

Brain Tumor Classification Using Deep Learning: A Review

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Abstract

Among the neurological diseases, brain tumors are one of the most dangerous and require an early and accurate localization. It can be achieved through medical image registration and brain tumor classification, which allow performing the precise alignment of multimodal medical images and the right determination of tumor features. This review highlights the state-of-the-art of the latest advances in deep learning image registration and brain tumor classification approaches. The related literature was systematically retrieved through IEEE Xplore, PubMed, ScienceDirect, SpringerLink and Google Scholar from 2018 to 2025 using the following keywords: brain tumor classification, medical image registration, deep learning, convolutional neural network, vision transformer and magnetic resonance imaging. Journal and conference papers relevant to the topic, innovative methodological approaches and the highest performance results were selected for inclusion into the review. The paper provides a review of mono-modal and multi-modal image registration approaches based on MRI, CT, PET, ultrasound and X-ray imaging technologies. In addition, the following deep learning approaches: CNN, FCN, U-Net, GAN, ViT, GNN and hybrid learning algorithms will be discussed. The issues related to benchmark datasets, evaluation criteria, clinical applications and comparison studies are also covered in this review. Moreover, important issues such as lack of annotated data, domain adaptation, computational complexity, explainability, privacy protection and generalizability to different imaging modalities have been emphasized. At the end of this study, new research directions related to foundation models, federated learning, XAI, multimodal transformers and intelligent decision-support systems for clinical decisions have been introduced for precision neuro-oncology.

Keywords: Artificial Intelligence, Brain Tumor Classification, Computer-aided Diagnosis (CAD), Deep Learning, Magnetic Resonance Imaging (MRI), Medical Image Analysis.

Introduction

Brain tumors can be considered one of the most difficult neurological diseases to diagnose and treat due to high rates of morbidity and mortality as well as a considerable influence on the quality of life of patients (1, 2). The early detection and identification of brain tumors are crucial factors in order to provide proper treatment, surgery, prognosis and follow-up care of patients (3, 4). Despite many developments in medical imaging systems and therapies for brain tumors, it is still a highly challenging task due to different appearances, growth patterns and presence of edema, necrosis and contrast enhancement (5, 6). Therefore, the necessity of using intelligent computer-assisted diagnostic systems grows day by day (7). Medical imaging is a crucial element in the diagnosis and monitoring of brain tumors. Different types of medical imaging techniques, like MRI, CT, PET, ultrasound imaging and X-ray imaging, contribute different forms of anatomical and functional data that help the clinicians to

determine the tumor borders, monitor the progression of disease and evaluate treatment results (8, 9). Among the different imaging modalities, MRI is the one that is considered to be a better option for the imaging procedure due to its soft tissue contrast, high resolution capability and ability to produce multiple imaging sequences, such as T1-weighted, T2-weighted, FLAIR, DWI and contrast enhanced images (10, 11). Even though current imaging techniques can produce high-resolution images, they require a lot of time to interpret (12). Image registration and tumor classification are two fundamental components of computer-assisted brain tumor diagnosis. Image registration can be defined as an alignment procedure of images captured from varying views or different imaging modalities at different time instances, which aims to provide spatial correspondence between different anatomical landmarks (13, 14). This procedure is vital for multimodal image fusion, image-guided surgery,

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treatment plan formulation, longitudinal follow-ups and motion compensation (15). Tumor classification means detection of the existence of tumors and classification of their types and grades based on imaging features and is very important in medical decision-making and selecting proper treatment (16). Conventional methods for solving problems of image registration and tumor classification are mostly dependent on manually engineered features, intensity-based similarity measures, optimization processes and conventional machine learning algorithms (17, 18). While these methods have shown promising results in many applications, they have been shown to suffer from heavy feature extraction and computation requirements and need careful parameters selection (19). Also, they are not robust enough in the case of large anatomical deformations and multi-modal images (20). With the advent of deep learning technology, medical image analysis has evolved to the stage where automatic hierarchical learning of features from raw imaging data is possible (21, 22). The use of deep learning techniques has revolutionized medical image registration, segmentation and classification through increased precision and automation. CNNs, FCNs, U-Net, ResNet, DenseNet, GANs, ViTs, GNNs and hybrid models are some of the successful examples of deep learning models that have been used for different medical imaging applications (23–27). Additionally, advances in attention mechanisms, multimodal learning, self-supervised learning, federated learning, foundation models and Explainable Artificial Intelligence (XAI) have contributed even more to the performance of intelligent diagnostic systems (28–31). A number of review studies have examined brain tumor classification and medical image registration independently. The existing review studies have pointed out the efficacy of CNNs, transformers and deformable registration techniques in enhancing diagnostic accuracy (32–34). Nevertheless, most of the previous reviews are concerned with brain tumor classification or image registration in isolation, thereby precluding a thorough examination of their combination in intelligent diagnostic pipelines (35). Furthermore, recent developments related to multimodal transformers, self-supervised learning, federated learning, foundation models and XAI have not been thoroughly analyzed in one single review (36–40).

Although there has been a great deal of advancement, still several issues persist that act as impediments in the wide adoption of deep learning-based algorithms for diagnosis (41–44). Some of these issues include small data sets, class imbalance and inconsistency in the imaging protocol, computational complexity, privacy issues, model interpretability and insufficient external validation (45–48). Hence, this literature review is expected to offer an extensive and state-of-the-art review of deep learning-based approaches for brain tumor classification and medical image registration. This review offers a systematic investigation of the imaging modalities, registration algorithms, segmentation techniques, feature extraction schemes, deep learning models, benchmarking databases, evaluation measures, clinical applications and performance comparison studies. Contrary to earlier surveys, this survey will present a unified framework of not only brain tumor classification and image registration but also recent advancements in multi-modal learning, transformer networks, self-supervised learning, federated learning, foundation models and explainable artificial intelligence. Finally, challenges and limitations faced in addition to possible future directions have been discussed critically for the development of intelligent CAD systems for precision neuro-oncology.

The main contributions of this review are briefly outlined below:

- (a) An extensive introduction to brain tumor imaging, clinical properties and medical image registration.
- (b) A systematic literature review of deep learning algorithms used for brain tumor classification, segmentation and multimodal image registration.
- (c) Benchmark datasets, performance evaluation, publicly available datasets and recent advances in the field.
- (d) Current challenges and limitations associated with the clinical application of advanced AI solutions.
- (e) Recent research directions in the field of Vision Transformers, multimodal foundation models, federated learning, explainable AI and intelligent healthcare systems.

Different from other studies that are either based on image registration or brain tumor classification alone, this paper gives a comprehensive review of

these two areas with the help of deep learning techniques. Moreover, the latest developments such as Vision Transformers, multimodal learning, self-supervised learning, foundation models, explainable AI and federated learning have been discussed in detail.

Despite significant progress, existing studies often focus on either image registration or tumor classification independently. Furthermore, challenges related to limited annotated datasets, model interpretability, domain adaptation and multimodal data integration remain unresolved.

The objective of this review is to provide a comprehensive analysis of deep learning-based image registration and brain tumor classification techniques while identifying current limitations and future research directions.

Brain Tumors: Clinical Overview

Brain tumors are amongst the complex neurologic diseases due to their complexity and the impact that they cause on the neurology of patients. They are caused by uncontrolled proliferation of abnormal cells in the brain or inside the skull. The presentation, prognosis and management of brain tumors vary depending on the cell type and molecular changes. Although there have been significant developments in neuroimaging, neurosurgery, radiation therapy and chemotherapeutic drugs, brain tumors continue to cause high morbidity and mortality rate, indicating the importance of proper diagnosis and treatment of these disorders (2, 4).

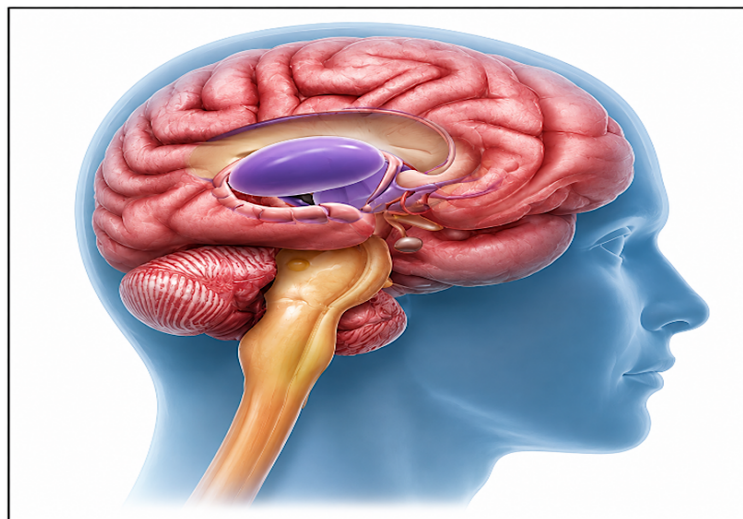


Figure 1: Basic Structure of Human Brain

Brain anatomy is represented in Figure 1. Figure 1 shows the structure of the human brain depicts the different parts that are responsible for various physiological actions within the brain. It is necessary to have a proper knowledge of the brain anatomy in order to understand where tumors occur.

WHO Classification of tumors of the Central Nervous System is a classification system for brain cancers based on the histological features as well as the presence of molecular biomarkers and not simply based on the histological characteristics. IDH mutation, 1p/19q codeletion, ATRX loss, TERT promoter mutation, MGMT promoter methylation and other genomic alterations are some of the molecular features that have been incorporated into the present WHO Classification to achieve greater precision in defining tumors and

treatment. Figure 2 represents WHO Brain Tumor Classification Overview. Clinically, brain tumours can be defined as either being primary or secondary. Brain parenchyma, meninges, cranial nerves, pituitary gland or glial cells and secondary brain tumours are caused by cancer of the lungs, breasts, kidneys, skin (melanoma) and gastrointestinal tract. Primary brain tumours are less common than metastatic tumours; however, they are much more challenging to treat due to their invasive nature and proximity to critical brain regions (6-8). Figure 2 represents the WHO brain tumor classification system that classifies the tumors according to their cell type of origin, histological features and malignancy grade. The WHO brain tumor classification system offers an organized method for diagnosing and managing brain tumor patients.

