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REVIEW PAPER

MRI brain tumor medical images analysis using deep learning techniques: a systematic review

Sabaa Ahmed Yahya Al-Galal[1] · Imad Fakhri Taha Alshaikhli[1] · M. M. Abdulrazzaq[1]

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Abstract

The substantial progress of medical imaging technology in the last decade makes it challenging for medical experts and radiologists to analyze and classify. Medical images contain massive information that can be used for diagnosis, surgical planning, training, and research. There is, therefore, a need for a technique that can automatically analyze and classify the images based on their respective contents. Deep Learning (DL) techniques have been recently used for medical image analysis, and this paper focuses on DL in the context of analyzing Magnetic Resonance Imaging (MRI) brain medical images. A comprehensive overview of the state-of-the-art processing of brain medical images using deep neural networks is detailed here. The scope of this research paper is restricted to three digital databases: (1) the Science Direct database, (2) the IEEEXplore Library of Engineering and Technology Technical Literature, and (3) Scopus database. 427 publications were evaluated and discussed in this research paper.

Keywords Deep learning · Convolutional neural network · Brain tumor · MRI medical images

1 Introduction

Medical images are critical towards surgical planning, as it is a crucial information source for many diseases. It can also be used for research and training purposes. The demand for digital medical images is steadily increasing, for instance, in 2002, the University Hospital of Geneva's Department of Radiology produced between 12,000 and 15,000 images per day. The daily number of images produced and stored in the department increased to ~ 50,000 in 2007, and 114,000 in 2009 [1]. Therefore, an efficient and precise medical image analysis scheme is needed for operational planning, preparation of medical reports, and medical research and development. The traditional technique of manual analyzes of medical images is time-consuming, and its interpretation imprecise (prone to human error). Deep learning (DL) has been demonstrated to be significantly superior to manual image analyses in terms of medical image segmentation, classification, detection, registration, biometric measurement, and quality evaluation [2]. The current work focus on deep convolution neural networks (CNN), which has resulted in significant advances in the analysis of medical images [3].

Medical imaging is essential for the early identification and diagnosis of cancer. Cancer is an abnormal and uncontrolled division of cells in any part of the body. If these abnormal cells appear in the brain tissue, it is called a brain tumor. Brain tumors, similar to other types of cancers, can be benign (non-cancerous) or malignant (cancerous). Brain tumors can also be classified into primary and secondary tumors, where the former originates in the brain and is mostly benign, while the latter (known as a metastatic brain tumor) occurs when the abnormal cells spread from other organs to the brain [4]. One common type of primary brain tumor is Glioma, which develops from glial cells [5]. Tumors and strokes have been the world's second and third leading causes of death, respectively, after heart disease. According to the World Health Organization (WHO), 40,000–50,000 people are diagnosed with a brain tumor annually in India, out of which ~ 20% are infants [6]. One of the most common

✉ Sabaa Ahmed Yahya Al-Galal
aljalalsaba@gmail.com

Imad Fakhri Taha Alshaikhli
imadf@iium.edu.my

M. M. Abdulrazzaq
dr.obay@aic4all.com

[1] Kulliyyah of Information and Communication Technology, International Islamic University Malaysia, Kuala Lumpur, Malaysia

forms of cancers is brain cancer, with a ~ 70% mortality rate. Early detection would help increase the survival rates of brain cancer patients [7]. The Eurostat reports indicated that one out of ten in Europe is subject to CT scan annually and one in thirteen is subject to MRI [8]. The majority of prior research involved MRI medical images [9, 10].

Previous studies implemented supervised machine learning (ML) algorithms (hand-designed features) for brain tumor classification and segmentation [11]. These techniques use the classical ML algorithm, which apply feature engineering. Alternatively, they develop a task-adapted algorithm, which is a hierarchy of increasingly complicated features to learn directly from within the domain [12]. DL network performed better compared to the classical ML algorithms. Previous studies confirmed that the most efficient way to analyze big datasets is to use DL [13–15]. According to Menze et al. there has been an exponential increase in the number of publications dedicated to automated brain tumor classification and segmentation. This reference highlights the need for automatic classification and segmentation of brain tumors [16].

DL is considered a state-of-the-art algorithm for medical image analysis and has been successfully applied in many areas [17]. Deep neural networks (DNNs) are widely used for brain image analysis. Many studies tended to classify brain diseases, brain tissue segmentation, and anatomy. According to the literature, image analytics are mostly done by DNNs. In brain tumors segments challenges (BRATS), the longitudinal MSLS 2015, the 2015 ischemic stroke lesion segmentation challenge (ISLES), and the MR brain imaging challenge (MRBrains) in 2013, all of the top teams used CNNs, focusing on the abovementioned techniques of MRI scans of the brain [18].

The following sections are comprehensive reviews elaborating on the literature on image analyses. The third section details the methodology and datasets being used. The fourth section details the conclusion and recommendations gleaned from this analysis.

2 Comprehensive review

This section provides an in-depth review. The following subsection presents the systematic review protocol for the brain tumor MRI medical images and deep learning algorithms.

