 3-D (axial, coronal, sagittal) images without the use of radiation. Other clinical radiology modes of scanning include functional MRI imaging, cardiovascular MRI and MRI-guided therapy.

Nuclear Medicine produces images by administering short-lived radiopharmaceuticals to the patient. The radiation released by the patient can be detected using a gamma camera or positron emission scanner to enable the overall image. Nuclear Medicine radiology modalities employed in the clinical setting are single photon emission computed tomography (SPECT), positron emission tomography (PET) and hybrids combining computed tomography (CT) and magnetic resonance imaging (MRI) scanners.

65.2 Diagnostic Imaging in Clinical Radiology: Radiography, CT, MRI, and Beyond

Radiography is a medical imaging technique that utilises X-rays to view internal structures in the human body. X-ray beams are generated and directed at the patient. These X-rays pass through the body, are detected, and then processed to obtain the image. The detector provides a superimposed 2-D representation of all the body's internal structures.

The advancement of radiography has enabled the principle of tomography. In this approach, the X-ray source and detector move to obscure structures that are not in the focal plane. Unlike plain film tomography, computed tomography (CT) generates 3-D representations used for computer-assisted reconstruction. The radiation dosages in this imaging process range from 3 mSv to 20 mSv, depending on the procedure. Today,

the role of radiography has expanded dramatically as a result of more advanced equipment for radiography.

65.3 PET Imaging with Radiopharmaceutical Agents: Molecular Imaging in Clinical Practice

Radiopharmaceuticals are radioactive drugs and/or imaging agents containing a radionuclide (radioisotope). Several radiotracers have been given FDA approval in the clinical setting for radiology diagnosis (e.g. fluorine-18 fludeoxyglucose, ProstaScint®, Octreoscan®, DaTscan™) and/or therapy (e.g. Zevalin®, Xofigo®, Bexxar®). Medical physicists calculate the dosimetry of the radiopharmaceutical to enable safe injection into the patient's systemic circulation. Occasionally, the radiopharmaceutical can be given orally, and this depends on the disease state and the imaging technique used.

Radiopharmaceuticals used for diagnosis contain an unstable radionuclide that decays by emitting electromagnetic radiation. The dose is usually in the form of gamma or röentgen radiation. During a typical decay process, positrons are released, which are capable of interacting with electrons. This electron-positron annihilation process generates two gamma rays of 511 keV in opposite directions.

65.4 A radiopharmaceutical is used to treat cancer

An important property of gamma radiation is its high penetrative power, capable of being absorbed partially by tissues in the human body. When a patient receives a diagnostic radiopharmaceutical, the resultant gamma or X-ray radiation can be detected externally from the body by using gamma or positron emission tomography (PET) cameras.

Radiopharmaceuticals, labelled with the radionuclides carbon-11 (t½= 20.4 mins), nitrogen-13 (t½= 10 mins), oxygen-15 (t½= 2.07 mins) and fluorine-18 (t½= 110 mins), are all employed in PET imaging due to their short half-life. Consequently, they must be prepared near the patient. Methods have also been developed to generate the radionuclide by using radionuclide generators (e.g. Drytec™) which prepare the gamma emitter technetium-99m (t½= 6 hours) labelled radiopharmaceuticals in the form of disposable labelling kits (Myoview™).

The continuing advancement of radiosynthesis technologies, especially in the area of automation rigs (FASTlab2), is establishing a broad range of radiopharmaceuticals to be used in the clinical setting. Currently, radiotherapeutics are of significant interest due to the approval of the first alpha particle-emitting therapeutic, Xofigo®. Further developments in this sphere lead to novel beta-gamma radiation based on medicinal drugs and/or radio-imaging agents.

65.5 Radiotherapeutics in Oncology: Combining Imaging and Treatment for Improved Outcomes

The therapeutic nature of ionising radiation is useful in medical imaging by applying X-rays to kill tumour cells for the different stages of cancer. These radiopharmaceuticals contain a therapeutic radionuclide which decays by emitting beta particles. Beta particles are fast, energetic electrons projecting over short

distances by transporting their energy to a defined target volume resulting in killing tumour cells or altering the cell function.

Consequently, radiotherapeutics designed in sealed sources (cobalt-60, radioactive seeds) are known as Brachytherapy or internal radiotherapy. These devices are placed strategically in the human body, so the emitted radiation kills the tumour. In addition to surgery, Brachytherapy is used in conjunction with other therapies, such as external beam radiotherapy (EBRT) and chemotherapy.

Another important approach is to use radionuclide antibody conjugates (RACs) to target cancer in a specific part of the body by firing the radiation in the form of alpha (targeted alpha radiotherapy) and beta particles to kill cancer cells. This approach depends on the radionuclide's linear energy transfer (LET).

A range of radionuclides (actinium-225, bismuth-213, astatine-211) is capable of emitting short-range particles such as alpha or beta. This property is beneficial in therapy because it can irradiate the energy over short distances and thus limit the damage to surrounding healthy cells.

Several therapeutic radioisotopes survive longer in the human body because the objective is to increase the efficiency of the treatment. These radionuclides used in the therapeutic mode are iodine-131 (Bexxar®), yttrium-90 (Zevalin®), rhenium-188 and lutetium-177. The emitted radiation used in medical procedures eventually decays in a reasonable time for the patient to leave the hospital.

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66 Medical Imaging Modalities involving X-rays and Medical Radiation

Medical imaging modalities, including MRI, CT, and ultrasound, facilitate accurate diagnoses and treatments.

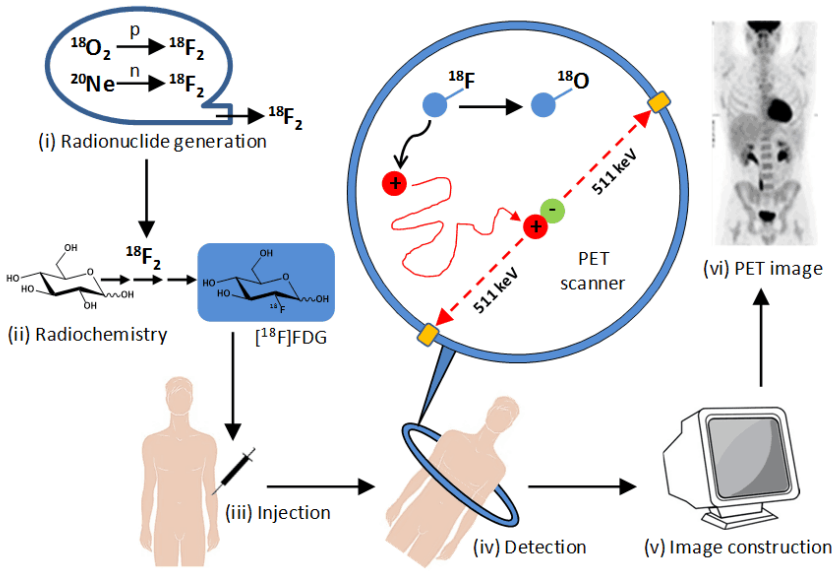
66.1 Introduction

Medical imaging modalities, for example, includes magnetic resonance imaging (MRI), ultrasound, medical radiation, angiography and computed tomography (CT) scanners. In addition, several scanning techniques are used to visualise the human body for diagnostic and treatment purposes. Also, these modalities are very useful for patient follow-up with regard to the progress of the disease state, which has already been diagnosed, and/or is undergoing a treatment plan. The vast majority of imaging is based on the application of X-rays and ultrasound (US). These medical imaging modalities are involved in all levels of hospital care. In addition, they are instrumental in public health and preventive medicine settings as well as in curative and further extending to palliative care. The main objective is to establish the correct diagnoses.

66.2 Positron Emission Tomography (PET): Medical Radiation in Molecular Imaging

Medical imaging modalities in a clinical setting are a vital contribution to the patient's overall diagnosis and help in the decision of an overall treatment plan. The utilisation of imaging techniques in medical radiation is increasing with new technological advances in medical sciences. Therefore, in the spectrum of a broad range of imaging modalities are the specialities of nuclear medicine, positron emission tomography (PET), magnetic resonance imaging (MRI) and ultrasound. Overall, imaging for medical radiation purposes involves a team of radiologists, radiographers and medical physicists.

