Chapter-2.

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RADIOMICS AND RADIOGENOMICS

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Abstract

This chapter explores the transformative realms of radiomics and radiogenomics, key domains in precision medicine that enhance the intersection of medical imaging and genomics. Radiomics extracts quantitative features from medical images, facilitating nuanced disease characterization and personalized treatment strategies. Radiogenomics integrates this data with genetic profiles to unravel the relationship between imaging phenotypes and molecular drivers of diseases, particularly cancer. Methodologies, including image acquisition, feature extraction, and machine learning applications, are dissected alongside their clinical implications. The chapter highlights advance in cancer diagnosis, prognosis, and therapeutic response prediction while addressing challenges like data standardization, clinical integration, and ethical considerations. It also emphasizes the future of multimodal data fusion and artificial intelligence-driven models, aiming to bridge research and clinical practice. Together, these fields hold unparalleled potential to revolutionize healthcare by fostering individualized care, optimizing outcomes, and advancing precision medicine.

Keywords: Radiomics, Radio Genomics, Tumours

Introduction

In ancient civilizations, physicians had limited ability to predict outcomes for oncology patients, often foreseeing only fatal or short life expectancies. The medical landscape changed dramatically with Wilhelm Conrad Rontgen's discovery of X- rays, revolutionizing diagnostics for malignant diseases, although treatment options remained constrained. Subsequent advancements in chemotherapy marked significant progress in oncology treatment. Today, numerous techniques exist for diagnosing and treating malignancies, but determining the most effective approach remains a challenge, particularly when interpretations of data vary among healthcare professionals, such as in the case of radiologists assessing CT scans differently. Precision medicine has emerged as a crucial approach to ensure patients receive optimal treatment. Within precision medicine, radiomics stands out as a subfield that leverages computer systems to aid in diagnosis and treatment selection. These systems also predict disease outcomes and prognoses based on correlations between historical and current patient data, facilitating personalized therapy decisions. Precision medicine encompasses a holistic approach that considers both the individual's genetic makeup (genotype) and observable traits (phenotype), integrating concepts from systems biology. This multidisciplinary approach incorporates mathematical modeling alongside genomics, transcriptomics, proteomics, and metabolomics.

Furthermore, medical imaging plays a central role in precision medicine. Radiomics involves extracting quantitative data from various medical images and integrating it with clinical and patient-specific information in a unified database. This database also supports radiogenomics, a field that combines genetic and radiomic data. Radiogenomics provides detailed genetic information at the voxel level for heterogeneous tumors or sets of tumors in metastatic disease, guiding tailored therapies based on individual genetic profiles. Additionally, radiogenomics aids in characterizing lesions, improving differentiation between benign and malignant entities, and enhancing patient screening processes. In recent decades, the convergence of medical imaging and genomics has catalysed ground-breaking advancements in disease diagnosis, treatment, and personalized medicine. Radiomics and radio genomics, two burgeoning fields at this intersection, have emerged as powerful tools for extracting actionable insights from medical images and integrating them with genomic data. This chapter delves into the intricacies of

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radiomics and radio genomics, exploring their methodologies, applications, challenges, and the transformative impact they are poised to have on healthcare. Radiomics, derived from "radiology" and "omics," entails the quantitative analysis of medical images to extract a wealth of features beyond what the human eye can perceive. This section traces the evolution of radiomics, from its origins in conventional imaging to the integration of advanced computational techniques and machine learning algorithms.

Methodologies in Radiomics

Methodologies in radiomics encompass a series of systematic steps and techniques used to extract and analyse quantitative features from medical images. These methodologies are crucial for understanding tissue characteristics, disease patterns, and treatment responses. Here's an overview of the methodologies in radiomics:

