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Survey Paper

Unfolding Explainable AI for Brain Tumor Segmentation

Muhammad Hassan [a], Ahmed Ameen Fateh [a], Jieqiong Lin [a], Yijiang Zhuang [a], Guisen Lin [a], Hairui Xiong [a], Zhou You [b], Peiwu Qin [c], Hongwu Zeng [a,*]

[a] Department of Radiology, Shenzhen Children's Hospital, Shenzhen, Guangdong, China
[b] College of Computer Science and Technology, Jilin University, Changchun, Jilin, China
[c] Shenzhen International Graduate School, Tsinghua University, China

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ABSTRACT

Brain tumor segmentation (BTS) has been studied from handcrafted engineered features to conventional machine learning (ML) methods, followed by the cutting-edge deep learning approaches. Each recent approach has attempted to overcome the challenges of previous methods and brought conveniences in efficacy, throughput, computation, explainability, investigation, and interpretability. Recently, deep learning (DL) algorithms show excellent performance regarding diverse fields, including image process, computer vision, health analytics, autonomous vehicles, and natural language processes; however, ultimately impediment in making the artificial intelligence explainable and interpretable to clinicians while dealing with critical health informatics and radiomics. Besides the sophisticated deep learning models for brain tumor segmentation, notorious notions like explainability, investigation, trust, and interpretability of DL raised significant concerns for clinicians in their domains. Among many DL methods, the neuro-symbolic learning (NSL) concept has gained more attention as it can contribute to explainable and interpretable AI. In the current study, we survey the prominent approaches, from handcrafted engineering conventional ML to deep learning algorithms, highlight the challenges in DL algorithms, and propose NSL architectures for BTS. Compared to existing surveys, our study not only outlines handcrafted to DL methods for BTS but also proposed explainable and interpretable pipelines appropriate for clinical practices. Our study can better facilitate novice learners in explainable AI and propose efficient, robust, interpretable DL models to facilitate the diagnosis, prognosis, and treatment of BTS.

1. Introduction

Brain tumor segmentation (BTS) identifies and outlines the regions containing tumor tissues from brain visuals [1–3]. Conventional and recent medical imaging techniques are used to segment brain regions into tissue classes including healthy, necrotic, and malignant (tumor) tissues. The process of BTS is critical for the accurate diagnosis and treatment planning of brain tumors. BTS enables clinical researchers to locate, target, outline, and measure tumor tissues precisely without damaging the surrounded healthy tissues [4]. The segmentation process is essential in numerous clinical applications, including diagnostic support systems, therapy planning assistance, intra-operative treatment, and tumor development monitoring. Intelligent segmentation techniques that speed up brain imaging processing, improve diagnosis results, and make disease follow-up easier by measuring tumor growth generate much interest, as shown by the thriving research environment [5]. A robust, practical, reasonably easy-to-use, and uncomplicated tumor segmentation pipeline is required to be implemented in ordinary clinical operations. This study aims to identify strategies to solve problems with current deep learning (DL) in clinical settings, especially when it comes to dividing up brain tumors. One way to do this is to use neuro-symbolic knowledge (NSL) to make DL more understandable.

Recent studies on tumor segmentation were described, along with their strengths and weaknesses and the use of several algorithms, including shallow ML (ML), region growth, and DL. In previous surveys, various DL modalities have been presented for tumor segmentation from brain magnetic resonance image (MRI) [6]. MRI-based brain tumor segmentation reviews mainly cover either conventional ML methods or recent DL approaches [7,8]. However, the existing surveys must outline BTS via handcrafted features engineering, conventional ML, and DL-based methods [6]. The recent automatic segmentation algorithms

* Corresponding author.
E-mail addresses: mhassandev@gmail.com (M. Hassan), Eng.Ahmed.a.d@outlook.com (A.A. Fateh), jacquielin@126.com (J. Lin), radiomichael2013@gmail.com (Y. Zhuang), gslintom@outlook.com (G. Lin), hairuixiong@126.com (H. Xiong), zyou@jlu.edu.cn (Z. You), pwqin@sz.tsinghua.edu.cn (P. Qin), homerzeng@126.com (H. Zeng).

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use DL methods to achieve state-of-the-art results and can address problems in previous conventional ML methods. DL methods enable efficient processing and objective evaluation of large amounts of MRI-based image data [8]. In the study of [5], conventional supervised and unsupervised segmentation techniques are briefly described. However, a shallow discussion was included in DL for segmentation and classification, and performance has yet to be evaluated. In the study [9], different algorithms based on thresholding, region growing, atlas, DL, and conventional supervised and unsupervised ML-based algorithms have been surveyed for the segmentation and classification of brain tumors. However, the recent algorithms need to be included, and more focus should be given to the distinction between segmentation and classification algorithms. The survey [10] presented DL algorithms for BTS with detailed building blocks; however, the corresponding conventional approaches are absent. Similarly, the studies [9,11] also presented their surveys on DL approaches, but the performance illustration needed to be extrapolated in detail.

Several substantiation reviews have been written on BTS; however, no recommendations for overcoming the limitations were made in the cutting-edge methods, such as DL modalities for BTS solutions [5–9,11,12]. The existing DL-based algorithm has achieved outstanding results. Still, it faces the challenges of interpretability, explainability, investigation, counterfactual, counter-intuitive, complexity, operating ability, justification, sensitivity, being data-driven and dependent, and the need for large datasets. Similarly, DL-based approaches may face the challenges of transferring effective configurations from one dataset to another, especially in 3D biomedical imaging, where dataset characteristics like imaging modality, image size, anisotropic (voxel spacing), and class ratio vary greatly. When modifying and training a neural network, numerous expert choices must be considered, including the precise network design, training schedule, and data augmentation or post-processing techniques. Therefore, the existing review study recalls the existing approaches with their pros and cons and emphasizes how to address the challenges.

In contrast to previous surveys [5–9,11,12], our research covers handcrafted to conventional algorithms and suggests a potential remedy for cutting-edge DL technologies. The following are the key highlights of our study:

- To the best of our understanding, this survey represents the inaugural attempt to incorporate explainable AI (as NSL) into the analysis of brain MRI visuals for the purpose of studying BTS.
- The present study provides an overview of various approaches employed in BTS, including handcrafted, semi-automated, automated, conventional ML, and DL methods.
- This study examines recent DL models utilized in the context of BTS and explores the limitations associated with DL modeling in the domain of critical healthcare.
- The study provides an overview of the strategies for addressing the difficulties encountered in DL modeling through the utilization of NSL.
- Hence, this research presents a range of innovative and comprehensive methodologies rooted in NSL principles for the purpose of BTS, with the aim of supporting radiomics.

To enhance readability, we have partitioned the content of the manuscript into eight sections: Section 1 introduces the contents together with the study objectives. The second section outlines preliminary concepts related to BTS, conventional and recent DL approaches to BTS, and the emerging concepts of combining symbolic and sub-symbolic AI to achieve more efficient, reliable, and reasonable outcomes for BTS. Section 3 outlines the approaches for BTS, from handcrafted algorithms to cutting-edge DL approaches. Section 4 points out the challenges of DL in a wide range of applications, specifically for BTs. Section 5 describes concepts relevant to NSL. Section 6 proposes solutions for BTS and future directions based on NSL. Section 7 discusses challenges in NSL. Finally, Section 8 concludes the achievements in the manuscript.

2. Brain tumor segmentation

2.1. Brain tumor

Gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) tissues are what distinguish normal brain tissues in MRI scan [13]. The unrestrained, abnormal development and division of bodily cells is what is referred to as cancer. A brain tumor occurs when the brain tissue has abnormal cell growth and division. Despite their frequency, brain tumors are among the deadliest malignancies [8]. In the tumorous brain scan, edema, necrosis, and core tumor are frequent findings. Discussion was held about the challenge of isolating the primary tumor from any associated inflammation [14]. The abnormal lump of tissue known as a brain tumor has cells that are proliferating and growing out of control. Clinically, it is challenging to comprehend the manifestation of a brain tumor due to the size variations, localization, pace of growth, and pathology using signal intensities [14]. For instance, two distinct forms of brain tumors could exhibit identical intensity characteristics surrounded by significant edema, which might make diagnosis difficult. Brain tumors can be categorized using a variety of factors. Following the WHO-proposed classification scheme that is more appropriate for radiological usage, brain tumors have been categorized into four levels [15]. In a 3D MRI scan, intensity levels, tumor morphologies, sizes, and positions might differ significantly from patient to patient. Additionally, tumor borders are frequently ambiguous, amorphous, and interrupted, which presents a severe barrier to studying tumor segmentation. Moreover, for each slice of the dataset's images, there may be intensity biases and changes imposed by the MRI machines and acquisition techniques that vary significantly from scan to scan. Such variable aspects highlight the requirement for sophisticated DL tumor segmentation models. Furthermore, in a 3D MRI scan, tumor forms, sizes, and locations might differ significantly from patient to patient. As a result, segmenting tumor sub-regions makes the DL-based models more complicated.

2.2. Segmentation

MRI is widely used in radiation therapy to capture soft tissue contrast. Using these features promotes automatic segmentation to reduce workload in clinical applications. BTS in medical images aids in the care and identification of tumor location, spread level, types, and grades. It eases in the initial diagnosis, prognosis, examination, monitoring, and treatment of the identified tumor lesion. Traditionally, tumor outlining, and sub-region delineation are manually accomplished by radiologists using handcrafted methods. This task requires careful attention and expertise, especially when dealing with a large number of patients, various contrast and multi-parametric images, and diverse tumor types. Computer-aided segmentation strategies can address these challenges by reducing the laborious task of labeling consistent annotations. However, segmentation using cutting-edge technologies needs sufficient annotated and qualitative data to deploy in clinical applications [16]. Various methods are available for tumor segmentation to assist in tumor diagnosis and prognosis [17]. The algorithms are classified as manual, automatic, ML, and DL, based on the nature of examination [18]. Radiologists utilize their anatomical and physiological expertise, acquired through training and experience, to manually segment using multi-modality attributes. The process involves a radiologist examination of multiple slices, identifying and diagnosing a tumor, and carefully outlining it manually. In addition to time-consuming drawbacks, the segmentation of tumors is dependent on radiologists, leading to variability in inter and intra features among different raters [19]. Manual segmentations are used to evaluate semi-automatic and fully automatic methods. User involvement in the semi-automatic method is necessary for obtaining feedback on interaction and initialization in the segmentation process.

Three segmentation techniques are commonly used: instance, semantic, and panoptic [20]. Semantic segmentation is a vital process in scientific research, as it transforms unstructured biomedical image data into organized and meaningful information. Semantic segmentation is essential in various therapeutic applications, such as AI-assisted tumor growth monitoring, intra-operative assistance, treatment planning support, and diagnostic systems [16]. Semantic segmentation is crucial for medical applications, including AI in diagnostic support systems, treatment planning, intra-operative assistance, and tumor development monitoring [5]. Instance segmentation, on the other hand, is a technique that focuses on analyzing and isolating specific objects in an image or video using bounding boxes or segmentation masks. Instance segmentation has not been used for tumor segmentation due to the datasets' characteristics. Panoptic segmentation combines semantic and instance segmentation to comprehensively and consistently record performance for all classes. Panoptic segmentation will greatly improve medical image segmentation in the near future. Panoptic segmentation of cancer cells from medical imaging can assist in locating tumors and diagnosing illnesses. Pathologists use morphological cues of cancerous cells to determine cancer stages. Panoptic segmentation schemes merge object detection, localization, and pixel-level class assignment for regions with overlaps, including the background. Most existing cell segmentation methods are based on semantic or instance cell segmentation. They can exceed state-of-the-art technologies [21].

2.3. Tumor segmentation from brain visuals

The brain's GM, WM, and CF are anatomically organized and can be visualized using MRI. Functional MRI (fMRI) sequences measure deoxyhemoglobin levels over time and are used to identify changes in brain activity in tissues during a behavioral task. Some work in diffusion tensor imaging (DTI) reveals information about water diffusion in the brain. Cell membranes, organelles, and myelin concentrations in WM influences DTI visuals. N-acetyl aspartate is a metabolite that can be measured by magnetic resonance spectroscopy (MRS) to assess brain neuron density and survival. Fetal MRI is a reliable and safe method for studying the embryonic brain [22]. CT, SPECT, PET, MRS, and MRI are common brain visuals as imaging techniques used for brain tumor diagnosis, providing information about shape, size, location, and metabolism [17]. BTS involves identifying, defining, and dividing tumor tissues, including active cells, necrotic core, and edema. Radiologists prefer to use MRI scans and their anatomical and physiological knowledge for segmentation. The procedure involves the radiologist manually outlining tumor areas by carefully reviewing multiple image slices. MRI produces three-dimensional brain image data in axial, sagittal, and coronal views at different depths and contrasts as T1, T1ce, T2, and FLAIR. The magnetic field intensity and sampling techniques influence the image quality, slice thickness, and inter-slice gap. In MRI acquisition, water molecules' protons align with the magnetic field in either parallel (low energy) or anti-parallel (high power) directions where the 3D anatomical visuals of the brain, heart, and other organs are used to diagnose diseases [13,23]. The variation in tissue structure in an MRI scan depends on water content.