Stages of PET scanning



66.3 Computed Tomography (CT): Expanding the Scope of X-ray Imaging in Diagnosis

Medical imaging modalities involve a multidisciplinary approach to obtain a correct diagnosis for the individual patient with the aim of providing a personalised approach to patient care. These imaging techniques can be applied as non-invasive methods to view inside the human body without any surgical intervention. They can be used to assist in the diagnosis or treat a variety of medical conditions. Medical imaging techniques utilise radiation that is part of the electromagnetic spectrum. These include imaging X-rays, the conventional X-ray, computed tomography (CT) and mammography. For example, a contrast agent can be used to improve X-ray image quality in angiography examinations.

66.4 Advances in Medical Imaging Modalities: Innovations in X-rays, MRI, and Ultrasound Technologies

Furthermore, imaging utilised in nuclear medicine and angiography can be attributed to several techniques to visualise biological processes. The radiopharmaceuticals used are usually small amounts of radioactive markers: these are used in molecular imaging. Other non-radioactive types of imaging include magnetic resonance imaging (MRI) and ultrasound (US) imaging. MRI uses strong magnetic fields, which do not produce any known irreversible biological effects in humans. Diagnostic ultrasound (US) systems use high-frequency sound waves to produce internal body organs and soft tissue images. Several medical imaging modalities use radiation using X-ray beams that are projected onto the body. When these X-ray beams pass through the human body, some are absorbed, and the resultant image is detected on the other side of the body.

66.5 Magnetic Resonance Angiography (MRA): Non-invasive Vascular Imaging with MRI

Some types of medical imaging function without ionising radiation; for example, magnetic resonance imaging (MRI), angiography, and ultrasound imaging have significant applications in diagnosing disease. Medical imaging modalities include single-photon emission computed tomography (SPECT), positron emission tomography (PET) and hybrid imaging systems such as PET/CT. Alternatively, other systems use the application of positron emission mammography (PEM) and radio-guided surgery (RGS). In addition, short and long-lived radioisotopes are applied to research and develop new imaging agents and associated targeted therapies. Other techniques include computed tomography (CT), magnetic resonance imaging (MRI), ultrasound imaging and planar X-ray (analogue, portable and digital) systems.

The main practical limitation of current medical imaging modalities is the special resolution required to elucidate detailed images of various structures within the human body. However, the rate of image acquisitions has increased over the last decade; this does not allow for the sensitivity required in order to express anatomical structure and function, which is limited by the radiation dose, amongst other factors.

66.6 Spatial Resolution in Medical Imaging: A Comparative Analysis of Different Modalities

Imaging modality	Spatial resolution (mm)	
	Animal	Clinical
PET	1-2	6-10
SPECT	0.5-2	7-15
OPTICAL	2-5 (Visible to IR)	
MRI	0.025-0.1	0.2
US	0.05-0.5	0.1-1
CT	0.03-0.4	0.5-1

The advancements will not dictate medical imaging modalities in imaging quality, but more likely, the objective will be to reduce the cost and scanning time, including exposure to radiation. These technical innovations allow for the rational conclusion that medical radiation dose, scanning speed, image resolution, and sensitivity, including cost per patient, will all be elements of personalised medicine in the future.

Consequently, the medical physicist will play a pivotal role in furthering these challenges: especially in extending knowledge and understanding of the effect of which signals are used to construct 3-D time-dependent images.

In particular, it is important to account for the physical and biological factors that modulate the behaviour of different energy forms within the human body. Moreover, to understand how to interpret images and derive more crucial information regarding the patient's disease state in order to formulate a treatment plan which is personal to the patient.

As with the continual development and improvements in imaging, it is essential to understand the specific biological episode associated with each specific disease state. It would be crucial to design medical imaging modalities that can recognise a 'fingerprint' that can be attributed to a specific disease state.

Furthermore, new imaging modalities would be used to evaluate changes in tissue composition resulting from a disease like fibrosis. In this case, the physiological parameter would be the reduction of blood flow in arteries according to angiography. Other techniques could evaluate the change in conductivity or magnetic susceptibility of brain tissue. All of these improvements could help in the understanding of the contrast mechanisms in several medical imaging modalities.

In essence, it is important to make use of the data within digital images to develop more quantitative tissue characterisation from these anatomical scans. For example, functional magnetic resonance imaging (fMRI) has transformed the understanding of brain construction.

This imaging technique has provided the exact relationship between the MRI signals that map neural activity. However, fundamental neurochemical and electrophysiological processes are not well defined.

Diagnostic imaging tools provide powerful techniques to locate biological processes within the human body. This includes spatial heterogeneity and related changes to the different regions within the anatomical structure's fine detail.

Advancements in medical imaging modalities will contribute to each patient's overall personalised treatment plan. This can only be guaranteed by continuing translational research in the design of novel radiopharmaceuticals and biomarkers in order to increase the efforts to devise robust personalised treatment plans for individual patients.

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67 Harnessing the Power of Deep Learning Reconstruction for Enhanced Medical Imaging and Diagnosis

Medical imaging advancements, aided by deep learning reconstruction, enhance diagnosis accuracy and efficiency, overcoming traditional limitations.

67.1 Introduction

Medical imaging is crucial in diagnosing diseases and monitoring treatment progress, significantly improving patient care. Over the years, numerous imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), have been developed to enhance the visualisation of anatomical structures and physiological processes within the human body. However, these techniques have limitations, including image noise, artefacts, and prolonged acquisition times. Deep learning reconstruction (DLR) has emerged as a promising solution to address these challenges, offering the potential for more accurate and efficient medical imaging.

Deep learning reconstruction leverages the power of artificial intelligence (AI) and advanced algorithms to enhance medical images. It incorporates deep neural networks (DNNs) trained to automatically learn and recognise patterns in imaging data, allowing for more accurate image interpretation and reconstruction. Using DNNs, DLR can significantly improve image quality, reduce acquisition times, minimise radiation exposure, and potentially aid in earlier disease detection and diagnosis.

67.2 Transforming Medical Imaging with Deep Learning Reconstruction: Enhanced Quality, Efficiency, and Diagnosis

One of the main benefits of DLR is the improvement in image quality. Traditional image reconstruction techniques often suffer from noise, artefacts, and low resolution. DLR can mitigate these issues by employing advanced algorithms that effectively differentiate between true signal and noise, thus enhancing image clarity and diagnostic confidence. This is particularly beneficial in cases where high-resolution images are crucial for accurate diagnoses, such as neurological disorders, cardiovascular diseases, and musculoskeletal conditions.

DLR can also help in reducing acquisition times for medical imaging procedures. By intelligently learning the optimal sampling patterns, DLR can accelerate data acquisition and produce high-quality images with fewer measurements. This not only

improves patient comfort but also increases the efficiency of imaging facilities, enabling more patients to be scanned in a shorter time.

In radiation-based imaging modalities, such as CT and PET, minimising radiation exposure is essential to ensure patient safety. DLR enables low-dose imaging protocols by effectively reconstructing images with lower radiation levels without compromising the image quality. This is particularly important for vulnerable patient populations, such as children and pregnant women, who are more susceptible to the harmful effects of ionising radiation.

By combining the power of deep-learning algorithms with high-quality imaging data, DLR can potentially aid in earlier disease detection and diagnosis. DLR-enhanced images can provide more detailed information about subtle pathological changes, enabling radiologists to identify abnormalities that might be missed using conventional imaging techniques. Moreover, DLR can help quantify various imaging biomarkers, thus providing valuable information for personalised treatment planning and therapy monitoring.

67.3 Overcoming Challenges in Deep Learning Reconstruction for Medical Imaging: Data, Integration, and Interpretability

Despite the potential benefits of DLR in medical imaging, several challenges must be addressed. First, the development and validation of DLR algorithms require large-scale, high-quality datasets, which can be difficult to obtain due to privacy concerns and data-sharing limitations. Second, integrating DLR into clinical workflows can be challenging, as it may require significant changes in the existing infrastructure and additional training for radiologists and other healthcare professionals.

Moreover, the interpretability of DLR algorithms is an essential aspect that warrants further investigation. Ensuring the transparency and explainability of the AI-driven decision-making process is crucial for establishing trust among clinicians and patients. Future research should focus on developing interpretable and robust DLR algorithms that can be seamlessly integrated into clinical practice.

67.4 Conclusion

Deep learning reconstruction is promising for revolutionising medical imaging by enhancing image quality, reducing acquisition times, minimising radiation exposure, and improving diagnostic accuracy. With the potential to transform healthcare delivery and patient care, DLR is poised to play a pivotal role in early disease detection, personalised treatment planning, and therapy monitoring. However, several challenges, including data acquisition, clinical integration, and algorithm interpretability, must be addressed to realise DLR's medical imaging benefits fully.