1. **Image Acquisition:** Radiomics begins with the acquisition of medical images using various imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), etc. Each modality provides unique insights into tissue structures and properties.
2. **Image Pre-processing:** This step involves several tasks to enhance the quality and reliability of the acquired images:
    - Noise Reduction: Removing background noise from images to improve clarity and accuracy.
    - Normalization: Ensuring uniformity in image intensities and scales across different scans or patients.
    - Segmentation: Identifying and delineating regions of interest (ROIs) within the images, such as tumours or organs, for focused analysis.
3. **Feature Extraction:** Radiomics algorithms extract quantitative features from the segmented ROIs. These features can be broadly categorized into:
    - First-Order Statistics: Basic statistical measures like mean, median, standard deviation, skewness, and kurtosis of pixel intensities within the ROI.
    - Texture Features: Descriptive measures capturing spatial patterns, coarseness, roughness, and homogeneity of pixel distributions.
    - Shape Features: Geometric attributes such as volume, surface area, compactness, and sphericity of the segmented object.
    - Spatial Relationships: Relationships between neighboring voxels or pixels, such as distance, clustering, and gradients.

4. Data Standardization: Ensuring consistency and comparability of radiomics features across different imaging platforms, protocols, and datasets. Standardization is crucial for robust analysis and validation of radiomics models.

5. Machine Learning and Statistical Analysis: Utilizing machine learning algorithms, such as support vector machines (SVM), random forests, neural networks, etc., to analyze extracted radiomics features. Statistical analysis helps in identifying patterns, correlations, and predictive models related to disease characteristics, prognosis, and treatment outcomes.

6. Validation and Interpretation: Validating radiomics models through independent datasets, cross-validation techniques, and clinical correlation studies. Interpretation of radiomics findings involves understanding the clinical relevance of extracted features and their implications for diagnosis, prognosis, and therapeutic decision-making. Overall, the methodologies in radiomics are interdisciplinary, involving expertise from radiology, medical imaging physics, computer science, statistics, and clinical oncology. These methodologies enable a data-driven approach to healthcare, offering insights into disease heterogeneity, treatment response variability, and personalized medicine strategies.

Applications of Radiomics

Radiomics plays a pivotal role in the diagnosis and prognosis of cancer, providing valuable insights into tumour characteristics, subtype classification, and predicting patient outcomes based on imaging features. This innovative approach has transformed cancer management by harnessing the power of advanced imaging technologies to extract quantitative data that holds significant clinical relevance. In the realm of cancer diagnosis, radiomics has revolutionized tumour characterization. By analysing a multitude of quantitative features extracted from medical images, radiomics enables clinicians to gain a comprehensive understanding of tumour morphology, heterogeneity, and spatial relationships. This detailed characterization facilitates precise tumour profiling, aiding in the identification of specific tumour subtypes and molecular signatures. Such subtype classification is crucial as it guides tailored treatment strategies based on the unique biological characteristics of each tumour. Moreover,

SPJP PROCEEDINGS
Volume-1 | Issue-1 | Page Number: 8-14
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ISSN: XXXX-XXXX

radiomics plays a crucial role in predicting patient outcomes in cancer. By correlating radiomics features with clinical data and genetic information, radiomics models can predict patient survival, recurrence risk, and overall prognosis. These predictive models empower clinicians to make informed decisions regarding treatment plans and follow-up strategies, ultimately improving patient care and outcomes.

Treatment response assessment is another critical area where radiomics demonstrates its utility. By monitoring changes in radiomics features over time, clinicians can objectively evaluate treatment efficacy and response. Radiomics-based biomarkers provide quantitative measures of treatment response, allowing for early detection of treatment resistance or disease progression. This data-driven approach enables clinicians to adjust treatment regimens promptly, optimizing therapeutic outcomes for cancer patients. Beyond its applications in oncology, radiomics extends its utility to various medical disciplines, including neuroimaging, cardiology, and musculoskeletal imaging. In neuroimaging, radiomics aids in the diagnosis and characterization of neurological disorders such as brain tumours, neurodegenerative diseases, and stroke. By extracting quantitative features from neuroimaging studies, radiomics enhances diagnostic accuracy and contributes to personalized treatment planning for neurological conditions. Similarly, in cardiology, radiomics holds promise in assessing cardiac function, identifying myocardial abnormalities, and predicting cardiovascular risk. By analysing cardiac imaging data, radiomics provides valuable insights into cardiac structure, function, and tissue composition, facilitating early detection of cardiac pathologies and guiding therapeutic interventions.

