

Deep Learning Based Segmentation of Brain MRI: Systematic Review (from 2018 to 2022) and Meta-Analysis

Priyanka Mahajan¹, Prabhpreet Kaur²

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Abstract:

Background This paper aims to perform an examination and statistical analysis of deep learning (DL) models utilized in the segmentation of brain tumor MR Images.

Methods The research systematically searched for pertinent research in databases such as PubMed, Science Direct, The Cochrane Library, and Web of Science. The studies related to deep learning (DL) in the context of brain tumor MR image segmentation are included for analysis. Meta-analysis focusing on the dice similarity coefficient (DSC) is conducted to evaluate the segmentation outcomes of these DL models. To categorize the research studies on the basis of sample size and method of segmentation, subgroup analysis is also carried out. Subgroup analysis is important to remove publication bias.

Results Thirty articles are selected from the published research works (n=445) and incorporated into the literature review scope. Eleven cohort studies met the inclusion criteria of the meta-analysis. For the performance of segmented tumors, the average DSC score for the included studies' DLAs is 0.93 (95% CI: 0.88–0.98). However, there is a large amount of variation amongst the papers that were included, and a bias toward publication can also be seen.

Conclusion The accuracy of DLAs used to automate the segmentation of gliomas is high, suggesting that they will be useful in neuroradiology in the future. However, accessible, high-quality public databases and extensive research validation are still required on a large scale.

Keywords Deep learning, Meta-analysis, segmentation, dice score, forest plots, publication bias.

1. Introduction

A tumor is when cancer cells grow uncontrollably in any part of the body. Brain tumors are the medical term for abnormal and unchecked expansion of brain or body tissue cells surrounding the brain (J. Liu et al., 2014). In terms of their point of origin, there exist two separate classifications of brain tumors: secondary and primary. Most primary brain tumors stay localized in the brain and never metastasize. In contrast, metastatic or secondary brain tumors originate from cancer that initially develops in another region of the body and later spreads to the brain. It is the rate of growth that determines whether a brain tumor is benign or malignant. Benign tumors have these hallmarks: a slow growth rate, a normal appearance, and well-defined borders,

while malignant tumors grow rapidly and have an irregular shape, both of which can be fatal (Nazir et al., 2021). Various tumor types along with their occurring percentages are shown in Fig.1

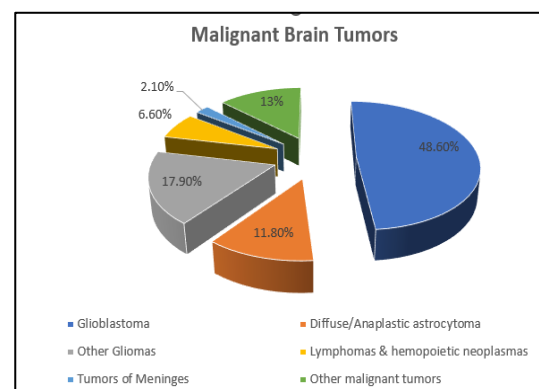


Fig. 1 Diverse brain tumor categories and their percentages of occurrence.

According to a survey by UNI, ten percent of all malignancies in India are brain tumors. The report refers to information provided by the International Association of Cancer Registries (IACR) affiliated with the World Health Organization (WHO) in their Globocan 2018 report. This analysis estimates that India diagnoses 28,142 new cases of brain tumors annually and, with 24,003 deaths as a direct result (M. I. Sharif et al., 2020). A news article from 'The

*1*Research Scholar,
Dept of Computer Engineering & Technology,
Guru Nanak Dev University,
Amritsar
Email: p_pankaj_gupta@yahoo.co.in
Orcid ID:0000-0002-6040-8943
*2*Assistant Professor,
Dept of Computer Engineering & Technology,
Guru Nanak Dev University,
Amritsar
Email: prabhpreet.cst@gndu.ac.in
Orcid ID: 0000-0001-8498-5940

Hindu' in 2016 stated that over 2,500 children in India are diagnosed with a type of brain tumor called medulloblastoma each year (A. Tiwari et al., 2020). Up until now, researchers have identified approximately 120 distinct tumor types (Kaur & Gill, 2017), each exhibiting various shapes and sizes (Shinde & Girish, 2020).

Brain tumor diagnosis involves three key steps: classification, detection, and segmentation. Tumor detection algorithms focus on identifying the presence of tumors. On the flip side, tumor segmentation techniques are used to precisely pinpoint and separate different tumor tissues that may contain multiple tumors. Furthermore, tumor categorization methods are used to label aberrant images as either benign or malignant tumors. Traditionally, radiologists conducted these tasks manually, which was time-consuming and error-prone. To address this, researchers turned to deep learning and machine learning (Kumari & Saxena, 2018). Despite existing scientific research, there hasn't been a thorough review of deep learning algorithms (MLAs) for accurate glioma segmentation. This study aimed to fill this gap by reviewing DLA-driven brain tumor segmentation tools using MRI data. We identified strengths and weaknesses and made suggestions for future studies.

2. Nuclear Magnetic Resonance Imaging (NMRI)

In recent years, medical imaging techniques have made significant advancements in aiding disease detection and precise location identification. Magnetic resonance imaging (MRI) stands out due to its safety and ability to provide detailed 3D images (Kaur & Gill, 2017). MRI excels at accurately detecting soft tissue abnormalities (M. Sharif et al., 2020).

Compared to CT scans, MRI offers superior diagnostic benefits with lower radiation exposure and improved contrast (Amin et al., 2020). MRI is valuable for diagnosing various brain-related diseases, including Alzheimer's, Parkinson's, dementia, and more (Acharya et al., 2019), Parkinson's disorder (Amoroso et al., 2018), dementia (Bruun et al., 2019), and many others.

Fig 2 (online source: (*MRI T1 vs T2*, n.d.)) illustrates three distinct MRI sequences: Fluid Attenuated Inversion Recovery (FLAIR), T1, and T2. FLAIR sequences are characterized by significantly prolonged Time to Echo and Repetition Time intervals, which are essential for effectively identifying anomalies within brain images (A. Tiwari et al., 2020).

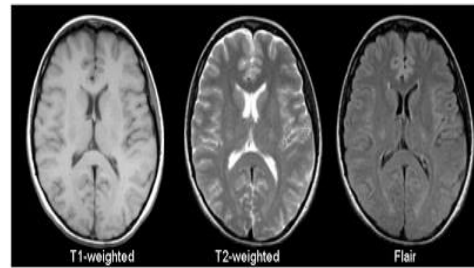


Fig 2. (a) T1- weighted (b) T2- weighted (c) FLAIR

3. Research Gaps

1. While there has been notable progress in diagnosing brain tumors, these improvements haven't been widely adopted in clinical settings. This could be because of limited collaboration between researchers and medical professionals, leading to continued reliance on manual tumor examinations. Additionally, only a few studies used data from multiple MRI techniques. Utilizing all four MRI methods during training can help reduce overfitting and enhance accuracy (Flair, T1-c, T1, T2).
2. Even though Deep Learning Algorithms (DLAs) have been useful for pinpointing and categorizing brain tumors, there are still challenges to be overcome. The existing literature on this topic lacks a combined summary or meta-analysis.
3. A system that can simultaneously pre-process, enhance, feature-extract, select, classify, and detect tumor is essential.
4. Relevant studies of previously published survey papers related to brain tumor diagnosis has shown that there was a publication bias because no interest was shown in publishing Deep Learning algorithms with poor performance.

