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Pseudo-Computed Tomography (PCT): Revolutionizing Imaging with Non-Ionizing Modalities

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Abstract
Pseudo-Computed Tomography (PCT) is an innovative imaging technique designed to simulate the high-resolution, cross-sectional images generated by traditional Computed Tomography (CT), without the associated risks of ionizing radiation. By integrating data from non-ionizing imaging modalities such as Magnetic Resonance Imaging (MRI), ultrasound, and other advanced imaging systems, PCT produces images that closely resemble those of conventional CT scans. This non-invasive technique holds considerable promise for medical diagnostics, treatment planning, and radiation-free imaging, particularly in radiation-sensitive settings. This review provides a comprehensive examination of the methodologies behind PCT, its current applications, the challenges it faces, and its future potential in advancing imaging technologies, especially in environments where minimizing radiation exposure is critical.

I. INTRODUCTION

Computed Tomography (CT) is typically used to image hard tissues, whereas Magnetic Resonance Imaging (MRI) provides superior clarity for soft tissues. In Radiation Therapy Treatment Planning (RTP), MRI plays a vital role not only in planning but also in confirming patient positioning for accurate treatment delivery. When CT and MRI are co-registered in RTP, it can lead to systematic errors. An MRI-only workflow for radiation therapy would be advantageous, as it could eliminate these errors, simplify patient care processes, and reduce the patient's exposure to radiation. Although MRI does not directly relate signal intensity to electron density like CT does, MRI-only methods for treatment planning have been successfully developed. CT images, on the other hand, enable dose calculation based on tissue electron density and voxel count, while a digitally reconstructed radiograph is derived from tissue attenuation (Dowling J A et al., 2015). In recent years, the preference for MRI-based treatment planning has increased, replacing CT images in many cases. The excellent contrast offered by MRI improves the ability to accurately identify tumor tissues and Organs at Risk (OAR). The main advantages of MRI-based planning include its ability to provide high-quality functional imaging, its lack of ionizing radiation, and its cost-effectiveness. MRI's superior soft tissue contrast makes it easier to differentiate tumor tissue from surrounding healthy tissues, allowing for more precise delineation of the affected regions. Furthermore, MRI scans can be performed before, during, or after treatment without any risk of radiation exposure to the patient. Technologies like MRI-Cobalt and MRI-Linac, which are already in use at several treatment centers, are being utilized for Image-Guided Radiation Therapy (IGRT). For accurate treatment planning and dose calculation with MR-Linac, the assumption of homogeneous electron densities throughout the patient's volume is essential. If the electron density is heterogeneous, dosimetric discrepancies exceeding 2% may arise compared to homogeneous assumptions. Although fusion techniques can align MRI data with CT scans, they come with limitations, such as increased costs and extended scanning times, especially for soft tissue imaging. Using MRI-based imaging systems can reduce reliance on CT, thus lowering both costs and patient discomfort while improving the accuracy of brain imaging. While MRI-only radiation therapy planning offers several advantages, it still faces challenges, particularly in addressing geometric distortions caused by non-uniform magnetic fields, gradient nonlinearity, and patient-induced susceptibilities. Additionally, conventional MRI-based treatment planning software cannot calibrate images based on electron density due to differences in imaging protocols.

II. METHODS

One approach to generating electron density maps involves registering MRI images with CT scans. The potential for replacing CT with MRI-only simulation systems for radiation therapy planning has been explored in several studies [16-19]. Recent advancements in MRI technology have led to the development of various methods for estimating electron density in external radiation therapy. In these methods, each homogeneous density value within an MRI scan is converted into a manual contour, which corresponds to a specific region of interest using bulk density assignment. While this approach was developed to simplify the use of MRI in radiation planning, its accuracy may not match that of CT, particularly in generating Digitally Reconstructed Radiographs (DRR). By combining MRI data with CT images, a pseudo-CT image can be generated, which offers a simpler alternative to mapping complex anatomy using Atlas-based registration techniques. These techniques allow for the full automation of the image creation process and are less susceptible to intensity variations between the images. However, a limitation of this method is its inability to align atlases with anatomical features that are not included in the atlas training sets, potentially compromising the accuracy of the image alignment.MRI images and CT scan slices can be merged and analyzed simultaneously, particularly in soft tissues (Wegener et al., 2018). However, fusion techniques come with their own limitations, including increased scan time and higher costs. On the other hand, MRI-only systems completely eliminate the need for CT, enhancing both the comfort and accuracy of brain segmentation. This approach effectively addresses the issues of increased costs, extended scan times, and other limitations associated with traditional fusion methods.