2.1 Systematic review protocol

The extent of this paper is determined by the use of the keywords ‘deep learning’, ‘brain tumor’, and ‘MRI’. The scope was restricted to three digital databases: (1) the Science Direct database providing highly reliable journals with access to science, technology, and articles; (2) the IEEEXplore Library of Engineering and Technology Technical Literature, and (3) Scopus database covering Peer-reviewed journals in essential subject areas: social sciences, physical sciences, and medical sciences. The literature search was performed up to Feb/2020. The process of selecting corresponding studies is relatively tricky, especially when accounting for the many research fields. Filtering papers is crucial and most important when investigating certain subjects. The first step was to remove duplicates, which was achieved using Mendeley. Then, the title and abstract were screened, and irrelevant documents excluded. The next step involves reading the selected papers, sometimes abstract does not give clear reflection of the whole contents, when we went deeper in some papers, we found that they are irrelevant references to the current work. So, we removed those papers, as per Fig. 1.

2.2 Taxonomy analysis

The search for the abovementioned query resulted in 427 papers. The field is relatively new, so we focused on recent years (2018–2020). Research alerts were set up for the same query in the three abovementioned databases (IEEE, Science Direct, and Scopus). Forty-four studies were duplicates and were removed, leaving a total of 383 papers. The papers were scanned by reading their titles and abstracts, and we ended up with 160 good papers. The number of papers that were available and downloaded was 108. The final set included 92 papers that were thoroughly read. The set of articles were divided into two main categories: segmentation and classification. The taxonomic review identified the general categories in deep learning for brain tumor medical images analysis. The mapping of the study illustrated in Fig. 2 represents the area of interest.

3 Segmentation

The segmentation method divides the image into areas that are not overlapping by a variety of rules/parameters, such as a collection of identical pixels/characteristics, encompassing contrasts, colors, and textures [19]. The number of publications devoted to automated brain tumor segmentation has grown exponentially over the past decade [11, 16]. The use of segmentation in medical images includes relevant information derived from the shape, length, organ location, and symptoms [20]. Tables 1 and 2 list the brain tumor medical images segmentation studies classified based on its used datasets. As per Table 1, more than forty studies within the research inclusion criteria used BRATS (more detail on this dataset explained in the upcoming sections), while other studies listed in Table 2 used different datasets.

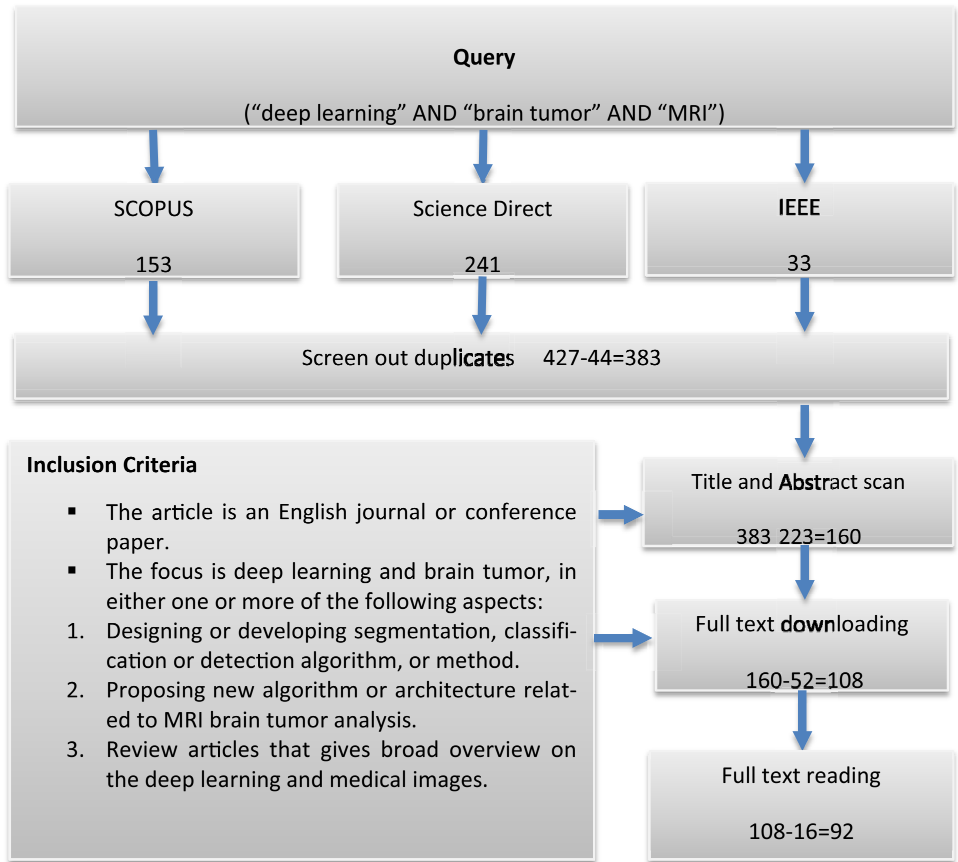

Fig. 1 The flowchart for research collection includes query words and inclusion criteria

In ML technology, the support vector machine (SVM) and random forest have been used extensively for the automatic segmentation of the brain tumor [21, 22]. These processes involve the feature engineering process to train the respective ML algorithms as per [23], where they achieved a Dice Similarity Coefficient (DSC) of 96% on BRATS (2015). However, this study depends on hand-crafted feature extraction. Pereira et al. applied a hybrid algorithm of random forest algorithm and Restricted Boltzmann Machine (RBM) and achieved a DSC of 84% on the complete, while they obtain ~ 74% on the core, tested on BRATS (2013) [24]. Thaha et al. developed an