This study seeks to fill gaps by conducting a meta-analysis of brain tumor segmentation research using Deep Learning Algorithms (DLAs). The goal is to summarize findings, point out strengths and weaknesses, and offer suggestions for future studies in this research area.

4. An Analysis of Segmentation-Related Literature

This section examines recent research on using deep learning for brain tumor MRI segmentation, covering articles published from 2018 to 2023. It's divided into three parts Part A summarizes commonly used datasets. Section B compares and contrasts different approaches. Section C provides a critical evaluation in a tabular format.

4.1 Datasets used for Brain Tumor diagnosis

When training a Deep Learning CAD system, a large trove of datasets are available for download for study ((M. I. Sharif et al., 2020); (Abd-Ellah et al., 2019)). Table 1 provides a basic list of the dataset names. The examined literature makes use of various datasets, still the BRATS dataset, with its larger size and better visualization

properties, is the most frequently cited. Fig 3 shows the usage of datasets for diagnosis of tumorous region.

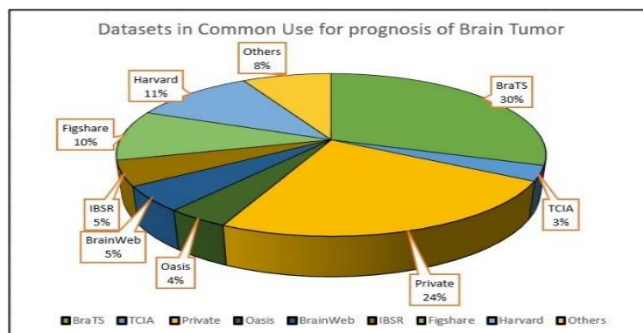


Fig 3 Datasets usage of brain tumor
Table 1. Datasets of Brain MRI available.

Dataset Name	Taken From	Modalities included	Types of images	No. of total images	Link to the dataset
“IBSR” (Internet Brain Segmentation Repository)	the CMA 'autoseg' biasfield	“T1- weighted”	I Normal II Segmentation	21 18	“ https://doi.org/10.18116/c6wc71 ”
“RIDER”	TCIA	“T1, T2-weighted”	Tumor	70,220	“ https://wiki.cancerimagingarchive.net/display/Public/RIDER+Collections ”
“AANLIB”	Harvard Medical School	“T1- and T2-weighted MRI”	Normal, Tumor	--	“ https://www.med.harvard.edu/aanlib/ ”
“Allen brain atlas”	Allen Institute Publications for Brain Science	“T1, T2, and DTI”	Normal	20	“MRI Donor Data :: Allen Human Brain Atlas :: Allen Brain Atlas: Human Brain (brain-map.org)”
“Brain Web”	McConnell Brain Imaging Centre	“T2-, T1- Proton Density-Weighted”	Simulated normal Simulated Multiple Sclerosis	20	“ https://brainweb.bic.mni.mcgill.ca/ ”
“CjData”	Harvard dataverse repository	“T1-weighted Contrast enhanced”	Pituitary, Glioma, Meningioma tumor	708,1426, 930	“ brain tumor dataset (figshare.com) ”
“BRATS_2012”	THE MICCAI challenge	“T1-weighted (T1Gd), T1, T2 FLAIR, T2-weighted (T2)”	GBM (Glioblastoma) / HGG and LGG	45 3D images	“ https://www.smir.ch/BRATS/Start2012 ”
“BRATS_2013”	THE MICCAI challenge	“T2 FLAIR, T1-weighted (T1Gd), T1, T2- weighted (T2)”	GBM (Glioblastoma) / HGG and LGG	65 3D images	“ https://www.smir.ch/BRATS/Start2013 ”
“BRATS_2014”	THE MICCAI challenge	“T2 FLAIR, T1-weighted (T1Gd), T1, T2- weighted (T2)”	GBM (Glioblastoma) / HGG and LGG	50 3D images	“ https://www.smir.ch/BRATS/Start2014 ”
“BRATS_2015”	THE MICCAI challenge	“T1-weighted (T1Gd), T1, T2 FLAIR, T2-weighted (T2)”	GBM (Glioblastoma) / HGG and LGG	300 3D images	“ https://www.smir.ch/BRATS/Start2015 ”
“BRATS_2016”	THE MICCAI BrainLes workshop	“T1-weighted (T1Gd), T1, T2 FLAIR, T2-weighted (T2)”	GBM (Glioblastoma) / HGG and LGG	300 3D images	“ https://www.smir.ch/BRATS/Start2016 ”

“BRATS_2017”	THE MICCAI-2017	“T1-weighted (T1Gd), T1, T2 FLAIR, T2-weighted (T2)”	GBM (Glioblastoma) / HGG and LGG	285 3D images	“https://www.cbica.upenn.edu/sbia/Spyridon.Bakas/MICCAI_BraTS/MICCAI_BraTS17_Data_Training.zip”
“BRATS_2018”	BraTS challenge	“T1-weighted (T1Gd), T1, T2 FLAIR, T2-weighted (T2)”	Glioblastoma (GBM/HGG) and lower grade glioma (LGG)	276 HGG and 75 LGG 3D images	“https://www.med.upenn.edu/sbia/brats2018/data.html”
BRATS_2019	MICCAI challenge	“T1, T2 FLAIR, T1(ce), T2”	Glioblastoma (GBM/HGG) and lower grade glioma (LGG)	384 HGG and 76 LGG 3D images	“https://www.smir.ch/BRATS/Star2019”
BRATS_2020	MICCAI challenge	“T1, T2 FLAIR, T1(ce), T2”	lower grade glioma (LGG) and glioblastoma (GBM/HGG)	418 HGG and 76 LGG 3D images	“https://www.smir.ch/BRATS/Star2020”

5. Brain Tumor segmentation methods

The primary motive behind segmentation is to identify tumor regions for easier detection and categorization of brain cancers by modifying the MR image representation. Differentiating tumor tissues like edema, necrosis, and active tumor from normal brain tissues is referred to as brain tumor splitting (Abd-Ellah et al., 2019). Brain MR scans are difficult to segment or classify due to their complex anatomy and significant level of inconsistency. Deep learning simultaneously handles feature extraction mechanism and efficient task performance. Few broad classifications are as in Fig. 4

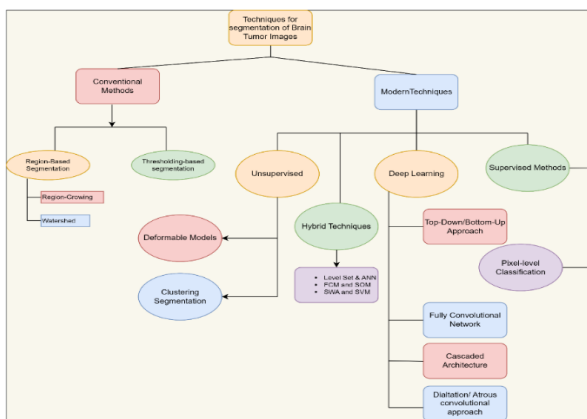


Fig. 4 Segmenting images of brain tumors using standard approaches.