While MRI-only radiation planning offers significant advantages, it is essential to consider geometric distortions caused by nonuniform magnetic fields, gradient nonlinearity, and patient susceptibility before accurate dose calculations and treatment planning can occur. MRI images used in radiation planning cannot be calibrated to electron density measurements due to differences in imaging protocols. To address this, electron density maps can be generated using techniques like rigid registration of MRI with CT, though this method becomes less feasible when the patient's positioning differs between MRI and CT scans.

Recent studies have explored the possibility of eliminating CT entirely from radiation therapy planning by implementing MRI-only simulation systems. Several methods for estimating electron density from MRI data have been developed in recent years, including the bulk density assignment approach, where a uniform density value is assigned to a specific area. While this method is more manageable, it does not provide the same level of precision as CT for generating reliable Digitally Reconstructed Radiographs (DRRs).

To generate a substitute for CT, a target MRI can be compared to a CT scan using an atlas-based approach, which simplifies the process compared to mapping complex anatomy. The Atlas-based method—which converts standard MRI sequences into quasi-CT images—is the only fully automated technique for creating pseudo-CT images from MRI, and it is more robust against intensity variations between images. However, a limitation of this approach is that it cannot deform atlas images to match anatomical features absent from the atlas training sets.

To address this, we propose a deformable registration method for semi-automatic segmentation using a selected atlas. Manually delineated MRI images were used to create a conjugated electron density atlas and a comprehensive MRI atlas, as described by Dowling et al. (2012). Our optimization method employs a robust block matching algorithm that ensures inverse consistency through a half-space definition. This algorithm optimizes both half-space transformations and their inverses simultaneously.

Additionally, a multi-atlas approach has been implemented, using the similarity of mapped morphological features between atlases and the target to create CT images from MRIs. For atlas-based learning of intensity maps, CT-MR images co-registered with a dictionary are commonly used as training sets. Other methods, such as Gaussian Mixture Regression and Random Forest Regression, have been applied to Dual Ultra-short Echo (dUTE) and multidimensional MRI images to generate pseudo-CT images.

Another approach for creating pseudo-CT images uses voxel-based techniques. These methods, based on functional MRI sequences and short echo time (UTE) sequences, utilize standard MRI sequences and ultrashort echo times. Voxel-based weighted summation techniques combine unwrapped UTE phase maps with water-fat maps to create a pseudo-CT. The MRI intensity values are adjusted based on a second-order polynomial model to match T1/T2 weighted CT images. This technique converts CT Hounsfield Units (HU) into T1/T2 weighted MRI intensities, allowing the creation of a pseudo-CT that can be used to optimize ion radiotherapy treatment plans with voxel-wise tissue classification.

Further studies by Chen et al. (2017), Cheng et al. (2018), and Chopra et al. (2005) introduced algorithms that combine Fuzzy Membership Functions (FCM) with the under-sampled UTE-mDixon pulse sequence to construct pseudo-CTs. Gaussian mixture regression was used in these studies to generate substitute CT images.

A machine learning approach introduced by Wang et al. (2019) demonstrated the potential of creating high-quality pseudo-CT images. Although the method showed promising image quality, the accuracy of dose calculation remains to be fully validated. Machine learning is also being explored to evaluate whether neurofocal Stereotactic Radiosurgery (SRS) dose calculations could be improved using pseudo-CT images derived from MRIs processed by this algorithm.