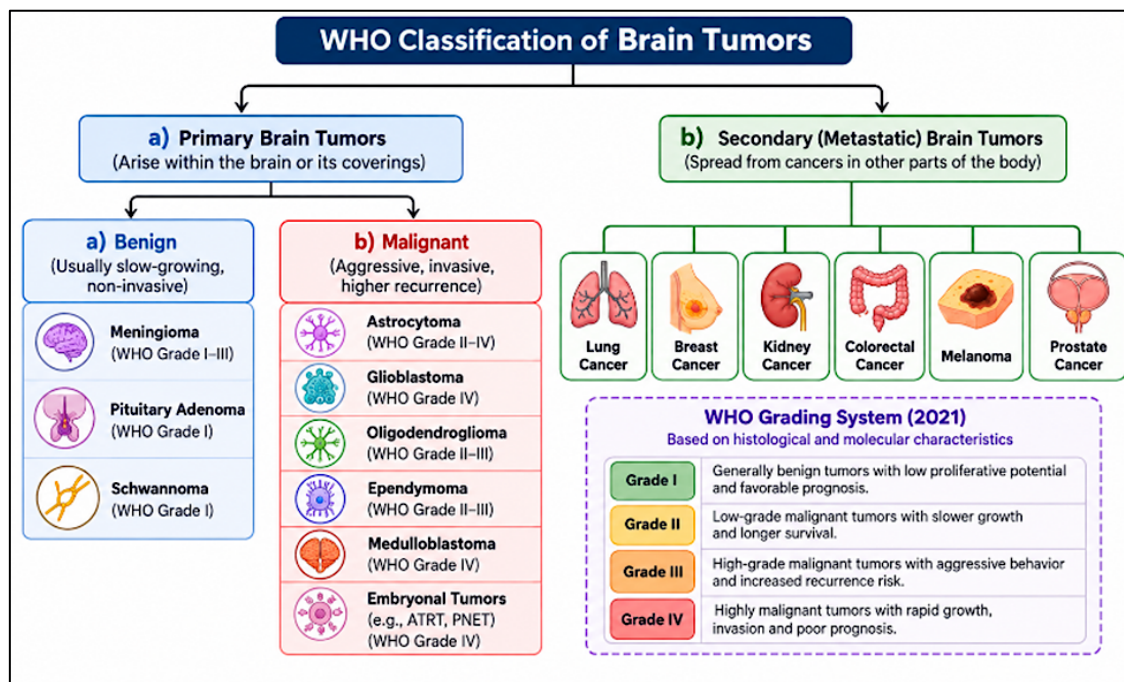


Figure 2: Overview of WHO Classification of Brain Tumors

The most common brain tumors are gliomas, meningiomas, pituitary adenomas, schwannomas and medulloblastomas. Almost all primary malignant brain tumors are gliomas that originate in the neuronal support glial cells. The various forms of gliomas are astrocytomas, oligodendrogliomas, ependymomas and glioblastomas depending upon their cell of origin and genetic characteristics. Glioblastoma (Grade IV WHO) is the most malignant and lethal form of primary brain tumor because of its rapid growth, invasive nature, angiogenesis, necrosis and higher tendency to recur (10-12). Mostly meningiomas are benign cap cell tumors of arachnoid origin but atypical and anaplastic meningiomas are highly aggressive. Medulloblastomas are highly aggressive embryonic brain tumors mostly seen in children, while pituitary adenomas occurring in the sellar region interfere with hormonal functions and vision.

Tumors of the brain are classified as benign or malignant according to their biological behavior.

Although benign tumors have moderate growth, well-defined margins and limited invasion, they can compress adjacent brain areas leading to neurological dysfunction. Malignant tumors grow quickly, invade widely, show increased mitosis and angiogenesis (15, 16). Furthermore, there is increased tendency for recurrence following treatment. WHO classifies brain tumors in four grades (Grades I-IV); the lower the grade, the slower is the growth with better prognosis and the higher the grade, the more aggressive it is with poor outcome. Clinical Classification of Common Brain Tumors is in Table 1. Table 1 presents the clinical classification of common brain tumors, including their origin, pathological characteristics and typical clinical behavior. The table provides a comparative overview of major tumor types, which assists in understanding diagnosis, prognosis, treatment planning and the development of automated classification systems for brain tumor analysis.

Table 1: Clinical Classification of Common Brain Tumors

Tumor Type	Origin	WHO Grade	Biological Nature	Clinical Characteristics
Glioblastoma	Astrocytes	IV	Highly malignant	Rapid growth, necrosis, poor prognosis
Astrocytoma	Astrocytes	II–IV	Variable	Diffuse infiltration, progressive behavior
Oligodendroglioma	Oligodendrocytes	II–III	Malignant	Slow growth, favorable prognosis with 1p/19q codeletion

Meningioma	Meninges	I-III	Mostly benign	Well-circumscribed, compressive growth
Pituitary Adenoma	Pituitary gland	I	Benign	Hormonal dysfunction, visual impairment
Medulloblastoma	Cerebellum	IV	Highly malignant	Predominantly pediatric, rapid dissemination
Schwannoma	Schwann cells	I	Benign	Cranial nerve involvement, slow growth

Note: WHO = World Health Organisation.

Medical Imaging Modalities for Brain Tumor Diagnosis

Tumor detection, characterization, treatment planning and follow-up assessment after treatment rely on medical imaging. Medical imaging has allowed doctors to detect brain anomalies at an early stage using high-resolution in both time and space. Anatomical, physiologic and functional details gained from medical imaging can help decide the tumor location, size, shape, vascularity, metabolic function and heterogeneous nature. MRI, CT, PET, US and X-ray imaging are extensively utilized for neuro-oncological purposes. Each technology has particular imaging, acquisition and diagnostic features. MRI is considered the gold standard of brain tumors assessment due to its high-quality soft-tissue contrast and multiparametric imaging, while CT rapidly shows blood vessel, calcifications and bone structures. US and X-ray imaging are commonly used for intraoperative and supplementary diagnostics, but PET uses a tumor's radiotracer uptake for metabolic and functional details (19, 20).

An appropriate imaging modality depends on the nature of the tumor, its location in the body, availability of imaging, diagnostic objective, time required for acquisition, amount of radiation received and cost. Multimodal imaging is becoming increasingly common in medical practice to utilize different aspects of anatomy and physiology information to enhance diagnostic accuracy, treatment planning, surgical guidance, radiation planning and follow-up disease monitoring. Imaging plays an essential role as the primary source of information for the automated detection of brain tumors through artificial intelligence (AI) and deep learning. These tasks are accomplished through deep learning techniques on multimodal images. Therefore, developing accurate CAD systems requires understanding the characteristics of imaging modalities. Table 2 gives an account of the different types of medical imaging systems which have been applied in the diagnosis of brain tumors. These include MRI, CT, PET, ultrasound imaging and X-ray imaging. This table discusses the imaging features of each of these modalities and their strengths and weaknesses as well.

Table 2: Comparison of Medical Imaging Modalities for Brain Tumor Diagnosis

Imaging Modality	Imaging Principle	Primary Clinical Application	Advantages	Limitations
MRI	Magnetic fields and radiofrequency pulses	Tumor detection, grading, surgical planning	Excellent soft-tissue contrast, no ionizing radiation	Higher cost, longer acquisition time
CT	X-ray attenuation	Emergency diagnosis, hemorrhage, calcification	Fast imaging, widely available	Ionizing radiation, limited soft-tissue contrast
PET	Radiotracer metabolic imaging	Tumor metabolism, recurrence assessment	Functional and metabolic information	High cost, limited spatial resolution
Ultrasound	High-frequency sound waves	Intraoperative navigation	Real-time imaging, portable	Limited penetration through the skull
X-ray	Differential X-ray absorption	Cranial bone assessment	Low cost, rapid acquisition	Poor soft-tissue visualization, limited role in brain tumor diagnosis

Note: MRI = Magnetic Resonance Imaging, CT = Computed Tomography, PET = Positron Emission Tomography, X-ray = X-radiography.

Magnetic Resonance Imaging (MRI)

The reason why Magnetic Resonance Imaging (MRI) is the most commonly used clinical method for diagnosing brain tumors lies in its superb contrast and spatial resolution in addition to being non-invasive. Unlike other imaging techniques such as X-rays and Computed Tomography (CT), MRI does not make use of any ionizing radiation; rather, it relies on a magnetic field, radiofrequency (RF) waves and magnetic resonance to produce a precise picture of the anatomy of the brain. Because of its superb tissue discrimination capabilities, MRI has emerged as the gold standard imaging procedure for diagnosing brain tumors (22-24).

The principle of MRI is based on the visualization of normal brain tissues as well as pathological abnormalities by virtue of their difference in the relaxation characteristics of hydrogen nuclei found in biological tissues. This method allows a

physician to determine such parameters of a tumor as its localization, shape, presence of edema and necrosis, hemorrhage and infiltration into adjacent normal tissues. Additionally, MRI can be used in the planning of surgery and radiotherapy, as well as for the evaluation of therapeutic efficacy and monitoring of brain tumors' patients. There exist several MRI sequences that are usually obtained in clinical studies of the brain (25, 26). The most widely used sequences are the T1-weighted images (T1WI), T2-weighted images (T2WI) and Fluid Attenuated Inversion Recovery (FLAIR) images. Figure 3 indicates the MRI sequences that can be used for detecting brain tumors. Such sequences include T1-weighted images, T2-weighted images and Fluid Attenuated Inversion Recovery (FLAIR). Each of them has unique features and can offer different contrasts for further detection of the tumor margins, edema, necrosis and surrounding anatomy.

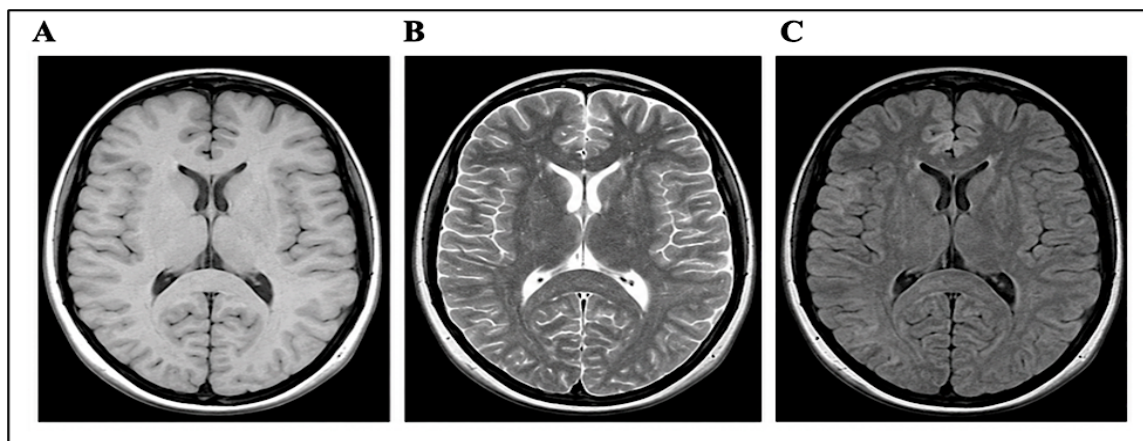


Figure 3: Representative MRI Sequences for Brain Tumor Diagnosis. A) T1-weighted B) T2-weighted and C) FLAIR Images. Images are displayed in pixel co-ordinates (256×256 pixels)

Note: FLAIR = Fluid Attenuated Inversion Recovery.

It is effective for showing normal anatomy due to its excellent anatomic resolution. The tissues containing fat appear hyper intense relative to hypo intense cerebrospinal fluid. The employment of the gadolinium enhancement agents makes tumor borders, the disrupted blood-brain barrier and contrast-enhancing lesions visible in the T1WI images. However, the edema and cerebrospinal fluid appear hyper intense compared to the T2WI image, which shows the amount of tissue water content. Therefore, T2-weighted image is effective for diagnosing peritumoral edema, inflammatory changes, cystic elements and infiltration tumors. The modified T2WI Fluid Attenuated Inversion Recovery (FLAIR) technique reduces the

cerebrospinal fluid signal but maintains the tissue signal intensity. Consequently, FLAIR detects low-grade gliomas, infiltrating tumors, white matter abnormalities and multiple sclerosis lesions adjacent to the ventricles and cortex surface (34, 35).