Fig 5 shows the exemplar of brain tumor segmentation of BraTs 2013 dataset implemented through U-Net mechanism in Python language.

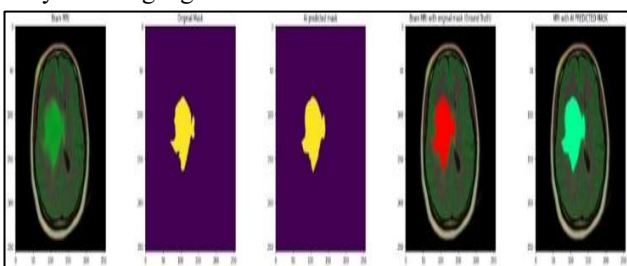


Fig. 5 Exemplar of segmentation of images of BraTS 2013 database through U-Net mechanism.

6. Meta -Analysis

In recent years, the use of deep learning, particularly Convolutional Neural Networks (CNNs), has surged for brain tumor image segmentation. These CNNs have excelled in recognizing objects in 2D and 3D images, driving the development of various CNN architectures aimed at improving accuracy. Some architectures focus on automatic segmentation, while others employ semi-automatic techniques, resulting in varying levels of tumor segmentation accuracy. This paper presents a comprehensive survey of popular methods for MRI brain tumor segmentation, highlighting potential for new approaches.

Our survey incorporates a wide range of papers and research from databases like Science Direct, PubMed, Scopus, and Web of Science. To ensure relevance, we applied specific criteria during selection, considering national and international journal papers and conference proceedings related to brain tumor segmentation. Studies that didn't meet these criteria, such as duplicates, inaccessible texts, or non-English articles, were excluded. Figure 1 summarizes the criteria used to identify the final publications for our study. Initially, a total of 3096 publications were identified through comprehensive searches of the databases selection. Additionally, 25 publications were discovered through cross-referencing. So, a total of 3121 publications were retrieved. After removing duplicate publications, 1783 papers remained for evaluation using the exclusion criteria. Further, 1338 publications were excluded based on the examination of their titles and abstracts. After screening 445 full-text research publications for suitability, 85 were chosen for this investigation. Fig. 6 shows the selection of research papers through the state- of -art PRISMA technique.

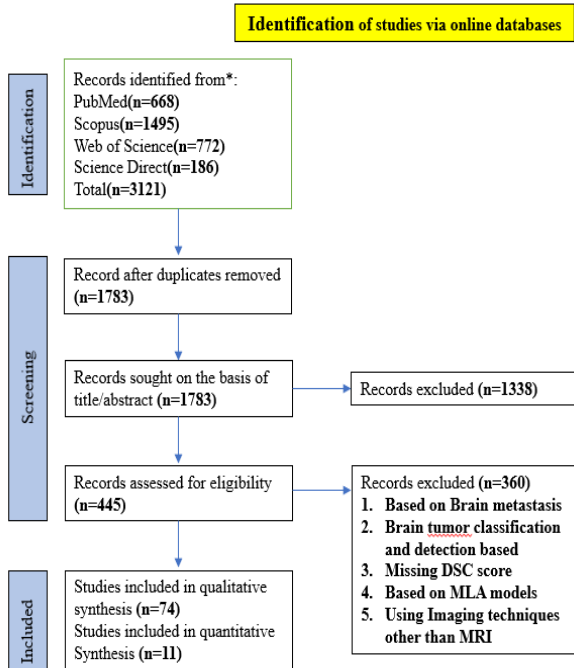


Fig 6. PRISMA technique used for inclusion of relevant classification and segmentation studies of Brain Tumor

Here, Section 2 provides a comprehensive background on MRI imaging and brain tumor characteristics followed by section 3 which addresses research gaps identified in prior studies. Then section 4 discusses the datasets used for brain tumor analysis. Also, section 5 outlines the brain tumor diagnosis process, including detection, classification, and segmentation and section 6 details the meta-analysis, including search methods, keywords, and inclusion criteria. Finally, section 7 concludes the survey, summarizing key findings and suggesting future research directions.

This extensive review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (van Kempen et al., 2021). The literature on deep learning algorithms for brain tumor segmentation is reviewed, searching MEDLINE (via PubMed), Scopus, Springer, and other databases from April 1, 2018, to May 19, 2023. Section 6 provides the search strings, including keywords and criteria. The studies that used DLA-based techniques to segment brain tumor patients' MRI images are included and their results using a dice similarity coefficient (DSC) score are defined. All non-human and duplicate studies are excluded.

6.1 Review of Included Studies This review draws heavily from searches conducted in (1) Google Scholar, (2) Springer Library, (3) PubMed, (4) Scopus, and (5) Web of Science. The search query is quoted as (((“Brain Tumor”) AND “Region Growing”) AND “Segmentation”) AND (“machine learning” OR “Deep Learning”). Pseudocode 1 elucidates the procedures that were followed while selecting the included works. In addition, the paper exclusion criteria (EC) and inclusion criteria (IC) are indicated on Table 3.

Table 2. Inclusion and Exclusion criterias of research papers in Meta-analysis procedure.

IC1: Only MR scans of are taken during study excluding X-Ray scans.	EC1: Research studies other than brain tumor diagnosis
IC2: The studies which are peer-reviewed are considered.	EC2: Research that makes use of other forms of medical imaging besides MRI.
IC3: Research article only for those which are either web of science indexed or scopus indexed	EC3: Study which is not related to segmentation and classification (like brain metastasis)
IC4: Research articles based only on segmentation through deep learning having the Mean Dice Score with std. deviation in that score.	EC4: Survey based papers of Brain tumor diagnosis
	EC5: Papers based on case study

The included research allowed us to extract the following types of data: (a) corresponding author and year of publication; (b) dataset used for segmentation purpose; (c) size of training set; (d) external validation was utilized or not; (e) study methodology, including MRI sequences utilized to determine the ground truth; (f) performance of the algorithm(s) in terms of accuracy, jaccard coefficient, f1-score, sensitivity, DSC score, and specificity for both the external/internal as well as training test sets.

Pseudocode 1 Algorithm for different databases search for collection of articles.

```

1: procedure COLLECT_FROM_DATABASE (Methods for Brain Tumor Segmentation Using Deep Learning)
2: Search_List_Databases ← Springer, Pubmed, Scopus, Web of Science
3: Search_Year ← 2018– 2022 AND Few papers from older years through references
4: j ← 1 #initialization of counter variable
5: M ← 5 #M is the count for online databases
6: for j ≤ M do
7: Searching_keywords ← brain tumor, deep learning, region growing, segmentation, classification
8: if Link_for_search ∈ Searching_Databases and Year ∈ Searching_Year then
9: Search (Region Growing AND Segmentation AND Deep Learning AND Classification AND Brain Tumor)
10: end if
11: end for
  
```

```
12:   if Count_Number of Papers  $\geq$  0 then
13:       Papers_refining
14:       Include_papers_in_database  $\leftarrow$  IC1, IC2, IC3
15:       Exclude_papers  $\leftarrow$  EC1, EC2, EC3, EC4, EC5
16:   end if
17: end procedure
```

6.2 Quantitative Evaluation

The meta-analysis with a random effects model to gauge the overall accuracy of existing DLAs has been conducted. The studies that reported the DSC score along with standard error (SE), standard deviation (SD), or the 95% confidence interval (95% CI) are considered for selection. For studies providing SE or 95% CI, statistical evaluation of the standard deviation is carried out.