In a study involving 14 patients, we analyzed 19 treatment plans using both CT simulations and MRI images. Dose distributions were calculated for both CT simulations and MRI-derived pseudo-CT images, comparing them with ground truth data. Dose-Volume Histograms (DVH) and gamma metrics were also evaluated for both pseudo-CT and ground truth images based on clinically relevant DVH metrics. The results showed a good comparison between the two imaging methods, with an adequate dose distribution. For the Planning Target Volumes (PTVs), the deviation was minimal (less than 0.6%), and there were no changes observed for the organs at risk. The gamma analysis yielded a pass rate of 99% for the pseudo-CT images. Using the proposed machine learning method, the researchers concluded that CT simulations could be replaced by their MRI-based method when treating the brain with Stereotactic Radiosurgery (SRS). According to the study, MRI images could eventually replace CT images entirely in the simulation and treatment planning processes.

In a separate study, Koike et al. (2020) explored the use of an adversarial network to generate pseudo-CT images from MRI sequences and assess their use in brain radiation therapy planning. The researchers created a three-channel image for 15 patients with glioblastoma by combining T1-weighted, T2-weighted, and fluid-attenuated inversion recovery images. They used a conditional Generative Adversarial Network (cGAN) to calculate the Mean Absolute Errors (MAE) of CT numbers from image patches. The study also performed a dosimetric evaluation of Volumetric Modulated Arc Therapy (VMAT) and 3D-Conformal Radiation Therapy (3D-CRT) using recalculated CT images and pseudo-CT data. The results showed no significant differences in isocenter doses, with dose differences for 2% of the volume (D2%), 50% of the volume (D50%), and 98% of the volume (D98%) all being less than 1.0%. The equivalent path length was slightly shorter in pseudo-CT images compared to CT by 0.6 ± 1.9 mm. This study demonstrated that pseudo-CT images can be reliably generated from MRI sequences using the cGAN algorithm, showcasing the potential for MRI-only radiation therapy planning.

Li et al. (2020) investigated the conversion of MR/CT images to synthetic MRI images using U-Nets and Cycle-Consistent Adversarial Networks (CycleGAN), two well-known deep learning methods. Their results showed that the U-Net approach produced synthetic images with lower Mean Absolute Errors (MAE), higher Structural Similarity Indices (SSIM), and better Peak Signal-to-Noise Ratios (PSNR) when generating synthetic CT images. While CycleGAN-generated images had less contrast information, the U-Net synthetic images were closer in pixel value profiles to real-world images, confirming the superiority of supervised deep learning over unsupervised methods for MR/CT synthesis tasks.

Xu et al. (2019) proposed using multiple Dixon MR images to create pseudo-CT (pCT) images for challenging abdominal regions, enabling MRI-only radiation therapy (RT). They employed a multichannel residual conditional generative adversarial network (MCRCGAN), which integrates various techniques to improve the accuracy of pseudo-CT generation. The MCRCGAN model captures more anatomical details from multiple MR images and produces accurate predictions even with limited training data. The study showed significant improvements in the quality and stability of pseudo-CT generation for MR-CT image pairs.

In Juan et al.'s (2020) study, CycleGANs were used to generate pseudo-CT images from unregistered MRI/CT images of patients with brain tumors. Thirty-one patients underwent both MRI and CT simulation of the entire brain. The researchers used CycleGAN to translate MRI images into pseudo-CT images without supervision, after preprocessing the MRI and CT images to correct for head frame influences, scanning range discrepancies, and imaging resolution differences. The study demonstrated that CycleGANs could successfully translate unregistered MRI and CT images, reducing errors caused by multi-modal image registration when delineating Gross Tumor Volumes (GTVs) in brain tumor patients.