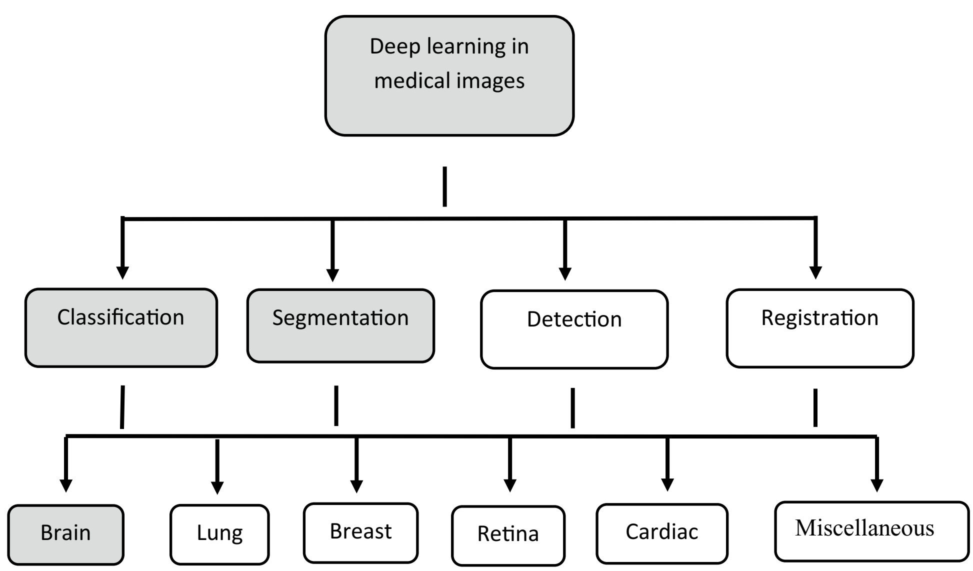

Fig. 2 Research taxonomy of deep learning in medical images showing the pattern recognition tasks and the anatomical regions, the grey highlighted boxes indicate the main focus of the paper

Table 1 brain tumor medical images segmentation studies that use BRATS Datasets

Ref	BRATS dataset	DL methods	Performance measures (DSC)
[23]	2015–2016-2017	LGR-DT-KNN-LDA-SVM-VGG19	DSC = 0.9636 on BRATS 2015
[28]	2015–2017	U-Net	DSC = 0.9401 on BRATS 2015 DSC = 0.9463 on BRATS 2017
[29]	2015–2017	U-Net	DSC = 0.89 on BRATS 2015 DSC = 0.86 on BRATS 2017
[33]	2013–2018	CNN AlexNet	Accuracy = 98.3%
[34]	2015	FCNN DMDF	DSC = 90. 89%
[35]	2018	GDL	DSC = 0.783
[30]	-	SVM V-Net	DSC = 64%, Precision (P) = 85% Recall (R) = 53%
[36]	2018	Hourglass U-NET	DSC (complete = 0.82, core = 0.72, enh. = 0.66)
[37]	2018	U-Net-RI U-Net-PR U-Net-DWP	DSC = 0.74
[2]	2015–2017	U-Net DeepMedic MLP	DSC = 85% on BRATS 2015 DSC = 89.30% on BRATS 2017
[38]	2017	2D-3D Model U-NET	DSC (complete = 0.918, core = 0.883, enh. = 0.854)
[39]	2018	CA-CNN U-Net	DSC = 61.0%
[25]	2015	CNN ECNN	Precision = (CNN: 82%, ECNN: 87%) Recall = (CNN:85%, ECNN: 90%) Accuracy = (CNN: 89%, ECNN:92%)
[12]	2013	CNN	DSC = 88%
[32]	2015	3D CNN	DSC = 90.1% Precision = 91.9% sensitivity = 89.1%
[31]	2015	CNN	DSC (complete = 0.78, core = 0.65, enh. = 0.75)
[40]	2015–2016	VGG-16	Accuracy = 82.2%
[41]	2015	3D CNN	DSC (complete = 0.84, core = 0.72, enh. = 0.62)
[42]	2015–2016-2017 ISLES 2018	Alex/ GoogleNet	DSC = 0.9891 on BRATS 2015
[24]	2013 SPES	RBM- RF	DSC (complete = 0.84, core = 0.74, enh. = 0.71)
[43]	2015–2017	HPU-Net	DSC (complete = 0.92, core = 0.80, enh. = 0.76) on BRATS 2017 DSC (complete = 0.90, core = 0.71, enh. = 0.78) on BRATS 2015
[44]	2016	DCNN	DSC (complete = 0.90, core = 0.85, enh. = 0.84)
[45]	2017	Cascade U-Net	DSC (complete = 0.81, core = 0.69, enh. = 0.55)
[46]	2015 -2016	FCNNs CRF-RNN	DSC (complete = 0.84, core = 0.73, enh. = 0.62)
[47]	2017	XCNet- ELOBA_λ	DSC (complete = 0.89, core = 0.76, enh. = 0.81)
[48]	2015	MLP/ U-Net	Precision = 84 Recall = 88 DSC = 85

Table 1 (continued)