J Jamovi, a user-friendly interface for R statistical software is employed, for the quantitative meta-analysis (Viechtbauer, 2010), offering a great alternative to software like SPSS and SAS. This research considered $p < 0.05$ as statistically significant for two-sided tests. The DSC score, a popular metric for assessing segmentation accuracy, is main focus. The repeatability by comparing DSC scores and manual and automatic segmentations (Yeghiazaryan & Voiculescu, 2018) is assessed. A DSC score of ≥ 0.8 was considered good, while scores ≤ 0.5 were deemed insufficient.

All estimated DSC scores from included studies in a forest plot are represented, displaying the overall performance. If there was overlap between the 95% Confidence Intervals in subgroup analyses, additional statistical analysis is not conducted. The Higgins I^2 -test is conducted to assess heterogeneity among studies; More than 75% indicates high heterogeneity, while 0-40% suggests modest heterogeneity (Higgins et al., 2003). Stata, a statistical software, is used to create a funnel plot, visualizing potential publication bias. Table 3 lists these DLA meta-analysis studies.

Table 3. Included studies after the filtration carried out using PRISMA technique.

First author (published year) (Ref.)	Training set	Testing Set	MRI Sequence	Dataset Name	Subgroups	Method used for segmentation	Specificity	Dice Score	Sensitivity
Kavitha et. al. (2023) (Kavitha & Palaniappan, 2023)	293 Training + 125 validation	166	No	BraTS 2019	Whole Tumor	Shuffled YOLO	0.93	0.978	0.921
Kavitha et. al. (2023) (Kavitha & Palaniappan, 2023)	BraTS 2020	BraTS 2020	No	BraTS 2020	Whole Tumor	Shuffled YOLO	0.952	0.986	0.943
Ladkat et. al. (2022) (Ladkat et al., 2022)	293 training + 125 validation	166	No	BraTS 2019	Whole Tumor	3-D attention U-Net Model	0.852+-0.004	0.823+-0.062	0.895+-0.042
Ladkat et. al. (2022) (Ladkat et al., 2022)	293 training + 125 validation	166	No	BraTS 2019	Tumor Core	3-D attention U-Net Model	0.721+-0.004	0.712+-0.132	0.793+-0.176
Ladkat et. al. (2022) (Ladkat et al., 2022)	293 training + 125 validation	166	No	BraTS 2019	Enhancing Tumor	3-D attention U-Net Model	0.934+-0.002	0.603+-0.293	0.723+-0.273
Jasmine et. al. (2022) (Anita Jasmine et al., 2022)	BraTS 2013 (700 T1 c+ and Flair images)		No	BraTS 2013	Whole Tumor Tumor core Enhanced Core	YOLO Deep Learning	--	0.89 0.9 0.92	--
Ranjbarzadeh et. al. (2022) (Ranjbarzadeh et al., 2021)	228 (HGG + LGG)	29 (HGG + LGG)	“FLAIR, T2-w, T1-w, T1-ce”	BraTS 2018	Whole Tumor Tumor core Enhanced Core	Cascaded CNN	--	0.9203 0.8726 0.9113	0.9386 0.9712 0.9217
Shidong et. al. (2022) (S. Li et al., 2022)	220 HGG +54 LGG (110 for testing)		“Flair, T1, T1c, T2 image”	BraTS 2015	Whole Tumor	ROI + U-Net	--	0.877 +- 0.060	--
Ilhan et. al. (2022) (Ilhan et al., 2022)	369 (HGG + LGG)		“Flair, T1, T1c, T2 image”	BraTS 2020	Whole Tumor	U-Net	0.9983	0.88+-0.32	0.8362
Ilhan et. al. (2022) (Ilhan et al., 2022)	335 (259 HGG + 76 LGG)		“Flair, T1, T1c, T2 image”	BraTS 2019	Whole Tumor	U-Net	0.9982	0.87+-0.32	0.8301

Aminian et. al. (2022) (Aminian & Khotanlou, 2022)	30 (HGG + LGG)	10 (HGG)	"Flair, T1-CE"	BraTS 2013 (Testing set)	Whole Tumor	Two-Path Caps-Net	--	0.90	0.91	
					Tumor core			0.85	0.82	
					Enhanced tumor			0.78	0.8	
Aminian et. al.(2022) (Aminian & Khotanlou, 2022)	164 (HGG + LGG)	110 (HGG + LGG)	"Flair, T1-CE, T1, T2 "	BraTS 2015 (Testing Set)	Whole Tumor	Two-Path Caps-Net	--	0.88	0.9	
					Tumor core			0.79	0.8	
					Enhanced tumor			0.77	0.78	
Swaraja et. al.(2022) (Meenakshi et al., 2022)	285 (210 HGG + 75 LGG)		"Flair, T1-CE, T1, T2"	BraTS 2017	Whole Tumor	Transfer Learning	0.986 (with MSVM)	0.9125	0.98 (with MSVM)	
Swaraja et. al. (2022) (Meenakshi et al., 2022)	274 (220 HGG + 54 LGG)		"Flair, T1-CE, T1, T2"	BraTS 2015	Whole Tumor	Transfer Learning	0.99 (with MSVM)	0.9225	0.982 (with MSVM)	
Swaraja et. al. (2022) (Meenakshi et al., 2022)	30 (20 HGG + 10 LGG)		"Flair, T1-CE, T1, T2"	BraTS 2013	Whole Tumor	Transfer Learning	0.993 (with MSVM)	0.94	0.987 (with MSVM)	
Ahmadi et. al. (2021) (Ahmadi et al., 2023)	1120	80	"T2-w"	Private dataset	Whole Tumor	CNN + PCA	0.998	0.912	0.999	
Futrega et. al. (2021) (Futrega et al., 2022)	1251 training + 219 validation	570	"T1, T1-weighted (T1Gd), T2-w and T2-FLAIR"	BraTS 2021	Whole Tumor	Optimized U-Net with Deep supervision	--	0.9149	--	
Elhamzi et. al. (2022) (Elhamzi et al., 2022)	285		"T1, T1c, T2, and FLAIR"	BraTS 2017	Whole Tumor	CNN for glioma segmentation		0.997	0.86+-0.016	0.8
					Tumor Core			0.997	0.82+-0.094	0.816
					Enhanced Tumor			0.997	0.6+-0.089	0.614
Elhamzi et. al. (2022)	285			BraTS 2018	Whole Tumor	CNN for glioma segmentation		0.998	0.88+-0.024	0.832
					Tumor Core			0.996	0.77+-0.161	0.828