3. Manual to DL algorithms and challenges in BTS

ML versions in the forms CNN [3] and GCN [24] can be utilized to identify, segment, and diagnose lesion details from MRI and other medical imaging modalities. Methods fall into manual or handcrafted, semi-automated, fully automatic, conventional ML, and various DL approaches are elaborated in the following subsections.

3.1. Handcrafted feature engineering for BTS

Traditional tumor segmentation techniques like atlas-based might perform better or worse depending on various factors, including image registration, label fusion, atlas generation, and dataset size variations. According to the study [18], there are three types of BTS methods: manual, semi-automated, and fully automatic. Radiologists utilize both the multi-modality data provided by the MR images and their training and experience-gained anatomical and physiological expertise to segment the images manually. The procedure entails the radiologist meticulously manually sketching the tumor areas after carefully looking over several slices of images, detecting and diagnosing the tumor. In addition to the time-consuming process, manual segmentation depends on the radiologist, and the results vary across different raters [19]. Manual segmentations are often utilized to assess the outcomes of fully automated and semi-automated techniques. User interaction is essential for semi-automatic approaches for three primary reasons: initialization, exchange, or feedback. Due to the large number of MRI slices, manually segmenting brain tumors from magnetic resonance (MR) images is a complex, time-consuming, and laborious task. Radiologists must utilize both the multi-modality data given by the MRIs and their training and expertise regarding anatomical and physiological expertise to segment the images manually. Examining several images slice by slice must be carried to diagnose the tumor, and its borders must be carefully manually outlined. The effectiveness of fully automatic and semi-automatic systems has sometimes been assessed using manual evaluation. It takes a lot of effort and time to manually segment brain tumors for malignant detection from an enormous volume of MRI data produced during regular clinical investigations and treatments. Segmenting brain tumor images automatically is necessary. Multiple slices throughout the 3D anatomical view comprise a single person's brain MRI scan. MR images of brain tumors must thus be manually segmented, which is a challenging and time-consuming process. BTS from MRI is vulnerable to both inter- and intra-observable variability.

3.2. Automatic methods

Different automated approaches have been presented in the literature to facilitate radiologists regarding BTS. The classification and segmentation of brain tumors from MRI images have been accomplished using ML with promising classification results. A conventional ML-based brain tumor classification technique often includes preprocessing, segmentation, feature extraction, and classification phases. There are several clinical applications for the automated segmentation of patient morphology from MRI data, including the diagnosis and prognosis of brain tumors. The initial efforts for segmenting brain tumors relied on manually handcrafted engineering together with classic ML techniques like decision forests [25], conditional random fields [1], and atlas-based [26]. The automatic algorithm can be independently applied to each MR modality (such as T1-w, T2-w, and FLAIR), and the final tumor volume is obtained by merging the data. Many brain-labeled MR images from various patients are typically needed to train ML-based BTS. Consequently, it becomes necessary to deal with noise and intensity bias correction. However, in this technique, the user initiates the procedure by choosing a subset of voxels from each tissue type. Variability among annotators continued to be a concern [27]. AI is primarily used to study fully automatic BTS to overcome the segmentation challenge. For BTS, ML classification algorithms typically need MRI images (with known ground truth) from various cases to train and test. Therefore, it becomes necessary to deal with noise and intensity bias correction. However, in the study [27], the user initiates the procedure by choosing a subset of voxels from a single example corresponding to each tissue type. Variability among raters and users continues to be a problem [27]. The majority of recent BTS research use completely automated techniques that integrate AI with prior knowledge to address the challenges in segmentation.

3.3. Conventional ML

Traditional ML methods have some of the most common features, including discrete wavelet transforms, textons, multifractal Brownian motion features, first-order statistical features, raw intensities, local image textures, intensity gradients, and edge-based. These features train different classifiers based on neural networks, support vector machines, AdaBoost, k-nearest neighbor classifiers, self-organizing maps, random forests, and conditional random fields. All of these feature-based approaches can provide helpful segmentation results. Decision forests, atlas-based algorithms, and conditional random fields are standard machine-learning methods that separate brain tumors into different parts. In traditional unsupervised approaches, an image is divided into disparate sections to locate the target region accurately. Region-based segmentation utilizes pixel grouping based on their values, such as the disparity and variability in gray levels, as well as their spatial proximity, such as Euclidean distance and region compactness. The most popular region-growing-based segmentation method for brain tumors is based on clustering algorithms [28]. In segmenting region-growing brain tumors, tissues, including tumorous areas, are divided based on similarity criteria such as homogeneity, texture, sharpness, and gray levels. The region-growing-based segmentation may effectively divide areas into spatially separated regions and regions with comparable features. The similarity criteria and noise sensitivity of the region-growing-based method are essential factors. Consequently, it can result in unconnected areas and a hole in the segmented region. Since tumor regions in the traditional supervised approach are often dispersed across the image, pixel classification techniques outperform conventional segmentation techniques. As a result, the segmentation of a brain tumor from a brain MRI image has been accomplished using conventional supervised ML techniques [29–33]. However, traditional ML techniques like k-means suffer from insufficient tumor region localization, poor initial centroid selection, and sensitivity to outliers. Many ideas have been put forward to solve these issues, such as using histogram-based k-means, k-means combined with other clustering algorithms, adaptive k-means to set up cluster centers that change over time and evolving adaptive k-means (MAKM) [6].

3.4. DL architectures

The popularity of DL techniques, in particular Convolutional Neural Networks (CNNs), among researchers has grown as a result of their recent successes in prediction [34], reconstruction [35], generation [36], and biological image segmentation problems [7,8,37]. CNNs learn salient and complex features from the fed visual and statistical information. DL is an advanced approach for creating sophisticated models and conducting training. It is particularly effective for processing high-dimensional data and accurately representing the 3-D characteristics of biological structures. DL approaches provide solutions for addressing segmentation problems. DL techniques also facilitate the effective processing and impartial assessment of voluminous MRI. Deep neural networks have gradually replaced traditional methods in several disciplines, including computer vision [38], NLP [39], and computational biology [40], thanks to the rising popularity of deep learning made possible by improvements in the computational capability of modern graphic processing units (GPU), the effectiveness of algorithms, and the availability of training data. DL techniques may also facilitate the successful processing and unbiased evaluation of enormous MRI-based image datasets. Deep convolutional neural networks (DCNNs), CNN, RNNs, long short-term memory (LSTM), deep neural networks (DNNs), deep autoencoders (AEs), and generative adversarial networks (GANs) are some of the excellent versions of DL networks.

3.4.1. DL models for BTS

The average brain tissues are typically classified into GM, WM, and CSF in an MRI scan, while the tumor tissues are categorized into core tumor, necrosis, and edema. These tissues often show similar intensity patterns in structural MRI sequences like T1-w, T2-w, and FLAIR [14]. It is challenging to distinguish the signal intensities between the primary tumor and associated inflammation [14]. For instance, two individuals can be identified as having the same tumor based on their intensity level while having distinct forms of brain tumors. The BTS investigations [6,41,42] have taken advantage of the freely accessible contrast-enhanced T1-s MRI imaging of brain tumors, which can be viewed from axial, sagittal, and coronal perspectives. The MRI images must be preprocessed using scaling and normalization methods before training via a neural network. A dataset may require augmentation to fulfill the desired DL of an enormous sample volume to expand the training dataset. The augmentation process may comprise flipping, rotation, and scaling [42]. In the literature, the study [43] ensembles multiple models' architectures to predict brain tumors from MR images using the combination of many 3D convolutional networks like DeepMedic [44,45], FCN [46], and U-Net [47]. To provide additional supervision and regularization, a study paired a 3D U-Net with an additional variational decoder pipeline [48,49]. The study [50] demonstrated strong performance using only minor adjustments to the traditional 3D U-Net by applying specific improvements. They achieved this by employing nnU-Net [50], a self-configuring framework that automatically adapts U-Net over the underlying dataset. A literature study [16] proposes a novel pathway between the current state of mainly data-driven AutoML techniques on the one side and primarily expert-driven method setup in biomedical segmentation on the other.

3.4.2. Varieties in DL modalities for tumor segmentation

The well-known DL modalities that have been utilized for BTS are included as custom CNN [51], HCNN ensemble CRF-RRNN [52], residual Network and Dilated convolution RDM-Net [53], Stack Multi-connection Simple Reducing (SMCSRNet) [54]. Ensemble of a 3D-CNN and U-Net [55], Two-PathGroup-CNN [56], Hybrid Two Track U-Net [57], P-Net with Bounding Box and Image Specific Fine Tuning (BIFSeg) [58], Multiscale CNN (MSCNN) [59], Cascaded 3D U-Nets [60], 3D Center-crop Dense Block [61], 3D FCN [62], DCNN (Dense-MultiOCM 4) [63], U-Net [64], AFPNet 5 + 3D CRF [65], Inception-based U-Net+ up skip connection + cascaded training [66], Tripple intersecting UNets (TIU-Net) [67], LSTM multi-modal UNet [68], nn-Unet [69], extended nnUnet [16]. In addition, various DL approaches have been proposed to segment malignant cells from the brain, with promising results in assisting radiotherapy [70–72]. The benefits of DL over the conventional image segmentation technique include minimal storage costs, high computing efficiency, and a wide field of perception range [73]. Nasopharyngeal carcinoma (NPC) is a malignant tumor whose survivability is greatly improved if early diagnosis and timely treatment are provided. Accurate segmentation of the primary NPC tumors and metastatic lymph nodes (MLNs) is crucial for patient staging and radiotherapy scheduling. Furthermore, GAN, transformer, and capsule neural networks have all been employed in the literature to segment brain tumors [74–76]. For instance, the study utilized the residual cyclic unpaired GAN network architecture based on the residual and reflecting concepts and principles [74]. In the literature, a transformer has been embedded into a 3D CNN to segregate brain tumors and presented a brand-new network called TransBTS that was built on an encoder–decoder structure [75]. The study improved a network called SegCaps, based on the capsule neural network, so it could accurately separate gliomas from MR images. The study [71] proposed a coarse-to-fine approach with fewer parameters in which the coarse mask is priorly predicted, followed by the rectification of pixels towards the tumor segmentation. The 3D U-Net-based designs have shown outstanding performance in biomedical segmentation among all segmentation modalities [69]. The majority of these techniques rely on datasets with complicated relationships. Reoptimizing pipeline parameters for each dataset may be necessary because network settings determined to be optimal for one dataset may not be generalized to another. Therefore, nnU-Net has comprehensively attempted these issues by defining solid design choices and explicitly modeling crucial relationships [69].

3.4.3. Segmentation improvement via prior knowledge embedding

In some earlier experiments, existing or prior knowledge in a blueprint, template, or shape was employed to effectively segment the brain tumor for automated cerebrovascular disease segmentation in brain MR images [77]. The study [78] developed an inference approach by modeling pathologies' intensity, shape, and spatial distribution to capture their anatomical antecedent. A multi-atlas and diffeomorphism-guided 3D fully convolutional network for brain segmentation was suggested and verified. Additionally, investigations using shape have been used as prior knowledge to carry out BTS. To automatically partition the brain, a level set-based context features are retrieved as an additional input for a neural network [79]. A DL-based hippocampal segmentation system that embeds the statistical structure of the hippocampus as context information was suggested successfully [80]. Some research also used parcellation (BP) in their segmentation processes in addition to the template and shape priors. A pre-defined brain atlas was used to get brain BP, and they showed that adding BP as prior to CNN may increase the accuracy of segmenting brain tumors [81] and accuracy of segmenting stroke lesions [82].

Different types of prior knowledge can be incorporated into DL models for tumor segmentation, including shape, texture, tumor locations, regions to which the tumor spreading and growth, templates, atlases, probabilistic shape, geometric representations that can be acquired from biomedical literature, expert annotations, or domain-specific knowledge bases. Prior knowledge can be obtained from various sources of BTS, such as biomedical literature, domain-specific knowledge bases, clinical guidelines, and atlases (location, shape, and appearance of tumors), as well as explicit encoded knowledge such as regularization constraints and probabilistic priors. For example, in the context of brain tumor segmentation, prior knowledge can be derived from radiology reports, clinical guidelines, or atlases that provide information about the location, shape, or appearance of different types of tumors [83–86]. Incorporating prior knowledge into DL models for BTS can be a promising approach for improving segmentation accuracy and reducing sample complexity. However, it requires careful consideration of the potential benefits and drawbacks. Incorporating prior knowledge into the DL-based segmentation models has the advantages of improving segmentation accuracy, enhancing labeling efficiency, reducing sample complexity and search space, overcoming data ambiguity and corruption, and increasing interpretability and explainability. Employing prior knowledge in the labeling task may outweigh potential disadvantages depending on various factors, such as the specific task, the nature of the prior knowledge, the available data, the properties of the model and expected outcomes, and alignment with the goal and objective. The prior knowledge of DL may lead to disadvantages of overfitting, limited generalizability, increased complexity, model misleading and collapse [86], erroneous segmentation [85], and resulting in unrealistic segmentations with missing or disconnected regions [83,84,86].