As medical imaging evolves, incorporating deep learning reconstruction technologies will likely become increasingly prevalent. Collaboration among researchers, clinicians, and industry partners will be crucial to overcoming the existing challenges and ensuring the successful integration of DLR into routine clinical practice. By harnessing the power of artificial intelligence and deep learning, medical imaging has the potential

to enter a new era of diagnostic precision, ultimately leading to improved patient outcomes and more efficient healthcare systems.

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68 Photon Counting Computed Tomography: Advancing Medical Imaging with Unparalleled Precision and Detail

Photon Counting Computed Tomography enhances image quality, tissue differentiation, radiation reduction, and material decomposition via precise photon detection.

68.1 Introduction

Photon Counting Computed Tomography (PCCT) has emerged as a groundbreaking innovation in the field of medical imaging. It offers numerous advantages over conventional energy-integrating computed tomography (EICT), including improved image quality, better tissue differentiation, reduced radiation dose, and advanced material decomposition capabilities. PCCT relies on photon-counting detectors that convert individual X-ray photons into digital signals, allowing for more accurate and detailed images. This article explores the fundamental principles, advantages, and potential applications of PCCT in medical imaging.

Photon Counting Computed Tomography (PCCT) is based on the same principles as conventional computed tomography (CT), which uses X-ray technology to create cross-sectional images of internal body structures. However, in PCCT, an X-ray source and photon-counting detectors are positioned on opposite sides of a rotating gantry, with the patient positioned in the centre. As the gantry rotates, the detectors register the X-ray photons that pass through the patient's body.

Unlike energy-integrating detectors used in conventional CT, which measure the cumulative energy of all photons within a specific time window, photon-counting detectors in PCCT identify and count individual photons. Each photon is assigned to an energy bin based on its energy level, resulting in a multi-energy spectrum for each detector pixel. This information is then used to reconstruct high-resolution images with superior contrast and material differentiation capabilities.

68.2 Enhancing Diagnostic Precision: The Multifaceted Benefits of Photon Counting Computed Tomography

Photon Counting Computed Tomography provides higher spatial resolution and better contrast-to-noise ratio (CNR) than conventional CT, enabling the visualisation of smaller anatomical structures and more accurate diagnosis. This is especially useful in identifying microcalcifications, small blood vessels, and important disease markers.

The multi-energy spectral information obtained from PCCT allows for enhanced differentiation between tissues, such as soft tissue, bone, and blood vessels. This can significantly improve diagnostic accuracy and help guide treatment decisions.

The higher sensitivity of photon-counting detectors in PCCT enables lower X-ray doses to achieve comparable image quality. This is crucial for reducing the risk of radiation-induced side effects, especially in paediatric and frequent-imaging patients.

PCCT's multi-energy spectral data enables the identification and quantification of different materials within the body. This can help detect and differentiate between iodine, calcium, and other contrast agents, essential for assessing various pathologies, including tumours, inflammation, and vascular diseases.

68.3 Revolutionising Medical Diagnostics: The Diverse Applications of Photon Counting Computed Tomography

Photon Counting Computed Tomography improves resolution and tissue differentiation capabilities. It can significantly enhance the visualisation of coronary arteries and myocardial perfusion, enabling earlier detection of coronary artery disease and better risk assessment for cardiovascular events.

PCCT can facilitate earlier and more accurate diagnosis of tumours, as well as improved monitoring of treatment response. Its material decomposition capabilities can help differentiate between tumour tissue and treatment-induced changes, such as necrosis or fibrosis.

The high resolution and contrast-to-noise ratio provided by PCCT can improve the detection and characterisation of brain lesions, such as ischemic stroke, haemorrhage, and brain tumours. Additionally, its ability to differentiate between different tissue types can help diagnose neurodegenerative diseases like Alzheimer's and Parkinson's.

PCCT can provide detailed images of bone microarchitecture, enabling the detection and monitoring of bone diseases, such as osteoporosis, and guiding orthopaedic surgery.

PCCT's material decomposition capabilities can be utilised to detect and quantify nanoparticles used as contrast agents for targeted imaging and drug delivery. This can provide valuable information on the biodistribution and accumulation of nanoparticles in tumours or other diseased tissues, enabling personalised therapy and monitoring of treatment efficacy.

Despite its numerous advantages and potential applications, PCCT also faces several challenges that must be addressed before becoming a widely adopted clinical tool.

68.4 Overcoming Challenges in Photon Counting Computed Tomography: Advancing Technology and Clinical Implementation

Developing photon-counting detectors with high count-rate capabilities, low noise, and stable performance is essential to implement PCCT successfully. Ongoing research focuses on optimising detector materials and designs to overcome these challenges.

Advanced image reconstruction algorithms and post-processing techniques are required to exploit the multi-energy spectral data provided by PCCT. Machine learning and artificial intelligence can enhance image quality and extract valuable diagnostic information from the data.

Rigorous clinical trials are needed to establish the diagnostic accuracy and clinical benefits of PCCT in various applications and define optimal imaging protocols and guidelines.

Adopting PCCT technology in clinical settings will require significant investment in infrastructure and training, which may be a barrier for smaller healthcare facilities. However, efforts to reduce costs and develop more compact systems can help facilitate widespread adoption.

68.5 Conclusion

Photon Counting Computed Tomography (PCCT) holds great promise in revolutionising medical imaging by offering improved image quality, better tissue differentiation, reduced radiation dose, and advanced material decomposition capabilities. Its potential applications span various clinical areas, including cardiovascular imaging, oncology, neuroimaging, orthopaedic imaging, and nanoparticle-based imaging. However, several challenges, such as detector technology, image reconstruction, clinical validation, and cost, must be addressed before PCCT becomes a standard medical imaging tool. Nevertheless, with ongoing research and technological advancements, PCCT has the potential to improve patient care and outcomes in the near future significantly.

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69 Dark Field Computed Tomography (DFCT): Medical Imaging with Enhanced Contrast and Resolution

Dark Field Computed Tomography enhances medical imaging by utilising X-ray scattering for improved contrast and resolution in soft tissues.

69.1 Introduction

Dark Field Computed Tomography (DFCT) is an advanced medical imaging technique that has gained prominence recently for its ability to provide high-contrast and detailed images of biological tissues. Traditional computed tomography (CT) scans rely on the attenuation of X-ray beams as they pass through the body, which can be limited in sensitivity and contrast when imaging soft tissues. In contrast, DFCT leverages the scattering of X-ray photons by small structures within the tissue, resulting in images with improved contrast and resolution. This article provides an overview of the principles, advantages, and potential applications of DFCT in the medical field.

The fundamental principle behind DFCT is the utilisation of X-ray scattering. This phenomenon occurs when X-ray photons interact with small structures within the tissue, such as collagen fibres, cell membranes, and blood vessels. When X-rays pass through the body, they are scattered by these structures, producing a unique pattern known as a dark field signal. This signal is then used to generate high-resolution images of the tissue.

DFCT systems typically employ a grating interferometer consisting of three main components: a source grating, a phase grating, and an analyser grating. The source grating collimates the X-ray beam, ensuring it is coherent and has a well-defined direction. The phase grating then imparts a periodic modulation on the X-ray beam, which results in interference patterns that depend on the X-ray's path through the sample. Finally, the analyser grating measures these interference patterns, enabling the reconstruction of the dark field image.

69.2 Unlocking High-Contrast Soft Tissue Imaging: Advantages of Dark Field Computed Tomography (DFCT) over Traditional CT Scans

The primary advantage of Dark Field Computed Tomography is its ability to provide high-contrast images of soft tissues. Traditional CT scans often struggle to distinguish between different types of soft tissues, as their attenuation coefficients are similar. However, DFCT's reliance on X-ray scattering enables it to differentiate between

tissues based on their unique scattering patterns. In addition, this increased sensitivity allows for better visualisation of subtle tissue composition and structure differences.

Dark Field Computed Tomography leverages scattered X-ray photons, requiring a lower X-ray dose than conventional CT scans. This reduced radiation exposure is particularly beneficial for paediatric patients and individuals who require multiple scans.

Dark Field Computed Tomography can be combined with conventional CT scans to provide multi-contrast imaging, where both attenuation and scattering information is used to generate images with a more comprehensive understanding of the tissue composition and structure.