In musculoskeletal imaging, radiomics enhances the evaluation of bone and soft tissue lesions, aiding in the differential diagnosis of musculoskeletal disorders such as fractures, tumours, and inflammatory conditions. Radiomics-based analyses of musculoskeletal images improve diagnostic accuracy, streamline patient management, and contribute to optimal treatment outcomes.

Challenges and Future Directions in Radiomics

Challenges and future directions in radiomics encompass a range of key areas that shape the evolution and application of this cutting-edge field within healthcare. Addressing these challenges and charting a clear path for future advancements is crucial for maximizing the potential of radiomics in improving patient care and outcomes. Here are the challenges and future directions in radiomics.

Challenges

Data Standardization: One of the primary challenges in radiomics is the lack of standardized protocols for data acquisition, pre- processing, and analysis. Variability in imaging parameters, equipment settings, and data handling practices can lead to inconsistencies and hinder the reproducibility of radiomics studies. Interpretability and Validation: Interpreting radiomics features and translating them into clinically meaningful insights can be complex. Robust validation studies in diverse patient cohorts are essential to validate the predictive and prognostic value of radiomics models and ensure their clinical relevance and reliability.

- Clinical Integration: Integrating radiomics into clinical workflows remains a challenge. Bridging the gap between radiomics research and clinical implementation requires collaboration between radiologists, clinicians, data scientists, and regulatory bodies to develop user-friendly tools and guidelines for incorporating radiomics-based analyses into routine clinical practice.
- Ethical and Regulatory Considerations: Ethical considerations regarding patient data privacy, informed consent, data sharing, and responsible data usage are paramount in radiomics research. Adhering to ethical standards and regulatory requirements is crucial to ensure patient confidentiality and data security. Data Quality and Reproducibility: Ensuring high-quality imaging data and reproducible radiomics analyses is essential for the reliability and validity of radiomics findings. Addressing issues such as image artifacts, variability in segmentation algorithms, and data pre-processing techniques is critical for enhancing data quality and reproducibility.

Future Directions

Standardization initiatives in radiomics, like the Image Biomarker Standardization Initiative (IBSI), are collaborative endeavors aimed at establishing uniform protocols, terminology, and benchmarks within radiomics research. These efforts are crucial for ensuring data harmonization, enhancing comparability across studies, and improving the reproducibility of radiomics findings. Furthermore, advancements in machine learning, such as

SPJP PROCEEDINGS
Volume-1 | Issue-1 | Page Number: 8-14
Website: https://journal.spjinternational.co/index.php/spjpp
ISSN: XXXX-XXXX

deep learning and artificial intelligence (AI), offer promising avenues for boosting the predictive capabilities and interpretability of radiomics models. By integrating sophisticated machine learning techniques with radiomics analyses, more accurate and clinically relevant insights can be derived, contributing to improved patient care and outcomes.

Another important aspect is the integration of radiomics data with other omics data sets, such as genomics, transcriptomics, proteomics, and metabolomics. This multi-omics integration enables a comprehensive understanding of disease biology and facilitates the development of personalized treatment strategies. Additionally, the development of explainable AI models and interpretable radiomics features is essential for unraveling the underlying biological mechanisms captured in imaging data. Enhancing the interpretability and transparency of radiomics analyses fosters trust among healthcare professionals and aids in making informed clinical decisions. Conducting large-scale clinical translation and validation studies, including multicenter trials, is imperative for translating radiomics research into clinical practice. Demonstrating the clinical utility, prognostic value, and cost-effectiveness of radiomics-based approaches is crucial for driving adoption and implementation in real-world healthcare settings. Moreover, adopting patient-centric approaches in radiomics research, which involve considering patient-reported outcomes, preferences, and values, can lead to personalized care, improved patient empowerment, and better health outcomes.