3.4.4. 3D and 2D ensemble models for BTS

An ensemble model gives a more stable solution with less variation than a single CNN model [87]. The ensemble versions based on 3D and 2D achieved high efficacy in the literature for various tasks [88,89]. The ensemble technique has also been used to separate brain tumors, such as models—CA-CNN, DKFZ Net, and 3D UNet were separately trained and joined the final BTS outcomes for ultimate goal [90]. Another study introduced eight models using a variety of network designs, input channels, and convolutional kernels. The model then combines the probability maps from all eight models and averaging them to achieve the desired segmented results [81]. The literature studies [88,89] performed better than all segmentation tasks.

Moreover, two potential CNN-based modalities exist: 2D slice-based and 3D patch-based. A brain tumor is separately predicted for each slice of a 3D volume partitioned into numerous 2D slices using 2D CNN algorithms [91–93]. For instance, 2D U-Nets have been used to independently treat MRI as slice-by-slice segments to perform BTS with promising results [94]. Furthermore, three multi-class segmentation-based models have been independently trained on axial, coronal, and sagittal slices and employ majority voting to provide the final predictions [95]. Further investigation proposed the incorporation of a pooling-free DenseNet into a UNet framework to create a distinctive DeepSCAN structure. 3D patch-based techniques are more often used in the BTS task compared to 2D slice-based methods because they are able to collect features along the volume dimension [48,81,90,96–99]. A 3D UNet has been presented that performs marginally better than DenseNet underlying TC as training dataset modality [96]. HDC-Net has been proposed [97] that uses convolution in the spatial and channel dimensions. However, it is pretty challenging to outperform a well-trained U-Net, and their publicly available U-Net code outperformed several state-of-the-art approaches on medical segmentation tasks [69].

4. Challenges in DL

After outlining numerous DL models, this section elaborates on the challenges that are faced by the DL architectures while diving into BTS. There are tribulations that DL models confront when mapping the issues into practicals, notwithstanding the tremendous work that DL has done in biomedical imaging, notably in tumor segmentation [69]. Therefore, this section highlights the limitations of DL in terms of BTS interpretation, data curation, task sensitivity, and the need to overcome DL impediments using NSL.

4.1. Challenges in DL regarding tumor segmentation

Since DL models are predominantly data-driven, factors such as inconsistent image contrast, insufficient training samples, and changing image quality may influence the learning process. DL models present several challenges, and one of the most difficult is dealing with parameters and hyperparameters. The choice of target spacing is an essential aspect of 3D segmentation. As the GPU capacity limits the patch size, more significant spacings produce smaller feature maps and cause a loss of detail. In contrast, lower spacings have larger images and prevent the network from acquiring enough contextual information. The limitations across several research directions using DL and motivation for NSL are elaborated on in the following subsections.

Clinically, it is challenging to comprehend the manifestation of a brain tumors owing to the variety in size, localization, rate of development, and pathology. The difficulties in diagnosing brain tumor from an MRI image are mainly brought on by ROI detection and the inadequacy of the descriptive data that may be derived using conventionally manual and handcrafted methods [100]. The enormous density and complicated brain architecture mainly contribute to this inefficiency. DL is based on learning data representations and hierarchical feature training instead of superficial ML methods. When classifying DL-based brain tumors, the DL models identify the qualitative statistics that best characterize various brain malignancies. Due to DL, categorizing brain tumors is now a data-driven issue rather than a challenge based on manually created features [101].

In DL models, the CNN network is often employed in tasks involving diagnosing, classifying, and segmenting brain tumors and has shown significant results [6]. The end-to-end training pipeline nnU-Net has been presented to address the problematic circumstances of configuration and optimization in DL [69]. Without any human interventions, the nnU-Net setup covers the complete segmentation process (including critical topological characteristics of the network architecture). This means that it requires no additional computing resources. The extraction of the dataset fingerprint and subsequent execution of heuristic rules are the first steps in the automated method setting for nnU-Net [16,69]. To avoid the control of DL training and evaluation, the attention mechanism received much attention recently [39]. The field of computer vision research is gradually embracing the self-attention mechanism. However, the computational cost of the attention mechanism rises quadratically with input size, making it hard to fit or train the network in a typical workstation configuration. This is one of the critical challenges when applying self-attention to vision issues. The additional dimension makes This constraint considerably worse when working with 3D data. Nevertheless, the use of axial attention [16] has been proposed as a means of applying attention to data with many dimensions. The computational complexity increases proportionally with the size of the image by independently applying self-attention to each axis. This allows for the incorporation of the attention mechanism even with 3D data, which enables the use of attention in segmentation from 3D visuals.

4.2. Data and task sensitivity in tumor segmentation

Regardless of the current success of DL-based segmentation techniques, these techniques often have confined application to specific image analysis challenges and limited generalizability to other datasets. Similarly, task-specific method design and configuration necessitate a degree of competence and experience since even little mistakes may significantly impact performance. The DL models for brain segmentation from MRI have gained popularity because they provide state-of-the-art results and are more effective at addressing the challenges [7,8] . The massive volumes of MRI-based image data may also be processed effectively and evaluated objectively using DL techniques. Similarly, many DL techniques have been given in the surveys for tumor segmentation from brain MRI [6]. Despite the DL model's successes, it has several drawbacks, including the need for large datasets, being data-driven and dependent, sensitivity, counterfactuality, complexity, operability, counterintuitiveness, investigateability, and explainability. The DL-based methods can be particularly challenging due to the limited transferability of practical configurations between datasets, especially in the context of 3D biomedical imaging and segmentation. This is because dataset properties such as imaging modality, image size, voxel spacing (which may be anisotropic), and class ratio vary significantly. When modifying and training a neural network, many expert decisions need to be taken, such as determining the specific network architecture, training schedule, and selecting data augmentation or post-processing procedures. In addition, when applying AutoML to new datasets, there are special expert choices that need to be employed, such as constructing a suitable search space tailored to the task at hand [69]. Using visual explanations to check the deep model's decision-making process, it is confirmed that a deep model for tumor segmentation must concentrate on the gray cube to identify situations as affirmative [102].

4.3. DL generalization for tumor segmentation

Following the rapid development of DL-based segmentation techniques, it is often difficult for end users to apply them to a particular image analysis challenge. In task-specific learning scenarios, small mistakes lead to an enormous drop in performance and a lack of transferring optimal configurations between datasets with variations in dimensions and features, leading to a lack of generalization. Therefore, a generalized system can be established by employing the NSL pipeline. It seeks to make a model explainable in that specific domain in addition to being generalized to a certain purpose. The terms generalization and NSL should be employed in various ways. In certain datasets, the generalized model nnUNet performed better than typical tumor segmentation methods [16,69]; however, it poorly performs on brain MR images. Performance enhancements based on architectural extensions suggested by the literature may not apply to all datasets in the domain for several reasons. First, the discipline of biomedicine necessitates the acquisition of certain skill sets to effectively handle the diverse range of datasets. The effectiveness of the examined architectural alterations may be overshadowed by the quality of the methodology implemented on a separate dataset [69]. Second, the assessment process in current research practices is limited to a maximum of two datasets, and these datasets often have comparable features. Assessing the multi-dataset investigation is inadequate for developing a universal methodology and inference system. Another drawback is the lack of transparency related to data-driven optimization, or "black box algorithms". Therefore, several DL algorithms for segmenting MRI-based brain tumor images are reviewed [6,8]. However, previous reviews failed to exploit DL shortcomings and solutions to the challenges. Therefore, our survey not only recalls the existing approaches with their pros and cons but also emphasizes how to address the challenges in BTS.

A claimed generalized architecture may face difficulties for unseen abnormal cases in fetal brain MRI segmentation [22]. The generalizing capacity of DL models may only partially overcome the difficulties of DL as black-box learning in practical scenarios. Therefore, the issues, specifically poor adaptation in out-of-distribution (OOD), can lead to serious consequences, such as misclassification or overconfidence in the model's predictions where its detection is indispensable for open-world ML models. Several approaches have addressed this issue, including data augmentation, domain adaptation, and uncertainty estimation [103,104]. However, there is still a research gap in this line of work to improve the robustness and reliability of DL models for handling OOD data to deal with BTS. Thus, NSL is necessary to present a generic pipeline that can not only accommodate a variety of segmentation issues but also produce structures that are rational and understandable to humans. NSL may incorporate existing models, such as the nnUNet technique, at the inferencing and reasoning levels.

4.4. Challenges in training and requirements for tumor segmentation

The DL models may be trained on different datasets by increasing and expanding the capacity of the network. Utilizing mixed-precision training in 3D convolution networks requires a substantial amount of GPU memory, hence reducing the batch size that can be used for training in comparison to 2D convolutional models. Group normalization has been implemented, exhibited impressive performance, and has been found to operate better than batch normalization for the small batch size regime [48]. Although cross-entropy and dice loss are often regarded as standard measurements, it is preferable to consider the assessment and inspection by radiologists. Because gathering and processing 3D medical images is essential, several data augmentation methods are implemented on the fly while training: rotations, scaling, Gaussian noise, Gaussian blur, brightness, contrast, simulation of poor resolution, gamma correction, and mirroring. The model's neural structure and depth should also be considered when selecting the appropriate batch and patch sizes. Batch size often aids in training stabilization by lowering errors from samples with sparse annotated samples. Like this, 3D segmentation uses specified learning with a decay rate and stochastic gradient descent with a Nesterov momentum of 0.99 as the optimizer.

4.5. AI limitations and emergence of NSL

Although AI has several uses in MRI segmentation, its use in clinical trials is hampered by the lack of suitable datasets and ML models. Annotated data from hospitals is often limited, especially for segmentation or detection when the ground truths demand experts' annotations. In rare cases, it is necessary to achieve more of a balance in the distribution

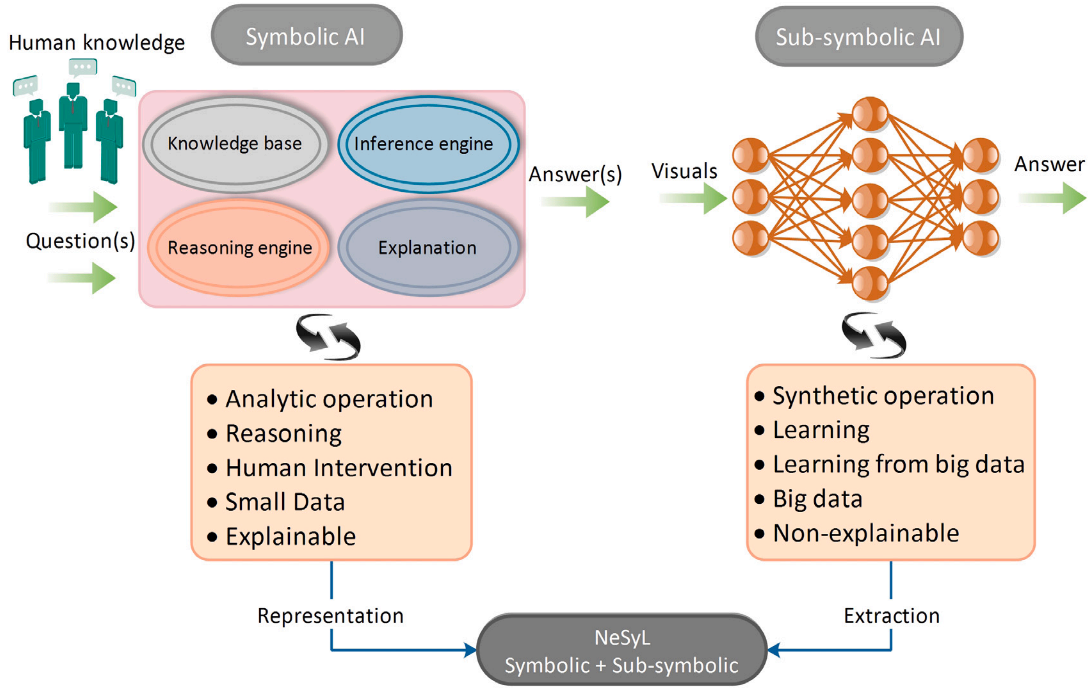

Fig. 1. The general purpose pipeline for symbolic and sub-symbolic (neural network) AI. On the left side, domain experts produce the symbolic knowledge for the symbolic AI unit. However, on the right side, sub-symbolic statistics are utilized. The parallel units utilize symbolic and sub-symbolic knowledge to construct a generic platform for solving clinical problems, specifically BTS. The symbolic AI should have a knowledge-based system, reasoning, and explanation platforms that further transform and translate to a matching learning process. The sub-symbolic unit utilizes expert knowledge in the early stages as symbols and latent space. Therefore, the depicted pipeline can generate a reliable and robust generic NSL-based platform.

and quality of data. Certain datasets have limited generalizability in practical scenarios and demonstrate uniformity across different ethnic groups. Granular distributions in healthcare scenarios are reflected in medical datasets, but even a little imbalance might result in poor performance for the minority labeled class in a deep learning model. Due to its capacity to extract characteristics, DL is the standard method used to perform tumor segmentation. According to [105], the black box representation may provide inferior interpretations, adaption, and reasoning-ability outcomes. This survey discusses the constraints mentioned earlier and presents the core concept of NSL, along with its possible uses in MRI, brain tumor detection, segmentation, classification, diagnosis, and circumventing DNNs' limitations.