69.3 Transforming Diagnostic Capabilities: Applications of Dark Field Computed Tomography (DFCT) in Lung, Bone, and Breast Imaging

Lung imaging is one of the most promising applications of DFCT. The technique has demonstrated superior sensitivity in detecting early-stage lung diseases, such as emphysema and fibrosis, compared to conventional CT scans. Additionally, DFCT has shown potential in identifying small lung nodules and distinguishing between malignant and benign lesions, which could significantly improve the early detection and treatment of lung cancer.

DFCT has been shown to provide detailed images of bone microstructure, which may improve the diagnosis and monitoring of osteoporosis and other bone diseases. Furthermore, DFCT's ability to visualise soft tissues, such as cartilage and tendons, could be invaluable in diagnosing and treating musculoskeletal disorders like arthritis and tendon injuries.

Preliminary studies have indicated that DFCT may offer improved contrast and resolution in breast imaging, potentially enhancing the early detection of breast cancer and reducing false positives associated with mammography.

69.4 Conclusion

Dark Field Computed Tomography is an emerging imaging technique that offers numerous advantages over traditional CT scans, including enhanced contrast, reduced radiation exposure, and multi-contrast imaging capabilities. In addition, by leveraging the unique scattering patterns of X-ray photons, DFCT can provide high-resolution and detailed images of soft tissues, which has the potential to revolutionise the diagnosis and treatment of various diseases.

Areas such as lung imaging, musculoskeletal imaging, and breast imaging are only a few of the many potential applications where DFCT could have a significant impact. As research continues and technology advances, it is expected that DFCT will become an increasingly valuable tool in the medical field, offering improved patient outcomes through early detection, accurate diagnosis, and more effective treatment strategies.

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70 X-ray Phase-Contrast Imaging: Enhancing Visualisation of Soft Tissues

X-ray phase-contrast imaging offers enhanced soft tissue visualisation, improved contrast, and resolution over conventional X-ray techniques.

70.1 Introduction

X-ray phase-contrast imaging (XPCI) is an advanced imaging technique that has gained significant attention in recent decades. It has evolved as a powerful tool for enhancing the visualisation of soft tissues and low-density materials that are typically challenging to image using conventional absorption-based X-ray techniques. XPCI exploits the X-ray phase shifts that pass through an object, providing increased contrast and resolution compared to conventional X-ray imaging methods. This article will discuss the basic principles, methods, applications, and advantages of X-ray phase-contrast imaging.

X-ray Phase-Contrast Imaging techniques typically rely on the attenuation of X-ray photons as they pass through an object, resulting in variations in the intensity of the transmitted X-rays. These intensity variations can generate an image of the object's internal structure. However, this approach is limited when imaging low-density materials or soft tissues, as the differences in X-ray attenuation coefficients are often small and result in poor contrast.

On the other hand, X-ray phase-contrast imaging takes advantage of the phase shifts an object induces as X-rays pass through it. These phase shifts are proportional to the object's refractive index and thickness, resulting in higher contrast and resolution images than conventional X-ray techniques. In addition, the phase shifts can be converted into intensity variations through different XPCI methods, which can then be used to create high-resolution images.

70.2 Exploring X-ray Phase-Contrast Imaging Methods: Talbot-Lau Interferometry, Propagation-Based Imaging, X-ray Holography, and Analyser-Based Imaging

Talbot-Lau Interferometry utilises an X-ray grating interferometer to detect X-ray phase shifts. The setup consists of three gratings: a source grating, a phase grating, and an analyser grating. The source grating creates a spatially coherent X-ray beam, the phase grating induces phase shifts, and the analyser grating converts these phase shifts into intensity variations that an X-ray detector can detect.

X-ray Propagation-Based Imaging (PBI) exploits the Fresnel diffraction patterns formed by the phase-shifted X-rays as they propagate through an object. A detector

placed at a certain distance from the object captures these patterns, and the images are then reconstructed using phase retrieval algorithms. PBI is a simple and cost-effective method but requires high spatial coherence and high-resolution detectors.

The X-ray Holography technique records the interference pattern between a reference X-ray beam and an object beam that has passed through the sample. The recorded hologram can then be reconstructed to generate a high-resolution image of the object. X-ray holography requires a coherent X-ray source, such as a synchrotron or an X-ray laser.

Analyser-Based Imaging (ABI) employs a perfect crystal as an analyser to transmit or reflect X-rays based on their phase shifts selectively. The transmitted or reflected X-rays are then detected to create an image of the object. ABI provides high sensitivity and can be used for phase-contrast and absorption imaging.

70.3 Expanding Horizons: Diverse Applications of X-ray Phase-Contrast Imaging in Medical, Materials Science, and Life Sciences Fields

Applications of X-Ray Phase-Contrast Imaging have a broad range of applications, including Medical Imaging: XPCI has shown great promise in improving the diagnosis and monitoring of various diseases, such as cancer, cardiovascular diseases, and bone-related disorders. It can provide high-resolution images of soft tissues, blood vessels, and cartilage, which are difficult to visualise using conventional X-ray techniques.

Materials Science: XPCI can be used to study the microstructure, defects, and phase transitions in materials. It is particularly useful for characterising low-density materials, porous structures, and composites, where traditional X-ray techniques struggle to produce sufficient contrast. Examples include studying the porosity of concrete, the distribution of fibres in composite materials, and the evolution of micro-cracks in metals under stress.

Biology and Life Sciences: XPCI has made significant contributions to biology by enabling the visualisation of delicate biological structures, such as cells, tissues, and organs. It can provide detailed images of soft tissues, revealing cellular structures and biological processes that were previously inaccessible with conventional X-ray methods. This has led to developmental biology, neuroscience, and plant biology advancements.

70.4 Advantages of X-ray Phase-Contrast Imaging: Enhanced Contrast, Higher Resolution, and Minimized Radiation Exposure for Non-Destructive Analysis

There are several advantages to using XPCI over traditional absorption-based X-ray imaging techniques:

- XPCI enhances the contrast in images of low-density materials and soft tissues, enabling the visualisation of previously difficult or impossible-to-detect structures.

- Due to the increased sensitivity to phase shifts, XPCI can provide higher-resolution images than conventional X-ray techniques, revealing finer details in the examined object.
- XPCI typically requires lower X-ray doses to achieve the same level of image quality compared to traditional methods. This is particularly important for medical imaging applications, where minimising patient exposure to ionising radiation is essential.
- Conventional X-ray techniques, XPCI, allows for the non-destructive investigation of objects, making it ideal for applications such as quality control, materials science, and cultural heritage studies.

70.5 Conclusion

X-ray phase-contrast imaging has emerged as a powerful tool for enhanced imaging, offering improved contrast and resolution over conventional X-ray methods. It has applications in various fields, including medical imaging, materials science, biology, cultural heritage studies, and non-destructive testing. With advancements in X-ray sources, detectors, and data processing techniques, XPCI will continue to play a vital role in our world knowledge.

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71 Dark-Field Radiography: Unveiling Hidden Structures for Advanced Medical Diagnostics

Dark-field radiography excels in early-stage lung disease detection, breast cancer diagnosis, microfracture visualisation, and soft tissue imaging.

71.1 Introduction

Dark-field radiography, a relatively new and emerging imaging technique, has gained significant attention in medical diagnostics. It provides a novel method to visualise internal structures and tissues, offering a unique perspective to clinicians and researchers alike. In addition, this technique relies on the scattering of X-rays rather than their direct absorption, enabling the visualisation of structures that would typically be difficult to see using conventional radiography. This article will explore the principles underlying dark-field radiography, its potential applications, and the challenges that must be addressed to harness its full potential.

The fundamental principle of dark-field radiography lies in the interaction between X-rays and matter. Unlike conventional radiography, which relies on the absorption of X-rays by tissues, dark-field imaging captures the scattered radiation resulting from the interaction between X-rays and the internal structures of a specimen. The scattered X-rays are detected and processed to create an image with a high contrast of soft tissues and small structures, which are usually not visible using traditional methods.

Dark-field radiography can be achieved using a technique called grating-based interferometry. This method involves placing a series of gratings, or periodic structures, between the X-ray source and the detector. The gratings diffract the incoming X-rays, creating an interference pattern sensitive to the phase shifts and scattering introduced by the sample. The dark-field signal can be extracted and used to generate a high-contrast image by analysing these interference patterns.