(Elhamzi et al., 2022)			“T1, T1c, T2, and FLAIR”		Enhanced Tumor		0.997	0.65+-0.1	0.612
Elhamzi et al. (2022) (Elhamzi et al., 2022)	369		“T1, T1c, T2, and FLAIR”	BraTS 2020	Whole Tumor	CNN for glioma segmentation	0.998	0.87+-0.027	0.765
					Tumor Core		0.998	0.91+-0.032	0.895
					Enhanced Tumor		0.998	0.79+-0.06	0.76
Liang et. al. (2022) (Liang et al., 2022)	285	66	“T1, T1c, T2-w, and FLAIR”	BraTS 2019	Whole Tumor	BTSwin-UNet	NA	90.28	NA
					Tumor Core			81.73	
					Enhanced Tumor			78.38	
Liang et. al. (2022) (Liang et al., 2022)	285	166	“T1, T1c, T2-w, and FLAIR”	BraTS 2018	Whole Tumor	BTSwin-UNet	NA	91.74	NA
					Tumor Core			85.53	
					Enhanced Tumor			81.93	
Zheng et. al. (2022) (Zheng et al., 2022)	2475	289	Not defined	Private Dataset	Whole Tumor	SCU-Net for segmentation	NA	0.9262	NA
Neelima et. al. (2022) (Neelima et al., 2022)	285	66	“T1, T1c, T2-w, and FLAIR”	BraTS 2019	Whole Tumor	U-Net Modified	NA	0.93	NA

6.3 Review of the included studies

The systematic review used a full-text search strategy to include 62 studies [Table 7] which performed both segmentation and classification, and the characteristics of the studies and their participants are shown in Table 4. The literature comprised of different DLAs and distinct categories of CNNs [(Anand et al., 2023), (ZainEldin et al., 2023), (Khan et al., 2022), (Balamurugan & Gnanamanoharan, 2023), (Athiyamani et al., 2023), (Svm & Maqsood, 2022)] and support vector machine [(Arif, Ajesh, et al., 2022), (Svm & Maqsood, 2022), (W. Wu et al., 2020), (Haq et al., 2022)], multiple classifier system [(Vankdothu et al., 2022), (M. I. Sharif et al., 2020), (Arif, Jims, et al., 2022)], and an auto encoder model [(Saeedi et al., 2023), (Kader et al., 2021)]. In addition, one experiment, employed a fully adversarial neural network [(Raja & Vijayachitra, 2023)], and one study used a Nakagami imaging method [(Alpar, 2023)]. Only 13 studies used external validation techniques for proving their correctness. Some studies omitted information about the MRI sequences they employed [(Shanthi et al., 2022), (Balamurugan & Gnanamanoharan, 2023), (Habib et al., 2022), (Srividya et al., 2023)]. Some studies used other than BraTS dataset [(Younis et al., 2022), (Rasool Reddy & Dhuli, 2022), (Tandel et al., 2022), (Reddy & Dhuli, 2023), (Srividya et al., 2023),]. The BraTS dataset has been used as the gold standard (i.e., the segmentations) in 27 separate researches. Four of these investigations [(Raja & Vijayachitra, 2023), (Srividya et al., 2023), (Shanthi et al., 2022), (Habib et al., 2022)] included the incorporation of original data segmentations. In ten of the researches, Figshare named dataset was used for segmentation purpose.

All analyses relied on previously acquired information. Five of the eleven studies in Table 4 dealt only with the separation of HGGs and LGGs. There were six more papers that talked about glioma segmentation, but they didn't break it down into LGG and HGG. Cross-validation was performed on the DLAs in 19 of the 74 papers that were included. The average DSC score among the included studies was 0.78, while the average sensitivity of the DLA tests was between 87 and 92%. Studies with a validated DSC score between 0.68 and 0.85 were selected. Sensitivity was (Haq et al., 2022) 89% (n = 2), whereas specificity was 98% (n = 1).

6.4 Meta- analysis of the involved research studies

Twenty DLAs were pooled from eleven trials for this meta-analysis, and their combined DSC was 0.93 (95% CI: 0.88 – 0.98) (Fig. 7). The results showed a heterogeneity of 90.4%, showing significant differences between the studies (p < 0.001) (Fig. 8).

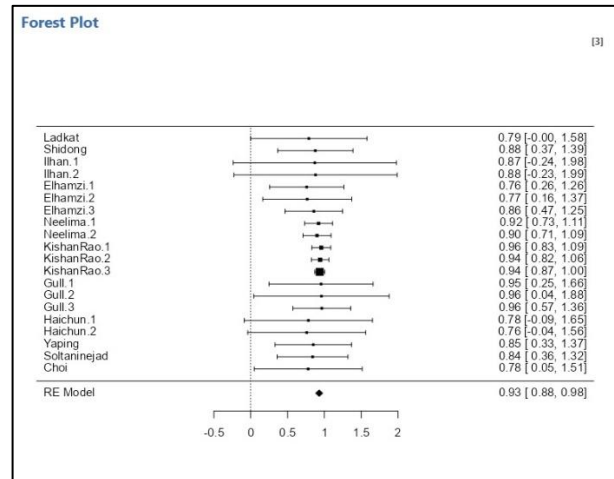


Fig. 7 Forests Plot showing the results of meta-analysis

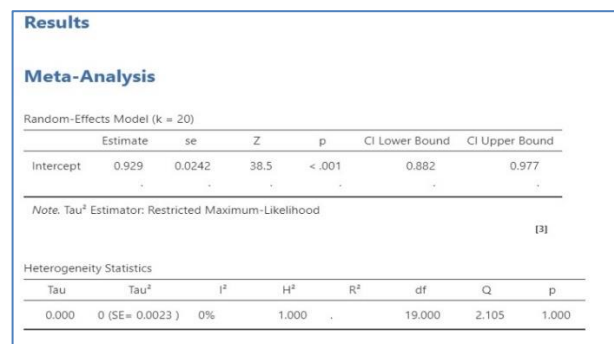


Fig. 8 Results of Heterogeneity

6.5 Publication Bias

The publication bias is also occurring this segmentation approach. Hence, a funnel plot (Fig. 9) is also plotted for further analysis.

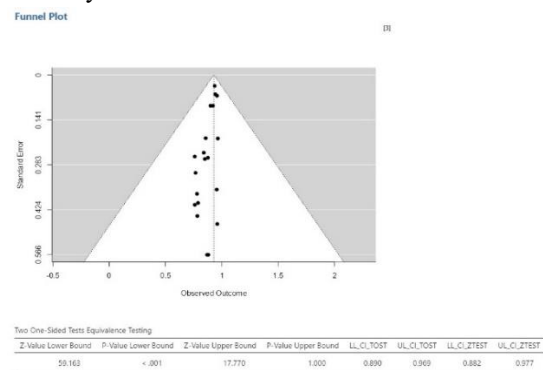


Fig. 9 Funnel plot in case of occurrence of publication bias. This research study also has the problem of publication bias. Hence, above funnel plot is drawn to overcome this problem.

6.6 Review of Included Studies

Analysis of the complete text reveals, 85 studies of brain tumor diagnosis were shortlisted. These collected studies used DL mechanism and performed the tasks of either segmentation or classification or both. All of them were shortlisted as systematic review participants, wherein Table 5 illustrates the demographics of the participants and the features of the study.