Lastly, Farhadi et al. (2019) proposed generating synthetic CT (sCT) and synthetic MR (sMR) images using an Atlas-based method. The study analyzed paired MR and CT data from 10 brain radiation therapy patients. The generated sCT/sMR images were compared to real CT/MR images by measuring the Mean Absolute Error (MAE). The results showed that sMR images (sT1w/sT2w) had lower MAEs compared to sCT images, and sCT images based on T1-weighted sequences correlated better with real CT images than those based on T2-weighted sequences. The study concluded that geometric details from CT targets were better transmitted to synthetic images than from MR targets.

III. PRE-PROCESSING

➢ *Local Symmetry and Global Symmetry Based Methods (LSBM/GSBM)*

In the Local Symmetry-Based Method (lSBM), symmetry measures are initially optimized locally by tracing the mid-section of the brain. Based on this, the symmetry measure is then derived. Since this method only considers a part of the brain, it requires longer computation time compared to Global Symmetry-Based Methods (GSBM). Stegmann et al. (2015) explain that local symmetry is a significant factor in the failure of Global Symmetry (GS) to accurately represent the brain's hemispherical symmetry. This failure occurs because local symmetry, by focusing on individual parts of the brain, is more complex and computation-heavy than GSBM. Shah et al. (2014) also suggest that GS methods often fail to fully capture hemisphere symmetry due to this limitation.

Kuijf et al. (2013) observed that local symmetry computations, which focus on smaller brain regions, can be completed in approximately 0.5 seconds. Despite being computationally efficient, these methods lack the global perspective that GSBM offers, leading to inaccuracies when considering the entire brain's symmetry.

In contrast, GSBM methods, which reflect brain images on a sagittal axis to achieve accurate registration, can take longer to compute. Kuijf et al. (2013) found that the 3D rigid registration for GSBM took 33.6 seconds, highlighting the computational burden. Additionally, patients with cerebral atrophy tend to have errors in symmetry due to the widening of the interhemispheric fissure, which complicates the symmetric division of the brain.

In 2003, researchers examined how Interhemispheric Fissure (IFP) influences the Symmetry Planes (SP), concluding that while the brain is symmetric, no two cases are identical. The difference between the Brain Symmetry Plane (BSP) and the Head Symmetry Plane (HSP) could be 0.53 (52/98), emphasizing the need for careful selection of the symmetry plane, particularly for abnormal subjects.

➢ *Techniques in Steganography*

Venna and Arivazhagan (2018) developed a method using weighted residuals and a small set of stereoscopic images to accurately determine spatial locations. This technique utilizes local weighting through a bivariate shrinkage function to enhance the spatial least significant bit (LSB) of stego images. Their method, which works without prior knowledge of the embedded algorithm, achieved 90% accuracy in estimating payload locations across 100 well-known stego images and five spatial LSB algorithms.

Similarly, Chakraborty et al. (2020) introduced a blind image steganography technique that uses Local Binary Pattern (LBP) functions. By embedding these patterns into an image, the cover image retains its local relationships while achieving comparable embedding rates. Their method, based on feature extraction through LBP, demonstrated advantages over traditional LSB-based steganography methods.

➢ *Area-Based Methods (ABM) in Registration*

Area-Based Methods (ABM) are suitable for image registration where the primary content is grayscale or color intensities, rather than local shapes or structures. ABM involves finding similarities between images and then applying a transformation function. Mambo et al. (2018) suggest that integrating deep learning algorithms with the registration process could help address challenges in densely sampled data.

In medical imaging, intensity-based registration is common, where image similarity is used to estimate transformations. Kuijf et al. (2013) and Fverstedt et al. (2019) demonstrated the advantages of this approach in medical image registration, particularly in non-rigid or multimodal scenarios. Kim et al. (2013) and Augusto et al. (2018) found that hybrid methods—combining intensity and feature-based approaches—often outperform purely feature-based methods in registering medical images.