71.2 Dark-Field Radiography's Impact on Early Diagnosis and Intervention

Dark-field radiography has shown great promise in lung imaging, particularly in detecting early-stage lung diseases such as emphysema, fibrosis, and chronic obstructive pulmonary disease (COPD). The technique's ability to visualise the delicate structures of the lungs, including the alveoli and bronchioles, allows for a detailed assessment of lung function and structure, enabling early diagnosis and timely intervention.

Conventional mammography is limited in detecting small or low-contrast tumours, particularly in dense breast tissue. Dark-field radiography, with its superior soft tissue

contrast, has the potential to detect early-stage breast cancer and distinguish between benign and malignant lesions, improving diagnostic accuracy and reducing unnecessary biopsies.

Microfractures, a precursor to stress fractures, are often difficult to detect using conventional X-ray imaging. However, dark-field radiography can visualise microfractures and assess bone quality, allowing for early intervention and prevention of stress fractures.

Dark-field radiography can generate high-resolution images of soft tissues, such as cartilage, tendons, and ligaments, which are typically challenging to visualise using conventional techniques. This capability can be invaluable in the early detection and management of musculoskeletal disorders.

71.3 Advancements Towards Clinical Implementation and Rapid Imaging

Despite its promising applications, dark-field radiography faces several challenges that must be addressed to exploit its potential fully. First, the technique requires specialised equipment, including high-resolution detectors and gratings, which can be expensive and challenging to implement in a clinical setting. Second, the acquisition and processing of dark-field images can be time-consuming, limiting its applicability in situations that require rapid imaging, such as emergency medicine.

To overcome these challenges, researchers are developing compact, cost-effective dark-field systems suitable for clinical use. Additionally, advanced computational methods are being explored to accelerate image acquisition and processing, making dark-field radiography more accessible and practical.

71.4 The Future of Diagnostic Imaging: Harnessing Dark-Field Radiography's Potential for Improved Patient Outcomes

Dark-field radiography is a promising imaging technique that offers a unique perspective on the body's internal structures. By capturing the scattered X-rays rather than relying on absorption, it can visualise structures that are difficult to see using conventional methods. With its potential applications in lung imaging, breast cancer detection, bone imaging, and soft tissue visualisation, dark-field radiography has the potential to revolutionise the field of medical diagnostics.

However, several challenges must be overcome to bring this technology to the forefront of clinical practice, including developing cost-effective equipment, faster image acquisition, and advanced processing techniques. Researchers and clinicians are working to address these challenges, making it increasingly likely that dark-field radiography will soon become an integral part of diagnostic imaging.

As dark-field radiography advances, it will improve our understanding of the body's internal structures and enable earlier detection and intervention for various diseases and conditions. Ultimately, this innovative technique holds the potential to transform medical diagnostics, leading to better patient outcomes and a more comprehensive understanding of human anatomy and physiology.

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72 Unveiling the Human Body's Secrets: Whole Body PET Imaging and Its Pivotal Role in Whole Person Research

Whole-body PET imaging transformed medical research, enabling personalised medicine and impacting diagnostics, therapy, and science.

72.1 Introduction

Whole-body positron emission tomography (PET) imaging is a non-invasive and susceptible imaging technique that has transformed the landscape of medical research and diagnostics. By enabling comprehensive visualisation of biological processes in real-time, whole-body PET imaging has paved the way for whole-person research, ultimately leading to the development of personalised and precision medicine. This article explores the role of whole-body PET imaging as a catalyst for whole-person research and its impact on diagnostics, therapy, and the future of medical science.

72.2 Whole-Body PET Imaging for Disease Management

PET is a functional imaging technique that relies on the detection of gamma rays emitted by a small quantity of radioactive tracer injected into the patient's body. These tracers, typically labelled with positron-emitting isotopes such as fluorine-18, carbon-11, or nitrogen-13, accumulate in specific tissues or organs, highlighting areas of increased metabolic activity or inflammation. PET imaging allows for the visualisation of physiological processes at the molecular level, providing unique insights into disease processes and responses to therapy.

Whole-body PET imaging extends the benefits of traditional PET imaging to encompass the entire body, generating three-dimensional images with exceptional resolution and sensitivity. As a result, this comprehensive imaging technique has become an indispensable tool in medical research, enabling the assessment of systemic diseases, tracking the progression of pathologies, and evaluating the efficacy of novel therapeutic interventions.

72.3 Whole-Person Research

PET imaging has given rise to whole-person research, a paradigm shift in human biology that emphasises the interconnectedness of various physiological processes and the holistic understanding of the disease. This research approach recognises that diseases are not isolated occurrences but result from complex interactions among biological systems, often influenced by genetics, environment, and lifestyle.

72.4 Whole-Body PET Imaging Impact on Oncology, Neurology, and Cardiology

Whole-body PET imaging has revolutionised the diagnostic landscape, particularly in oncology, neurology, and cardiology. In oncology, this imaging technique enables the precise localisation and staging of tumours and the detection of metastatic lesions throughout the body. This comprehensive assessment of cancerous growth greatly aids clinicians in determining the most appropriate treatment strategies and monitoring patients' responses to therapy.

In neurology, whole-body PET has proven invaluable for the early detection of neurodegenerative diseases such as Alzheimer's, Parkinson's, and multiple sclerosis. Researchers can develop targeted therapies and monitor their effectiveness by visualising the accumulation of pathological proteins in the brain and tracking the progression of neuronal damage.

Cardiologists also benefit from whole-body PET imaging, which can detect areas of reduced blood flow or inflammation in the heart, providing critical information for the management of patients with cardiovascular diseases. Additionally, this imaging technique offers a unique opportunity to study the effects of systemic conditions, such as diabetes or obesity, on cardiovascular health.

72.5 Therapeutic Insights

Whole-body PET imaging has significantly contributed to the development of personalised medicine, enabling the identification of patient-specific molecular targets to design tailored therapeutic interventions. This imaging technique can also monitor the efficacy of these targeted therapies in real-time, allowing for rapid adjustments to treatment strategies and minimising the risk of adverse side effects.

Furthermore, whole-body PET imaging facilitates the study of drug distribution and metabolism within the body, offering invaluable insights into the optimisation of drug dosages and delivery systems. This knowledge can significantly enhance the safety and efficacy of novel therapies, ultimately improving patient outcomes.

72.6 Future Directions

As whole-body PET imaging advances, its impact on whole-person research will only grow. Combining this imaging technique with other diagnostic modalities, such as magnetic resonance imaging (MRI) or computed tomography (CT), can provide even greater insights into human biology and disease processes. Additionally, the integration of artificial intelligence and machine learning algorithms into the analysis of whole-body PET imaging data can potentially uncover previously unrecognised patterns and associations, further enhancing our understanding of the complex interplay between various biological systems.

The future of whole-person research will likely involve the development of integrated diagnostic platforms, combining whole-body PET imaging with other cutting-edge technologies such as genomics, proteomics, and metabolomics. This integration will enable a more comprehensive understanding of the molecular underpinnings of

diseases, ultimately leading to the development of more effective, personalised, and targeted therapies.

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73 Targeting Metastatic Castration-Resistant Prostate Cancer: The Promising Role of Lutetium-177 labelled PSMA Radioligand Therapy

Prostate cancer's global impact persists; mCRPC, demanding advanced strategies, finds hope in ^{177}Lu-PSMA targeted radioligand therapy.

73.1 Introduction

Prostate cancer remains one of the leading causes of cancer-related death among men worldwide. Although numerous advances in treatment options, metastatic castration-resistant prostate cancer (mCRPC) remains a clinical challenge, often requiring aggressive and innovative approaches for effective management. Recently, targeted radioligand therapy utilising lutetium-177-labelled prostate-specific membrane antigen (^{177}Lu-PSMA) has emerged as a promising treatment for mCRPC patients, demonstrating significant clinical benefit and an acceptable safety profile.

73.2 ^{177}Lu-PSMA: A Novel Radioligand Therapy

Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein highly overexpressed in prostate cancer cells. This characteristic has made PSMA an attractive target for targeted cancer therapies, particularly in the management of mCRPC. Lutetium-177 is a beta-emitting radionuclide that delivers cytotoxic radiation directly to tumour cells when bound to a PSMA-targeting ligand. By targeting PSMA-expressing cells, ^{177}Lu-PSMA therapy selectively delivers radiation to cancerous cells while sparing healthy tissues, minimising the risk of side effects.