In essence, the MRI contrast is mainly determined by the following acquisition variables: Repetition Time (TR) and Echo Time. The former refers to the interval between two pulses of the radiofrequency. On the other hand, the latter represents the time interval between the RF pulse and the peak of the echo signal. Figure 4 show the Relationship between Repetition Time (TR) and Echo Time (TE) in MRI Pulse Sequences. Figure 4 shows the

interaction between the repetition time (TR) and the echo time (TE) in the pulse sequence of MRI scans and the effect on the image contrast. There are different combinations of the two that can

result in either a T1-, T2- or proton density-weighted images and therefore, be able to show varying tissue characteristics.

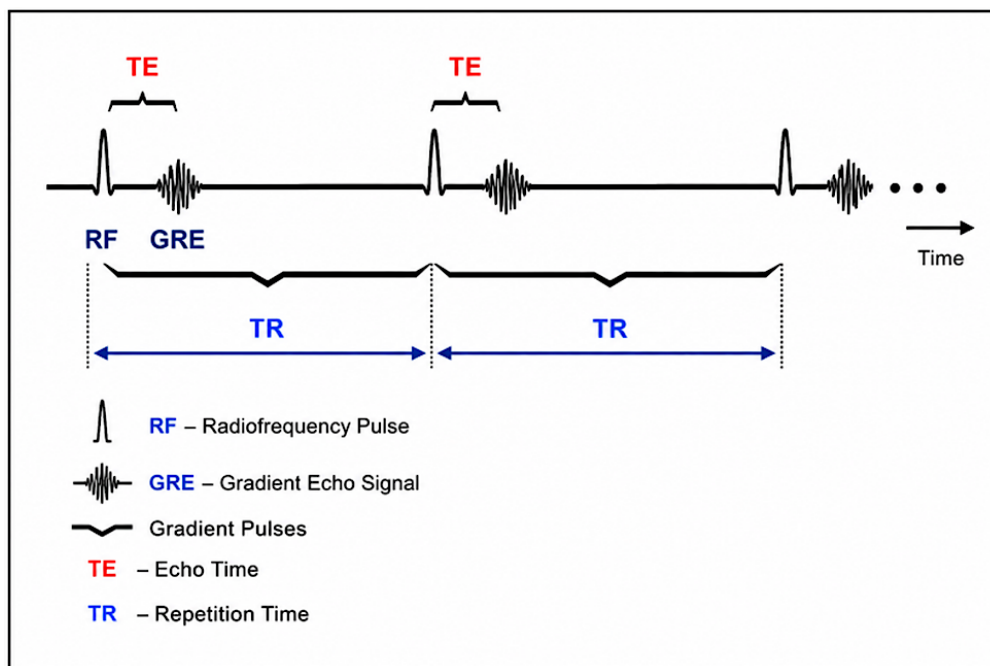


Figure 4: Relationship between Repetition Time (TR) and Echo Time (TE) in MRI Pulse Sequences

Generally, T1-weighted images are obtained using short TR and TE, which results in good anatomical contrast. On the other hand, T2-weighted images are obtained using long TR and TE, which highlight the contrast between water content in the tissues. FLAIR images also use long TR and TE along with an inversion pulse to remove cerebrospinal fluid. The acquisition parameters for commonly used MRI scans are shown in Table 3 below. Table 3 summarizes the typical MRI acquisition

parameters used in brain imaging, including Repetition Time (TR), Echo Time (TE), slice thickness and imaging sequence characteristics. These parameters influence image quality, tissue contrast and diagnostic accuracy. Understanding their selection is important for optimizing brain tumor visualization, segmentation and classification in clinical and research applications.

Table 3: Typical MRI Acquisition Parameters for Brain Imaging

MRI Sequence	TR (ms)	TE (ms)	Clinical Characteristics
T1-weighted	400–800	10–30	Excellent anatomical visualization and contrast-enhanced tumor detection
T2-weighted	2000–6000	80–120	Visualization of edema, cystic regions and fluid-containing tissues
FLAIR	6000–10000	80–140	Suppression of CSF signal and improved lesion visualization

Note: TR = Repetition Time, TE = Echo Time, ms = millisecond, T1-weighted = T1-weighted Magnetic Resonance Imaging Sequence, T2-weighted = T2-weighted Magnetic Resonance Imaging sequence, FLAIR = Fluid-Attenuated Inversion Recovery, CSF = Cerebrospinal Fluid.

There have been many innovative MRI techniques developed in addition to structural MRIs to better characterize brain tumors. DWI evaluates the diffusion properties of water molecules and cell densities, while PWI provides information on the vascularity and angiogenesis of the tumor. Because of its capability to visualize white matter fiber tracts, DTI is very helpful for planning neurosurgical procedures due to the preservation of brain networks. In addition, MRS provides

information about the biochemical aspects of tumor metabolism and is capable of differentiating between recurrence of the tumor and the changes caused by treatment. MRI is the most common modality used for brain tumor analysis using deep learning techniques. The BraTS challenge datasets and other open benchmark datasets consist of multimodal MRI scans including T1, T1CE, T2 and FLAIR images. There are many advantages of MRI technology, but at the same time there are

disadvantages. The process of image acquisition can take time and thus cause patient motion artifacts. MRI machine setup and maintenance are costly, while the type of the scanner, acquisition methods and magnetic field strength will influence the image quality. MRI data sets can differ greatly from each other and therefore it is hard to create universal deep learning algorithms that will be used in different medical institutions. MRI is considered to be the gold standard in diagnosing brain tumors because of its ability to visualize soft tissues (37, 38).

Brain Tumor Detection Methods

Computer-aided detection of brain tumor has become a crucial tool for modern medical image processing technology, allowing automatic diagnosis and improved decision making and treatment planning. Artificial intelligence, machine learning and deep learning have increased the precision and efficiency of brain tumor detection using multimodal medical images to a considerable degree. There are typically four consecutive steps in the brain tumor detection system: image pre-processing, tumor segmentation, feature extraction and classification, shown in the figure below. All these steps contribute towards improving the process of diagnosis through reduction of image artifacts, precise identification of tumors, feature extraction and classification (4,6,8).

Image Pre-processing

The first phase in the process of detecting brain tumor is the pre-processing of images where the objective is to refine image quality before any other processing. The medical images obtained from MRI, CT and PET are usually noisy and are prone to intensity inhomogeneities, motion artifact and unwanted anatomical elements that may hinder the performance of image segmentation and classification tasks. Particularly, MRI images tend to have Rician noise, making tissue borders hard to visualize. Several methods of pre-processing are used to counteract these problems. Such methods include noise removal, bias field removal, intensity normalization, contrast improvement, histogram equalization, skull removal and image registration (18,19).

Brain Tumor Segmentation

Segmentation is among the most important tasks for automated analysis of brain tumors as it seeks to distinguish tumor from normal tissues.

Segmentation ensures that tumor size can be estimated and its growth monitored. The common segmentation methodologies include thresholding, region growing, atlas, watershed, edge detection and K-means, FCM. Optimization techniques such as particle swarm optimization and genetic algorithms have also been used to segment the tumor region. The recent approaches are based on the use of deep learning to learn the spatially complex structure of tumors and segment different parts of tumors, such as edema, necrosis, enhancing tumor and gliomas from multimodal MRI images. The most successful deep learning-based segmentation approaches include FCNs, U-Net, Attention U-Net, Mask R-CNN and DeepLab (20, 22, 25).

Feature Extraction

Feature extraction converts segmented tumor regions into relevant numerical features for automatic tumor classification. In conventional machine learning methods, manually engineered features are extracted that are used to represent the morphological, statistical and textural attributes of tumors. Some of the most commonly used handcrafted features include GLCM, LBP, HOG, Gabor filtering, DWT and shape features. Tumor features include tumor texture, contrast, homogeneity, entropy, energy and shape features (32, 33, 37). Dimensionality reduction is applied to decrease the number of redundant and irrelevant features to simplify computations. Dimensionality reduction is achieved through PCA, LDA and optimization-based feature selection methods. In contrast to traditional methods, deep learning methods extract hierarchical features from medical images automatically. Such architectures as CNN, ResNet, DenseNet, EfficientNet, ViT and capsule networks do not require manual feature engineering.

Brain Tumor Classification

Classification of brain tumors based on the pathological features of brain tumors forms the final step of the detection paradigm. Clinically, the brain tumors can be grouped as benign or malignant tumors. The malignant brain tumors can further be subdivided as glioma, meningioma, pituitary adenoma, medulloblastoma and metastatic tumors. Gliomas can also be classified into grades I to IV as per the World Health Organization (WHO) classification criteria based on histopathology and molecular analysis. Machine

learning classifiers like SVM, RF, DT, KNN, NB and ANNs have been traditionally employed in brain tumor classification. But recent developments in deep learning have considerably improved the diagnostic capabilities of these classifiers using automatic feature learning. State-of-the-art architectures like CNNs, ResNet, DenseNet, EfficientNet, ViTs, Swin Transformers and Hybrid CNN-Transformers have performed excellently in

the case of multiclass brain tumor classification with multimodal MRI data sets like BraTS, TCGA and Figshare (4, 16, 18). These networks do not only improve the classification performance but also offer robustness, scalability and generalizability for clinical imaging data sets. Figure 5 shows the General Pipeline for Deep Learning-Based Brain Tumor Detection.

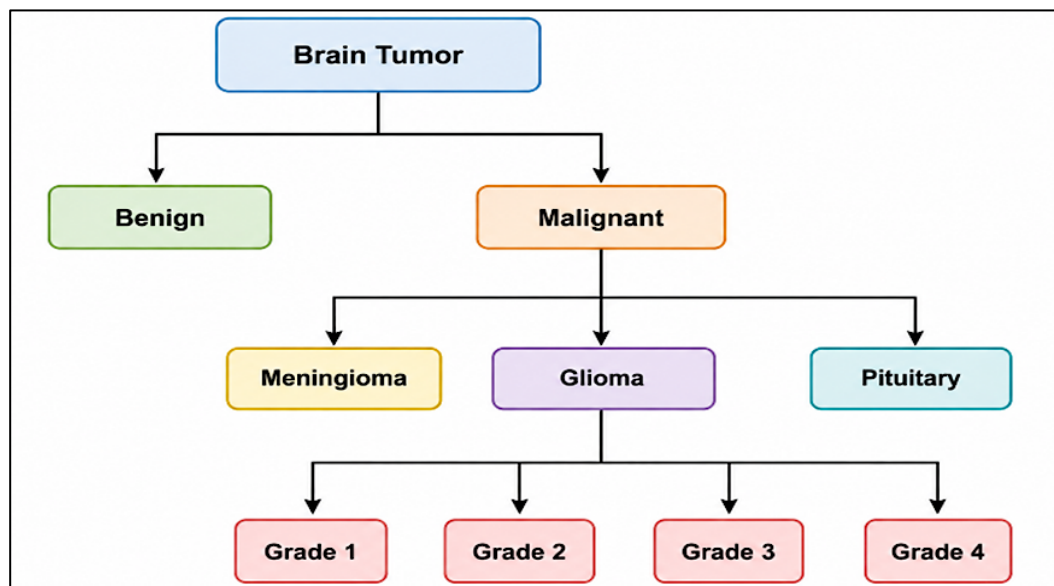


Figure 5: General Pipeline for Deep Learning-Based Brain Tumor Detection

Figure 5 shows the process of brain tumor detection using deep learning models. This process involves the following stages: acquiring medical images, preprocessing the acquired images, segmenting these images, extracting the features and then classifying them. This pipeline shows how deep learning models can automatically detect discriminative features of brain images. This model can be used in development of intelligent computer aided systems for brain tumor analysis.