Ref	BRATS dataset	DL methods	Performance measures (DSC)
[49]	2015	3D-CNN DEEPMEDIC	DSC = 79%
[50]	2015	DCR RESNET 50	DSC = 87%
[51]	2015	SkipNet SENet IntNet (VGG)	SkipNet DSC = 87% SENet. DSC = 88% IntNet(VGG) DSC = 90%
[52]	2013–2015	CNN Linear nexus	DSC (complete = 0.86, core = 0.87, enh. = 0.90)
[53]	2015	TLN / ITCN FCN	DSC (complete = 0.89, core = 0.77, enh. = 0.80)
[54]	2017	PIXELNET VGG16	DSC = 87.6%
[55]	2013	ERT	DSC = 85%
[56]	2018	3D CNN	DSC (complete = 0.87, core = 0.84, enh. = 0.81)
[57]	2013	RF-DTI	DSC = 96%
[58]	2017	VGG16	DSC (complete = 0.86, core = 0.78, enh. = 0.66)
[59]	2015	CNN	DSC = 86.13%
[60]	2015–2018	WRN RESNET	DSC = 0.91 Sensitivity score = 0.94 PPV = 0.89
[61]	2017	CNN	DSC = 72%
[62]	2015	Saliency map U-Net	Precision = 86%

Enhanced Convolutional Neural Networks (ECNN) with the BAT algorithm by optimizing the loss function for the automatic segmentation process [25]. The findings of the experiments confirmed a better efficiency relative to the conventional methods. The parameters compared are precision (CNN: 82%; ECNN: 87%) recall (CNN: 85%; ECNN: 90%) and accuracy (CNN: 89%; ECNN: 92%). However, various selection schemes can be implemented to increase the accuracy.

CNN architecture called U-Net is a breakthrough in the automated segmentation of images [26]. Ronnebergers's U-Net has a contraction direction and a symmetrical expanding direction with intermediate overhead links. The mirroring method is used for the estimation of the boundary pixels [27]. Table 1 detail recent studies that utilize the U-Net architecture. Nema and Dudhane achieved a DSC of ~ 94% on BRATS (2015) and ~ 94.63% on BRATS (2017). They used the U-Net alongside the skip connection method [28]. Li et al. reported a novel brain tumor segmentation using U-Net and added a skip connection and up skip connection when using two datasets (2015) and BRATS (2017) [29]. They achieved a DCS of ~ 89% and ~ 86%, respectively. V-net has a similar architecture to U-Net but is associated with 3D images. Gonella et al. applied the V-net algorithm on 3D MRI images and achieved a DCS of ~ 64% on a BRATS dataset [30].

Pereira et al. introduced the idea of using small-sized kernels due to its positive impact against overfitting [31]. The use of small kernels resulted in a deeper architecture due to the smaller weights in the system. They took part in the on-site BRATS (2015) challenge using their model, placing second with DSC matrices of 0.78, 0.65, and 0.75 for the full, core, and enhancing regions, respectively. Havaei et al. introduced a novel CNN architecture that incorporates a two-way architecture that can absorb local brain information in a broader context [12]. The two-phase training method is crucial for resolving unbalanced label distributions. They achieved an accuracy of ~ 88%. Kamnitsas et al. merged the previously mentioned algorithms (small kernel size and two pathway (normal resolution and low resolution)) and applied the 3D CNN; dense training on image segments and building deeper networks with 3D kernels [32]. The results using BRATS (2015) were DSC (~ 90.1%), precision (~ 91.9%), and sensitivity (~ 89.1%).

Among all of the reviewed articles of brain tumor segmentation studies, ten did not use the BRATS datasets; those studies are listed in Table 2. According to [63], they achieved ~ 84% accuracy using a dataset of only 40 MRI images. Similarly, many researchers used different datasets which have a limited number of images for the same purpose [64–66]. However, researchers also reported better

Table 2 Segmentation studies that use different datasets

Ref	Dataset	DL methods	Performance measures
[63]	Dataset: 40 MRI mixed images (normal and abnormal)	M-SVM CNN	Accuracy = 84%
[68]	FLAIR images in the dataset and only segment the whole tumor. We randomly selected 234 cases for training and used the remaining 40 cases for testing	CNN (P-Net) (R-Net)	DSC = 89.93 ± 6.49%
[69]	The MRI data of 5 subjects (2 male and 3 female, varying degrees of atrophy and white matter lesions) were provided as training database. The MRI data of another 15 subjects were collected as the testing database of MRBrainS	Multi-modality aggregation network	DSC = 86.40%
[14]	2457 images from BRAINIX MRI images	GCNN SWT	Recall = 98% Precision = 98%
[70]	NAMIC Brainweb Turmobase	CNN ROBEX	DSC = 95%
[66]	Sixty cases from three centers were released as a public training set	U-Net	DSC = 80%
[64]	2013 MICCAI MRBrainS, which consist only of 5 training and 15 testing	RELU BN RESNET	DSC = 86%
[71]	ISBR dataset ABIDE	3D FCNN	DSC = Thalamus, Caudate, Putamen Pallidum (0.92,0.87 0.13,0.25)
[65]	IBSR 2(Internet Brain Segmentation Repository), which consists of 18 manually segmented MR images of the brain	Densenet Growth rate Bottleneck	Accuracy = 92%
[72]	256 SAMPLES	SVM- CNN	Accuracy = 67%

accuracies when using DL algorithms as being associated with the usage of a large number of images in the datasets [18, 67].