Introduction to Radio-genomics

Radio genomics bridges the gap between imaging phenotypes and underlying genetic drivers of disease, offering a holistic understanding of disease biology and personalized treatment strategies. Radio genomics is an emerging field at the intersection of radiology and genomics, combining advanced imaging techniques with genetic analysis to gain deeper insights into disease mechanisms, treatment responses, and patient outcomes. This interdisciplinary approach holds tremendous promise for personalized medicine, as it allows clinicians to tailor treatments based on individual genetic profiles and imaging characteristics. By integrating radiomics data extracted from medical images with genomic data obtained from techniques like next-generation sequencing (NGS) or microarray analysis, radio genomics aims to unravel the complex interplay between genetic factors and imaging features in various diseases, particularly cancer. The fundamental premise of radio genomics lies in understanding how genetic variations influence radiographic phenotypes, such as tumor morphology, vascularity, and metabolic activity captured in imaging studies. This knowledge enables the identification of imaging-genomic associations and potential biomarkers that can inform prognosis, treatment selection, and therapeutic response monitoring. Radio genomics also plays a crucial role in characterizing tumor subtypes, predicting patient outcomes, and guiding precision medicine approaches tailored to individual patients.

Key areas of focus in radio genomics include the development of predictive models that integrate radiomics and genomics data to forecast treatment responses and disease progression. By leveraging machine learning algorithms and statistical analyses, radio genomics models can identify imaging-genomic signatures associated with specific clinical endpoints, such as survival rates, recurrence risk, and treatment efficacy. These models empower clinicians to make data-driven decisions, optimize treatment strategies, and improve patient care. Moreover, radio genomics contributes to advancing our understanding of disease heterogeneity, therapeutic resistance mechanisms, and molecular pathways involved in disease progression. By elucidating the genetic underpinnings of imaging phenotypes, radio genomics offers a comprehensive view of disease biology, facilitating targeted interventions and personalized treatment approaches.

Methodologies in Radio genomics

Methodologies in radio genomics encompass systematic approaches and techniques that integrate radiological imaging with genomic analysis to gain insights into disease mechanisms, treatment responses, and patient outcomes. Here are the key methodologies in radio genomics:

- Genomic Data Acquisition: This involves obtaining genetic information using advanced techniques such as next-generation sequencing (NGS), microarray analysis, or other molecular profiling methods. Genomic data acquisition provides insights into genetic mutations, gene expression profiles, epigenetic modifications, and other genomic alterations associated with diseases.
- Radiological Imaging: Radiological imaging techniques like MRI, CT scans, PET scans, and others capture detailed anatomical and functional information about tissues and organs. Radiological images serve as the basis for extracting radiomic features related to tumor morphology, vascularity, metabolic activity, and other imaging characteristics.

SPJP PROCEEDINGS
Volume-1 | Issue-1 | Page Number: 8-14
Website: https://journal.spjinternational.co/index.php/spjpp
ISSN: XXXX-XXXX

- Image Preprocessing: Before extracting radiomic features, image preprocessing steps are performed to enhance image quality and remove artifacts. This may include noise reduction, intensity normalization, image registration, and segmentation to delineate regions of interest (ROIs) within the images.
- Feature Extraction: Radiomic features are quantitative metrics extracted from radiological images and genomic data. These features encompass a wide range of characteristics, including intensity, texture, shape, spatial relationships, and functional parameters derived from imaging and genomic analyses.
- Correlation Analysis: Statistical methods are employed to correlate radiomic features with genomic data. This correlation analysis helps identify imaging-genomic associations, biomarkers, and predictive signatures that are indicative of disease subtypes, treatment responses, prognosis, and patient outcomes.
- Machine Learning and Predictive Modeling: Machine learning algorithms, such as supervised and unsupervised learning techniques, are utilized to develop predictive models based on integrated radiomic and genomic data. These models can predict treatment responses, disease progression, survival rates, and other clinical endpoints, aiding in personalized treatment planning and decision-making.
- Validation Studies: Validation of radiogenomics models is essential to assess their accuracy, reliability, and clinical relevance. Validation studies involve evaluating model performance using independent datasets, cross-validation techniques, and assessing predictive capabilities in real-world clinical settings.
- Clinical Translation: Translating radiogenomics findings into clinical practice requires collaboration between radiologists, geneticists, oncologists, and other healthcare professionals. It involves integrating radiogenomics insights into patient care pathways, implementing personalized treatment strategies, and evaluating the impact on patient outcomes through prospective clinical trials and observational studies.