Discussion

CADD systems for brain tumor classification and medical picture registration have improved greatly due to deep learning improvements. Diagnostic accuracy, computational efficiency and clinical application have been improved via convolutional neural networks, transformer-based architectures, segmentation models and image registration frameworks. Following are current studies' key contributions to this study topic.

MRI scans of the brain were employed to automatically detect and classify gliomas using a convolutional neural network framework. The

model learns the hierarchical structure of the images directly from the MRI scans and improves the performance of traditional feature extraction approaches on classification accuracy, thereby exhibiting the potential of deep learning in detecting brain tumors (1). To improve the detection of brain tumors, multiple MRI sequences have been combined in a multimodal deep learning-based decision support system. Complementing imaging information results in greater classification accuracy and robustness for brain tumors, indicating the therapeutic benefits of multimodal learning (2).

A lightweight deep super-resolution network has been proposed to create high-resolution medical images from low-resolution images. High-resolution images help in improving feature representation and visual appearance of images, thus becoming more suitable for tumor segmentation, classification and medical image registration (3). An extensive survey has investigated the topic of medical image diagnosis using machine learning and deep learning techniques. The paper analyzed neural network

architectures, feature learning techniques and clinical applications of artificial intelligence (4). The convolutional neural network and the highly advanced classification algorithm were used for the development of the hybrid deep learning model for chest X-ray disease diagnosis. Initially designed for pulmonary disease detection, the hybrid architecture model proved to be promising in medical image classification and brain tumor study (5).

Biomechanically constrained deep learning was proposed for the deformable MR-TRUS image registration. The proposed registration approach enhanced the multimodal image alignment for treatment purposes through applying biomechanical constraints on estimating deformation and anatomy correspondences (6). The hybrid affine-deformable neural network model for 3D brain MRI registration was offered. The combination of the methods improved registration accuracy, computing complexity and anatomical consistency of brain MRI images (7). LungRegNet is an unsupervised deep learning model for four-dimensional CT image deformable registration. It has demonstrated unsupervised learning of complex medical image registration through learning spatial transformations from the images without the manual labeling of the deformation field (8). The unsupervised joint learning model was employed in the development of a multiscale convolutional neural network for the deformable image registration in the lungs. The hierarchical model combined both the anatomical features globally and the local deformation patterns and enhanced the robustness of the model under enormous non-linear deformations in the tissues (9). The application of deep learning for image registration with spatial gradients and noisy segmentation labeling increased the registration accuracy. The method involved weakly-supervised and less reliance on highly-annotated data and thus it was acceptable in practical applications with little ground truth labels (10). Evaluation was done for breast cancer screening and detection through artificial neural networks. The deep learning techniques can be applied to several aspects of medical imaging, from the neural network architectures, feature extraction processes and classifiers (11).

A novel hybrid deep learning model that integrated image segmentation and deformable registration

was proposed for optimization purposes. There was improvement in the anatomical consistency, segmentation accuracy and registration errors during medical imaging (12). The semi-supervised DeepAtlas system taught medical picture registration and segmentation from minimal labeled data. The suggested strategy optimised feature representation, anatomical alignment and segmentation while decreasing the need for huge annotated medical datasets (13). VoxelMorph developed an end-to-end convolutional neural network system for deformable medical picture registration. One of the most prominent deep learning-based registration frameworks, the network immediately predicted dense deformation fields instead of iterative optimization, decreasing computing time and retaining good registration accuracy (14). Smooth and topology-preserving deformation fields between medical pictures were estimated using an unsupervised probabilistic diffeomorphic registration approach. Deformable medical image registration became more robust and reliable once the probabilistic framework quantified registration uncertainty and ensured anatomically reasonable transformations (15).

We created an unsupervised three-dimensional end-to-end medical image registration framework using a volume tweening network to predict dense deformation fields from volumetric medical pictures. High registration accuracy and low computing time were achieved using unsupervised deep learning for large-scale deformable picture registration (16). A poorly supervised convolutional neural network was presented for multimodal medical picture registration with minimal anatomical annotations. This approach learnt cross-modal correspondences across imaging modalities, boosting alignment accuracy and minimizing dependency on fully annotated training datasets (17). A thorough study examined magnetic resonance imaging-based brain tumor segmentation methods utilizing conventional and deep learning. Critical analysis of thresholding, clustering, atlas-based, optimization, convolutional neural network and U-Net designs showed the shift from conventional segmentation to fully automated deep learning models (18). Multimodal brain tumor segmentation approaches utilizing BraTS benchmarking dataset were covered extensively in the literature. The study

considered state-of-the-art deep learning approaches, performance metrics and clinical applications, emphasizing the growing importance of multi-modality MRI in brain tumor segmentation (19). A thorough evaluation was done of the brain MRI convolutional neural network architectures for tumor identification, segmentation, classification and disease diagnosis. Transfer learning, feature learning and optimization approaches were discussed, in addition to future research directions in intelligent medical image analysis (20). This comprehensive analysis assessed the role of deep learning in medical image processing and its application in clinical settings. This research revealed that convolutional, recurrent, autoencoder, generative adversarial and fully convolutional networks influence medical picture classification, segmentation, detection and registration (21). The latest studies analyzed deep learning approaches to brain MRI segmentation and the advantages of fully convolutional networks, U-Net modifications and encoder-decoder architectures. The limitations associated with annotated data sets, computational difficulties and clinical implementation of deep learning models were identified as well (22).

Deep learning techniques are actively employed in the healthcare field for disease detection, medical imaging, genomics and clinical decision support systems based on a comprehensive review. The research emphasized the ways in which AI changes diagnosis accuracy, process automation and personalized medicine (23). A systematic analysis assessed convolutional neural network architecture, detection algorithms and feature extraction approaches for general object detection through deep learning techniques. While being related to computer vision, many of these models have been successfully adapted for medical image classification, localization and lesion detection (24). Using deep learning models, an AI system made predictions regarding the spread of illness and resource usage in the healthcare sector (25). Artificial intelligence approaches for data-driven medical diagnosis were covered, including machine learning, deep learning, medical image analysis and clinical decision support systems. The research stressed the need of intelligent healthcare technology for illness detection, prognosis and treatment planning (26).

The recent study analyzed transformer-based medical image processing from CNNs to Vision Transformers. Self-attention mechanisms, transformer architectures, multimodal learning models and their application to image classification, segmentation and medical image registration were investigated, together with future research directions (27). Vision Transformers and U-Net were integrated to produce TransUNet – a transformer-based encoder-decoder model for biomedical image segmentation. The novel architecture enhanced image segmentation performance on multiple medical image databases utilizing the benefits of both global context learning and local feature extraction (28). Vision Transformers for medical image processing were comprehensively evaluated against the state-of-the-art CNNs. Currently, the challenges include computational overhead and limited availability of training data, but it was found that vision transformers exhibit better global feature learning capabilities, long-term dependencies modeling and generalization capabilities (29). The comprehensive review evaluated explainable AI techniques for deep learning-based medical image analysis. It was found that visualization techniques, attention mechanism, saliency maps, Grad-CAM, SHAP and interpretable learning frameworks boost model interpretability and clinician trust (30). The applications of convolutional neural networks, recurrent neural networks, autoencoders and generative adversarial networks in a clinical setting have been discussed to evaluate the progress of deep learning in medical image processing. Deep learning increases the picture recognition, segmentation, registration and disease detection capabilities and lays the foundation for modern computer-aided medical imaging systems (31).

In-depth investigation has been done about the design of deep convolutional neural networks for brain MRI analysis. Deep learning techniques have surpassed the traditional manual techniques for tumor detection, segmentation, classification and grading (32). The rapid evolution of brain MRI segmentation techniques with the help of deep learning techniques has been observed. According to a recent study, the issues of dataset availability, computation and complexity and generalization of the model in clinical practice have been the

important issues (33). Deep learning has been studied in medical imaging, disease diagnosis, clinical decision-making, drug discovery and personalized medicine in a comprehensive manner. Data-driven AI technologies improve the diagnostic accuracy and health care efficiency (34). The study evaluated multimodal brain tumor segmentation using benchmark MRI data sets. A comparison between different deep learning models, assessment measures and segmentation approaches revealed that multimodal MRI employing convolutional neural networks is superior to delineate the tumor borders and segmentation accuracy (35). Brain tumor segmentation techniques were investigated using traditional image processing and deep learning. Convolutional neural networks, encoder-decoder models and automatic segmentation techniques received positive remarks, while clinical application and variability of data sets were considered to be limiting factors (36).

An extensive evaluation of thresholding, region growing, clustering, atlas based and deformable MR image-based brain tumor segmentation techniques was conducted. The study concluded that conventional segmentation techniques are not able to deal with complex tumor morphology (37). Complete research has been done on segmentation of tumors from MRI images involving preprocessing, feature extraction, segmentation and classification approaches. Research proved that numerous stages of image processing improve clinical identification and diagnosis of tumors. Complete textbook has been written on artificial neural networks, convolutional neural networks, optimization techniques, regularization techniques, representation learning and probabilistic models giving the foundation of deep learning. These concepts are the basis of current applications of deep learning in medical imaging and computer-aided diagnoses (38). Deep Learning has transformed computer vision, speech recognition, natural language processing and medical image analysis, a landmark report says. The research proves that hierarchical feature learning beats traditional machine learning in prediction accuracy speeding up the intelligent healthcare applications.