73.3 Clinical Evidence for ^{177}Lu-PSMA in mCRPC

Several clinical trials have investigated the safety and efficacy of ^{177}Lu-PSMA therapy in mCRPC patients. For example, a landmark phase 2 trial demonstrated that ^{177}Lu-PSMA-617 significantly reduced prostate-specific antigen (PSA) levels in mCRPC patients who had exhausted other treatment options.

The study reported a 50% or greater reduction in PSA levels in 57% of patients, with a median progression-free survival (PFS) of 7.6 months and overall survival (OS) of 13.5 months. The treatment was generally well-tolerated, with the most common side effects being fatigue, nausea, and transient thrombocytopenia.

Building on these positive results, the phase 3 VISION trial (2021) confirmed the clinical benefits of ^{177}Lu-PSMA-617 in mCRPC patients who had previously received at least one androgen receptor pathway inhibitor and taxane-based chemotherapy.

The trial reported a significant improvement in PFS and OS for patients receiving ^{177}Lu-PSMA-617 in combination with standard of care compared to those receiving standard of care alone (median PFS: 8.7 months vs 3.4 months; median OS: 15.3 months vs 11.3 months). However, treatment-related adverse events were consistent with previous studies, with the most common side effects being fatigue, anaemia, and thrombocytopenia.

73.4 Extended Treatment with ^{177}Lu-PSMA

As the clinical evidence supporting the use of ^{177}Lu-PSMA in mCRPC patients grows, researchers have begun to explore the potential benefits of extended treatment with this novel radioligand therapy. Preliminary data from ongoing studies suggest that patients may derive additional benefits from receiving more than the standard four cycles of ^{177}Lu-PSMA-617. For example, a recent retrospective analysis demonstrated that mCRPC patients who received more than four cycles of ^{177}Lu-PSMA-617 experienced a significantly longer median OS than those who received four or fewer cycles (22.0 months vs 12.0 months).

However, balancing extended treatment's potential benefits with cumulative toxicity risks is important. The safety profile of extended ^{177}Lu-PSMA treatment remains relatively unexplored, and limited data is available on the long-term effects of repeated cycles. While the existing clinical trials indicate an acceptable safety profile for ^{177}Lu-PSMA therapy, further research is needed to understand extended treatment's tolerability better and identify potential dose-limiting toxicities.

73.5 Strategies to Optimise ^{177}Lu-PSMA Therapy

To maximise the therapeutic potential of ^{177}Lu-PSMA in mCRPC patients, several strategies are being investigated to optimise treatment outcomes and minimise adverse events. These strategies include:

- Identifying patients most likely to benefit from ^{177}Lu-PSMA therapy is crucial for optimising treatment outcomes. Therefore, PSMA expression levels, prior treatment history, and overall health should be considered when selecting patients for this therapy.
- Combining ^{177}Lu-PSMA with other therapies, such as androgen receptor pathway inhibitors or immune checkpoint inhibitors, may improve treatment outcomes by targeting cancer cells through multiple mechanisms. Clinical trials are currently underway to assess the safety and efficacy of these combination approaches.
- Using radioprotective agents, such as amifostine, may help reduce the risk of treatment-related toxicities in patients undergoing ^{177}Lu-PSMA therapy. However, more research is needed to determine the most effective radioprotective agents and to establish optimal dosing regimens.
- By using personalised dosimetry, clinicians can tailor the administered activity of ^{177}Lu-PSMA to each patient's individual needs, potentially maximising treatment efficacy while minimising the risk of toxicities.

73.6 Conclusion

^{177}Lu-PSMA therapy has demonstrated significant clinical benefits for patients with metastatic castration-resistant prostate cancer, offering a new treatment option for those who have exhausted other therapies. As the evidence supporting using ^{177}Lu-PSMA grows, extended treatment regimens may provide additional benefits for select patients. However, further research is needed to fully understand the safety and tolerability of extended treatment and optimise treatment strategies for this promising therapy. Through ongoing clinical trials and translational research, ^{177}Lu-PSMA has the potential to significantly improve the management of metastatic castration-resistant prostate cancer, offering hope for patients and their families.

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74 Prognostic Accuracy in Resected Pancreatic Cancer: Using Radiomic PET Imaging

Pancreatic cancer demands an accurate prognosis, improved treatment strategies, and PET radiomic analysis for optimised post-resection outcomes.

74.1 Introduction

Pancreatic cancer is one of the most lethal malignancies worldwide, with a 5-year survival rate of approximately 9%. However, despite significant advances in diagnostic and therapeutic modalities, the prognosis of pancreatic cancer remains dismal. Curative resection is the primary treatment for localised pancreatic cancer; however, the disease often recurs even after successful surgery. Therefore, identifying accurate prognostic factors is crucial for improving patient outcomes and optimising therapeutic strategies. This article aims to provide an overview of the prognostic analysis of curatively resected pancreatic cancer using harmonised positron emission tomography (PET) radiomic features.

74.2 Emerging Radiomics: Prognostic Power in Medical Imaging Modalities

Radiomics is an emerging medical imaging field involving the extraction of quantitative imaging features for diagnostic and prognostic purposes. Radiomic features are extracted from various imaging modalities, including computed tomography (CT) and magnetic resonance imaging (MRI). In addition, PET is a nuclear medicine imaging technique that utilises radiolabelled tracers, such as ^{18}F-fluorodeoxyglucose (FDG), to provide functional and metabolic information about tissues. PET has been used to assess various malignancies, including pancreatic cancer, and has shown promise in providing valuable prognostic information.

74.3 Harmonisation of Radiomic Features

The lack of standardisation in radiomic feature extraction methods has led to inconsistencies in the reported prognostic value of these features across different studies. Therefore, the harmonisation of radiomic features is essential to improve the reproducibility and reliability of radiomic analysis. Harmonisation involves the implementation of standardised protocols for image acquisition, reconstruction, preprocessing, and feature extraction. In PET imaging, harmonisation efforts include standardised uptake value (SUV) normalisation, the implementation of standardised segmentation methods, and the adoption of standard radiomic feature extraction software packages.

74.4 Prognostic Analysis of Curatively Resected Pancreatic Cancer

Several studies have investigated the prognostic value of PET radiomic features in curatively resected pancreatic cancer. These studies have reported that specific radiomic features are significantly associated with overall survival (OS), disease-free survival (DFS), and recurrence-free survival (RFS).

As measured by PET radiomic features, tumour heterogeneity has been associated with a poor prognosis in pancreatic cancer. In addition, high intratumoral heterogeneity, as indicated by increased entropy, irregular shapes, and non-uniform intensity distributions, has been linked to aggressive tumour biology and higher recurrence rates.

Elevated metabolic activity, as indicated by high maximum and mean standardised uptake values (SUVmax and SUVmean), has been correlated with poor survival outcomes in pancreatic cancer. This is likely because high metabolic activity reflects aggressive tumour behaviour and the presence of viable tumour cells after resection.

PET-derived textural features, such as coarseness, contrast, and homogeneity, have been shown to hold prognostic value in pancreatic cancer. In addition, these features provide information about the spatial distribution of tracer uptake within the tumour, which can indicate tumour aggressiveness and potential for recurrence.

By incorporating PET radiomic features with clinicopathological factors, researchers have developed prognostic models to predict survival and recurrence in curatively resected pancreatic cancer patients. These models have shown improved predictive accuracy compared to models based on clinicopathological factors alone.

74.5 Conclusion

The integration of harmonised PET radiomic features in the prognostic analysis of curatively resected pancreatic cancer has shown promising results. By providing valuable information on tumour biology and aggressiveness, PET radiomics may aid in tailoring personalised treatment plans and improving patient outcomes.

Future research should focus on validating these findings in larger, multicenter studies and developing standardised radiomic feature extraction methods to enhance these results' reproducibility and clinical applicability. Additionally, the integration of radiomic features from other imaging modalities, such as CT and MRI, may provide a more comprehensive understanding of tumour characteristics and further enhance prognostic accuracy.

Ultimately, the incorporation of harmonised PET radiomic features into clinical practice has the potential to significantly impact the management of pancreatic cancer patients and contribute to the advancement of precision oncology.

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75 Diagnosis of Large Vessel Vasculitis and Polymyalgia Rheumatica with FDG-PET/CT

Large vessel vasculitis and polymyalgia rheumatica are both inflammatory rheumatic diseases that can result in serious illness if not diagnosed.