5. NSL and relevant concepts

Identifying systemic flaws either in the data or the algorithm may lead to the failure of ML algorithms. The human expert leverages their deep understanding of the field and relevant information to identify systemic deficiencies. A new system has been developed to assist individuals in distinguishing their language abilities from their visual perception. This system utilizes a neuro-symbolic approach to visual question answering (VQA) [106]. Symbolic learning and AI are coupled in the relatively new discipline of NSL. The fundamental comparison of sub-symbolic (Neural Network-NN) or connectionist AI (cAI) and symbolic AI (sAI) systems is shown in Fig. 1. NSLs have increased AI performance and surpassed cutting-edge DL models with superior accuracy in various fields, particularly visual reasoning and medical imaging. Scientists in this domain are fascinated by the mechanisms through which the brain learns and processes information as they seek to create AI-driven systems. This section discusses the essential concepts of NSL and brings attention to significant challenges that need to be addressed in the medical industry. Thus, this section emphasizes the potential opportunities for NSL's expansion into various significant industries, particularly BTS.

5.1. Symbolic versus sub-symbolic AI

The sAI and the sub-symbolic have long been the two major schools of thought: symbolic AI (sAI) and connectionist AI (cAI). Making a mind versus modeling the brain is how described the relationship between sAI and cAI [107]. The formation of a mind (sAI), by human cognitive capabilities, often begins at a higher cognitive level through symbolic manipulation and language processing. On the other hand, the development of neurons and their connections forms the foundation of how the brain (cAI) is built. Additionally, study [108] placed the idea of a binary architecture (System-1 and System-2) to explain the outcomes of processing speed variations in people on various mental tasks. Fig. 1 illustrates the primary differences. A list of the sAI's aliases usually includes old-fashioned AI, rule-based AI, and classic AI [109]. Most AI research from the middle of the 1950s to the 1990s concentrated on sAI, which relies on encoding human knowledge and social conventions into computer algorithms [110]. The sAI takes symbols to be the fundamental building blocks of human intelligence. The cognitive processes of humans also involve a series of explicit assumptions about symbolic representations. The cognitive focus of sAI lies in the analytical activities that involve high-level, decomposable, conscious, and reasoning tasks. Analytical processes involve cognitive abilities and deliberate actions guided by specialized knowledge. Language is a subject that is encompassed by symbolic and propositional knowledge. There are several similarities that have been found between the sAI and analytical procedures, such as sequential decomposability and propositional knowledge. The sAI program interprets and analyzes text that utilizes symbols to represent concepts or objects in the real world. The algorithmic relationship between symbols is determined by how each symbol is structured, which may be accomplished hierarchically or via lists and networks [111].

The sAI system deduces reasoning, logical inference, and specific search algorithms that are designed to address the restrictions of a given model [112]. This system includes an expert system based on human-generated information and often contains if-then statements directing algorithms on what to perform. An inference engine model analyzes the knowledge and understanding and determines the rules appropriate for a particular symbol or collection of symbols. The sAI has been extensively employed in tasks with precise rules and objectives [113,114]. However, the algorithmic complexity of discontinuous reasoning makes such algorithms difficult to use for solving complicated issues and is challenging for nondeterministic polynomial time. The modeling of ambiguous and uncertain knowledge by the sAI is intricate. Alternatively, sAI can be created by individuals using manually programmed algorithms. The cAI encompasses a wide range of neural networks, such as CNN, DNNs, and graph neural networks (GNN). When it comes to pattern recognition and generalization, the cAI demonstrates impressive performance. When it comes to safety–critical industries such as self-driving vehicles and medicine, there is often a need for more transparency in explaining how a solution was reached. Obtaining high training and testing accuracy often requires a significant amount of data, which may need to be more practical for specific applications.

There is broad consensus among scientists that the composition and organization of information vary depending on the level of abstraction. They presumptively believe that greater degrees of abstraction are symbolic, whereas lower ones are sub-symbolic. The study [115] claimed that knowledge at any level of abstraction incorporates neural-symbolic information, i.e., symbolic and sub-symbolic information is included in all groups. This suggests that connectionist (cAI) and symbolic (sAI) characteristics might be combined as neural-symbolic models (NSL) to create a natural mimic machine for information processing. NSL AI, often known as NSL, can change features from knowledge by first extracting them from the data using connectionist methods. It has been shown that neural-symbolic AI can converge rapidly with just 10th of the training data. According to scientists, NSL will provide computers the power to learn and reason while carrying out various activities without requiring lengthy training. The symbolic component regularizes the neural learning, while the neural components support model scaling and direct discrete choices.

5.2. NSL components

This section covers every aspect of an NSL system, such as attention mechanisms, knowledge graphs, representation methods, and mutual collaboration. These components play a crucial role in the development and effectiveness of NSL.

5.2.1. Attention mechanism

By employing an attention mechanism, Bahdanau [116] successfully addressed the challenge of fixed-length encoding in NLP. Incorporating the attention mechanism primarily enhances the performance of a DL model [39]. However, the attention mechanism persuades the neural network architecture to focus on and enforce a specific function as needed, all while allowing for reasoning and inference. Thus, the attention mechanism plays a vital role in the fusion of symbolic and sub-symbolic learning. Attention mechanisms have also been computed in other tasks, such as alignment score, weight, and context vector. Moreover, removing irrelevant terms from the symbolic reasoning process is important where excessive logical combinations make computation challenging. Combinatorial search over symbolic code can be changed to scalable gradient-based techniques by symbolic distillation and relaxing symbolic programs into neural networks. Distillation emerges as an alternative solution for learning symbolic and neuro-symbolic programs. Latapie [115] applied attention mechanisms to neuro-symbolic reasoning to filter huge data combinations and realize parallel calculations of different varieties.

5.2.2. Knowledge graphs

The graph is the connection between all components or vertices. Learning graphs are an excellent approach that allows end users to retrieve information from knowledge graphs (KG) more effectively and efficiently, which can be better used for segmenting tumors, inferencing, and reasoning. A knowledge base for a reason and storing information may be created using the graph [117]. By replicating the connections between neurons in the brain, graphs connect elements and vertices. This capacity also applies to neuro-symbolic systems, which gain from KG as a bionic technology. Graphs provide AI with the ability to reason and learn using logic, information from the past, and statistics. A graph-based AI will use logic to incorporate new information into the more extensive graph. Such models may continue to learn further details long after training is finished, which helps massive systems run more efficiently [118]. The attention mechanism and graph are also used to calculate independent correlations among the weights of adjacent nodes in a network [119]. The KG unifies objects, logical expressions, and semantic networks [120]. Equivocation in natural language may result in illogical representations, making it challenging to correlate and correspond to logical representations [121]. To categorize items and describe interrelationships via connections for ease of network extension, the KG may also be represented using a semantic network [121]. For a better knowledge representation, the gap between semantic networks and KG must be filled [118].

There are two possibilities for knowledge representation: localist and distributed representation [122]. On basic models, the localist representation offers benefits in terms of interpretation and great computational efficiency. Most significantly, it keeps the relationship between characteristics intact [123]. The knowledge base is supplemented with distributed representation, which calculates similarity [123]. Natural languages and entities have extensively used distributed representation [124,125]. To apply the knowledge representation, the structured embedding [122], single layer model [126], semantic matching energy [127,128], and latent factor model [129,130] based approaches are attempted. The neural tensor network has been created for knowledge basis. Knowledge representation is more accurate and may reduce computing costs when compared to knowledge graphs [123]. Once neural networks are integrated, there will be even more opportunities to delve into knowledge representation. Knowledge graphs are widely recognized as the industry standard for expert explanation and can be seamlessly integrated with cAI. Using knowledge graphs makes it easier to represent, infer, and explain things better, which in turn makes it easier to add a more complete model of symbolics and sub-symbolics to NSL.

5.2.3. Role of knowledge graph in the fusion of symbolic-AI and sub-symbolic AI

DL models typically bypasses a significant portion of the centuries-long expertise from domain specialists as annotations. Although most traditional symbolic AI systems are intelligible, they still need to achieve comparable levels of performance or scalability. The introduction of xAI provides explanations and justifications for its learning process [131,132]. Many studies have shown the sensitivity and weaknesses of black box notorious in DL algorithms and developed visual interpretation approaches like attribution or saliency maps to make these methods more interpretable [133]. However, the explanations offered by these methods, often in heatmaps, are not always sufficient since they are difficult to measure, correct, or communicate to technologically-minded audiences. In addition, as recommended in [134], expanding the involvement of various minorities and audiences may make it easier to evaluate AI models when the objective is to deploy human-centered AI systems. As a result, the motivation of the NSL learning paradigm is to sub-symbolic and symbolic AI components. Connecting such learned and symbolic representations makes it possible to provide explainability as fusion. The explainable xAI-based learning approach bridges the gap between DL and domain expert representations. The xAI technique aims to create explainable neural symbolic models while giving general explanations to end-users and domain specialists.

Table 1
The neuro-symbolic learning taxonomy composed of 5 structures.

Structure	Description
NN prior symbolics pipeline	Processing data and passing it to either logic or functional symbolic codes, such as, Houdini searches through a library of functions and a neural module in order to train and learn [135].
NN post symbolics pipeline	First symbolic components apply followed by a neural network.
Purely Neural module	A number of neural modules appear and work simultaneously to provide high-level functionality.
Composition via algebra	Symbolic and sub-symbolic run independently and cumulative results achieve via imitation-**pro**jected **p**rogrammatic **re**inforcement **l**earning (PROPEL) and **co**ntrol **re**gularized **r**einforcement **l**earning (CORE-RL) as operators.
Program acceleration through NN	Employing ML to execute the program efficiently without effecting functionality.

Table 2
The 6 structures overview of neuro-symbolic learning.

Structure	Description
Symbolic→Neuro→Symbolic	Symbolic representations first convert into NN as vector embedding followed by symbolics.
Symbolic [Neuro]	NN as sub-routines of symbolics as designed by Monte Carlo search tree.
Neuro; Symbolic	Symbolic and NN systems run in parallel and communicate the results to improve performance.
Neuro: Symbolic → Neuro	Symbolics as knowledge embedded into NN.
NeuroSymbolic	Symbolics as rules to regularize NN parameters and loss function.
Neuro [Symbolic]	Employing symbolic reasoning into NN.

5.3. Task adaptive NSL structure

Various classification systems have been created to categorize neuro-symbolic structures. In this section, we present the scenarios that are widely recognized, and then we provide some prominent examples in their respective fields. There are five different structures included for the task adaptive NSL structure, as shown in Table 1.

Another system of taxonomy has many of the same qualities as the one that has been presented (Table 1), and it is widely recognized by the relevant body of research [122,136,137]. It is possible to use pointer networks or GNNs to solve graph issues using attention methods. The overview based on the six different structures is shown in Table 2.

5.4. Knowledge incorporation and decision rules

The decision rules are an essential component regarding the inclusion of knowledge representation. Because of their close resemblance to regular language, decision rules are excellent for interpretation [138]. One possible solution to address the combination issue is to utilize decision lists and decision sets. These can help prevent any overlap or omission of rules. The processing of the data by algorithms may result in the production of new rules. Therefore, the OneR algorithm uses the entire dataset and acquires different rules per the inaccuracy made [139]. On the other hand, OneR cannot be applied to a dataset since it contains more than one rule. A study [138] suggested RIPPER as an advancement on sequential coverage, which employed rule reduction for optimization. Another approach to learning rules is using Bayesian Rule Lists [140]. In the first stage of this methodology, frequent patterns are pre-mined using recurring pattern growth or Apriori. NSL uses knowledge improvement techniques to develop a dependable system; nevertheless, it is challenging to increase generalization and domain adaptability simultaneously [141]. Other different algorithms may be used to produce decision rules [142]. The DL models have also been used with decision rules in certain scenarios [143]. It is widely acknowledged that decision rules are valuable for interpretation and making precise yet efficient predictions; however, they may encounter challenges when it comes to regression [138].