4 Classification

Image classification is assigning one or more object labels to a category. It is one of the essential computer vision and pattern recognition tasks. In conventional image classification systems, an image is represented with low or medium-level characteristics, which are used for label assignments by a trainable classifier, while in DL, the process can be carried out without the handcrafted features, and both steps of feature extraction and classification are combined [73]. Many research institutions use the classification systems to classify brain tumors, where ~ 120 types of tumors are found in the brain and central nervous system (CNS). The tumor is classified according to their cellular origin and actions from the less active (benign) to the more aggressive (malignant). Tumors are assigned to grades I (least malignant) to IV (most malignant), representing its growth rate [4].

The classification of brain tumors helps predict its possible behavior and improve health systems. One common dataset that many researchers used to train their systems is the 3064 T1-CE MR images, consisting of three types of brain tumors (meningioma, Glioma, and pituitary tumors) obtained from 233 patients [74]. Table 3 lists the studies involved in applying the abovementioned datasets. They used different DL methods, except one study [75], which used the snake contour detection algorithm; however, the latter's accuracy was lower than those using the DL algorithms. The best accuracy was reported by [76]; however, it suffers from considerable misclassification of samples from the class of meningioma. Another study used the same dataset to compare two CNN archaicities and reported that the method with the Softmax output layer performs better than the method with the sigmoid output layer [77] (see Table 4)

Table 4 summarizes articles involving brain tumor classification using datasets other than the ones introduced earlier. Brunese et al. reported an excellent precision rate, reaching ~ 99% for grades (I, II and IV), and 97% for grade III, however, its method requires handcrafted features [7]. Talo et al. and Lu et al. used the same dataset from Harvard Medical School (HMS), with extensive data augmentation for the first mentioned reference. Their results are impressive at an accuracy of 100%, which is due to its limited range of images [15, 83]. Saxena et al.applied the CNN architecture, consisting of five fully connected layers and the softmax layer on the REMBRANDT dataset, but they obtained a relatively a low accuracy rate relative to that reported in another

Table 3 Classification studies that used the same dataset

Ref	Methods	Result
[78]	CNN	93.01% on the introduced split and 95.6% on a random split
[79]	VGG19	88.41%, 96.12%, and 94.58% for sensitivity. specificity, and accuracy respectively
[75]	Snake Contour detection	DSC was calculated as 0.78, 0.59 and 0.49 For Meningioma, Glioma and Pituitary tumor respectively
[77]	CNN DENSE SOFTMAX SIGMOID	The method with Softmax output layer performs better than the method with sigmoid output layer
[80]	VGG19	Achieve average accuracy of 94.82% under five-fold cross-validation
[76]	googleNet CNN SVM	Classification accuracy of 98%
[81]	KELM CNN KE-CNN	The accuracy of KE-CNN method on this dataset is = 93.68%
[82]	CapsNet	Segmented tumor = 86%

research [84]. Özyurt et al. used the super-resolution Fuzzy C-Means (SR-FCM) for tumor detection on the TCIA datasets of 500 samples, followed by classification using the CNN extreme learning machine [85]. They proved that the accuracy with a super-resolution is 10% better than without super-resolution, but the main drawback of the SR-FCM-CNN strategy is that it relies on the training dataset. Mallick et al. did not use CNN, they implemented the Deep Wavelet Autoencoder (DWA) on RIDER (Reference Image Database to Evaluate Therapy Response) dataset from TCIA and reported an excellent accuracy rate of ~93% [13]. However, researchers recommended using CNN, especially for the classification of medical images.

Table 4 classification table with different datasets

Ref	Dataset	Methods	Result
[7]	3 DATASETS: 1. JeffersonUniversity Hospitals (110,020) MRI From 130 patients 2. BRATS 2019 3. dataset is gathered from the Radiopaedia Repository	ML algorithms (SVM-KNN-RF-QDA)	A precision of 0.991(Grade I), 0.994 (Grade II), 0.976 (Grade III) and 0.990 (Grade IV)
[85]	TCIA was preferred. In the relevant database, approximately 500 samples were selected per different types of cancer and tissues	SR-FCM squeezeNet ELM classifier	98.33% accuracy rate has been detected in the diagnosis of segmented tumor
[83]	From Harvard medical school contains contain 38 normal and 177 pathological ones	Transfer learning AlexNet	They have achieved 100% accuracy
[84]	REMBRANDT which consists of MR scans of 130 patients suffering from glioma tumors of different types and at different stages. From this dataset, a total of 38,952 images	CNN Softmax Layer	The model gives a training accuracy of 63.17%, validation accuracy of 56.67% and test accuracy of 65.24%
[86]	20 FLAIR and T1-T2 weight brain images from the Tianjin Medical University Hospital, China	Fuzzy C-Mean CNN	Network for 24 epochs achieved Dice similarity 86,785%, and accuracy 98%
[13]	RIDER (19 subjects)	DWA-DNN	Accuracy 93%
[15]	613 images only including augmentation from Harvard medical school website	(CNN) based ResNet34	Accuracy 100% after 3 stages and 50 epochs
[87]	9 HGG with pre- and post-surgery MRI data and 9 metastasis patients with pre-surgery MRI data	SVM	Misclassification error of 8.4%
[88]	BRATS 2017contains 3D brain volume images from Mayo Clinic in USA	7 layers 2D CNN	Test accuracy of 90.87% for former case, and 89.39% for the latter case

5 Datasets

There are several medical images of brain tumors mentioned in the previous sections, but the most common datasets used by researchers are BraTS and TCIA due to its availability and reliability. More details on the datasets are given below.

