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Review article

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Context aware machine learning techniques for brain tumor classification and detection – A review

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ABSTRACT

Background: Machine learning has tremendous potential in acute medical care, particularly in the field of precise medical diagnosis, prediction, and classification of brain tumors. Malignant gliomas, due to their aggressive growth and dismal prognosis, stand out among various brain tumor types. Recent advancements in understanding the genetic abnormalities that underlie these tumors have shed light on their histo-pathological and biological characteristics, which support in better classification and prognosis.

Objectives: This review aims to predict gene alterations and establish structured correlations among various tumor types, extending the prediction of genetic mutations and structures using the latest machine learning techniques. Specifically, it focuses on multi-modalities of Magnetic Resonance Imaging (MRI) and histopathology, utilizing Convolutional Neural Networks (CNN) for image processing and analysis.

Methods: The review encompasses the most recent developments in MRI, and histology image processing methods across multiple tumor classes, including Glioma, Meningioma, Pituitary, Oligodendroglioma, and Astrocytoma. It identifies challenges in tumor classification, segmentation, datasets, and modalities, employing various neural network architectures. A competitive analysis assesses the performance of CNN. Furthermore it also implies K-MEANS clustering to predict Genetic structure, Genes Clusters prediction and Molecular Alteration of various types and grades of tumors e.g. Glioma, Meningioma, Pituitary, Oligodendroglioma, and Astrocytoma.

Results: CNN and KNN structures, with their ability to extract highlights in image-based information, prove effective in tumor classification and segmentation, surmounting challenges in image analysis. Competitive analysis reveals that CNN and outperform others algorithms on publicly available datasets, suggesting their potential for precise tumor diagnosis and treatment planning.

Conclusion: Machine learning, especially through CNN and SVM algorithms, demonstrates significant potential in the accurate diagnosis and classification of brain tumors based on imaging and histo-pathological data. Further advancements in this area hold promise for improving the accuracy and efficiency of intra-operative tumor diagnosis and treatment.

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1. Introduction

The modern medical world is transitioning towards artificial intelligence [1] in biological and medical information [2]. Considering complex medical tests, machine learning can improve efficiency and prediction [3] with the optimum accuracy and precision in cancer [4], equivalent to interpretations by medical practitioners (e.g. pathologists) [5]. Revolutionary¹ algorithms for ML and DL demonstrate greater validity and reliability in image processing, especially in cancer patient data and morphology.

In the recent, many technology and medical experts focused on Deep Convolutional Neural Network (DCNN) [6], considered the most power full and frequently used algorithm for computer vision and image processing. ML Algorithms associated with neural networks may further be applied to patients in early tumor diagnosis, X-ray [7] and CT scan [8]. Tumor rapidly changes is density and mitotic activity [9] which can be rectified and diagnosed by Histopathology [10] of different organs for cancer prediction and treatment like kidney [11], prostate [12], liver [13], brain [14], breast cancer [15] and heart [16]. According to current statistics, the growth in numbers of cancer incidence is different in various regions. It is significantly lower in the African continent and higher in Northern Europe REF.

The death rate of the brain, other CNS, and intracranial tumors are proportional life span of different people, older or adult might have high fatality rates. UK reported [17] 34 % of deaths per year among people of 75 years and older on average between 2016 and 2018. When compared to most cancers, there is a smaller percentage of mortality in older age groups as brain tumor considered to be one of the vital death caused among men and women of all ages [18]. Recent research trends depict the fact that brain tumors are extremely heterogeneous [19,20]. This means that they may rapidly change their color, size, region and mutation that cause the main problem for histopathology's or medical experts to diagnose and classify brain tumor by the virtue of its type.