5.5. The role of NSL for the transition of manual to DL learning algorithms

NSL has the potential to play a significant role in enhancing the performance of algorithms ranging from manually handcrafted engineering to recent DL architectures in clinical settings. As manual approaches for BTS from MRI may be challenging and time-consuming owing to the numerous slices in MRI images, NSL adopts a human-like approach to reasoning and inferencing. Integrating NSL into standard ML techniques can increase performance by adopting human-like problem-solving tactics and reasoning against the generated outcomes, which can be accomplished by selecting feature-specific features as desired. Recent DL upsurges in the prominence of these approaches among the researcher community [7,8,37]. The character of biological structures can be more accurately represented through high-dimensional processing, which is considered the most innovative method for modeling sophisticated representation, training, and learning. In recent times, there has been a growing interest in axial attention as a promising solution to effectively apply attention to multidimensional data [16]. This makes it viable to incorporate the attention mechanism even with 3D data since it only scales linearly. Similarly, based on the ROI using of DL, there might be a necessity for intervention, inference, and feedback response and evaluation to comprehend ordinary and non-technical subjects and novice learners [7,37]. Recently, automated segmentation using DL techniques has been more popular because of the involvement of DL, which provided feasible solutions [8]. Similarly, several DL techniques have been provided in the previously conducted surveys for tumor segmentation from brain MRI [6]. The DL-based algorithm has achieved remarkable achievements but still faces the issues of interpretability, explainability, research, causality, complexity, operateability, and the necessity for massive datasets to function effectively.

5.6. Transition of data driven to symbolic learning

The CNN models have made significant contributions to image processing over the last ten years, particularly in neuroimaging, but more attention needs to be paid to tumor prediction, classification, and segmentation together with explainability and interpretability. In contrast to DL modeling, NSL incorporates expert knowledge to guarantee that the decision-making process is reliable and explainable to people. A transparent system in the clinical sector becomes necessary; as a result, CNN is being replaced by the research potential and advancement in NSL. Therefore, an NSL technique was used for clinical applications to extract human-readable symbolic representation for decision-making [12]. The NSL model produced results equivalent to those of cutting-edge investigation, interpretability, and explainability techniques. The study [144] showed an emergent language-based classification framework, including a sender, generator, and receiver for classifying medical images to combine the representational capacity of DL with the interpretable powers of symbols. An innovative technique for automatically producing a spinal medical report was presented [145]. The work [133] used symbolic representations and offered explainable NSL (X-NSL) strategies to combine DL representations with domain knowledge that annotates architectural elements and image classification. To correct miss classification, the study [146] built a semantic referee that pulls features from profound CNN errors as additional image channels. Despite outstanding performance in visual question answering on synthetic images, long-tail distribution of visual conceptions and uneven reasoning processes are problems for neural symbolic approaches in actual images. To handle distribution imbalance, study [147] presented the calibrating concepts and operations paradigm, which included an executor to record the underlying data features and an operation weight predictor to emphasize critical functions and suppress unnecessary ones. The study [148] built a neural-symbolic-neural architecture to train an end-to-end neural-to-symbolic model offering an innovative approach to image generation and reconstruction. To impose logical restrictions on the training of the convolutional layers, the study [149] used logic tensor networks and a neural-symbolic method to avoid data dependency. Thus, a symbolic learning module in the neural network may enhance the model's interpretability and extensibility.

5.7. NSL versus classical DL applications

NSL can be employed for a wide range of potential applications with the benefits of cheaper costs, improved generalization and resilience, interpretation and explainability, quick training, and the ability to imitate human cognitive capacity. Various efficient and effective attempts have been made towards developing a DL-based paradigm [150]. Several studies have used symbolic reasoning to improve the DNN's learning process and create a more accurate loss function [151]. As a result, using an NSL to choose the loss function before the DNN may assist in improving the performance of the entire system. Without additional information, a GNN model may not be capable of determining and computing significant graph features [152]. Standard methods such as structure optimization, message addition, and synthesis can trim the CNN model by making the polynomial more specific so that the regression can be trained better [153]. NSL, in contrast, offers excellent benefits while being less expensive to annotate. It is more challenging to balance time and resource consumption due to research showing that the depth and breadth of a network matter in DL [154]. The NSL uses fewer resources and performs better in numerous cases than CNN. DNNs are susceptible to adversarial perturbations, which may be prevented using domain knowledge from driverless driving like road markings [155]. Applying knowledge-based improvement techniques would enable NSL to create a solid system. System generalization is another area that merits investigation; however, it is challenging to combine generalization and domain adaptation [141]. Additionally, there is an issue with overfitting in DL networks, which reduces their resistance to adversarial attacks [156]. Large-scale pretraining networks have also been used to execute neural symbolic regression successfully and re-discover fundamental equations [157]. To increase the effectiveness and performance of the symmetrical neural network in computer vision and medical image processing, an equivariant network with promising fusion NSL [158]. The top 10 research areas of CNN and the NSL are similar, including computer science, engineering, and mathematics computational biology [12]. Given the advantages of NSL over traditional networks, it is critical to place a greater emphasis on conducting thorough research in NSL.

6. NSL based solutions and directions for BTS

Clinically, it is challenging to understand the appearance of a brain tumor and the segmentation because of the wide range factors including variation in size, localization, rate of growth, and pathology. Recently, DL networks are highly regarded for their potent magic in resolving a wide range of issues; nonetheless, concerns like inferencing, reasoning, and counterfactual situations still need to be handled. NSL combines symbolic learning and reasoning elements with modern neural networks. This section addresses the deficiencies observed in current DL models while exploring potential solutions and prospects in clinical settings.

6.1. NSL for generic and fine-grained tumor identification

A novel route between expert-driven symbolic and data-driven sub-symbolic configurations in biomedical image segmentation has been attempted [69]. The search area for empirical alternatives when given a new task is drastically reduced by this method, which systematizes the configuration process on a task-agnostic level. This selection process has been streamlined by including symbolic selections for practical model training and output. Datasets and network configurations may be used to choose designs automatically. As a result, selecting parameters and hyper-parameters for a network model may automatically produce the symbolics or rule-based setup. This would allow picking options using inference and rule-based techniques at various levels. Meanwhile, NSL uses in clinical settings are favorable when investigation and interpretability are more demanded. It has the potential to be applied to medical imaging techniques such as MRI-based disease classification [159]. Medical imaging frequently needs the help of experts for the costly task of object labeling, especially when it comes to predicting, classifying, and segmenting brain tumors [160]. On the other hand, fine-grained images have a meager signal-to-noise ratio because information with enough discrimination often only exists in tiny local regions. The effectiveness of fine-grained image categorization systems has come down to the efficient use of local area information. Trustworthy datasets must be extracted using fine-grained image classification to reflect lesions with distinct forms, outlines, appearances, and criteria on a large scale. NSL manipulates features using symbolic AI techniques and extracts features using cAI methods. NSL has shown superior performance despite needing small training data and the capacity to learn and reason while carrying out different tasks. NSL thus offers promising application potential in biomedical imaging, classification, registration, and segmentation.

6.2. Knowledge as symbolics prior to embedding

In addition to being independent of programming language and effectively preserving the relationship between symbolic and sub-symbolic information, the topological dependence of data is held by the integration through graphs and hypergraph [161]. The compositional structure of graph representations makes it possible to represent entities, attributes, and relations scaleably. Thus, the literature study suggested using a multimodal GNN to resolve the problem of compositional generalization for visual reasoning and question-answer sessions [162]. Knowledge as KG typically exhibits hierarchies at once, such as hyperbolic space, which may represent a continuous replica of discrete trees, enabling it to describe hierarchical and graphical data [163]. Additionally, the ConceptNet ontology incorporates a symbolic model with a DL-based sentence-based image retrieval procedure to represent general-purpose information, which is utilized to enhance learning performance [164]. The DL method's outputs are linked with information about various concepts' affordances and relationships with other items [165]. To generate exact predictions for tumor segmentation, combine DL and ML with expert knowledge of several relevant concepts. Combining information from several expert domains while receiving training would enhance clinic participants' capacity for analysis and decision-making.

6.3. Knowledge embedding and clinical practices

Incorporating domain knowledge into learning algorithms improves data efficiency and learning rates. Integrating and using domain knowledge to allow a customized healthcare system is necessary to facilitate a patient's health [166]. Therefore, combining DL representations with domain-specific information is a critical task. For clinical applications, there has been an effort to integrate biological or domain information into GNNs [167]. Domain knowledge like patient personal knowledge might benefit from the symbolic representation of information in domain knowledge. The patient history, such as patient's health, food, nutrition, lifestyle, and history, which may be required to model the healthcare decision-making process [168]. A CNN-model can be trained to reason about health informatics such as meal suggestions, allergy limitations, and carbohydrate prescriptions, given patient's health history as a symbolics. The trained NSL network may be used to forecast patient diagnoses and recommend treatment for segmented tumors. Collecting specific tumor information, incorporating it into neural networks, and, most crucially, comparing it to the same patient's clinical data to map their medical history. Thus, NSL makes health decisions more rationally like human practitioners. In addition, a generalized model for tumor segmentation receives domain information about the tumor, such as tumor grades, types, volume, location, outline, brain architecture, and patient history about food and medicine. At the evaluation, the model's output (Fig. 2 can be reasoned and queried for examination purposes.

6.4. Diseases diagnosis, prognosis, and treatment

The accuracy of disease diagnosis has risen when using a comprehensible ML technique [134]. Increasing the number of feature dimensions might enhance the framework's importance; but, it would also complicate symbolic reasoning. Domain expert knowledge has a significant role in the diagnosis, prognosis, and therapy based on medical imaging modalities at various levels of integration. The latent space is an appropriate level for integrating domain knowledge with symbolic information to enhance reasoning abilities in segmented regions [169, 170]. To diagnose and evaluate the prognosis of tumor using medical imaging techniques, clinicians must acquire precise information regarding biomarkers and lesions to perform detection, segmentation, and classification. Multitasking may be required to identify tumor outcomes accurately using domain knowledge and symbolic reasoning. Similar changes in contrast and intensity may be present in the segmented lesions, and their association is essential for prognosis and therapy. To implement symbolic logic, neural network computing must focus on embedding domain knowledge in symbols to assist tumor diagnosis. The segmented and delineated tumor is the only exception to the generic framework shown in Fig. 2. The size and structure of segmented tumor may vary, and a clinician can compare tumor before and after surgery, forecast if tumor will spread, and vice versa.

6.4.1. Recent breakthroughs and NSL for BTS

Pre-trained generative models, such as large language models (LLM), are gaining popularity recently due to favorable user feedback [39]. NSL and LLM ML algorithms have pros and cons depending on the tasks [171]. NSL, combined with DL and symbolic reasoning, excels in complex pattern recognition and symbolic manipulation tasks [172]. A neural network extracts features from raw data and sends them to an extended reasoning system for decision-making or output synthesis in NSL. This method has shown promising outcomes for sophisticated inference, planning, and reasoning tasks using noisy or partial data. LLMs, such as chatbots, language translation, and content creation tools, rely entirely on DL and offer human-like answers to textual input [173–175]. It is a generative model that uses massive text data processing to produce human-like text answers, making it ideal for chatbots, language translation, and other NLP tasks. If pattern recognition and symbolic manipulation are needed, NSL learning may be the optimal choice. Thus, this area seeks to gain from NSL and LLM in clinical applications, specifically in BTS. Using LLMs, doctor-patient interactions can be automatically translated into notes, where clinical notes can be summarized, medical images can be captioned, and disease progression can be predicted artificially [176–178]. The Transformer, developed by the Google Brain team in 2017 with tremendous improvement in NLP [39]. The NLP breakthrough of transformers was applied to vision with SwinT [179]. However, discrepancies between language and image, such as substantial scale, make Transformer adaptation difficult.

New developments in LLMs improve neural symbolic reasoning by making it easier to understand and use natural language [180–183]. Bridging the gap between symbolic logic, language, and perception is a significant difficulty in NSL [184]. By generating and comprehending language, LLMs like GPT-3 can improve symbolic logic and neural reasoning systems' natural language knowledge. Integrating LLMs into reasoning systems enhances understanding of natural language input, improving accuracy and efficiency and adapting to crucial tasks like BTS [185]. OpenAI published DALL-E and DALL-E 2 in 2021 for language processing-based image generation [186]. Where DALL-E 2 generates better images from textual descriptions since it is trained on a larger dataset with more parameters. The Contrastive Language-Image Pre-Training (CLIP) model is an extensive neural network trained on text and images [187]. CLIP-DALL-E combines DALL-E with CLIP, which produces images that match the text and its context. The ViT-DALL-E model combines DALL-E with the Vision Transformer (ViT) architecture [180]. DALL-E 2 and ViT-DALL-E use GANs to generate images and need a lot of annotated visuals and text data for training, which can be difficult in some fields. The creative characteristics in DALL-E allow the generation to be actual to input, visually appealing, and aesthetically pleasant. GPT-3 must be equipped with symbolic reasoning to create and combine new visual notions. Grad-CAM and shapely-additive-explanation-like techniques aim to simplify NSL for complex tasks like BTS by interpreting the model's learned weights [188–190]. However, these models can be more challenging to understand because of how they arrive at their outputs. NSL, on the other hand, can work with smaller amounts of data, have more transparency, and generate human-interpretable rules and explanations. Thus, the combination of NSL and NLP may be used to accomplish symbolic reasoning in healthcare decision-making for BTS.