5.1 BraTS

In MRI research, BraTS has been the focus of the assessment of state-of-the-art techniques for the segmentation of brain tumors. BraTS use MRT multi-institutional pre-operative scans to target the segmentation of brain tumors, namely gliomas, that are fundamentally heterogeneous (in their look, shape, and histology). Also, BraTS focuses on the patient's overall survival via integrative radiometric characteristics analysis and ML algorithms to define the clinical importance of this segmentation task. BraTS have six successful subsequent collections between 2012—2018, as per Table 5. However, several unprocessed or partially pre-processed images were found in a testing collection for BraTS (2016) [46].

5.2 The cancer imaging archive (TCIA)

The TCIA is an online resource sharing repository that is publicly available for download from different organizations; therefore, no approval is needed from the Institute Review Board (IRB). It contains many collections of different areas of the human body, with most being either CT/MRI types of medical images. The first published dataset was for Prostate Cancer in June 2011. One example of these collections was a dataset for a brain tumor published in February 2019 as shown in Table 6. This collection contains datasets of 20 newly diagnosed primary glioblastoma patients who underwent surgery and conventional concomitant chemotherapy (CRT) and adjuvant chemotherapy. For each patient, two IRM examinations were included: within 90 days after completion and advancement of a CRT (clinically determined and based on clinical results or imagery and marked by treatment or intervention change).

All images are in the form of DICOM format and included T1w (pre-post contrasting agent), FLAIR, T2w, ADC, normalized cerebral blood flow, normalized relative cerebral blood volume, standardized relative cerebral blood volume and binary tumor masks (created with T1w photographs). The pictures of perfusion were created after a preload of the contrast agent from the dynamic susceptibility comparison (GRE-EPI DSC). The T1 + C pictures are co-recorded for all of the series. The dataset evaluated the efficiency of a detailed learning algorithm for forecasting the development of the tumor [90]. More than 40 studies used this dataset; Table 7 includes some detail of these studies.

Table 5 Details of BraTS datasets [89]

BraTS	Country	Cases for training	Cases for testing
BraTS 2012	Nice, France	5 LGG, 10 HGG	-
BraTS 2013	Nagoya, Japan	10 LGG, 20 HGG	-
BraTS 2014	Boston, USA	16 LGG, 175 HGG	-
BraTS 2015	Munich, Germany	54 LGG, 220 HGG	110 (HGG, LGG)
BraTS 2016	Athens, Greece	54 LGG, 220 HGG	191(HGG, LGG)
BraTS 2017	Quebec City, Canada	75 LGG, 210 HGG	146(HGG, LGG)
BraTS 2018	Granada, Spain	75LGG, 210 HGG	66(LGG, HGG)

Table 6 One Example of TCIA collections on brain tumor [90]

Collection Statistics	
Number of Studies	40
Number of Series	383
Number of Patients	20
Number of Images	8798
Modalities	MRI
Image Size (GB)	3.2

6 Data augmentation

A broad dataset is essential for the success of the DL model. By increasing the existing data, the model's efficiency can be increased. Data augmentation allows researchers to increase the variety of data for learning models without actively acquiring new data. Some conventional techniques for data augmentation include rotation, cropping, padding, horizontal flipping, Gaussian blur, sharpen, edge detection [79], cross-modality image generation [111], and synthetic data [112, 113]. Other researchers also suggested image translation [114], but it could lead to a wrong class to the patch for segmentation [31]. Data augmentation is an excellent method for increasing the datasets in DL applications as long as it is carefully used.

7 Convolutional neural networks (CNN)

DL in medical images analysis is triggered by CNN. The second-best image classifying error was halved by a DL algorithm (a convolutional neural network) in 2012 in ImageNet Large-Scale Visual Recognition Challenge (ILSVRC) [114]. Over the

Table 7 The studies that refers to the TCIA Brain-Tumor-Progression datasets

Ref	Field of study	Algorithm used
[91]	Medical and Biological Engineering	Seed detection algorithm
[92]	Medicine	Topological data analysis
[93]	Computer Science	Unsupervised clustering by Euclidean distance
[94]	Medicine	quantified using algorithmic analysis of MR images
[95]	Biomedical Engineering	SVM and a radial basis function
[96]	Computer Science	Random forest, Gaussian Naive Bayes, KNN
[97]	Medicine	Velocity AI FSL 3D slicer
[98]	Medicine	Rigid registration tool Gary Level co- occurrence matrix (GLCM)
[99]	Computer Science	SVM
[100]	Medicine	(BraTumIA)
[101]	Computers and Electrical Engineering	SVM-KNN-NSC—k-Means Gaussian-Euclidean city block-Sparse
[102]	Computer Science	SVM, Neural network
[103]	Computer Science	Random Forest (RF)
[104]	Medicine	radiologists' toolbox Consensus matrix, CDF curve, and delta curve for all clusters
[105]	Computer Science	CRNN
[106]	Medicine	Measured in terms of overall survival time
[107]	Medicine	VASARI feature-set
[108]	Medicine	Expectation Maximization (EM) algorithm
[109]	Medicine	overall survival (OS) and progression-free survival (PFS) were
[110]	Medicine	leave-one-out cross validation approach to automatically extract imaging features