Recent studies also highlight the integration of deep learning into image registration, where CNNs (Convolutional Neural Networks) are employed to improve similarity computation and transformation estimation. For instance, Davatzikos et al. (2013) and Thijs Kooi et al. (2017) focused on enhancing registration accuracy by using deep learning architectures designed to compute similarities.

➢ *Optical Flow Methods in Image Registration*

Optical Flow Methods are employed to match corresponding pixels between two images, useful in applications like vehicle tracking, motion tracking, and pose recognition. These methods work by comparing pixel displacement between images, which is often a challenge due to variations in lighting, viewing conditions, and occlusions.

Fortun et al. (2015) discussed various image transformation techniques, such as pixel-level displacement, affine transformation, and free-form transformation, used in optical flow analysis. CNNs and classical differential algorithms are commonly employed for this task. FlowNet (Dosovitskiy et al., 2015) and its later iterations, such as FlowNet2 (Ilg et al., 2017), have been proposed to estimate dense pixel displacement by analyzing the correlation between image pairs.

Uzunova et al. (2017) used FlowNet to identify deformations in brain MRI images. Their research demonstrated that CNNs could effectively register images by focusing on contours and shapes, showing significant promise in medical image registration. These advances in deep learning and optical flow aim to improve the accuracy and efficiency of image alignment, particularly in large datasets like KITTI and Middlebury.

➢ *Feature-Based Methods (FBM) in Medical Imaging*

Feature-Based Methods (FBM) are widely used for image registration, especially in applications like brain MRI. These methods involve extracting distinctive features such as edges, blobs, and corners, which are then matched across images to estimate a transformation. Common feature extraction algorithms include SIFT, SURF, and ORB.

Mizotin et al. (2013) applied feature-based methods to early-stage Alzheimer's diagnosis by using SIFT features in medical images. This approach improved accuracy in detecting abnormalities by considering early imaging data and integrating additional classification steps.

In the context of image registration, FBMs typically use similarity measures like L1-NORM, L2-NORM, or cosine correlation to match features, followed by transformation estimation using methods like RANSAC.

➢ *Stereo Matching and Remote Sensing*

In stereo vision applications, deep neural networks (CNNs) are increasingly used for 3D modeling, robotic vision, and tracking. These networks use Siamese architectures to compute the similarity between image patches and match corresponding features across different viewpoints. Luo et al. (2016) and others have worked on improving stereo matching by incorporating fine-grained approaches that reduce registration times and enhance accuracy.

Researchers have also extended stereo matching techniques to work with LIDAR and 3D point clouds (Elbaz et al., 2017), with autoencoders and deep learning models providing improvements in registration accuracy. These advancements make stereo vision systems more efficient and applicable in real-time environments.

IV. IMAGE SEGMENTATION

➢ *Threshold-Based-Segmentation Methods*

Threshold-based-segmentation involves dividing an image into distinct regions based on predefined intensity values, which can be either hard or soft thresholds. This approach works best when there is a significant contrast between different regions in the image. However, it struggles with low-contrast images as it becomes sensitive to noise and intensity variations, leading to scattered, disconnected regions. Researchers have explored different variations of thresholding, often combining it with other techniques to enhance segmentation accuracy.

For instance, Evelin et al. (2013) used thresholding to classify brain tissues such as white matter, gray matter, and cerebrospinal fluid (CSF) in MRI scans. By employing a single fixed threshold, the method split the image into two classes. While thresholding is not ideal for segmenting multi-channel images, it proves effective for detecting tumor regions. Aja-Fernandez et al. (2010) proposed an automated soft computing approach, comparing it to hard thresholding, k-means, Fuzzy C-Means (FCM), and traditional thresholding. They concluded that soft computing was more efficient and fully automated, offering a robust alternative to manual threshold selection, especially in noisy images like ultrasound and radiographic scans.

➢ *Region Growing*

In region growing, segmentation begins with a seed pixel (or group of pixels) and expands to neighboring pixels that share similar intensity characteristics. The process continues until no more pixels meet the intensity criteria for inclusion in the region. This method works best for segmenting regions with homogeneous intensity but can be less effective when intensity variations are minimal. A significant drawback is the manual selection of the seed point.