By employing these methodologies, radiogenomics aims to bridge the gap between radiological imaging and genomic analysis, providing a comprehensive understanding of disease biology and facilitating personalized medicine approaches tailored to individual patient needs.

Applications of Radiogenomics

Radiogenomics, the integration of radiological imaging with genomic analysis, has a wide range of applications across various medical fields. Here are some key applications of radiogenomics:

- Cancer Diagnosis and Prognosis: Radiogenomics plays a crucial role in cancer diagnosis by providing insights into tumor characteristics, subtypes, and genetic profiles. By correlating radiomic features extracted from imaging data with genomic data, radiogenomics aids in tumor classification, prognostication, and risk stratification. This information is valuable for predicting patient outcomes, treatment responses, and developing personalized treatment plans for cancer patients.
- Treatment Response Prediction: Radiogenomics helps predict how tumors will respond to specific treatments, such as chemotherapy, immunotherapy, or targeted therapy. By identifying imaging-genomic biomarkers associated with treatment response, radiogenomics enables clinicians to tailor treatment strategies and optimize therapeutic outcomes.
- Therapeutic Decision-Making: Integrating radiomic and genomic data guides therapeutic decision-making by providing valuable insights into disease biology, molecular pathways, and potential therapeutic targets. Radiogenomics assists in selecting the most effective treatment options, monitoring treatment responses, and adjusting treatment regimens based on individual patient characteristics.
- Prognostic Assessment: Radiogenomics aids in prognostic assessment by identifying imaging-genomic signatures associated with disease progression, recurrence risk, and overall survival. This information helps clinicians stratify patients into risk categories, estimate prognosis, and develop personalized follow-up plans for long-term monitoring.
- Precision Medicine: Radiogenomics is a cornerstone of precision medicine, enabling personalized treatment approaches tailored to individual patient profiles. By combining radiomic and genomic data, precision medicine aims to maximize treatment efficacy, minimize side effects, and improve patient outcomes through targeted interventions.
- Therapeutic Monitoring: Radiogenomics facilitates therapeutic monitoring by tracking changes in

SPJP PROCEEDINGS
Volume-1 | Issue-1 | Page Number: 8-14
Website: https://journal.spjinternational.co/index.php/spjpp
ISSN: XXXX-XXXX

radiomic and genomic biomarkers over time. This continuous monitoring allows clinicians to assess treatment responses, detect treatment resistance or disease progression early, and make timely adjustments to treatment plans.

- Research and Biomarker Discovery: Radiogenomics contributes to research and biomarker discovery by identifying novel imaging-genomic associations, biomarkers, and predictive signatures. These discoveries drive advances in understanding disease mechanisms, developing new therapies, and improving diagnostic and prognostic tools for various medical conditions.

Challenges and Future Perspectives in Radio genomics

- Data Integration and Privacy: Managing diverse datasets while ensuring patient privacy and data security is a paramount concern in radiogenomics research.
- Validation and Clinical Translation: Robust validation studies and regulatory approvals are essential for translating radiogenomics findings into clinical practice.
- Ethical Considerations: Ethical guidelines governing data usage, patient consent, and equitable access to radio genomic technologies require ongoing attention and adherence.

Emerging Trends and Innovations

- Multimodal Fusion and Integrated Diagnostics: Advancements in multimodal imaging and data fusion techniques enable comprehensive disease characterization and integrated diagnostic approaches. Artificial Intelligence and Deep Learning: The role of AI and deep learning continues to expand, driving innovation in radiomics and radiogenomics analyses and enhancing predictive modeling capabilities.
- Clinical Implementation and Precision Medicine: Bridging the gap between research and clinical practice is crucial for realizing the full potential of radiomics and radiogenomics in delivering personalized, precision medicine.

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