Biomedical image segmentation uses fully convolutional encoder-decoder U-Net. The proposed architecture maintains spatial

information and achieves high segmentation accuracy through skip connection in encoder and decoder path (39). The concept of deep residual learning architecture was formulated to address problems related to deterioration of extremely deep neural networks. Improvement of gradient propagation through residual connections contributed to faster convergence and classification of the neural network. ResNet is among the best backbone networks used in the field of medical image classification, feature extraction and transfer learning. Inter-layer connections in a densely connected convolutional neural network architecture enhance reusability of features in the network. DenseNet proposed here reduced the number of trainable parameters, enhanced feature propagation, computational efficiency and classification accuracy, making it suitable for application in medical image processing tasks where there is limited amount of training data (40). Medical image registration approaches were reviewed in detail, including rigid, affine, deformable, feature-based and intensity-based methods. Transformation models, similarity measures, interpolation strategies and optimization techniques were discussed to identify the strengths and weaknesses of conventional registration approaches and provide a solid theoretical foundation for modern deep learning-based registration frameworks. VoxelMorph, an end-to-end deformable image registration method, replaces iterative optimization with convolutional neural network-based deformation field prediction. The technique lowered registration time and maintained good anatomical alignment accuracy, making it one of the most prominent deep learning models for medical image registration (41). A semi-supervised learning system called DeepAtlas improved picture registration and segmentation in one deep learning architecture. Simultaneous learning enhanced feature representation, anatomical consistency and segmentation accuracy without huge annotated medical datasets. Deep learning-based deformation initialization was presented for quick groupwise registration of diverse medical picture populations. The approach improved computational efficiency and registration accuracy by giving correct starting deformation estimates, accelerating convergence of standard registration methods (42). SVF-Net, a shape-driven registration

network, uses stationary velocity field estimates for deformable medical image registration. The design provided smooth deformation fields while conserving anatomical topology, proving resilient to complicated nonlinear deformations (43). Quicksilver used input photos to estimate deformation parameters for rapid deformable image registration using predictive deep learning. Compared to optimization-based techniques, the strategy lowered computing time and maintained fMRI registration accuracy. A reinforcement learning-based multimodal image registration framework optimises picture alignment via sequential decision-making. The technique increase-ed multimodal medical picture registration resilience by learning optimum transformation rules instead of similarity optimization (44).

A dilated fully convolutional network was presented for multi-agent two- and three-dimensional medical picture registration. The design collected multiscale contextual information and improved transformation estimates, proving dilated convolutions useful for complicated registration challenges (45). No manual labeling was needed for non-rigid picture registration using a self-supervised fully convolutional neural network. The approach learnt deformation mappings using image similarity measurements, proving that self-supervised learning can accurately register medical images without

annotation. An adversarial similarity network assessed picture alignment quality in deep learning-based registration systems. Using adversarial learning in similarity estimation improved deformation accuracy and multimodal image registration under demanding imaging settings (46). Sparse anatomical labeling were used to propose a poorly supervised convolutional neural network for multimodal medical picture registration. Learning cross-modal correspondences across imaging modalities while minimizing the need for highly annotated datasets improved clinical applicability (47). An intra-modality similarity-supervised deep learning-based inter-modality picture registration framework improved multimodal image alignment. The proposed approach used structural similarity between anatomical regions to estimate accurate deformation fields, outperforming conventional multimodal registration methods and emphasizing the importance of deep learning in intelligent medical image registration (48). Deep Learning Solutions and Whole Tumor Dice Score from 2012 to 2020 indicated in Figure 6. Figure 6 shows the evolution of deep learning methods in relation to brain tumor analysis along with the Whole Tumor Dice Score obtained from 2012 to 2020. It is clear from Figure 6 that there has been steady progress over the years, which can be attributed to the effectiveness of advanced deep learning architectures and optimization methods.

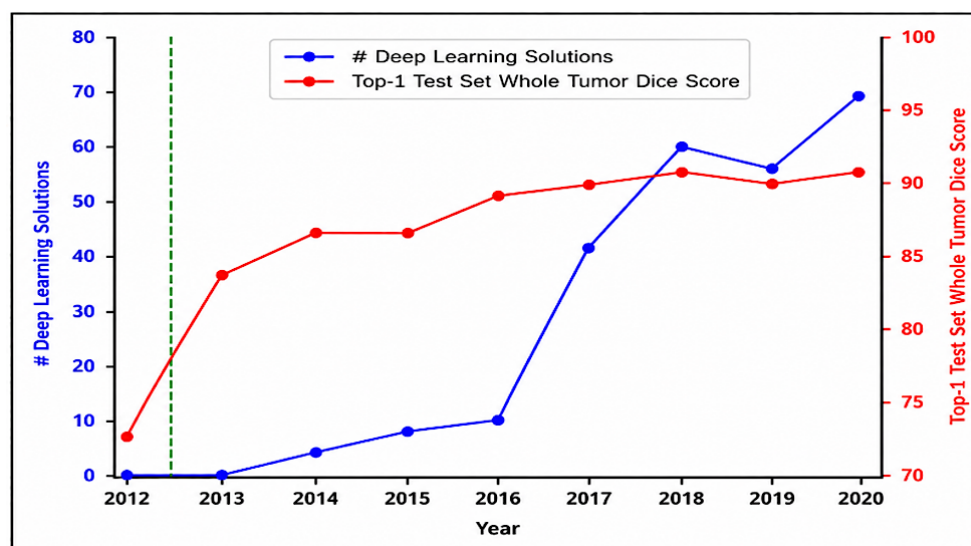


Figure 6: Deep Learning Solutions and Whole Tumor Dice Score from 2012 to 2020

Figure 7 illustrates the representative images of brain tumors that are collected using four different modalities of Magnetic Resonance Imaging (MRI):

T1-weighted (T1), T1-contrast enhanced (T1ce), T2-weighted (T2) and Fluid Attenuated Inversion Recovery (FLAIR). Multimodal MRI Images give

complementary information about the brain tumor structures, contrast enhancement, edema and their surroundings. On the right side of the figure, the ground truth segmentation maps are illustrated in which different regions of the brain tumor are annotated manually by clinicians. In the ground truth segmentation maps, the red region indicates Necrotic and Non-Enhancing Tumor Core (NCR/NET), the yellow region shows Peritumoral Edema (ED) and the green region represents GD-Enhancing Tumor (ET), while the black region indicates the background of the brain. Figure 8 shows some typical brain MRIs from the Brain

Tumor Segmentation (BraTS) data set. The images show various forms of brain tumors taken from various patients and viewpoints. It is a collection of multimodal MRI images that are frequently utilized for brain tumor detection, classification, segmentation and image registration studies. The images shown have diverse sizes, shapes, locations and intensities of the tumors, emphasizing the difficulty of automating brain tumor analysis. The BraTS data set is a gold standard benchmark to evaluate the performance of deep learning models in neuro-oncology and computer-aided diagnosis.

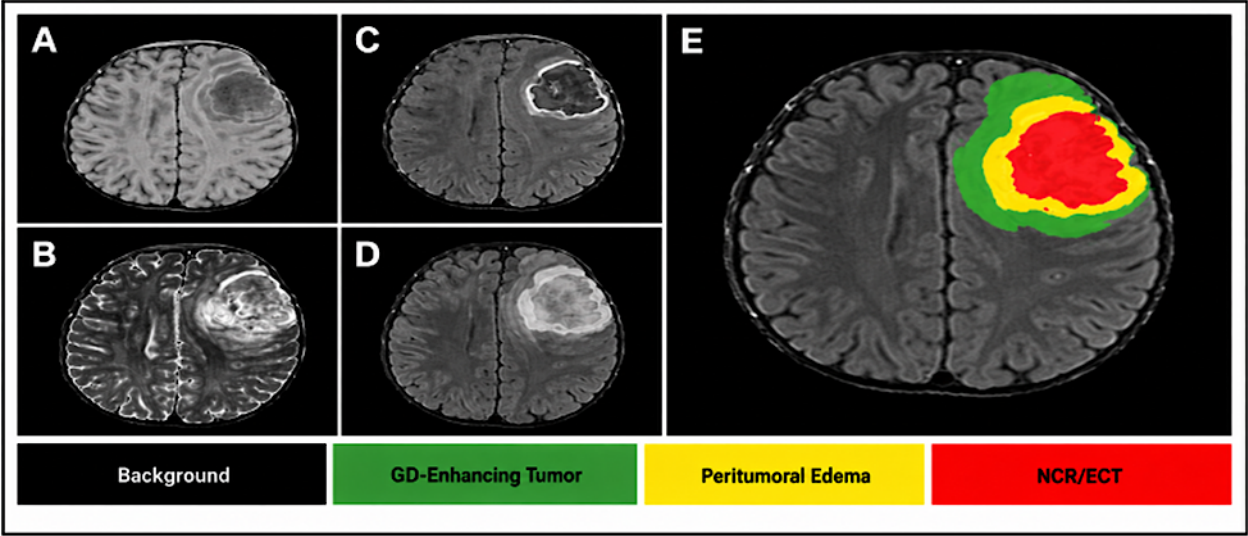


Figure 7: Ground fact segmentation map for different MRI modalities. A) T1, B) T2, C) T1ce, D) FLAIR, E) Ground Truth. Images are displayed in pixel co-ordinates (256×256 pixels)

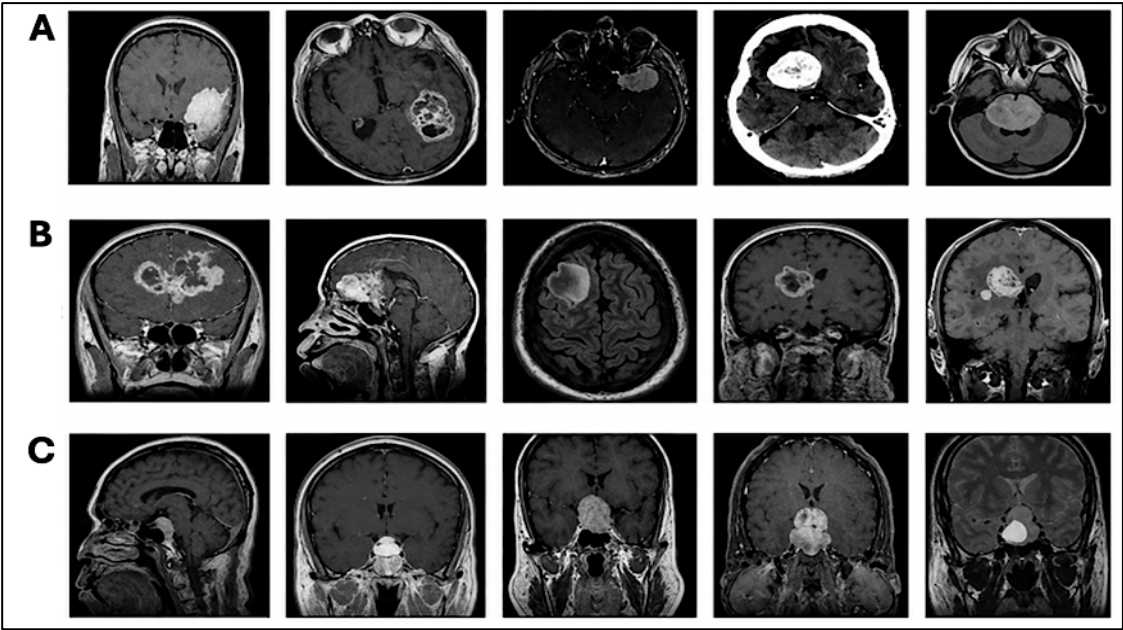


Figure 8: BraTS dataset sample brain MR images. A) Benign, B) Malignant, C) Pituitary. Images are displayed in pixel co-ordinates (256×256 pixels)

Table 4 contains the Comparative Analysis of Existing Deep Learning-Based Brain Tumor Classification and Medical Image Registration Studies. Table 4 is a comparative analysis of the literature review done on existing research work based on deep learning algorithms that have been

conducted on brain tumor classification and medical image registration. This comparative study comprises various aspects such as datasets, deep learning techniques used, evaluation metrics, major findings and performance results.