Deng et al. (2010) addressed the challenge of seed-point selection by considering variances and gradients along boundary curves in their region-growing method. This approach was successful in creating segmented images useful for detecting tumors and other abnormalities in brain MRIs. Zabir et al. (2015) applied region-growing combined with level set analysis to detect gliomas (malignant tumors) in MRI images. In a similar vein, Xiang et al. (2002) developed a hybrid 3D segmentation method, combining fuzzy region growing, mathematical morphology, and the Sobel 3D edge detector to segment white matter and the entire brain. The results demonstrated that hybrid models outperform individual algorithms in 3D segmentation, offering greater robustness and accuracy. Alia et al. (2010) used Fuzzy C-Means clustering to segment brain regions affected by sclerosis lesions, proving the method's ability to automatically identify the number of clusters for MRI scans.

➢ *Morphological Segmentation*

Morphological operators are often used for detecting structures in images, such as tumors, by emphasizing the shape and structure of regions. These operators can be combined with other methods for more effective segmentation results. For example, Roger et al. (2001) and Zhang et al. (2002) used morphological operators to detect brain tumors in MRI images. Nandi (2002) combined these operators with thresholding and watershed algorithms to enhance tumor detection. The combination proved more effective than clustering algorithms like k-means for tumor segmentation. Additionally, Roger Hult (2001) used grey-level morphology to segment the cortex in MRI slices, helping classify tumors as benign or malignant. A histogram-based approach was employed to identify threshold values for separating brain tissue from surrounding body regions, with binary and morphological operators providing effective segmentation.

➢ *Cluster-Based Segmentation*

Cluster-based segmentation groups pixels into clusters based on shared intensity or probability values, without prior knowledge of the image content. k-means and FCM clustering methods are commonly used to detect brain tumors. Combining clustering with other techniques often enhances segmentation accuracy.

For example, Qurat-ul et al. (2010) developed a system using naive Bayes classification to identify tumor regions and k-means clustering with boundary detection to segment them, achieving a 99% accuracy rate. Agarwal et al. (2015) demonstrated that level-set segmentation combined with bias field-corrected fuzzy c-means outperformed individual techniques in segmenting brain MRIs, offering a method well-suited for tumor detection in developing countries.

In a study by Vinu et al., a multifaceted machine learning approach was used to improve brain tumor segmentation in MRI images. This approach integrated various models such as CNN, SVM, RNN, KNN, and Random Forest. The CNN model achieved the highest accuracy (91.3%), followed by RNN (87.6%), KNN (85.4%), SVM (94.3%), and RF (9.78%). The results highlight the effectiveness of combining multiple machine learning techniques for precise tumor segmentation.

Senthilkumar et al. (2019) developed an algorithm that automatically segments both normal tissues (white matter, gray matter, CSF) and abnormal tissues (tumors) from MR images. The algorithm utilizes a curvelet transformation for noise removal and modified spatial fuzzy c-means (FCM) for tissue segmentation. This approach improves accuracy by incorporating spatial information and smoothing regions to reduce background noise.

Hua et al. (2021) introduced an improved version of Fuzzy C-Means (IMV-FCM), which addresses uncertainty in segmentation tasks. The method adapts clustering by assigning different weights to views based on their contribution to the overall segmentation, overcoming the noise sensitivity issues that often affect traditional FCM.

- *Neural Network-Based Segmentation*

Neural networks, particularly Convolutional Neural Networks (CNNs), have become a key tool in the segmentation of gray matter (GM), white matter (WM), and CSF in brain MRIs. Mahbod et al. (2018) developed an ANN framework that integrates volumetric shape models for brain segmentation. Their method combined intensity-based texture fitting with level-set-based statistical shape fitting, achieving high accuracy in segmenting GM, WM, and CSF. The results demonstrated that this approach is effective for brain tissue segmentation.