6.5. Exploiting BTS using NSL

6.5.1. Reasoning, inferencing, and decision making using NSL

Users' confidence increases when the underlying processes are better understood, and they can grasp a ML model's prediction. The absence of a white-box concept poses one of the biggest problems for ML and DL-based modeling regarding interpretability and reasoning. A range of application disciplines, particularly the natural sciences, where comprehension and prediction are crucial for decision-making, emphasize the importance of the model's interpretability [191–193]. Extensive study has been conducted to convert the complex and opaque nature of a black-box into a transparent and comprehensible feature represented by explicit mathematical equations that can be readily understood and evaluated by humans [105]. Inferencing may also be done by embedding information and attention processes in DL to tackle black-box notorious features. Attention may be given to NLP in the form of embedding, in which words, phrases, and structure levels can all be provided with various chunks of information. Given the optimized module's knowledge, a specific module with poor performance may be reparametrized for global-level attention that provides a vital route while facilitating a global attention mechanism. The local attention mechanism (LA) prioritizes and penalizes specific neuron(s) at a submodule level. Thus, a symbolic learning module included in

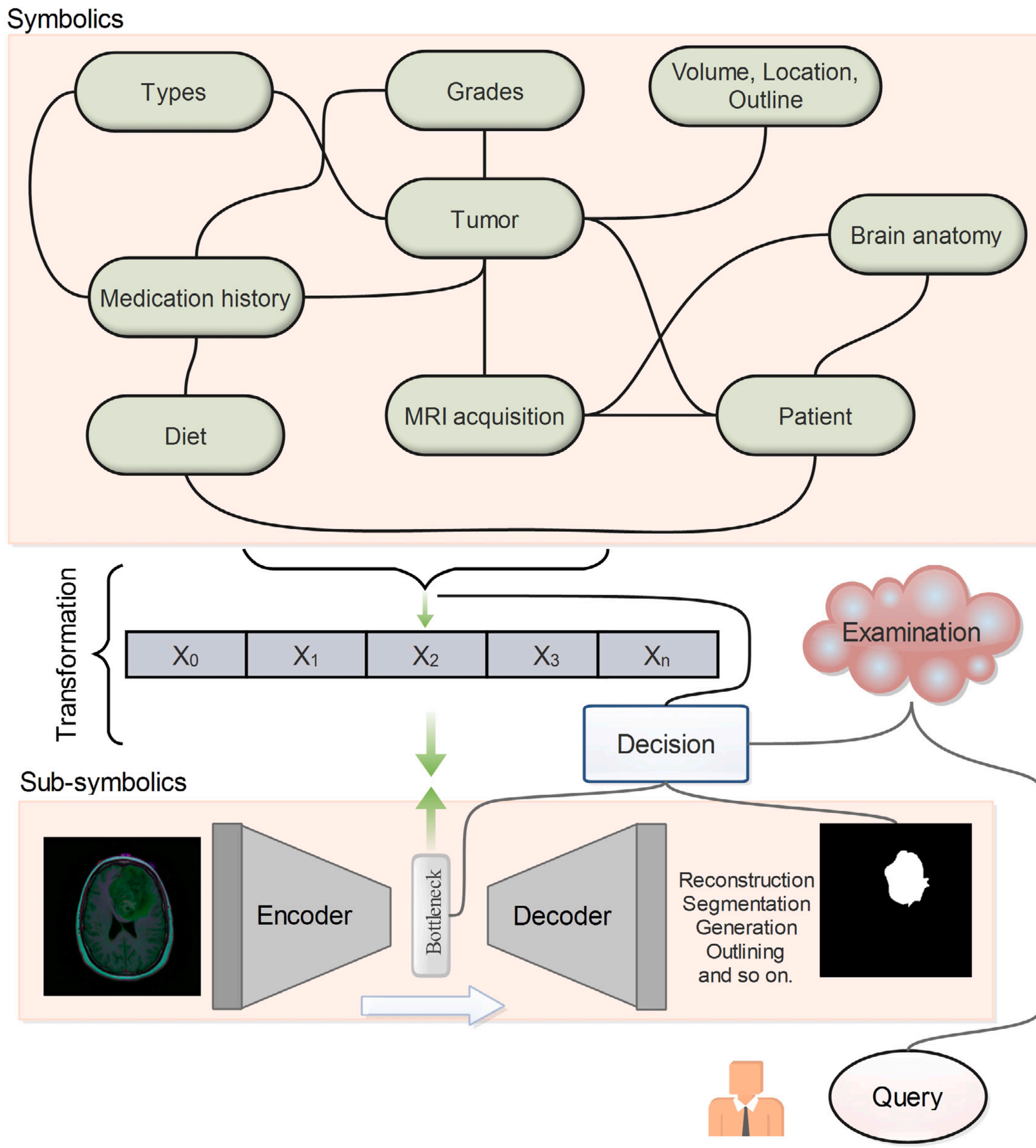

Fig. 2. Information on the tumor, including its grade, volume, location, circumference, brain anatomy, diet, type, medicine, and corresponding collection MRI, is embedded in the knowledge. It is possible to make use of the symbolic information during training and testing at many levels, particularly at the bottleneck layer. Prior to the embedding process, the information about the symbols is transmitted to the neural network computation through a representation that is similar to a transformer and has a variety of attention methods.

the neural network may aid in improving the model's interpretability and extensibility. The research [16] has convincingly shown high-quality configurations on fresh datasets and task-specific empirical optimization that can further enhance segmentation performance. In the future, DL architectures could serve as a foundation for comprehensive automation, enhancing the practical optimization of specific design decisions like data augmentation or network architecture. Graph-based techniques have the potential to facilitate smoother scaling and more effectively handle complex fine-grained multi-modal reasoning. A holistic model is outfitted with symbolic learning that may be carried out for inferencing, reasoning, and decision-making about segmented tumors.

NSL is broken down into symbolics and sub-symbolics parts, in which the neural network reads a brain MRI into a U-Net-like architecture (Fig. 3). The input encodes to the bottleneck layer. The symbolic representations will receive and fuse at the proper location and coating during encoding. Similarly, conditioning in the form of attention can be incorporated at specific layers. The method segments the tumor, along with symbolic information describing the cancer in terms of its kind, area, outlines, coordinates, and grades. In human contact, physicians may interact to question, reason, or infer and make appropriate decisions regarding diagnosis and prognosis.

6.5.2. *Conditioning on neural network and feasible segmentation*

The objective of conditioning in a neural network is to separate a process from several manifestations that go towards the intended direction. Numerous research, including text-to-speech [194], style generation [195], attention mechanisms [196], literature production, and text-to-image synthesis [197], have used conditioning on neural networks. In the field of neural networking, efforts are made to harness the innate ability of inborn to engage in conditioned thinking, particularly via the visualization of information based on textual descriptions. For text-to-image synthesis, hypergraph-based conditioning may be used at several levels, such as sentence and word level conditioning, to increase generating flexibility. Beyond the training dimensions, continuous and discrete image production is made easier by embedding hypergraphs as conditioning. As a further condition on the network

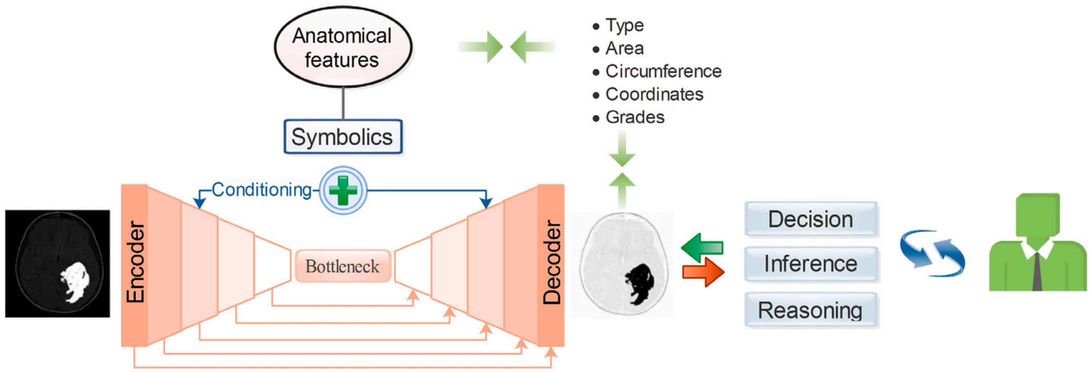

Fig. 3. The pipeline that was just presented illustrates neuro-symbolic learning, which is made up of symbolics and sub-symbolics. An MRI of the brain is received by the neural network in U-Net, which then encodes the information into the bottleneck layer. In addition, the symbolic representations receive and fuse at the right position and layer when the encoding process is taking place. In a similar fashion, conditioning in the form of attention at a certain layer is also utilized. In addition to providing symbolic information on the type of tumor, its extent, its outline, its coordinates, and its grades, the mode subdivided the tumor. Human interaction allows doctors to communicate with one another in order to question, reason, infer, and make conclusions that are acceptable.

statistics, such as one-hot vector, vector signature, conditional signal, style as condition, and conditioning hypernetwork, meta internal learning is used for image synthesis [198]. In this case, a Variational Autoencoder (VAE) has been constructed using a hypernetwork. The purpose of this VAE is to predict the uncertain actions of multidimensional agents in settings that are influenced by context and may be generalized [199]. Using different circumstances to encourage NN learning towards the desired goal is legitimate. Incorporating adversarial hypernetworks and meta-learning techniques like few-shot learning may also lead to improvement [198]. One potential future route for reasoning in ML models is implicit learning, in which the overall result is built on sub-solutions [200]. Similarly, when segmenting tumors, a segmentation model may be trained using diverse expert knowledge and information on the tumor morphology. In this regard, a proposed generalized DL model shown in Fig. 3 utilizes the output for not only decision, inferencing, and reasoning purposes but also conditions in the form of attention that can be embedded at a particular level and position.

6.5.3. Interpretation through NSL

Most DL explanation techniques return relevance estimates for a model's prediction to its original input region. By allowing human user involvement with the explanations in the training loop, explanatory interactive learning integrates xAI into the learning process [133]. Similar to how the potential explanations in DL may be divided into local descriptions, saliency map explanations, compositional part-based classification models, and so on [133]. Visual explanations fall short if a task demands a concept-level explanation of a model's decision [102]. Nevertheless, when provided a scenario during training, a deep network only perceives scenes with big, gray cubes. Visual explanations used to check the deep model's decision-making process show that it learns to primarily concentrate on the gray cube when classifying scenes as positive. Decomposing a visual image into an object-based, symbolic representation may be the answer, making it possible to calculate and engage with neuro-symbolic explanations and interpretation [102]. The work [102] develops a revolutionary neuro-symbolic idea learner via end-to-end differentiating slot attention [201] and set transformer [202] approaches. A collection of output vectors with permutation symmetry is produced via slot attention. Slot Attention windows are not specialized to a single kind or class of item, which might harm generalization. As a result, slot attention may systematically generalize to unobserved compositions, more objects, and more slots [201]. Set Transformer creates unique relationships between items in the input set [202]. The work given by [203] proposes a learning system based on a long-term convolutional network that explains the classifier's judgments for visual descriptions of recognition and description [131]. To segregate brain tumors and explain them, xAI may be a beneficial technique [132]. Finally, the proposal of an NSL model for tumor segmentation should be explainable, interpretable, and trusted by clinical and non-clinical stakeholders in healthcare and high-risk scenarios.

6.6. NSL translation, fusion, and integration

6.6.1. Translation

There must be a systematic mechanism to convert logical constraints to symbolic representation for neural networks. When the weights employed for learning and propagating gradients are not like those used in deep learning models, it becomes impossible to discriminate logical symbolic representations [204]. A hypergraph may need to be translated into a neural network with additional precautions to introduce cycle dependencies in the symbolic representation (see Fig. 4). Applying numerical constraints is challenging in practice. A unique mathematical tool and the inclusion of domain knowledge are required to perform the optimization since a loss term is complex and inappropriate for critical scenarios. Therefore, a study [161] presented a deep fusion-based reasoning engine to encode and transform knowledge into four levels, where L_0 is like the unprocessed sensor data collected from physical systems. This work seeks to represent, integrate, and translate knowledge by replicating a human method. Additionally, the physical, inferencing, and causal levels have been separated from the layer-wise translation [205]. One or more knowledge hierarchies may be represented simultaneously using a knowledge graph [163]. Hierarchical and graphical data may be modeled using a spatial network, such as hyperbolic space, representing a continuous replication of discrete trees (see Fig. 4).