Table 4: Comparative Analysis of Existing Deep Learning-Based Brain Tumor Classification and Medical Image Registration Studies

Deep Learning Technique	Medical Imaging Modality	Application	Dataset	Strengths	Limitations	References
CNN	MRI	Glioma Classification	MRI Dataset	High classification accuracy, automatic feature extraction	Limited generalization	(1)
Multimodal Deep Learning	MRI	Brain Tumor Classification	Multimodal MRI	Improved robustness using multimodal fusion	Higher computational complexity	(2)
Super-Resolution CNN	Medical Images	Image Enhancement	Multiple	Improved image quality	Not specifically designed for tumor analysis	(3)
Deep Point Cloud Matching	MR-TRUS	Image Registration	Prostate MRI	Accurate non-rigid registration	Limited to prostate imaging	(6)
Joint Affine + Deformable CNN	MRI	Brain Registration	Brain MRI	Simultaneous global and local alignment	High GPU requirement	(7)
LungRegNet	4D CT	Deformable Registration	Lung CT	Fully unsupervised learning	Application limited to lung CT	(8)
Multi-scale CNN	CT	Deformable Registration	Lung CT	Robust multiscale registration	Not validated on MRI	(9)
CNN + Spatial Gradient	MRI	Registration	Brain MRI	Works with noisy labels	Moderate computational cost	(10)
Hybrid DL	MRI	Segmentation + Registration	MRI	Joint optimization improves accuracy	Complex architecture	(12)
DeepAtlas	MRI	Registration + Segmentation	Brain MRI	Semi-supervised learning	Requires partial annotations	(13)
VoxelMorph	MRI	Deformable Registration	Brain MRI	Extremely fast registration	Registration accuracy depends on training data	(14)
Probabilistic Diffeomorphic CNN	MRI	Registration	MRI	Topology-preserving deformation	Computationally intensive	(15)
Weakly Supervised CNN	MRI/CT	Multimodal Registration	Medical Images	Reduced annotation requirement	Lower accuracy than supervised learning	(17)
Survey	MRI	Brain Segmentation	Multiple	Comprehensive review	No quantitative comparison	(18)
Survey	MRI	Brain Segmentation	BraTS	Benchmark comparison	Limited registration discussion	(19)
Review	MRI	Brain Analysis	MRI	Covers CNN applications	Older transformer	(20)

Survey	Multiple	Medical Image Analysis	Multiple	Landmark DL survey	methods excluded Does not include recent transformers	(21)
Review	MRI	Brain Segmentation	MRI	Clinical perspective	Earlier CNN architectures only	(22)
Vision Transformer	MRI	Medical Image Analysis	Multiple	Global feature learning	Requires large datasets	(27)
TransUNet	MRI	Segmentation	BraTS	CNN + Transformer hybrid	High computational complexity	(28)
Vision Transformer Review	MRI	Medical Image Analysis	Multiple	Excellent review of ViTs	Limited clinical validation	(29)
Explainable AI	Multiple	Medical Imaging	Multiple	Improves model interpretability	Still limited in real-world deployment	(30)

Note: MRI = Magnetic Resonance Imaging, AI = Artificial Intelligence, ViTs = Vision Transformers, CT = Computed Tomography, 4D = Four-dimensional.

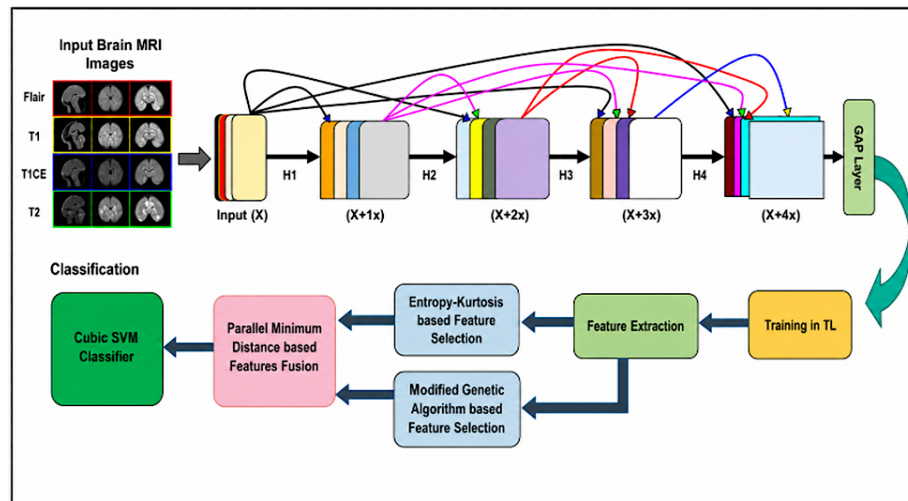


Figure 9: Deep learning (DL) based Multimodal Brain Tumor Classification

Note: DenseNet201 = Densely Connected Convolutional Network-201, TL = Transfer Learning, SVM = Support Vector Machine, MRI = Magnetic Resonance Imaging, T1CE = T1-weighted Contrast Enhanced, FLAIR = Fluid-Attenuated Inversion Recovery

Figure 9 presents a framework for multimodal brain tumor classification using deep learning architecture. Several MRI modes such as T1, T1CE, T2 and FLAIR are input into the deep feature extraction neural network based on the DenseNet201 architecture. Features obtained from feature extraction process are subjected to feature selection and fusion and then classification is performed using Cubic SVM Classifier. Figure 10 indicates the DenseNet201 architecture for image classification. The network employs densely connected convolutional blocks to enable efficient

feature reuse, enhanced feature propagation and improved classification accuracy while reducing the number of trainable parameters. Figure 11 describes the Fine-tuned DenseNet201 deep learning model for multimodal brain tumor classification. The model processes BRATS MRI modalities (T1, T1CE, T2 and FLAIR) through a DenseNet201 feature extraction network, followed by feature selection, feature fusion and Cubic SVM classification to improve brain tumor detection and classification performance.

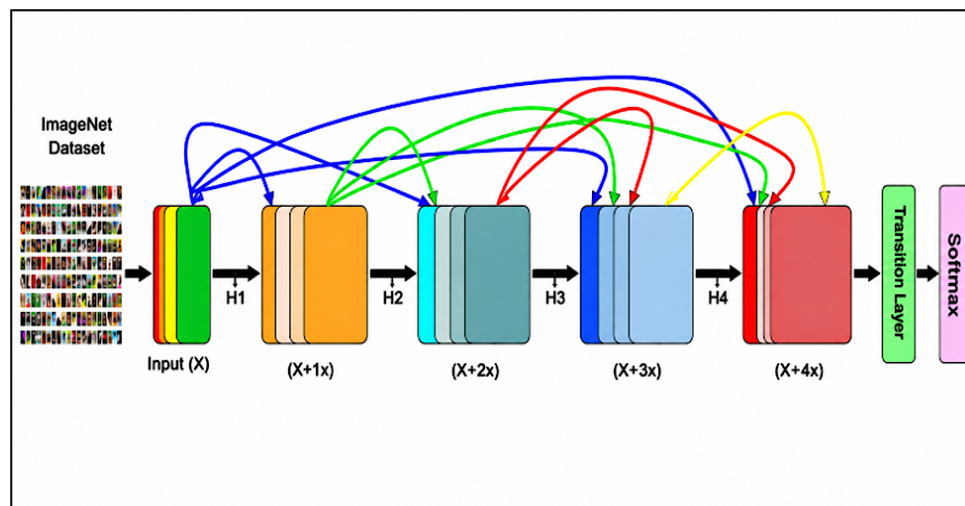


Figure 10: DenseNet 201 Architecture for Image Classification

Note: BN = Batch Normalization, ReLU = Rectified Linear Unit, Conv = Convolution Layer; Softmax = Softmax Classifier. X, X+1x, X+2x, X+3x and X+4x denote successive feature extraction stages within DenseNet201.

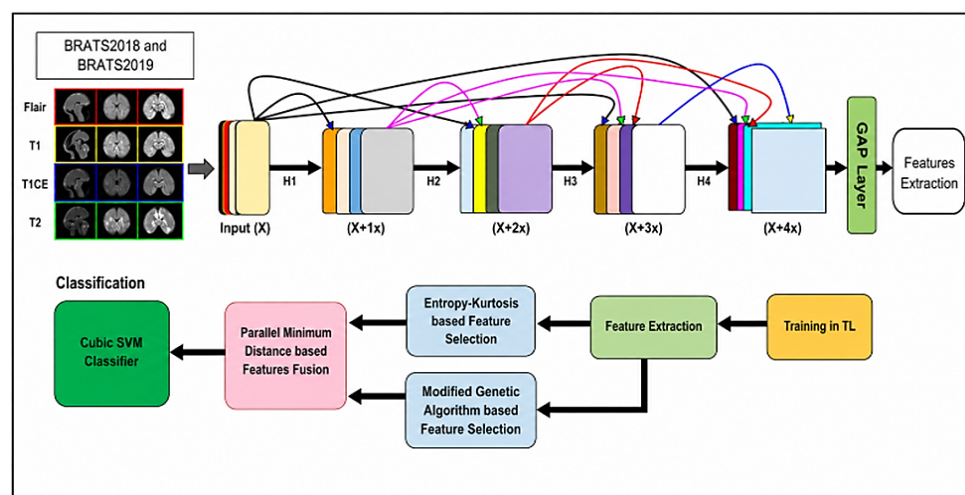


Figure 11: Fine-tuned DenseNet201 deep learning model

Note: BRATS = Brain Tumor Segmentation Challenge dataset, T1 = T1-weighted Magnetic Resonance Imaging, T1CE = T1-weighted Contrast-Enhanced Magnetic Resonance Imaging, T2 = T2-weighted Magnetic Resonance Imaging, FLAIR = Fluid-Attenuated Inversion Recovery, H1-H4 = Hidden feature extraction blocks/layers, GAP = Global Average Pooling, TL = Transfer Learning, SVM = Support Vector Machine.

Comparative Analysis of Existing Deep Learning Approaches

Feature learning and end-to-end optimization of automated systems have been used to revolutionize brain tumor classification and medical image registration through deep learning. Some of the CNN architectures that have enhanced classification and image registration accuracy include CNNs, U-Net, ResNet, DenseNet, ViT, GANs, VoxelMorph, DeepAtlas and hybrid CNN-Transformer architectures. Even though advancements in image recognition technology have been made through these networks, each network has advantages and disadvantages relative to the dataset, computation complexity,

need for annotation and application in medicine. The most common classification brain tumor architectures are the CNN architectures because they are automated to learn features hierarchically in pictures from MRI images. Densely connected architecture and residual learning enhance feature propagation, network convergence and classification accuracy. Transformer-based models have recently gained attention since the self-attention mechanism represents the long-range spatial dependencies that convolutional neural networks cannot. Models such as TransUNet improve segmentation and classification tasks through the combination of feature extraction capabilities of CNNs and the global context modeling capabilities of the transformer network.