McClure et al. (2019) introduced a Bayesian Deep Neural Network (DNN) that can predict structural MRI volume segmentation in a fraction of the time, making it highly efficient. By using spike-and-slab dropout-based variational inference, the method outperformed previous segmentation techniques, particularly in estimating the uncertainty of segmentation predictions, which is crucial for quality control.

Havaei et al. (2017) explored the use of Deep Neural Networks (DNNs) for automatically segmenting glioblastomas (brain tumors) in MRI images. Their CNN-based method incorporated both local and global context for improved segmentation performance, offering a 40-fold speed improvement over conventional CNN architectures. Their work also introduced a cascade architecture, where the output of one CNN served as input for a second CNN, further enhancing tumor segmentation accuracy.

In McCinley et al. (2021), two CNN-based methods were compared for segmenting gray matter and lesions in multi-modal MRI scans. The methods—3D Unet and DeepSCAN—were retrained and tested on a larger dataset. The study found that DeepSCAN provided the most accurate results, particularly when weak anatomical labels were included, making it a powerful tool for lesion detection and anatomical label prediction.

V. FEATURE EXTRACTION AND FEATURE SELECTION

- *Feature Extraction and Segmentation Techniques*

The identification of brain tumors through Magnetic Resonance Imaging (MRI) is a sophisticated process, requiring detailed examination of features such as shape, texture, intensity, and binary patterns. These characteristics are fed into classifiers that categorize tumors based on their distinct traits. However, extracting relevant features from complex brain tissues like white matter, gray matter, and cerebral spinal fluid remains a significant challenge due to their diverse structures.

- *Texture Features Based on Second-Order Gray Level Co-occurrence Matrices (GLCM)*

Texture analysis encompasses not just shape, size, and color, but also pixel intensity variations. A prominent method for extracting texture features in medical images is the Gray Level Co-occurrence Matrix (GLCM), which captures the spatial relationships between pixel intensities.

In a study by Usha et al. (2019), GLCM texture features were extracted from MRI brain images in three distinct phases: 1) Hierarchical Transformation Technique (HTT) for mask selection, 2) texture feature extraction, and 3) classification. HTT utilizes morphological operations, including top-hat and bottom-hat transforms, to enhance the image quality before extracting statistical texture attributes like contrast, correlation, energy, entropy, and homogeneity. The extracted features are subsequently used for classification with Support Vector Machines (SVM). This method was compared against conventional approaches, showing promising results.

Similarly, Kanchana et al. (2017) proposed a method for detecting ischemic stroke lesions using bin-based histogram analysis combined with GLCM. This statistical approach achieved a confidence interval of 95% for distinguishing between affected and unaffected regions, providing a reliable classification.

Rastogi et al. (2020) introduced a deep learning approach using Convolutional Neural Networks (CNNs) to classify brain tumors, emphasizing the role of radiologists in diagnosis. Their CNN model, which utilized multi-branch networks and inception blocks, demonstrated exceptional accuracy (99.30%) when applied to the Br35H dataset, outperforming conventional models like Support Vector Classifiers (SVC) and Decision Trees.

Dastmalchian et al. (2021) incorporated Magnetic Resonance Fingerprinting (MRF) to extract texture features from both gliomas and metastases. Statistical analysis of these features, including rank-sum tests and Kaplan-Meier survival analysis, further refined tumor classification.

In another study, Li et al. (2020) used GLCM features in conjunction with SVM-Recursive Feature Elimination (SVM-RFE) for tumor segmentation. By selecting key features, they achieved a Dice Similarity Coefficient (DSC) of 0.60, indicating a strong segmentation capability.

- *Intensity-Based or First-Order Histogram Features*

First-order histogram features are based on the individual pixel intensities rather than their spatial relationships. These include mean, variance, skewness, and kurtosis, which can help differentiate between tumor and non-tumor regions.