6.6.2. Fusion

DL models pose serious risks when used in highly sensitive and important applications such as healthcare simply because of their lack of transparency, complexity, and complexity in diagnosing. The outputs of DL are usually produced employing correlation approximations, which makes them sensitive and difficult to correct. The majority of traditional symbolic AI systems, on the other hand, are comprehensible but need to achieve comparable levels of performance or scalability. xAI generates explanations or justifications for how it works. Numerous studies have shown the sensitivity and weaknesses of black box DL systems and developed visual interpretation techniques like attribution or saliency maps to make them more understandable [133]. These approaches provide explanations, often in the form of heatmaps, but they are only sometimes sufficient since they are difficult to measure, rectify, or communicate to non-technical audiences. Performance considerations increase the requirement for combining neural and symbolic

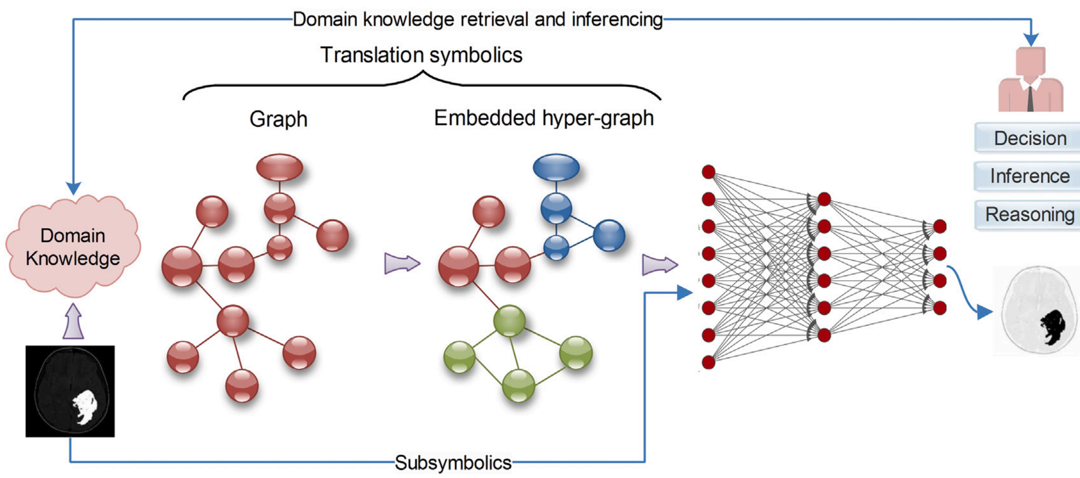

Fig. 4. Radiology specialists were consulted in order to obtain domain knowledge on brain tumors in MRI. This information was then transferred to graphs, and hyper-graphs were embedded as symbolics. While this is going on, the visual information represents the input of the brain tumor in the form of sub-symbolics. This information is then jointly given to neural networks in order to learn how to segment the brain tumor. The segmented tumor is utilized by the radiologist in the process of decision-making, inferencing, and providing rationale.

AI for explainable AI utilizing KG. Introducing explainability to a model by combining the alignment of learnt and symbolic representations is an intriguing obstacle. Expert knowledge may be considered a knowledge graph to explore this concept better. As the fusion of DL and domain expert representations is our ultimate objective, an X-NSL idea and learning approach have been presented to close this gap. To combine DL representations with specialist subject knowledge, the research [133] used symbolic expressions and proposed the X-NSL technique. DNNs may enhance AI by including manually designed features for human-centric applications.

6.6.3. Integration

Graph-based integration: The best method for representing domain and expert information in graphs and hyper-graphs before integration to the neural network. The data's topological dependence is maintained, and the integration using Graph and hypergraph accurately represents the interconnection between symbolic and sub-symbolic representations [161]. Graph representations are inherently compositional, allowing us to efficiently represent entities, properties, and relations. To generate a factor matrix for the question-answering session and to address the issue of compositional generalization for visual reasoning, the research [162] presented a multi model graph neural network. Different locations have been allowed for the integration of information into NSL models. In this regard, Fig. 5(a) depicts the domain knowledge integration into the NSL platform. First, the domain knowledge extracts BTS information from the domain experts such as tumor outlining, shape, stage, grade, lesion from radiologists. The collected domain knowledge translates into a Graph or hypergraph as a KG. The KG can then be fed into a sub-symbolic module. The graph and hyper-graph Graphs provide the ability to reason and learn using logic, prior knowledge and information about tumors, and statistics. A more extensive graph comes into existence from a smaller sub-graph in a synchronized way. The knowledge integration using KG allows end users (clinicians) to retrieve information from knowledge graphs more effectively and efficiently, which can be better used to segment tumors, inferencing, and reasoning. Knowledge graphs can represent a variety of data on the underlying issue of tumor classification and segmentation (Fig. 5(a)) together with patient history (Fig. 2). Ultimately, the pipeline generates data that allows domain specialists to analyze and investigate the segmented tumor. The input may then be sent to the domain expertise for further improvement in results.

Layer-wise Integration: Different attention-like methods are used in the investigation [115] between the symbolic and sub-symbolic levels. Similar to how high- and low-level information in terms of symbolic and sub-symbolic representations have been combined at various abstraction layers [161]. These layers (L_0, L_1, …, L_n) should have cognitively synergistic attention mechanisms. Complex procedures are required to deal with attention coming from symbolic and sub-symbolic systems, and it is essential to ensure their coordination, integration, harmonization, and coherence in connections. The importance of the attention mechanism for modeling NSL may be seen in how it activates specific neurons in the neural system when certain symbols are perceived [206]. Another option is to incorporate the domain information into a layer-wise neural network design (Fig. 5(b)). Each layer may receive labeled information in terms of a caption individually, and a particular layer can be singled out through an attention function. In language modeling, caption information can be provided, in which the layer-based information is converted into a vectorial representation that includes objects, characteristics, dimensions, and a message-passing mechanism between levels. Additionally, various positions may consist of domain information, including the input level, as well as biases, weights, and loss terms (Fig. 5(b)). Such domain information allows us to prepare a methodical symbolic translation into the domain of neural networks, addressing differentiability and logical constraints in representation. In Fig. 5(b), caption-C_3 has been utilized for an arbitrary attention mechanism that can be employed as desirable. For NLP, integration and embedding may be accomplished at the syllable, word, sentence, and structure levels. The proposed NSL concept-based model utilizes black-box learning, enabling optimization across several layers and incorporating diverse scenarios to create a robust model with enhanced interpretability and extensibility.

Position-wise Integration of Domain Knowledge: The incorporation of domain knowledge has been investigated in research [207] at many levels, including the input level, the loss function, and bias and weights parameters. Integrating domain knowledge aims to empower a responsible and stable neural network with fairness and investigation principles. The input would be converted and supplied to a DNN model if it consisted of raw features plus information obtained from the domain. The domain knowledge may also be included in the loss function as a penalty term that reflects recommendations and directions based on the domain knowledge. These concepts include regularization terms, embeddings, and semantic domain constraints. Similarly, a deep network's model parameters as weights may be constrained through domain knowledge, or its architectural layout can be chosen. As previously stated in the latent representation, such inclusion may be accomplished directly in Bayesian formulation [169,170,208].

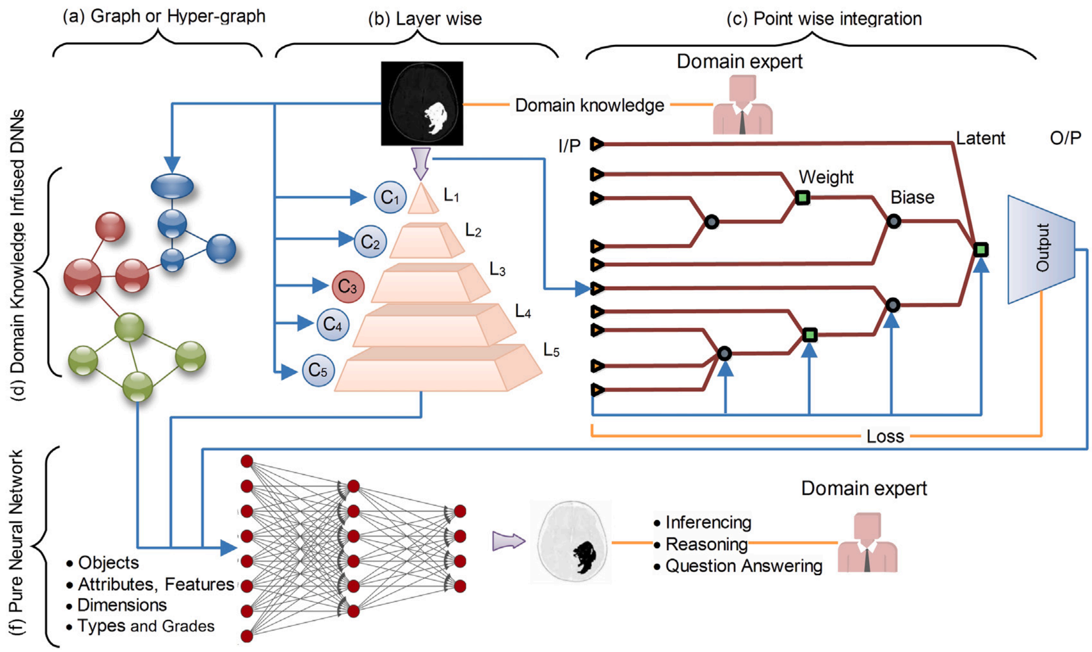

Fig. 5. A generalized pipeline to demonstrate translation, integration, and embedding of domain knowledge in different ways into deep neural networks to facilitate tumor segmentation. Three types of domain knowledge representation are used before a pure neural network-based operation. (a) The extracted domain knowledge first passes to a graph and hyper-graph-based neural network representation. (a) Domain knowledge feeds to a layer-wise neural network, which is further composed of different layers ($L_1, L_2, \ldots, L_5$) where a particular layer (L_3) has been conditioned (C_3) emphasizing learning certain features. (c) Similarly, the domain knowledge also passes to point-wise or position-wise neural networks to influence the model learning at different positions (weight, bias, latent space, and decoding side). After learning and knowledge representation into feature maps, a pure neural network (sub-symbolic module) utilizes these features for BTS. An expert or clinician infers, reasons, and examines the segmented tumors toward an explainable AI.

Transfer-learning as a prior distribution across the model parameters may transfer domain knowledge or symbolic information to DL models [209]. To further obtain the desired outcome, domain knowledge stored as a set of propositional rules and domain constraints must be applied to the neural network's structure [151,210,211]. Domain knowledge can be expressed by metapaths as to how biological components may be integrated in a latent space. Overall, the network performance will improve by point-wise integrating domain knowledge acquired from experts, where the experts can reason, infer the output, and provide feedback regarding improvement.

6.6.4. Optimization of DL and NSL

Integrating data-driven learning techniques with symbolics is generally regarded as one of the most challenging AI domain. There are many ways to incorporate low- and high-level details, including abduction-induction, structural alignment, and neural-symbolic. The design and development of neural-symbolic systems have rapidly attracted the attention of several sectors in AI due to their learning process [146]. To optimize a DL network's parameters and hyperparameters, several strategies have been suggested [212]. Nevertheless, several precise combinatorial optimization methods will find the optimal solution despite the worst-case exponential time complexity [213]. Branch-and-bound was changed into a Markov decision process, a common and accurate way to solve systems and equations with mixed integers [214]. A Bayesian optimization technique for combinatorial search spaces was put forward in the study [215]. Most Bayesian optimization techniques concentrate on continuous rather than combinatorial search spaces [216]. The novel frameworks convert discrete restrictions into differentiable, gradient-descent-optimized smooth functions. Most of the segmentation approaches use U-Net as the leading architecture. The optimization of U-Net-based NNs given symbolics from domain knowledge can be utilized for optimization purposes. The domain knowledge regarding tumor lesions must be translated to enable differentiable and gradient optimizations.

6.7. Clinical interactive NSL

The interaction between a human and a computer has been attempted to become convenient and simple [132,217]. There are extensive and vital thoughts of study on how individuals define, develop, choose, and provide answers in philosophy, psychology, and cognitive science, which claim that humans use cognitive biases and social expectations in the explanation process [132]. The prevailing theory is that users will be better able to comprehend and, as a result, trust the intelligent agents if systems are made more transparent, interpretable, or explicable [132]. Applications of explanation are being studied in a variety of AI subfields, including explaining medical decisions [218], debugging ML models [219], justifying autonomous agent behavior [220], and interpreting predictions [221]. The experts who understand decision-making models the best are not in the correct position to judge the usefulness of explanations to lay users, as "the inmates running the asylum" [222]. Based on the assumptions, studies, and conclusions above, the interactive system between humans and machines would be an exciting application for biomedical image processing, especially for BTS, classification, and segmentation.