The iterative approach to optimize has been replaced by deep learning models to perform medical image registration. VoxelMorph, BIRNet, DeepAtlas and SVF-Net models estimate the deformation field directly which results in better efficiency and precision in registration. Tables 5 describe the Comparative Analysis of Representative Deep Learning Architectures. Table 5 compares representative deep learning models

that are utilized in brain tumor recognition and medical image registration. The comparison includes the design aspects, learning capacity, pros, cons and application in medical imaging of these models. The comparison allows one to understand which models can be applied in certain diagnostic procedures and to select suitable architecture for further investigations and practice.

Table 5: Comparative Analysis of Representative Deep Learning Architectures

Architecture	Primary Application	Advantages	Limitations
CNN	Classification	Automatic feature extraction	Limited global context
ResNet	Classification	Mitigates vanishing gradients	High computational cost
DenseNet	Classification	Efficient feature reuse	Increased memory usage
U-Net	Segmentation	Accurate localization	Requires extensive labeled data
Attention U-Net	Segmentation	Improved boundary detection	Higher computational complexity
Vision Transformer	Classification and Segmentation	Captures long-range dependencies	Requires large-scale datasets
TransUNet	Segmentation	Combines local and global features	Computationally intensive
GAN	Image synthesis and augmentation	Data augmentation	Difficult training
VoxelMorph	Registration	Fast deformable registration	Reduced interpretability

Note: CNN = Convolutional Neural Network, ResNet = Residual Neural Network, DenseNet = Densely Connected Convolutional Network, U-Net = U-shaped Convolutional Neural Network, Attention U-Net = Attention-based U-Net Architecture, ViT = Vision Transformer, TransUNet = Transformer-based U-Net Architecture, GAN = Generative Adversarial Network.

Benchmark Datasets

Benchmark datasets which are made publicly accessible have proven to be quite essential in the research on deep learning for brain tumor classification and registration of medical images. Benchmark datasets offer a platform for fair comparison of various algorithms in a standardized manner while encouraging reproducible research. In all benchmark datasets, the one which is widely used for testing segmentation, classification and registration algorithms is the Brain Tumor Segmentation (BraTS) challenge. The BraTS dataset includes multimodal MRI sequences comprising T1, enhanced T1 (T1CE), T2 and FLAIR images as well

as expert annotations for segmentation of tumor, tumor core and whole tumor. Other publicly accessible datasets such as TCIA, REMBRANDT, Figshare, IXI, LPBA40, OASIS and TCGA have been widely used for diagnosing brain tumors and deformable image registration. Commonly Used Benchmark Datasets shown in Table 6. Table 6 highlights the benchmarking data sets which are widely used for brain tumor classification, segmentation and medical image registration studies. The information provided in the table includes the characteristics of the data set, modality, number of patients and application. These publicly available data sets have an important role to play in the development of deep learning algorithms.

Table 6: Commonly Used Benchmark Datasets

Dataset	Modality	Application	Availability
BraTS	MRI	Segmentation, Classification	Public
TCIA	MRI, CT	Classification	Public
Figshare	MRI	Brain Tumor Classification	Public
REMBRANDT	MRI	Glioma Analysis	Public
IXI	MRI	Registration	Public
LPBA40	MRI	Brain Registration	Public
OASIS	MRI	Brain Anatomy	Public
TCGA	MRI	Cancer Genomics	Public

Note: BraTS = Brain Tumor Segmentation Challenge, MRI = Magnetic Resonance Imaging, TCIA = The Cancer Imaging Archive, CT = Computed Tomography, REMBRANDT = Repository for Molecular Brain Neoplasia Data, IXI = Information eXtraction from Images

Dataset, LPBA40 = LONI Probabilistic Brain Atlas 40 Dataset, OASIS = Open Access Series of Imaging Studies, TCGA = The Cancer Genome Atlas.

Evaluation Metrics

The efficiency of deep learning models can be quantitatively judged by several performance measures. Accuracy, Precision, Recall, Sensitivity, Specificity, F1-Score and Area under the Receiver Operating Characteristic curve are the most common performance measures for classification algorithms. Performance measures used for evaluating segmentation tasks include Dices similarity coefficient, Intersection over Union and Hausdorff distance. Performance measures for deformable image registration include Target Registration Error, Mean Squared Error,

Normalized Cross Correlation, Structural Similarity Index and Peak Signal to Noise Ratio. Common Evaluation Metrics shown in Table 7. Table 7 shows some of the evaluation criteria that are commonly applied to evaluate the performance of brain tumor classification, segmentation and medical image registration models. Evaluation criteria include accuracy, precision, recall, F1-score, Dice Similarity Coefficient (DSC), Jaccard Index, sensitivity, specificity and registration errors. These evaluation criteria form the basis of comparison of different deep learning algorithms and their effectiveness.

Table 7: Common Evaluation Metrics

Metric	Application	Objective
Accuracy	Classification	Overall correctness
Precision	Classification	Positive predictive value
Recall	Classification	Detection sensitivity
F1-score	Classification	Precision-Recall balance
Dice Score	Segmentation	Region overlap
IoU	Segmentation	Segmentation accuracy
Hausdorff Distance	Segmentation	Boundary similarity
TRE	Registration	Registration error
NCC	Registration	Image similarity
SSIM	Registration	Structural similarity

Note: IoU = Intersection over Union, TRE = Target Registration Error, NCC = Normalized Cross-Correlation, SSIM = Structural Similarity Index Measure.

Current Research Challenges

Despite improvements in brain tumor analysis brought about by deep learning techniques, there are many research problems that hinder its extensive use in the clinical field. The problem of lack of large annotated data sets is attributed to the cost involved in acquiring such datasets. In addition, class imbalance, imaging artifacts, scanner variability and heterogeneity of acquisition protocol decrease the generalization capacity of the model across different clinical institutions. The use of deep learning models entails large computing power, which poses a challenge for real-time implementation. Moreover, most of the state-of-the-art deep learning models function as black boxes. Data protection laws also hinder the collaboration of different parties using the same dataset because of the issue of sharing data.

Based on the comparative analysis, CNN-based models continue to be quite useful in feature extraction, but Vision Transformers and the

combination of both of these approaches outperform others in terms of their ability to extract information from both local and global levels of images. The same applies to VoxelMorph and DeepAtlas when it comes to deformable image registration, where computation is less complex.

Future Research Directions

Future works need to be directed toward the development of foundation models that can learn the universal representation of medical images using different imaging modalities and clinical applications. It is anticipated that Transformer architecture, multimodal learning, self-supervised representation learning and federated learning will provide better generalization of the models without compromising the patient's privacy. The integration of Explainable Artificial Intelligence (XAI) methods into diagnostic models is essential to increase transparency and clinical acceptance of AI. LVLMS, digital twins, graph neural network and multimodal foundation models are potential areas for future work in intelligent healthcare systems.

Besides, integration of image registration, segmentation, classification, radiomics and clinical report generation will significantly improve the efficiency of computer-aided diagnosis.

Conclusion

This review gives a complete summary of recent developments in deep learning-based brain tumor classification and medical image registration. It underscores the importance of the latter two concepts for computer-aided diagnosis systems. The review has conducted an extensive investigation of medical imaging techniques, image registration methods, segmentation algorithms, feature extraction approaches, deep learning algorithms, datasets, evaluation measures and applications in the literature. It was found out that the performance of deep learning models, namely CNN, U-net, Resnet, Densenet, GAN, ViT and hybrid architectures, in brain tumor analysis has significantly increased compared to machine learning and image processing methods.

An important contribution of this review lies in combining brain tumor classification and medical image registration into one framework. In contrast to the existing surveys which usually consider either one of the two concepts separately, this review explores the recent progress in multimodal learning, transformers, self-supervised, federated, foundation models and Explainable Artificial Intelligence (XAI). Moreover, it discusses recent methodologies, reveals key challenges of the field and describes emerging trends.

The significance of these developments is quite obvious in clinical practice, as better image registration allows achieving better results when it comes to image fusion and planning treatment and monitoring the progression of diseases, while classification can help detect tumors early and make correct diagnoses and grade and plan treatment accordingly. Thus, the use of deep learning tools can improve the accuracy of diagnostics, relieve the work of radiologists and help achieve better results in precision neuro-oncology.

Despite the impressive progress that has been made in recent years, several drawbacks still exist. There is not enough large and well-annotated data sets for medical images, as well as class imbalance are still an issue. Also, problems associated with domain adaptation, data privacy, high computa-

tional costs, lack of explainability and external clinical validation prevent deep learning models from being widely used in practical medicine.

For future studies, it is important to develop a robust, interpretable and clinically validated diagnostic model framework that can work within heterogeneous medical imaging data sets. Future directions like multimodal transformers, foundation models, self-supervised learning, federated learning, explainable artificial intelligence and integration of end-to-end systems that can perform registration, segmentation, classification, prognosis prediction and clinical decision support will become extremely significant in this context. These trends can be expected to speed up the implementation of deep learning technology into practical use in intelligent health care.

Abbreviations

CNN: Convolutional Neural Network, CT: Computed Tomography, DenseNet: Densely Connected Convolutional Network, DWI: Diffusion-Weighted Imaging, FCN: Fully Convolutional Network, FLAIR: Fluid Attenuated Inversion Recovery, MRI: Magnetic Resonance Imaging, PET: Positron Emission Tomography, ResNet: Residual Neural Network, U-Net: U-Shaped Convolutional Network.

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Author contributions

All authors contribute equally to the research, design the study, analyzed data and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Artificial Intelligence (AI) Assistance

The authors acknowledge the use of generative AI to assist in the paraphrasing of certain parts of the manuscript. All content generated through AI was critically reviewed, edited and verified by the authors to ensure accuracy, originality and compliance with academic standards. The authors take full responsibility for the integrity and validity of the manuscript.

Ethics Approval

This study does not involve human participants, animals, or any biological materials. Therefore, ethical approval was not required for conducting this research work.