Rehman et al. (2020) explored the use of intensity-based features from FLAIR MRI images to locate brain tumors. By generating texton maps from segmented superpixels and applying Gabor filters for noise removal, their model was able to achieve an 88% Dice overlap score using a Leave-One-Out Cross-Validation (LOOCV) approach. Their findings demonstrate the utility of combining first-order statistical features with advanced segmentation techniques.

Sharma et al. (2019) also explored the use of GLCM and first-order statistics for classifying brain images into normal and abnormal categories. Using Principal Component Analysis (PCA) to reduce dimensionality, they achieved a high classification rate of 95.45% with SVM and 77.27% with K-Nearest Neighbors (KNN).

Carré et al. (2020) evaluated various intensity normalization techniques for MRI images, including Nyul, WhiteStripe, and Z-Score normalization. Their study indicated that normalization could significantly improve classification performance, especially in tumor grading, yielding balanced accuracy scores above 80%.

VI. CLASSIFICATION METHODS

Classification of brain tumors from MRI images can be significantly enhanced by incorporating advanced machine learning techniques, such as Generative Adversarial Networks (GANs) and Convolutional Neural Networks (CNNs).

Frid-Adar et al. (2018) demonstrated that GANs could generate synthetic medical images to augment training datasets, leading to improved classification performance. Their approach, which focused on liver lesions, showed that adding synthetic data increased sensitivity and specificity, improving classification accuracy to 88.4%.

Emami et al. (2018) used GANs and ResNet architectures for generating synthetic CT images (synCT) from T1-weighted MRI data. Their approach, validated through cross-validation, resulted in highly accurate synCT images, contributing to better treatment planning for brain cancer patients.

Hane et al. (2017) proposed a method for generating synthetic CT images (sCT) from MRI data using a deep CNN model. Their approach utilized a 27-layer convolutional network and demonstrated impressive accuracy in comparing sCT with true CT images, furthering the application of CNNs in image synthesis for medical imaging.

Li et al. (2018) developed a u-net-based Fully Convolutional Network (FCN) model to predict MR/CT image transformations. Their model was able to synthesize accurate CT images from MRI data, contributing to more efficient radiation therapy planning.

Li et al. (2019) introduced a cycle-GAN-based method for generating synthetic CT images from MR data. Their approach was validated on 14 patient datasets, achieving highly accurate results with a Mean Absolute Error (MAE) of 60.9 HU, making it suitable for clinical radiation therapy planning.

Gholamiankhah et al. (2021) compared GANs and Residual Networks (ResNets) for generating synthetic CT images from MRI data. Their results showed that ResNets outperformed GANs in terms of CT value accuracy, with a Mean Absolute Error (MAE) of 114.1 HU, compared to the MAE of 147.0 HU from GANs.

Singh et al. (2021) proposed a CNN-LSTM model for detecting tooth decay. Their model achieved a remarkable accuracy of 96%, outperforming traditional CNN models like AlexNet and GoogleNet in classifying dental images.

These advancements in image segmentation, feature extraction, and classification highlight the significant potential of deep learning and advanced statistical methods in improving brain tumor diagnosis and treatment planning. The integration of various techniques, from GLCM texture analysis to generative models like GANs, continues to push the boundaries of medical imaging and radiology.

VII. CONCLUSION

MRI-only radiation therapy planning offers significant advantages by eliminating many of the issues associated with using CT images, such as the need for additional CT scans, repeated dosing, and image validation. However, a major challenge lies in the fact that MRI signal intensities do not correlate directly with the biological tissue attenuation coefficients, making it difficult to generate accurate electron density maps. This discrepancy leads to complications such as increased workloads, ambiguities from inter-modality image registration, and unnecessary patient exposure to radiation. While MRI is the preferred modality, the creation of a pseudo-CT (pCT) from MRI is essential for generating reliable electron density maps and patient reference images. Given the transformative impact of deep learning across various fields, developing a precise and reliable model for generating pCTs from MRI data is crucial to advancing radiation therapy planning.

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