years, scientists developed different CNN architectures, which led to a massive improvement in the field. The error rate in competition represents this development, as per the ILSVRC, where the top-5 error rate for images classification fells from over 15% to over 3% in just three years. The top five error rate is the number of test images for which the system's prediction did not include the correct answer [115]. CNN started in 1998 with 60,000 parameters, and in 2012, AlexNet won the ILSVRC challenge with an error rate of 15.3% and 60 million parameters [114]. GoogleNet was introduced in 2014, and the error rate dropped to only 6.67%, with only 4 million parameters. Also, ResNet won the challenge in 2015, and its error rate dropped dramatically to 3.6%, which surpassed the human performance of 5.1%, rendering ResNet the current state-of-art CNN architecture [116]. It has been previously assumed that object identification in nature is difficult for computers, but CNN has now exceeded even humans in ILSVRC, effectively addressing the classification problem [117]. In CNNs, there are clear preferences based on their architecture that helps understand why they are so popular. The following sections explain the CNN building layer.

7.1 The convolutional layer (the kernel)

Convolution is the first layer where the functionality of an input image is captured. In order to learn the image features, convolution preserves the relationship of pixels using tiny squares of input data [118]. It is a mathematical operation that requires the two inputs, which are image matrix and filter/kernel. The convolution process aims to extract from the input image high-level features. The ConvNets should not be limited to a single layer. The first ConvLayer conventionally captures the low-level characteristics, encompassing, including the borders, color, orientation, and gradients. With additional layers, the architecture also adapts to the requirements of the high-level features, providing us with a network that understands the images within a complete dataset.

The role of ConvNet is to reduce the images to a more easy-to-work form without sacrificing the essential features to realize the right prediction, which is critical when designing an architecture that is not only useful for learning but can also be scaled to large datasets [119].

7.2 Activation function

Neurons are passed into a non-linear activation function in the activation process. The standard function activation is in sigmoid form, as follows:

$$f_{sigmoid} = \frac{1}{1 + exp^{(-x)}} \quad (1)$$

It has been demonstrated that the saturation of the sigmoid function resulted in poor performances when training the network. The rectified linear unit (ReLU) has been populated to solve this problem since the stochastic gradient downward convergence accelerated relative to the sigmoid function [120]. Also, an activation map at the threshold of zero can be applied. (ReLU) is defined as follows:

$$f_{relu} = max(0, x) \quad (2)$$

7.3 Pooling layer

When the images are too large, the pooling layers' segment will decrease the number of the parameters. Spatial pooling is also known as sub-sampling/sampling, where it reduces the dimensionality of each map while maintaining important details. The pooling layer is, like the convolved layer, responsible for the convolved feature's spatial dimension. It decreases the computing power required to process data by reducing the dimensionality [121]. Also, the efficient shaping of the model can be used to extract the dominant features, which are rotating and position invariant. Examples of rates of swimming are Max and Average Pooling. The maximum value of the portion of the image projected by the kernel is returned by Max Pooling [122]. In comparison, the Average Pooling gives the cumulative sum of the values in the Kernel portion of the image, as per Fig. 3.

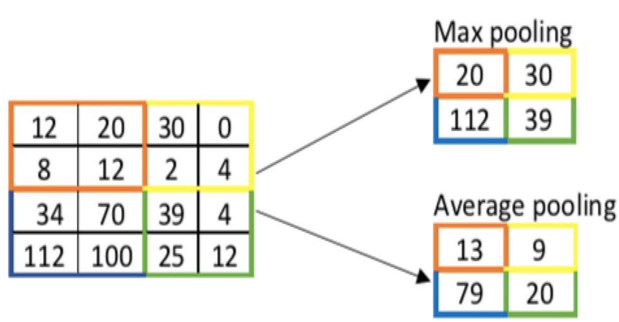

Fig. 3 Example of Pooling layer

7.4 Fully connected layer (FC Layer)

Neurons in an ultimately linked layer have complete ties, as seen in standard Neural Networks, to all the activations of the previous layer. Their activations can be determined by multiplying the matrix with an offset bias.

7.5 Evaluation metrics for the medical image analysis system

Various primary performance indicators, such as accuracy, F1-score, precision, recall, sensitivity, specificity, and the dice coefficient, can be used to test the standard medical image analysis method [31].

$$F1_{score} = 2x\frac{(PrecisionxRecall)}{(Precision + Recall)} \quad (3)$$

where:

$$Precision = \frac{(TP)}{(TP + FP)} \quad (4)$$

$$Recall = \frac{(TP)}{(TP + TN)} \quad (5)$$

$$Sensitivity = \frac{(TP)}{(TP + FN)} \quad (6)$$

$$Specificity = \frac{(TN)}{(TN + FP)} \quad (7)$$

$$DiceScore = \frac{2x|P \cap GT|}{|P| + |GT|} \quad (8)$$

The symbols in the previous equations are (TP), which stands for true positive, representing the number of cases correctly classified as defected, (FP), which stands for false positive, representing the number of cases that are incorrectly classified as defected, (TN), which stands for true negative, representing the number of cases correctly classified as non-defected, and (FN), which stands for false negative representing the number of cases incorrectly classified as non-defected. In the last Eq. (8), P stands for the prediction provided to a test sample by the method being evaluated, while GT demonstrates the ground truth of the respective test sample [20].