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References

1. Saravanan S, Kumar VV, Sarveshwaran V, Indirajithu A, Elangovan D, Allayear SM. Computational and mathematical methods in medicine glioma brain tumor detection and classification using convolutional neural network. *Computational and mathematical methods in medicine*. 2022;2022(1):4380901. doi:10.1155/2022/4380901
2. Sharif MI, Khan MA, Alhussein M, Aurangzeb K, Raza M. A decision support system for multimodal brain tumor classification using deep learning. *Complex & Intelligent Systems*. 2022;8:3007-3020. doi:10.1007/s40747-021-00321-0
3. Esmaeilzahi A, Ahmad MO, Swamy MNS. SRNMSM: A deep light-weight image super resolution network using multi-scale spatial and morphological feature generating residual blocks. *IEEE Transactions on Broadcasting*. 2021;68(1):58-68. doi:10.1109/TBC.2021.3126275
4. Mondal MR, Bharati S, Podder P. Diagnosis of COVID-19 using machine learning and deep learning: a review. *Current Medical Imaging Reviews*. 2021;17(12):1403-1418. doi:10.2174/1573405617666210713113439
5. Bharati S, Podder P, Mondal MR. Hybrid deep learning for detecting lung diseases from X-ray images. *Informatics in Medicine Unlocked*. 2020;20:100391. doi:10.1016/j.imu.2020.100391.
6. Fu Y, Lei Y, Wang T, Patel P, Jani AB, Mao H, Curran WJ, Liu T, Yang X. Biomechanically constrained non-rigid MR-TRUS prostate registration using deep learning based 3D point cloud matching. *Medical image analysis*. 2021;67:101845. doi:10.1016/j.media.2020.101845
7. Buizza G, Paganelli C, Ballati F, Sacco S, Preda L, Iannafi A, Alexander DC, Baroni G, Palombo M. Improving the characterization of meningioma microstructure in proton therapy from conventional apparent diffusion coefficient measurements using Monte Carlo simulations of diffusion MRI. *Medical Physics*. 2021;48(3):1250-1261. doi:10.1002/mp.14689
8. Jones S, Hargrave C, Deegan T, Holt T, Mengersen K. Comparison of statistical machine learning models for rectal protocol compliance in prostate external beam radiation therapy. *Medical Physics*. 2020;47(4):1452-1459. doi:10.1002/mp.14044
9. Jiang Z, Yin FF, Ge Y, Ren L. A multi-scale framework with unsupervised joint training of convolutional neural networks for pulmonary deformable image registration. *Physics in Medicine & Biology*. 2020;65(1):015011. doi:10.1088/1361-6560/ab5da0
10. Avants BB, Epstein CL, Grossman M, Gee JC. Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain. *Medical image analysis*. 2008;12(1):26-41. doi:10.1016/j.media.2007.06.004
11. Zhu Z, Cao Y, Qin C, Rao Y, Lin D, Dou Q, Ni D, Wang Y. Joint affine and deformable three-dimensional networks for brain MRI registration. *Medical Physics*. 2021;48(3):1182-1196. doi:10.1002/mp.14674
12. Fu Y, Lei Y, Wang T, Higgins K, Bradley JD, Curran WJ, Liu T, Yang X. LungRegNet: an unsupervised deformable image registration method for 4D-CT lung. *Medical physics*. 2020;47(4):1763-1774. doi:10.1002/mp.14065
13. Bharati S, Podder P, Mondal RH. Artificial neural network based breast cancer screening: a comprehensive review. *arXiv preprint arXiv:2006.01767*. 2020. doi:10.48550/arXiv.2006.01767
14. Avants B, Gee JC. Geodesic estimation for large deformation anatomical shape averaging and interpolation. *Neuroimage*. 2004;23:S139-50. doi:10.1016/j.neuroimage.2004.07.010
15. Gibson E, Giganti F, Hu Y, Bonmati E, Bandula S, Gurusamy K, Davidson B, Pereira SP, Clarkson MJ, Barratt DC. Automatic multi-organ segmentation on abdominal CT with dense V-networks. *IEEE transactions on medical imaging*. 2018;37(8):1822-1834. doi:10.1109/TMI.2018.2806309
16. Balakrishnan G, Zhao A, Sabuncu MR, Guttag J, Dalca AV. Voxelmorph: a learning framework for deformable medical image registration. *IEEE transactions on medical imaging*. 2019;38(8):1788-800. doi:10.1109/TMI.2019.2897538
17. Dalca AV, Balakrishnan G, Guttag J, Sabuncu MR. Unsupervised learning of probabilistic diffeomor-

- phic registration for images and surfaces. *Medical image analysis*. 2019;57:226-236.
doi:10.1016/j.media.2019.07.006
18. Zhao S, Lau T, Luo J, Chang EI, Xu Y. Unsupervised 3D end-to-end medical image registration with volume tweening network. *IEEE journal of biomedical and health informatics*. 2020;24(5):1394-1404.
doi:10.1109/JBHI.2019.2951024
 19. Hu Y, Modat M, Gibson E, *et al*. Weakly-supervised convolutional neural networks for multimodal image registration. *Medical image analysis*. 2018;49:1-13.
doi:10.1016/j.media.2018.07.002
 20. Hameurlaine M, Moussaoui A. Survey of brain tumor segmentation techniques on magnetic resonance imaging. *Nano Biomedicine and Engineering*. 2019;11(2):178-191.
doi:10.5101/nbe.v11i2.p178-191
 21. Ghaffari M, Sowmya A, Oliver R. Automated brain tumor segmentation using multimodal brain scans: a survey based on models submitted to the BraTS 2012–2018 challenges. *IEEE reviews in biomedical engineering*. 2020;13:156-168.
doi:10.1109/RBME.2019.2946868
 22. Litjens G, Kooi T, Bejnordi BE, *et al*. A survey on deep learning in medical image analysis. *Medical image analysis*. 2017;42:60-88.
doi:10.1016/j.media.2017.07.005
 23. Akkus Z, Galimzianova A, Hoogi A, Rubin DL, Erickson BJ. Deep learning for brain MRI segmentation: state of the art and future directions. *Journal of digital imaging*. 2017;30(4):449-459.
doi:10.1007/s10278-017-9983-4
 24. Esteva A, Robicquet A, Ramsundar B, Kuleshov V, DePristo M, Chou K, Cui C, Corrado G, Thrun S, Dean J. A guide to deep learning in healthcare. *Nature medicine*. 2019;25:24-29.
doi:10.1038/s41591-018-0316-z
 25. Liu L, Ouyang W, Wang X, Fieguth P, Chen J, Liu X, Pietikäinen M. Deep learning for generic object detection: A survey. *International journal of computer vision*. 2020;128(2):261-318.
doi:10.1007/s11263-019-01247-4
 26. Podder P, Khamparia A, Mondal MR, Rahman MA, Bharati S. Forecasting the Spread of COVID-19 and ICU Requirements. *International Journal of Online and Biomedical Engineering (ijOE)*. 2021;17(05):81–99.
doi:10.3991/ijoe.v17i05.20009
 27. Cerrolaza JJ, Reyes M, Summers RM, González-Ballester MÁ, Linguraru MG. Automatic multi-resolution shape modeling of multi-organ structures. *Medical image analysis*. 2015;25(1):11-21.
doi:10.1016/j.media.2015.04.003
 28. Al-Antari MA. Artificial intelligence for medical diagnostics—existing and future AI technology!. *Diagnostics*. 2023;13(4):688.
doi:10.3390/diagnostics13040688
 29. Chen J, Lu Y, Yu Q, Luo X, Adeli E, Wang Y, Lu L, Yuille AL, Zhou Y. Transunet: Transformers make strong encoders for medical image segmentation. *arXiv preprint arXiv:2102.04306*. 2021.
doi:10.48550/arXiv.2102.04306
 30. Nguyen DC, Pham QV, Pathirana PN, Ding M, Seneviratne A, Lin Z, Dobre O, Hwang WJ. Federated learning for smart healthcare: A survey. *ACM Computing Surveys (Csur)*. 2022;55(3):1-37.
doi:10.1145/3501296
 31. Wang J, Wang S, Zhang Y. Deep learning on medical image analysis. *CAAI Transactions on Intelligence Technology*. 2025;10(1):1-35.
doi:10.1049/cit2.12356
 32. Bernal J, Kushibar K, Asfaw DS, Valverde S, Oliver A, Martí R, Lladó X. Deep convolutional neural networks for brain image analysis on magnetic resonance imaging: a review. *Artificial intelligence in medicine*. 2019;95:64-81.
doi:10.1016/j.artmed.2018.08.008
 33. Gordillo-Castillo N, Montseny E, Sobrevilla P. State of the art survey on MRI brain tumor segmentation. *Magnetic resonance imaging*. 2013;31(8):1426-1438.
doi:10.1016/j.mri.2013.05.002
 34. Liu J, Li M, Wang J, Wu F, Liu T, Pan Y. A survey of MRI-based brain tumor segmentation methods. *Tsinghua science and technology*. 2014;19(6):578-595.
doi:10.1109/TST.2014.6961028
 35. Cerrolaza JJ, Villanueva A, Cabeza R. Hierarchical statistical shape models of multiobject anatomical structures: application to brain MRI. *IEEE Transactions on Medical Imaging*. 2012;31(3):713-724.
doi:10.1109/TMI.2011.2175940
 36. LeCun Y, Bengio Y, Hinton G. Deep learning. *nature*. 2015;521(7553):436-444.
doi:10.1038/nature14539
 37. Islam A, Reza SM, Iftekharuddin KM. Multifractal texture estimation for detection and segmentation of brain tumors. *IEEE transactions on biomedical engineering*. 2013;60(11):3204-3215.
doi:10.1109/TBME.2013.2271383
 38. Gatys LA, Ecker AS, Bethge M. A neural algorithm of artistic style. *arXiv*. 2015.
doi:10.48550/arXiv.1508.06576
 39. Gardner JR, Upchurch P, Kusner MJ, Li Y, Weinberger KQ, Bala K, Hopcroft JE. Deep manifold traversal: Changing labels with convolutional features. *arXiv*. 2015.
doi:10.48550/arXiv.1511.06421
 40. Hill DL, Batchelor PG, Holden M, Hawkes DJ. Medical image registration. *Physics in medicine & biology*. 2001;46(3):R1-45.
doi:10.1088/0031-9155/46/3/201
 41. Zitova B, Flusser J. Image registration methods: a survey. *Image and vision computing*. 2003;21(11):977-1000.
doi:10.1016/S0262-8856(03)00137-9
 42. Oliveira FPM, Tavares JMRS. Medical image registration: a review. *Computer methods in biomechanics and biomedical engineering*. 2014;17(2):73-93.
doi:10.1080/10255842.2012.670855
 43. Fan J, Cao X, Yap PT, Shen D. BIRNet: Brain image registration using dual-supervised fully convolutional networks. *Medical image analysis*. 2019;54:193-206.
doi:10.1016/j.media.2019.03.006
 44. De Vos BD, Berendsen FF, Viergever MA, Sokooti H, Staring M, Išgum I. A deep learning framework for unsupervised affine and deformable image registration. *Medical image analysis*. 2019;52:128-43.
doi:10.1016/j.media.2018.11.010

45. Wu G, Qi F, Shen D. Learning-based deformable registration of MR brain images. IEEE transactions on medical imaging. 2006;25(9):1145-1157. doi:10.1109/TMI.2006.879320
46. Christensen GE, Johnson HJ. Consistent image registration. IEEE transactions on medical imaging. 2001;20(7):568-582. doi:10.1109/42.932742
47. Shen D, Davatzikos C. HAMMER: hierarchical attribute matching mechanism for elastic registration. IEEE transactions on medical imaging. 2002;21(11):1421-1439. doi:10.1109/TMI.2002.803111
48. Davatzikos C. Spatial transformation and registration of brain images using elastically deformable models. Computer Vision and Image Understanding. 1997;66(2):207-222. doi:10.1006/cviu.1997.0605

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