75.1 Introduction

Large vessel vasculitis (LVV) and polymyalgia rheumatica (PMR) are both inflammatory rheumatic diseases that can result in serious illness if not diagnosed. Unfortunately, these conditions remain challenging to diagnose due to their nonspecific symptoms and the absence of pathognomonic laboratory findings. In recent years, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has emerged as an essential tool in evaluating and managing LVV and PMR. This article aims to discuss the role of ^{18}F-FDG PET/CT in the diagnosis, management, and follow-up of patients with LVV and PMR.

75.2 The Role of ^{18}F-FDG PET/CT in Diagnosis

LVV encompasses a group of disorders, including giant cell arteritis (GCA) and Takayasu arteritis (TA), which involve the inflammation of the large arteries. PMR, conversely, is a clinical syndrome characterised by pain and stiffness in the shoulder and pelvic girdles. Although PMR and GCA may present as separate entities, there is significant overlap between these conditions, as approximately 40-60% of GCA patients may also have PMR symptoms.

Conventional diagnostic methods for LVV and PMR include laboratory tests such as erythrocyte sedimentation rate and C-reactive protein and modern imaging modalities like ultrasound, magnetic resonance imaging (MRI), and computed tomography (CT). However, these tests may have limitations regarding sensitivity, specificity, and ability to detect disease activity.

^{18}F-FDG PET/CT has shown promise in diagnosing LVV and PMR due to its ability to detect increased metabolic activity and inflammation in the affected vessels and musculoskeletal structures. In addition, it has demonstrated high sensitivity and specificity in diagnosing GCA and TA, with studies reporting sensitivity rates of 85-100% and specificity rates of 75-93%.

In PMR, ^{18}F-FDG PET/CT has shown high sensitivity in detecting subclinical inflammation of the shoulder and pelvic girdles, which may aid in early diagnosis and initiation of therapy.

75.3 Optimising Management of Large Vessel Vasculitis and Polymyalgia Rheumatica

^{18}F-FDG PET/CT can be crucial in managing LVV and PMR by assessing the extent of vascular involvement, evaluating response to treatment, and detecting complications. The extent of vascular involvement in LVV is an important determinant of treatment strategy and prognosis. ^{18}F-FDG PET/CT can help identify the affected arteries and potential complications such as stenosis, occlusion, or aneurysm formation, allowing for tailored treatment approaches.

Monitoring treatment response is vital in managing LVV and PMR, as it can help guide therapy adjustments and prevent unnecessary treatment-related side effects. ^{18}F-FDG PET/CT can be used to assess the effectiveness of treatment by evaluating changes in metabolic activity and inflammation in the affected structures. A decrease in ^{18}F-FDG uptake after treatment initiation indicates a favourable response to therapy, while persistent or increased uptake may suggest the need for alternative treatments or further investigations.

Given the chronic and relapsing nature of LVV and PMR, long-term follow-up is necessary to monitor disease activity and detect relapses. ^{18}F-FDG PET/CT can be used to monitor patients for disease recurrence, particularly in cases where clinical and laboratory findings are inconclusive. Early detection of relapse can prompt timely intervention and prevent disease progression and complications.

75.4 Conclusion

The role of ^{18}F-FDG PET/CT in the diagnosis, management, and follow-up of large vessel vasculitis and polymyalgia rheumatica is invaluable. Its ability to detect increased metabolic activity and inflammation in affected vessels and musculoskeletal structures enables timely diagnosis and initiation of appropriate therapies. In addition, ^{18}F-FDG PET/CT can help guide tailored treatment approaches and monitor for disease recurrence by assessing the extent of vascular involvement, evaluating treatment response, and detecting complications.

Although the growing evidence supporting the use of ^{18}F-FDG PET/CT in evaluating LVV and PMR, specific challenges and limitations still exist. These include variability in image interpretation, patient factors such as age, glucose levels, and inflammatory comorbidities impact on 18F-FDG uptake and exposure to ionising radiation. To optimise ^{18}F-FDG PET/CT in clinical practice, further research is needed to establish standardised protocols, improve image interpretation, and develop novel radiotracers with higher specificity for inflammation.

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76 Predicting Neoadjuvant Chemotherapy Response in Breast Cancer Patients

Radiomics offers non-invasive, quantitative image analysis for predicting breast cancer patients' response to neoadjuvant chemotherapy, enhancing personalised treatment.

76.1 Introduction

Radiomics is an emerging field in medical imaging that aims to extract quantitative data from medical images for predicting neoadjuvant chemotherapy. Medical scanners, such as computed tomography, magnetic resonance imaging, and positron emission tomography, improve diagnostic and prognostic accuracy toward personalised treatment plans. This innovative approach leverages advanced image processing techniques and machine learning algorithms to identify complex patterns and relationships within the images, which the human eye often does not discern.

The foundation of radiomics lies in the extraction of numerous high-dimensional features from medical images, known as radiomic features. These features capture a wide range of information, such as tumour shape, size, intensity distribution, and texture patterns. By analysing these features, radiomic models can provide valuable insights into the tumour's biology, heterogeneity, and aggressiveness and predict patient outcomes and treatment response.

Radiomics has found its application in various oncological settings, including diagnosis, prognosis, treatment planning, and response assessment. In addition, the field has demonstrated its potential in the management of several cancers, such as lung, breast, brain, and prostate cancers, among others. By offering a non-invasive method to assess tumour characteristics, radiomics has the potential to revolutionise cancer care, paving the way for precision medicine.

Despite the promising results, several challenges must be addressed to ensure the successful integration of radiomics into clinical practice. These challenges include standardisation of image acquisition and pre-processing, feature selection and validation, and the development of robust, generalisable models. Nevertheless, as the field of radiomics continues to evolve, it holds significant potential in improving patient outcomes and advancing the field of personalised medicine.

76.2 Radiomics for Predicting Neoadjuvant Chemotherapy Response in Breast Cancer Patients

Breast cancer is the most widespread cancer in women and is estimated at 2.3 million new cases diagnosed annually worldwide. However, neoadjuvant chemotherapy (NAC) is a locally advanced and high-risk early-stage breast cancer treatment strategy. The efficacy of NAC is variable, and predicting the response to treatment is crucial in guiding therapy and improving patient outcomes. Radiomics, a rapidly developing field, employs quantitative image features to create models that can predict clinical outcomes. This article will discuss a radiomic model that classifies responses to predicting neoadjuvant chemotherapy in breast cancer patients.

76.3 The Radiomic Model

The radiomic model proposed in this paper utilises quantitative imaging features extracted from pre-treatment magnetic resonance imaging (MRI) scans to predict the likelihood of achieving pathological complete response (pCR) following NAC. The development of the model involved three main steps:

- Image acquisition and pre-processing step involve obtaining pre-treatment breast MRI scans from a cohort of patients who underwent NAC. The scans are then pre-processed to ensure uniformity in voxel size and intensity values. In addition, image normalisation, resampling, and noise reduction optimise image quality and reduce scan variability.
- Radiomic features are extracted from the MRI scans' tumour regions. These features are categorised into several groups, including shape-based, first-order, and higher-order texture features. Shape-based attributes describe the size and shape of the tumour; first-order features describe the distribution of voxel intensities within the tumour, and higher-order texture features capture spatial patterns and relationships between voxel intensities. In total, hundreds of features are extracted, providing a comprehensive characterisation of the tumour's radiomic signature.
- Feature selection and model development avoid overfitting and improve the model's generalizability. This feature selection is employed to identify a subset of radiomic characteristics most predictive of pCR. This is achieved using various statistical methods, such as mutual information, correlation coefficients, and recursive feature elimination. A machine learning algorithm, such as logistic regression, support vector machines, or random forests, is then used to develop a predictive model based on the selected features.

76.4 Evaluation and Validation

The performance of the radiomic model is evaluated using various metrics, such as accuracy, sensitivity, specificity, and the area under the receiver operating characteristic (ROC) curve. Cross-validation techniques, such as k-fold cross-validation or bootstrapping, are employed to assess the model's robustness and

generalizability. Furthermore, external validation using an independent dataset is essential to confirm the model's utility in a clinical setting.

76.5 Clinical Implications

The proposed radiomic model has significant implications for the management of breast cancer patients. By predicting the response to NAC, the model can help clinicians identify patients likely to benefit from the treatment, sparing non-responders from the toxic effects of chemotherapy and allowing for alternative treatment strategies to be employed earlier in the treatment course.