Table 5 Final table for all the included studies

Study ID/Year/Reference	Dataset Name	Purpose	MR Imaging Modalities	Algorithm Used	Training Images (N)	Performance Metrics	Pre-processing/Features Extracted	External Validation
Tiwari et. al(P. Tiwari et al., 2022) (2022)	Figshare (public dataset)	Classification	T1-w CE	CNN	2870	Accuracy, Precision, Recall	None	NO
Younis et. al(Younis et al., 2022) (2022)	MRI (public dataset)	Classification	Not Defined	CNN, VGG-16, Ensemble model	202	Accuracy, Recall, F1-Score	Preprocessing	No
Gamel et. al(ZainEldin et al., 2023) (2023)	BraTS 2021	Classification	T1, T1 CE, T2, FLAIR	Inception ResNet V2	1251 cases with 4 modalities	Accuracy, Sensitivity, Specificity, Precision, NPV, F1-Score	Both Preprocessing and Feature Extraction	NO
Rasool et. al(Rasool et al., 2022) (2022)	Public dataset	Classification	T1-w CE	Google-Net	2451	Accuracy	Fine Tuning	NO
Arkapravo et al.(Chattopadhyay & Maitra, 2022) (2022)	BraTS 2020	Classification	T1, T2, and FLAIR	CNN	2602	Accuracy	None	NO
Monirujjaman et. al(Khan et al., 2022) (2022)	Public Dataset from Kaggle	Classification	Not Defined	MobileNetV2 & VGG-19	3220	F1-score, Accuracy	Pre-processing & Post-processing	NO
Rahman et. al(Rahman & Islam, 2023) (2023)	Public Dataset + Figshare dataset+ Dataset from Kaggle	Classification	T1-w CE	PDCNN	Varied	Accuracy, Error Time, Kappa values	Preprocessing	NO
Shanthi et. al.(Shanthi et al., 2022) (2022)	Public dataset from clinics of Karnataka	Classification	Not Defined	Optimized Hybrid CNN + LSTM	600	Accuracy	Pre-processing	NO
Tandel et. al.(Tandel et al., 2023) (2023)	Molecular brain tumor data (REMBRANDT)	Classification	FLAIR, T1 (w), T2 (w)	5 different transfer learning models are tested	13,472 data points	Accuracy, Sensitivity, Specificity, AUC, PPV, NPV	Pre-processing & Feature Extraction	Yes (5-fold)
Suganya et. al.(Athisayamani et al., 2023) (2023)	Figshare + BraTS 2019 + BraTS 2021	Segmentation + Classification	FLAIR, T1 (w), T2 (w), T1-CE	ResNet-152 based DCNN	—	Accuracy, Precision, Recall	Pre-processing & Feature Extraction	NO

Gomez et. al.(Gómez-Guzmán et al., 2023) (2023)	Figshare +SARTAJ+ Br-35	Classification	FLAIR, T1(w), T2-(w), T1-(w) CE	Generic CNN, ResNet50, InceptionV3, InceptionResNetV2, Xception, MobileNetV2, and EfficientNetB0	6397	Accuracy, Specificity, precision, Recall, AUC	Pre-processing	NO
Vatsala et. al.(Anand et al., 2023) (2023)	The Cancer Genome Atlas (TCGA)	Classification	Not Defined	Weighted Avg. Ensemble Model	3536	Accuracy, Sensitivity, Precision, F1-Score	Feature Extraction	NO
Ramdas et. al.(Vankdothu et al., 2022) (2022)	Kaggle dataset (32/harvard64 images)	Detection + Classification	Not Defined	CNN + LSTM	2870	Accuracy, Precision, Recall	Feature extraction & Pre-processing	NO
Ghazanfar Latif (Latif, 2022) (2022)	BraTS 2015 + PIMS -MRI dataset	Segmentation + Classification	T1, T1(c), T2 and FLAIR + T1, T2	Deep CNN for classification + FCM for segmentation	1,69,880	Accuracy, Recall, Precision, F1- Score	Feature extraction	Yes
Muhammad Arif et. al. (Arif, Ajesh, et al., 2022) (2022)	From AANLIB/Harvard	Segmentation + Classification	Axial, T2(W)	BWT for segmentation + SVM classifier	66 brain MRI	Accuracy, error, sensitivity, specificity	Pre-processing & Feature extraction	NO
Maqsood et. al. (Svm & Maqsood, 2022) (2022)	BraTS-2018 + Figshare	Classification + Segmentation	T1w, T2w, T1w CE, and FLAIR image + T1-w CE	17-layered CNN, MobileNetV2 & M-SVM	285 from BraTs + 2451 from figshare	Accuracy, Sensitivity, specificity, Dice coefficient index	Contrast Enhancement + Feature Extraction	Yes
Rasool Reddy et. al. (Rasool Reddy & Dhuli, 2022) (2022)	BraTs 2015	Classification + Segmentation in 2 Phases	T1, T1c, T2 and FLAIR	Bi-dimensional empirical mode decomposition (BEMD) + Modified Quasi-Bivariate variational mode decomposition (MQBVMD)	274 training gliomas	ACC, Recall, Precision, Spec, AUC, F-Measure	Median Filtering + Feature Extraction	Yes
Balamurugan et. al. (Balamurugan & Gnanamanoharan, 2023) (2023)	253 images dataset	Segmentation + Classification	Not Defined	DCNN + LuNet	173: 64 tumor and 109 non-tumor data	Acc, Sen, Spec, Precision, F-Score, Dice-Similarity Index	Preprocessing + feature extraction	NO

RamPrasad et. al. (Ramprasad et al., 2022) (2022)	BraTS 2020	Segmentation + Classification	T1-w, T1ce-w, T2-w and Flair sequences	HFCMIK for segmentation + DLPNN for classification	369 images	Acc, Sen, Spec, Recall, F-measure, NPV, MCC	Pre-processing + Feature Extraction	NO
Tandel et. al. (Tandel et al., 2022) (2022)	3- datasets from TCIA-REMEMBRAND T	Segmentation + Classification	T1-w, T2-w, FLAIR, diffusion-weighted imaging (DWI)	Major Voting Algorithm	80% of WBM, RSM, SSM	Acc, Sen, Spec, AUC, PPV, NPV, ITR, TIME	Feature Extraction	Yes
Saeedi et. al. (Saeedi et al., 2023) (2023)	Public dataset of 3264 images	Segmentation + Classification	T1-w (CE) MRI	2-D CNN + Auto-encoder CNN	After augmentation 8812 images	Acc, Sen, Spec, F-measure	Pre-processing + Feature Extraction	Yes
Raja et. al.(Raja & Vijayachitra, 2023) (2023)	Dataset from hospitals of USA (65 images)	Segmentation + Classification	Not Defined	Generative Adversarial Network	52 images	Acc, Sen, Spec, Computation time, Dice score, PSNR, SSIM, NMSE	---	NO
Liu et. al. (Y. Liu et al., n.d.) (2023)	BraTS-2019 + BraTS-2020	Segmentation	FLAIR, T1 (w), T2 (w), T1-CE	PIF-Net, the MSFF module and the V-Net	335 + 369 MR Images	Dice score, Hausdroff distance	—	NO
Liang et. al.(Liang et al., 2022) (2022)	BraTS 2018 + BraTS 2019	Segmentation	T1-w, T1 (CE), T2-w and (FLAIR)	BT Swin-Unet	285 + 335 training subjects	Dice score, Hausdroff distance	—	NO
Elhamzi et. al.(Elhamzi et al., 2022) (2022)	BraTS 2017 + BraTS 2018 + BraTS 2020	Segmentation	T1, T2, T1 CE, and FLAIR	CNN architecture	285 + 285 + 369 training subjects	Dice Score, Sen, Spec, Hausdorff distance, Avg. Time	None	NO
Nyo et. al.(Nyo et al., 2022) (2022)	BraTS 2015	Segmentation	Not defined	OTSU thresholding method	—	Accuracy, Jaccard	Pre-processing	NO
Mahesh et. al.(Mahesh Kumar & Parthasarathy, 2023) (2023)	BraTS-2019	Segmentation	T1-w, T1- (CE), FLAIR and T2- w	Enhanced U-Net	Not defined	Acc, Dice Coeff, Jaccard Coeff, Precision, Sen, Spec	Pre-processing	NO
Srividya et. al.(Srividya et al., 2023) (2023)	CPTAC-GBM from National Cancer institute	Segmentation	Not-defined	Histo-quartic graph + Stack entropy based DNN	Not discussed	PSNR, RMSE, Accuracy, Loss	Pre-processing	NO