7.6 CNN popular architectures

The design of the CNN for a specific task includes the under-representation of the task, its criteria, and optimal usage of the computing and resource usage plan for the system. A simple combination of layers was used in the early designs of CNN, such as the one in AlexNet [114]. Further CNN architectures are relatively more complex, and each evolution relies on previous technological ideas and experiences for updating its developments. The next list detail some state-of-the-art CNN architectures.

1 *AlexNet*
AlexNet is the network that triggered the DL revolution since researchers made outstanding efforts to improve the ILSVRC 2012. It has 60 million parameters and 650,000 neurons, with five convolutional layers, max-pooling layers, activation function (RELU), and 1000-way softmax layer [114].
2 *VGG*
VGG is the culmination of the idea of small kernels and deeper networks, such as VGG 19, which is made up of 19 layers compared to only 7 layers in AlexNet. It comprises mainly of a sequence of convoluted layers using small kernels followed by three full-connected (FC) layers, with the last layer is the soft-max layer [123].
3 *GoogleNet*
The main idea introduced in GoogleNet is the better stacking of CNN layers, similar to the ones in the deep NIN (network-in-network) [124]. The key concept behind the inception architecture is handling and coping with readily accessible dense components in a convolutional network [125]. GoogleNet is also famous for reducing the parameters of the network since it does not fully apply the connected layer at the end; instead, it uses the average pooling, which enables it to compete with more complex architectures to achieve a similar accuracy [125].
4 *ResNet*
This CNN architecture was developed by Kaiming He et al., who won first place at the ILSVRC 2015 [126]. One of ResNet's key advantages is that it enables the creation of an incredibly deep neural network by implementing the skip connection principle to skip one/more layers to solve the degrading precision and vanishing/exploding gradients issue [127]. ResNet was used to develop extensive computer vision applications, but little work has been performed involving the segmentation of medical images [41]. ResNext is the extension version of ResNet introduced by Xie et al. [128] which combines the inception model from GoogleNet and skip connection from ResNet [129].
5 *U-Net*
It is a popular and efficient 2D image segmentation network. The image is first processed using a conventional CNN architecture, and once an image is obtained, a symmetric network is used for the up-sampling path to revert the image to its original size. This network also applies the skip connection technique, similar to the way it is used in ResNet [27]. The 3D version of U-Net is called V-Net [130].
6 *SE-Net*
The Squeeze and Execution (SE) network won the ILSVRC 2017 challenge. It focuses on the ResNext but added easy-to-train parameters that can be used by the network to measure each feature map, while previous networks only implemented it. They SE-Net layers enable the network to individually model the channel and space data to increase the model's capability. The Squeeze-Net layers can be applied to any CNN model, but doing so will increase its competitional costs [131].

7.7 Transfer learning

Transfer learning is a collection of ML techniques that can be used to save knowledge from a problem/dataset for application to a similar problem. If the intended dataset size is not enough, the network parameters can be preserved to prevent overfitting [132]. Transfer learning methods are standard practice when the goal size is insufficient, and many researchers used this technique in DL architectures. Two transfer learning techniques can be utilized when the processed data is broad, as is the case in MRI medical images: first is the pre-trained network for extracting functions, and second is the fine-tuning a pre-trained network with the data [18]. Kuzina and Egorov's experiments have been conducted using a basic U-Net (transfer learning of the U-Net) model and using a subset of BraTS 2018 [37]. Transfer learning has also been applied to AlexNet and GoogleNet by Amin et al. [42], Talo and Baloglu applied transfer learning using the pre-trained CNN ResNet34, while Swati and Zhao applied transfer learning and fine-tuning on CNN (VGG19) [23, 80, 133, 134]. Deepak and Ameer applied transfer learning on GoogleNet [76], while Gonella and Binaghi applied transfer learning on V-Net [30]. Many others adopted similar approaches [15, 23, 83, 135–137].

8 Discussion

The vast number of medical images make it difficult for accurate expert analyses [15]. Manual analyses of medical images analysis are limited in their effectiveness (prone to human error) and are time-consuming [15]. Although ML and DL techniques are better than manual analyses, research is ongoing on improving both approaches in terms of its accuracy [16]. The challenges of DL technology due to insufficient data and restricted labels are addressed via strategies such as data augmentation and transfer learning. Since DNN rely on convoluted complex structural models of the training data for predictions, it makes it difficult to interpret these predictions. The concern with the DNN is "black box," which means that it can make exact predictions, but the extracted features are ambiguous [18, 117]. Despite these challenges, DL networks for the analyses of medical images continue to persist. Medical attention can also be leveraged in the area of computer-aided diagnosis (CAD) systems for the improvement of the general attitude of computer science researchers.

The significant advantage of the techniques of DL is its computability and consistency with many conventional techniques. This merger has excellent advantages in the context of innovations. Typically, CNN architectures are known to be computationally very powerful.

9 Conclusion

A systematic study of DL approaches for MRI brain medical images processing has been conducted. DL methods focusing on convolutional neural networks (CNN) are more applicable to all sub-fields of medical image processing, such as classification, identification, and segmentation. The issues associated with DL approaches due to minimal data and labels are addressed using strategies such as data augmentation and transfer learning. Nonetheless, it is also assumed that other issues can be addressed with the collection of resources provided in this paper. It is expected that DL is likely to remain an essential field of research in MRI brain tumor medical image analyses.

Compliance with ethical standards

Conflict of interest The author has no conflict of interest in submitting the manuscript to this journal.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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