Additionally, the radiomic model may contribute to personalised medicine by providing insights into the underlying tumour biology and identifying potential molecular targets for therapy. Radiomic features can be associated with specific molecular pathways or gene expression profiles, enabling the development of targeted therapies and improving patient outcomes.

76.6 Conclusion

The radiomic model can potentially transform the management of breast cancer patients by predicting their response to predicting neoadjuvant chemotherapy. This model can help clinicians make informed treatment decisions and pave the way for personalised medicine in breast cancer care by harnessing the power of quantitative imaging features. However, further research and validation are necessary to refine and optimise the model, ensuring its successful integration into clinical practice.

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77 Comparing Ultrasound and MRI in Brachial Plexus Imaging

Brachial plexus imaging is vital for diagnosing nerve conditions, ultrasound's potential challenges MRI's traditional dominance in this area.

77.1 Introduction

The brachial plexus is a complex network of nerves that extends from the spinal cord, through the neck and armpit, and into the arm. Imaging the brachial plexus is crucial for diagnosing and managing conditions such as traumatic nerve injuries, nerve compression syndromes, and tumours. For decades, magnetic resonance imaging (MRI) has been the gold standard for brachial plexus imaging due to its excellent soft tissue contrast and ability to visualise the entire plexus in great detail. However, ultrasound has emerged as a promising alternative in recent years, offering specific advantages over MRI. This article explores the potential of ultrasound to replace MRI for brachial plexus imaging.

77.2 Advantages of Ultrasound

Ultrasound machines are significantly more affordable than MRI machines in terms of initial investment and ongoing operational costs. As a result, using ultrasound for brachial plexus imaging could reduce the financial burden on patients and healthcare providers.

Ultrasound is more widely available than MRI, particularly in remote or under-resourced areas. This increased accessibility could lead to earlier diagnosis and treatment of brachial plexus-related conditions, ultimately improving patient outcomes.

MRI examinations often require patients to remain confined for extended periods, which can be uncomfortable or even impossible for some patients (e.g., those with claustrophobia or severe pain). On the other hand, ultrasound is performed at the bedside and does not involve any confinement, making it a more patient-friendly option.

Ultrasound allows real-time visualisation of the brachial plexus, whereas MRI does not. This can be particularly helpful for guiding interventional procedures, such as nerve blocks or biopsies, as it enables the clinician to adjust their approach as needed.

Ultrasound does not involve ionising radiation, which is a concern with other imaging modalities like computed tomography (CT). This makes it a safer option for patients,

particularly pregnant women and children, who are more susceptible to the harmful effects of radiation.

77.3 Challenges for Ultrasound

Although these advantages, there are also several challenges associated with using ultrasound for brachial plexus imaging:

- The quality of ultrasound images is highly dependent on the skill of the operator. This is in contrast to MRI, which provides more consistent and reproducible results across different operators. Therefore, ensuring that ultrasound operators are well-trained and experienced in brachial plexus imaging is essential for obtaining accurate diagnostic information.
- Ultrasound has a smaller field of view than MRI, making it more challenging to visualise the entire brachial plexus. This limitation may be particularly problematic in cases where the full extent of nerve involvement is unclear.
- Although modern ultrasound machines have improved image resolution, MRI provides superior soft tissue contrast and overall image quality. MRI may be better suited for detecting subtle abnormalities within the brachial plexus, such as small nerve injuries or early-stage tumours.
- Ultrasound is prone to certain artefacts, such as shadowing from bones or gas-filled structures, which can obscure the brachial plexus and limit the diagnostic accuracy of the examination.

77.4 Conclusion

Ultrasound has several advantages over MRI for brachial plexus imaging, including cost-effectiveness, accessibility, patient comfort, real-time imaging capabilities, and the absence of ionising radiation. However, it also faces challenges regarding operator dependence, limited field of view, image resolution, and imaging artefacts. These challenges may limit the diagnostic accuracy of ultrasound in certain cases and make it less suitable for detecting subtle abnormalities within the brachial plexus.

Despite these limitations, ultrasound has shown great potential as an alternative to MRI for brachial plexus imaging, particularly when MRI is unavailable, contraindicated, or not feasible for the patient. However, operators must be well-trained and experienced in brachial plexus imaging to optimise the diagnostic accuracy of ultrasound. Additionally, advances in ultrasound technology, such as the development of high-frequency transducers and enhanced image processing algorithms, may further improve image quality and resolution, helping to overcome current limitations.

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78 Lung Cancer Screening: Low Dose CT and the Potential of Photon Counting CT

Lung cancer's high mortality demands early detection; advances like low-dose CT and photon-counting CT improve noninvasive, accurate screening outcomes.

78.1 Introduction

Lung cancer is a significant cause of cancer-related deaths worldwide, with a high mortality rate mainly due to late diagnosis. Early detection and appropriate intervention can significantly improve survival rates. Recent advances in imaging technology have allowed for the development of lung cancer screening methods that are less invasive and more accurate. Low dose computed tomography (LDCT) has emerged as a viable screening tool, reducing radiation exposure while maintaining diagnostic accuracy. Photon-counting CT (PCCT), a cutting-edge technology, holds promise to enhance LDCT's capabilities further.

LDCT is a computed tomography (CT) type that uses a lower radiation dose than standard-dose CT. This approach has been increasingly utilised in lung cancer screening for high-risk populations, such as individuals with a significant smoking history. The National Lung Screening Trial (NLST) demonstrated that LDCT screening can reduce lung cancer mortality by 20% compared to chest radiography. Consequently, multiple professional societies, including the American College of Radiology (ACR) and the National Comprehensive Cancer Network (NCCN), now endorse LDCT for lung cancer screening in high-risk populations.

78.2 LDCT for Lung Cancer Screening: Balancing Benefits and Limitations in Early Detection

The main advantage of LDCT is reduced radiation exposure, which lessens the risk of radiation-induced malignancies. Additionally, LDCT has demonstrated superior sensitivity in detecting early-stage lung cancers compared to chest radiography. Early detection is crucial for improving patient outcomes, as it enables timely intervention and increases the chances of successful treatment.

However, LDCT is not without limitations. One significant challenge is the high false-positive rate, which can lead to unnecessary invasive procedures and patient anxiety. False positives often occur due to the detection of benign pulmonary nodules indistinguishable from malignant ones. LDCT is less effective in identifying ground-glass opacities and can miss cancers with non-solid components. Consequently, there is a need for more advanced imaging technologies to address these limitations.

78.3 Photon Counting CT (PCCT) as a Potential Solution

Photon-counting CT (PCCT) is an emerging technology that holds promise for addressing the limitations of LDCT. PCCT uses advanced detectors that can count individual photons, providing more detailed and accurate information about the X-ray attenuation properties of scanned tissues. This technology can potentially improve the diagnostic accuracy of LDCT in several ways:

- PCCT can achieve higher spatial resolution and better contrast-to-noise ratio than conventional CT. This improvement can help differentiate between benign and malignant pulmonary nodules, reducing the rate of false positives.
- PCCT can differentiate between various tissue types based on their unique attenuation properties. This ability to distinguish between materials can help identify ground-glass opacities and non-solid components of lung cancers often missed by LDCT.
- Due to the advanced detector technology, PCCT can potentially achieve lower radiation doses than LDCT, further reducing the risk of radiation-induced malignancies.
- PCCT can provide functional information, such as blood flow and perfusion, to help assess tumour aggressiveness and guide treatment decisions.

78.4 Challenges and Future Directions

Although PCCT shows great promise, it is still experimental and not yet widely available. Large-scale clinical trials are needed to establish its efficacy and safety for lung cancer screening. Additionally, cost and accessibility may be barriers to widespread adoption. However, as technology advances and costs decrease, PCCT may become an essential tool in the fight against lung cancer.

78.5 Conclusion

Lung cancer screening using low dose computed tomography (LDCT) has proven to be an effective method for early detection of lung cancer in high-risk populations. Although its benefits, LDCT faces challenges such as high false-positive rates and limitations in identifying specific types of lung cancers. Photon-counting CT (PCCT) is an emerging technology that has the potential to overcome these challenges by offering improved image resolution, material decomposition, lower radiation doses, and functional imaging capabilities. As further research and clinical trials are conducted, PCCT may become an essential tool in the fight against lung cancer, ultimately leading to improved patient outcomes and reduced mortality rates.

Suggested reading

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