Alpar (Alpar, 2023) (2023)	BraTS 2012	Segmentation	T1, T1 (C), T2, FLAIR	Nakagami Imaging + Fuzzy Fusion	Not discussed	DSc, TPR, TNR, Avg. IOU	Preprocessing	NO
Wentao et. al.(W. Wu et al., 2020) (2020)	BraTS 2018	Classification + Segmentation	T1w, T2w, T1w c+, and FLAIR images	DCNN-F-SVM model	285 training set	DSc, Sensitivity, Specificity	Both	Yes
Kader et. al. (Kader et al., 2021) (2021)	MRIs from BraTS 2012, BraTS2013, BraTS2014, BraTS2015, ISLES	Classification+ Segmentation	T1w, T2w, T1w c+, and FLAIR images	Deep Wavelet Auto Encoder Model	2500 Images combined	Acc, Sen, Spec Precision, DSc, FPR, FNR, JSI	Pre-processing	NO
Irfan et. al. (M. I. Sharif et al., 2020) (2019)	BraTS 2013, BraTS 2015, BraTS 2017, BraTS 2018	Classification & Segmentation	T1w, T2w, T1w c+, and FLAIR images	Saliency-based Segmentation + Softmax classifier	588 HGG + 198 LGG	Error + Accuracy + Time	Feature Extraction	NO
Archana et. al. (Ingle et al., 2022) (2022)	Nanfeng hospital	Classification + Segmentation	T1-w	Modified UNet	2479 images	mIOU + DSc	Pre-processing	NO
Dang et. al. (Dang et al., 2022) (2022)	BraTS 2019	Classification + Segmentation	T1, T1 (CE) + T2-w, FLAIR	UNet + VGG + GoogleNet	--	Dice Score + Precision + Recall + Housdorff distance + Accuracy	Pre-processing	Yes
Arif et. al.(Arif, Jims, et al., 2022) (2022)	REMBRANDT	Classification + Segmentation	Not Defined	Genetic Algorithm & U-Net	--	Acc, Sen, Spec, Precision, recall, Detection rate, FPR + TPR	Pre-processing + Feature extraction	NO
Ejaz et. al. (Haq et al., 2022) (2022)	Two distinct public datasets	Classification + Segmentation	T1-w	Deep CNN + SVM-RBF	--	Acc, PSNR, MSE, FPR, DSc	Pre-processing	NO
Samee et. al. (Samee et al., 2022) (2022)	BraTS2015	Classification + Segmentation	T1, T1 (CE) + T2-w, FLAIR	U-Net and CNN Cascaded framework	736 HGG + LGG MRIs	DSc, Sensitivity and Acc, Specificity	Pre-processing & Feature extraction	Yes
Pranjal et. al.(Agrawal et al., 2022) (2022)	BraTS2020	Classification + Segmentation	T1, T1 (CE), T2-w, FLAIR	3D-UNet + CNN	—	DSc, Accuracy, Precision, recall, F1-score	Feature Extraction	NO

Neelima et al. (Neelima et al., 2022) (2022)	BraTS2018 + Figshare Dataset	Classification + Segmentation	T1, T1 (CE), T2-w, FLAIR	Deep MRSeg + GAN	Variational	DSc, Sens, Spec, Accuracy	Pre-processing + Feature Extraction	NO
KishanRao et al. (Kishanrao & Jondhale, 2023) (2023)	BraTS2015, BraTS 2017 and BraTS 2019	Segmentation + Classification	T1, T1 (CE), T2-w, FLAIR	Hybrid DCNN with deer hunting	90% of combination of datasets	DSc, Sen, Spec, Acc, FPR, FNR, PPV, Precision	Pre-processing + Feature Extraction	NO
Deepa et al. (Deepa et al., 2023) (2023)	BraTS2018 + Figshare	Segmentation + Classification	T1, T1 (CE), T2-w, FLAIR + T1-w	Deep MRSeg + DRN	285 training sets + 2758 from figshare	Acc, Specificity, Sensitivity	Pre-processing + Feature Extraction	NO
Kamireddy et al. (Reddy & Dhuli, 2023) (2023)	Dataset from Harvard medical school	Segmentation + Classification	T2-w	CNN + FL-MSCM	185 training MRIs	TPR, TNR, PPV, F-Score, AUC, Accuracy, DSc	Pre-processing + Feature Extraction	Yes
Nacer et al. (Farajzadeh et al., 2023) (2023)	BraTS2020	Segmentation + Classification	T1, T1 (CE), T2-w, FLAIR + T1-w	CNNs + UNet	369 MR Images	Accuracy, Precision, Recall, F1-Score	Preprocessing + Feature Extraction	Yes
Nirmala et al. (Ramesh et al., 2021) (2021)	BraTS2015	Segmentation + Classification	T1, T1 (CE), T2-w, FLAIR + T1-w	VGG-16 + kPCA	—	PSNR, SSIM, MSE, Accuracy, Sen, Spec, Precision, F-measure	Preprocessing + Feature Extraction	NO
Srinath et al. (Kokkalla et al., 2021) (2021)	Figshare dataset	Classification	T1-w (CE)	Deep Dense Inception ResNet	2298 MR Images	Accuracy, Precision, Recall, F1-Score	None	NO
Polat Ozlem (Polat & Güngen, 2021) (2021)	Figshare dataset	Classification	T1-w (CE)	VGG-16 + VGG-19 + ResNet50 + DenseNet-121	2145 MR Images	AUC, Accuracy	None	NO
Habib hassan et al. (Habib et al., 2022) (2021)	A private dataset of 512 images gathered from Nishtar Hospital, Pakistan, and the second one is a slice dataset of 940 images	Classification + Segmentation	--	Segmentation methods + ML-based Classifiers	1161 (80% of total images) MR Images	Accuracy, Precision, Specificity, TPR, TNR	Pre-processing + Feature Extraction	NO