To mimic human-like actions in the ML, it is necessary to understand humans with their social, cognitive, and psychological aspects. Researchers argued that while producing and evaluating explanations, humans use certain biases and social expectations [223]. These biases and expectations may enhance interactions between people and AI [108]. It is often the responsibility of a human expert to identify systemic flaws in the data or the algorithm using domain expertise and contextual information to understand why ML algorithms fail. The study [224] demonstrates that AI research often acknowledge or build on social science explanation frameworks. Therefore, it is necessary to define, produce, choose, evaluate, and provide optimal response in interactive system [132]. Adopting such behaviors in machines for critical environments, such as BTS and explanation, is inevitable because people attribute human-like traits to artificial agents and anticipate the same conceptual framework used to explain human behaviors.

According to the prevailing theory, by creating more transparent, interpretable, or explicable systems, users would be better able to comprehend and, thus, have greater faith in the intelligent agents [132]. This comeback is motivated by evidence that many AI applications are not or only partially adopted owing to ethical reservations and a lack of user trust.

6.8. Generalized future directions in NSL

To include the innovative aspects of symbolic learning in terms of integration, translation, reasoning, and applications, special attentions must be paid to the application-specific mechanisms while developing NSL models. Therefore, future DL models should include domain knowledge and reasoning capabilities. The segmentation of brain tumors would thus need a generalized neural network. Sub-symbolic learning often involves feeding the model with new knowledge for attaining a more generic structure. Nonetheless, it must be emphasized that a NSL model performs better even with little input domain knowledge compared to typical DL models. Developing methods to maximize AI's information acquisition while minimizing reliance on human knowledge data poses a substantial problem. When multiple clusters are evaluated at the same time, it can be more challenging to encode domain information into latent space. However, given that humans are involved in data curation, domain knowledge design, and interpretation, and their coupling should be protected against human intrusion. Revisiting CNN for NSL can be one of the fascinating future directions. Introducing specialized CNN layer-based models would bring significance to the futuristic NSL shape. Brain tumors may be diagnosed and clinically managed using both invasive and non-invasive imaging techniques. Creating a trustworthy decision support system for prediction depends on automatically identifying and accurately segmenting tumors. However, since slices in MR images vary in size, placement, and non-uniform alignment, it is a challenging to introduce reliable BTS algorithm with interpretable nature.

7. Discussion

AI faces many challenges, including emulating human learning, intuition, and reasoning skills while incorporating comprehensibility into its existing architecture [225]. Fundamental developmental principles govern how environmental stimuli are transformed into programmable symbols. Numerous ideas have been proposed, ranging from biologically acceptable Hebbian-style processes that still need to be shown to solve complex real-world learning challenges to a learning method that works but has some biologically doubtful features [226]. The current investigation aims to ascertain if precise measures of temporal activation patterns, synaptic features or paired-neuron input–output correlations can provide quantitatively accurate predictions regarding which learning rule the data is more likely to correspond to. Identifying the patterns of neuronal alterations that result from specific learning rules is a challenging task. However, it becomes easier when consider overall network architecture and loss function of the learning system, based on theoretical grounds [226]. It takes much study to determine if NSL's bias, robustness, generalization, and architecture are universal benefits over DL. NSL brings the development of a human brain mimic algorithm one step closer, opening new research possibilities and fascinating applications.

When performing manual segmentation, a radiologist via NSL must utilize the multi-modality information from MRI scans and apply their anatomical and physiological expertise acquired by means of education and practice. The procedure entails the radiologist examining several slices of images slice by slice, identifying the tumor, and meticulously drawing the malignant spots. In addition to taking much time, manual segmentation depends on the radiologist, and the results are often very heterogeneous both within and across raters. However, human segmentations are often employed to assess the outcomes of fully automated and semi-automated techniques. Neural networks have become increasingly widespread in recent years due to the emergence of novel designs and applications. Even though they must be addressed for crucial applications like tumor prediction, classification, and segmentation, difficulties with interpretability, explainability, inquiry, counterfactual, robustness, safety, and sensitivity still exist in neural network technology. Efforts have been made to address the difficulties in neural network computation by expressing and embedding domain information in symbolic representations. Thus, the idea of neuro-symbolic learning (NSL), which incorporates symbolic representation and common sense into neural networks, led to NSL. This study thoroughly analyzes the most recent NSL techniques, their guiding principles, developments in DL and ML algorithms, applications for BTS and classification, and, most importantly, prospects in clinics.

Numerous imaging modalities, including CT, SPECT, PET, MRS, and MRI, assist in diagnosis by disclosing essential details about the form, location, size, and metabolism of brain tumor lesions [17]. Automatic segmentation using DL techniques across several imaging modalities has recently gained popularity due to its ability to provide cutting-edge findings. The massive volumes of MRI-based image data may also be processed effectively and evaluated objectively using DL techniques. In MRIs, the T1 image series is often utilized to differentiate between healthy tissues, whereas T2 defines the edematous area that appears as a strong signal on the image. The prominent sign of the accumulated contrast agent (gadolinium ions) in the active cell area of the tumor tissue in T1-Gd images makes it simple to identify the tumor boundary. Since necrotic cells do not interact with the contrast agent, it is simple to distinguish them from the active cell area on the same sequence by seeing them in the tumor core's hypo-intense region. Water molecule signals are attenuated in FLAIR images, making it easier to distinguish edema from cerebrospinal fluid (CSF). Segmenting brain tumors entails identifying, characterizing, and partitioning tumor tissues such as active cells, necrotic core, and edema.

Conventional research on prediction, classification, and segmentation based on supervised and unsupervised data briefly presents a superficial debate about the integration of DL. At the same time, performance has yet to be examined. Many techniques based on thresholding, atlas, region growing, deep knowledge, and traditional supervised and unsupervised ML-based algorithms have been extended to segment and classify brain tumors. The contrast between segmentation and classification algorithms, however, receives little attention, and the most recent algorithms are neglected [7,8]. DL and shallow ML have mainly been used for tumor segmentation. Each technique has strengths and limitations, but the rules in the previous research still need to be addressed. The shortcomings of DL-based BTS and solutions to those problems may not be included in the review on MRI-based brain tumor image segmentation [8]. Our study involves both traditional methods and potential remedies for cutting-edge machine and DL technologies, as well as the use of NSL. Similarly to the above, many DL techniques have been given in the previous surveys for tumor segmentation from brain MRI [6]. Although the last DL-based methods yielded successful performance, they still need attention to issues like interpretability, explainability, research, causality, complexity, operability, and the need for large datasets. Therefore, our study emphasizes addressing the difficulties and recalling previous approaches to develop sophisticated NSL models.

Besides numerous advantages, domain knowledge as symbolics have several challenges in translation, embedding, and translation. Before transferring domain information into a neural network, it must be constrained by logical constraints. However, there is no standard framework for logical controls regarding embedding integration with D. Thus, particular consideration must be given prior to integration. Furthermore, given domain information, no simple method exists to generate a loss term for critical and safety scenarios. Graph-based approaches in robotic control and autonomous navigation applications can enhance scalability and improve the handling of sophisticated multimodal reasoning. The difficulties of fairness in handling multidimensional associations and interpretability may be solved by incorporating heterogeneous graph-based networks [200]. Another option is combining the domain information into a layer-by-layer neural network design. When a particular layer has been called out via an attention method, each layer gets labeled news individually in terms of a caption. Information about the captions is derived through language modeling. After that, the layer-based information is transformed into a vectorial representation that includes objects, characteristics, dimensions, and a message-passing mechanism between levels. Moreover, various aspects, including the input level, biases, weights, and loss terms, can integrate domain knowledge into an NSL platform. Incorporating domain knowledge can be achieved by mapping symbolic representations into the architecture of neural networks. This prepared the way for a methodical symbolic translation into the domain of neural networks, addressing differentiability and representation of logical constraints. Along with the advantages of making DL models understandable, plausible, and interpretable, NSL may also have some notable drawbacks. Probabilistic models based on symbols impose strict and limiting parametric assumptions, and when these assumptions are false, high-dimensional data bias occurs. Like this, NSL construction spaces need in-depth subject matter expertise. On the other hand, humans construct complex internal models immediately from raw data and generate hypotheses on a domain's conceptual characteristics and generative grammar.

8. Conclusion

DL has attracted much interest in various fields, including image analysis, NLP, healthcare informatics, and particularly in the prediction and segmentation of tumors. The wide range of applications of DL and ML are critical. However, their usage is limited to unavoidable circumstances, such as healthcare situations and medical imaging with major challenges such as interpretability, explainability, investigation, and black-box issues. The issues of explainability, reasoning, and inferencing in a realistic environment still need consideration. In addition to white-box characteristics and domain-rich knowledge, symbolic learning has yet to attain the computational level of neural learning. In order to attain human-like intuitive abilities such as transparency, interpretability, explainability, investigation, and reasoning in AI algorithms, it is necessary to incorporate symbolic AI into DL structures in a suitable manner. The fusion and embedding of symbolics and sub-symbolics are inevitable for achieving desirable results in a critical environment. With a focus on BTS, this study offers related ideas and NSL principles and solves DL problems with suggested future perspectives. Compared to previous research, our survey covers traditional DL methods and addresses the challenges in DL models with recommended, possible, and efficient NSL models. The recommended NSL-based modalities would enable clinicians to interpret, analyze, and reason about the detected, predicted, classified, and segmented brain tumors. This study will guide novice learners in ML in biomedical science with innovative NSL ideas for specialized and generalized domains.

CRediT authorship contribution statement

Muhammad Hassan: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ahmed Ameen Fateh:** Writing – original draft, Software, Formal analysis, Data curation. **Jieqiong Lin:** Writing – original draft, Visualization, Investigation, Data curation. **Yijiang Zhuang:** Visualization, Investigation, Formal analysis. **Guisen Lin:** Software, Resources, Data curation. **Hairui Xiong:** Validation, Software, Formal analysis. **Zhou You:** Formal analysis, Writing – review & editing. **Peiwu Qin:** Writing – review & editing, Validation, Methodology. **Hongwu Zeng:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Funding acquisition, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.neucom.2024.128058.

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Muhammad Hassan has received his Ph.D. in computer applied technology from Jilin University in 2022. His research interests are included image processing, medical imaging, computer vision, machine learning, and bioinformatics. He was a research assistant in Shenzhen International Graduate School, Tsinghua University, China. Dr. Hassan is currently a research fellow in Shenzhen Children's Hospital, Guangdong, China.

Ahmed Ameen Fateh received the B.Sc. degree in Biomedical Engineering from LIU, in 2012, the M.Sc. and Ph.D. degrees in Biomedical Engineering from UESTC, in 2014 and 2021 respectively. He is currently a researcher at Shenzhen Children's Hospital. His current research includes Brain imaging and image processing.

Lin jieqiong graduated from Shantou University Medical School in 2022 with a master's degree. Her research interests include pediatric neuroimaging, functional MRI, and medical imaging; She is currently a doctor at Shenzhen Children's Hospital, Guangdong Province, China.

Yijiag Zhuang Graduated from Shantou University Medical School in 2021 with a master's degree. His research interests include pediatric neuroimaging, machine learning, and medical imaging; He is currently a doctor at Shenzhen Children's Hospital, Guangdong Province, China.

Guisen Lin has received his master degree in medicine from Shantou University in 2019. His research interest is medical imaging. Guisen Lin is a radiologist in Shenzhen Children's Hospital, Gungdong, China.

Hairui Xiong received her M.Med. in medical imaging and nuclear medicine in Fudan University. She is interested in pediatrics neurological and abdominal imaging. Dr. Hairui Xiong is the attending doctor of Shenzhen Children's Hospital, Guangdong, China.

Zhou You received the bachelor's and Ph.D. degrees from Jilin University, Changchun, China, in 2002 and 2008, respectively, where he is currently a Professor with the College of Computer Science and Technology. His research interests include machine learning, pattern recognition, and bioinformatics.

Peiwu Qing received Ph.D. degree in biochemistry from the University of Missouri in 2013. He has been a Post-Doctoral Fellow with the Department of Physics, University of California at Berkeley, Berkeley, CA, USA, from 2013 to 2018. He is currently an Assistant Professor with Tsinghua–UC Berkeley Shenzhen Institute, Shenzhen, China. His research interests include optical imaging and signal processing.

Hongwu Zeng received his Ph.D. in imaging medicine and nuclear medicine from Southern Medical University in 2016. His research interests include child imaging, neuroimaging, fMRI, and brain function. Dr Hongwu Zeng is the Vice President and Research Scholar of Shenzhen Children's Hospital. Guangdong China.