	selected for experimentation.							
Badza et al. (Autoencoder & Badža, 2021) (2021)	Figshare Dataset	Segmentation	T1-w(CE)	Convolutional neural auto encoder	1838 MR scans	Acc, Sen, Spec, Precision, DSc	Pre-processing	Yes
Saeed Usman et al. (Saeed et al., 2021) (2021)	BraTS2018, BraTS2019, BraTS2020	Segmentation	T1-w, T1-w(T1ce), T2-w, and Flair	RMU-Net	285 + 335+ 369 both HGG and LGG cases	Dice Score, Jaccard Score	Pre-processing	NO
Huang et al. (Huang et al., 2021) (2021)	BraTS2018, BraTS2019, BraTS2020	Segmentation	T1-w, T1-w(T1ce), T2-w, and Flair	Multitask deep Framework	285 + 335+ 369 both HGG and LGG cases	Dice Score, Hausdorff distance, Sensitivity and specificity	Pre-processing	NO
Kalpana et al. (Kalpana et al., 2022) (2022)	BraTS2016, BraTS2017, BraTS2018	Segmentation	T1-w, T1-w(T1ce), T2-w, and Flair	PLA + DenseNet-169	274 + 285+ 285 Training images for all datasets respectively	Acc, Sen, Spec	Both	Yes
Neelima et al. (Neelima et al., 2022) (2022)	BraTS 2018, Figshare	Segmentation	T1, T1-w+T1 (CE), T2, FLAIR	CAViaR-SPO	3064 slices for figshare + 130-176 slices for BraTs2018	Seg acc, Sensitivity, Specificity	Both; feature extraction done using DeepMRSeg	No
Kishanrao et al. (Kishanrao & Jondhale, 2023) (2023)	BraTs 2015, BraTS 2017, BraTS 2019	Segmentation + Classification	T1-w, T1c), T2-w, and T2 - Flair	Hybrid Deep CNN + Deer Hunting Optimization with SFO	2446.23 M voxels of BraTs 2015 + 2544.33 M voxels of BraTs 2017 + 2972.91 M voxels of BraTs 2019	Accuracy, Sensitivity, Specificity, Dice Score, Jaccard Indexes, Balanced Error rate	Both	NO
Yaping et al. (Y. Wu et al., 2019)(2019)	BraTS 2017	Segmentation	T1, T2, FLAIR and CET1	Otsu Algorithm + SVM	228 training + 57 testing cases	Dice Score, Housdorff distance, specificity and Sensitivity	Both	Yes (5-fold cross validation)
Soltaninejad et al. (Soltaninejad et al., 2018) (2018)	Private dataset :11 Multimodal Images + BraTS 2013 : 30	Classification + Segmentation	Single modal FLAIR, multi-modal	Random Forest + Multimodal Supervoxel	11 multimodal from private dataset and 30 (20 HGG + 10	Dice Score, Precision, Sesitivity and	Both	Yes (4-fold cross validation)

	multimodal Images		cMRI (FLAIR, T1, T2 and T1 + contrast)		LGG from BraTS 2013)	Balanced Error Rate (BER)		
Li et. al.(H. Li et al., 2019)(2019)	BraTS 2015 + BraTS 2016 +BraTS 2017	Segmentation	T1-w, T1-CE, T2-w and FLAIR	Inception based U-Net + Up-skip connection + cascaded training strategy	220 HGGs and 54 LGGs from training in BraTS 2015 + 110 x 620 images for testing in BraTS 2015 + 210 HGGs and 75 LGGs (BraTS 2017)	Dice, Sensitivity, PPV and Jaccard Index	Pre-processing	Yes (5-fold cross validation)
Elhamzi et. al.(Elhamzi et al., 2022)(2022)	BraTS 2017, BraTS 2018, BraTS 2020	Segmentation	FLAIR, T1, T1c, T2	CNN with seven convolution, four Batch Normalization, and four pooling layers	BraTS 2017 and BraTS 2018 have 285 training images and BraTS 2020 have 369 images	Sensitivity, Specificity, Housdorff distance	Post-processing	NO
Shidong et. al. (S. Li et al., 2022)(2022)	BraTS 2015	Segmentation	FLAIR, T1, T1c, T2	2D U-Net for localization + 3D U-Net for segmentation	220 HGG and 54 LGG	Dice Similarity Coefficient, Mean surface distance, Housdorff distance	Slice Extraction + Pre-processing(cropping)	Yes (10-fold cross validation)
Ahmet et. al.(Ilhan et al., 2022) (2022)	BraTS 2012, BraTS 2019, BraTS 2020	Segmentation	T1, T2, T1c, FLAIR	Tumor localization and enhancement + U-Net	5633 FLAIR images from 2012, 51,925 FLAIR images from BraTS 2019 + 57,195 FLAIR images from BraTS 2020	Dice score, Matthew's correlation coefficient, Jaccard, Sensitivity, specificity, precision	Filtration for noise removal	Yes (5-fold cross-validation)
Ajay et. al.(Ladkat et al., 2022)(2022)	BraTS 2019	Segmentation	FLAIR, T1ce, T1, T2	Mathematical model embedded with 3-D attention U-Net	335 cases (259 HGG + 76 LGG)	Dice, Sensitivity, Specificity, Housdorff, accuracy, precision	Feature Extraction	No

7. Future Directions

This study's findings highlight the superior accuracy and robustness of deep learning compared to traditional methods, making it a more efficient and precise diagnostic tool. Deep learning in medical imaging holds the potential to transform healthcare by enabling earlier disease detection and treatment, particularly in brain MRI image diagnosis.

However, it's important to acknowledge that training deep learning models demands substantial time, effort, data, and computing power. Despite this challenge, the benefits of applying deep learning to brain MRI image diagnosis are substantial. Several key points emerge

1. Access to large, high-quality real-world databases remains a significant hurdle, but data augmentation offers a potential solution.
2. Developing a pre-processing system for color-balancing textured MRI images to unlock new features is crucial, with an emphasis on tumor detection.
3. There's an urgent need for a versatile system capable of processing both 2D and 3D images, encouraging innovative approaches that merge shallow and deep systems.
4. Incorporating optimization strategies for deep learning models is a potential avenue for improvement.
5. To Create an integrated framework encompassing multiple tasks, from pre-processing to tumor type identification, is required for aiding neurosurgeons with automated tumor segmentation. In conclusion, deep learning holds great promise for brain tumor research, with a focus on translating these experiments from the lab to clinical settings with strategic direction and effort.

8. Conclusion

This report includes a comprehensive literature analysis covering the years 2018–2023 on the topic of utilizing Deep Learning to Separate Brain Tumors from Normal Tissue in MRI Images. There are a plethora of practical and efficient algorithms available today, yet there is still room for improvement due to a lack of uniformity. In-depth benefits and cons of every previously-mentioned method are discussed here. DL has been applied to several problems, including brain tumor prediction, diagnostics, detection, segmentation and classification. When compared to other methods, there is no denying the efficacy of Deep Learning methods and algorithms and can process big datasets with ease. Unfortunately, their usefulness in the investigation of brain tumors is still not fully utilized. Despite the promising outcomes, successfully applying DL methods to advance diseased clinical images will require significant additional time, effort, and a secure partnership between various official higher authorities, industries, and academic groups. Hence, it is clear from the above extensive

review that a single, fully-automated system capable of identifying brain tumors and classifying them effectively with a minimum of complication is urgently needed.

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