Inception V3, particularly in CNN, Deep Learning techniques, may be applied to detect and diagnose multiple types of tumors, such as Glioma, Meningioma, Pituitary, and Glioblastoma [21]. Machine learning for diagnosis and inspection encompasses a broad spectrum, extending beyond MRI and CT scan classification. It also includes Histopathology [22] (SVM/CNN) combined in the field of Histopathological diagnosis for brain and breast cancer of two different classes, namely LGG/HGG. This self-learning method identifies images of brain and breast tissues using Google Inception V3 and CNN. A label-free soft tissue staining method called H&E [23], along with CNN, can predict and diagnose tumors in real-time environments. A single biopsy is insufficient to reflect the physical characteristics of a tumor and its spatial genes, a significant mechanism for tumor therapy known to be intra-tumoral genetics and chromosomes. The labor-intensive workflow for intra-operative diagnosis based on H&E staining is a time-consuming process. Providing secure and efficient treatment during cancer surgery, along with spatial gene and intra-operative diagnosis at the patient's bedside, is more important in the modern world [24].

An Artificial Neural Network (ANN) based programmed network model for classification and segmentation approaches MRI cerebrum tumors by utilizing ANN, which includes ROI and texture features as well [25]. The acquired precision value is 92.14 %, with 89 % sensitivity and 94 % specificity, respectively. DNN segmentation and detection of tumors (Glioma) further combine with two effective techniques, such as a combination of modalities for identifying brain tumors [26]. Separate processing algorithms are employed for segmentation, using the Brats 2018 dataset, depicting 61.0 % accuracy.

Effective features are identified by employing decision trees and cross-validation of the BraTS 2018 dataset, which is used to rectify different tumor intensity levels, such as T2-FLAIR, T2, and T1-Gd for diagnosis [27]. The CNN based on the VGG-19 architecture, combines with WND-CHRM, an open-source classifier, to analyze Low-grade Glioma [28]. The programming structure can separate and classify tumors (Glioma, Meningioma, Pituitary) accurately, based on contrast-based high-resolution MRI images.

The authors [29] also discuss the possibility of improving the classification performance by interposing optical diffractive layers between the microfluidic channel and the camera, which can be directly generalized to the interposition of other arbitrary diffractive layers. This could lead to hardware-based improvements in the classification technique. The authors propose a simple and versatile machine learning approach that achieves high classification accuracy at an extremely low computational cost. They use a lens less micro flow cytometer and a simple visible laser, a pinhole, a microfluidic channel with pumping mechanism, and a camera to classify particles based on their 2D interference patterns. The classification is performed using a linear classifier (logistic regression), which does not require any feature extraction based on domain knowledge.

The authors [30] introduce a novel strategy for brain tumor segmentation, subtype classification, and survival prediction using radiology images. They propose a 3D context-aware deep learning method that takes into consideration the uncertainty of tumor location in radiology MRI image sub-regions to ensure precise tumor segmentation. This method is then applied to subtype classification and survival prediction through a hybrid approach that combines deep learning and machine learning techniques.

The study demonstrates the efficacy of the proposed method in accurately segmenting brain tumors and predicting their subtypes and survival rates. The BraTS 2019 dataset, which consists of the Multimodal Brain Tumor Segmentation Challenge 2019, was used to evaluate the method's performance in tumor segmentation and overall survival prediction. The CPM-RadPath Challenge on Brain Tumor Classification 2019 dataset was used to evaluate the method's performance in tumor classification. The results indicate that the proposed method achieved excellent tumor segmentation and survival prediction, with the tumor classification results ranking second in the testing phase of the 2019 CPM-RadPath global challenge.

The study investigated the diagnostic assurance of both radiologists and Convolutional Neural Networks (CNNs) in identifying small hypoattenuating hepatic nodules (SHHN) on computed tomography (CT) scans. The results indicated that radiologists had a higher number of nodules with low confidence compared to the CNN, which had fewer nodules with low confidence, especially when liver metastases were present. In another study, the authors propose a machine learning technique that utilizes a lensless microflow cytometer and a simple visible laser, pinhole, microfluidic channel with a pumping mechanism, and a camera to classify particles based

on their 2D interference patterns. The classification is accomplished using a linear classifier (logistic regression) without requiring any feature extraction based on domain knowledge. The authors suggest that the classification performance could be improved by interposing optical diffractive layers between the microfluidic channel and the camera, which could lead to hardware-based improvements in the classification technique [31].

1.1. History OF NON-INVASIVE techniques

MRI is generally the primary modality for structural neuroscience research because it provides images with excellent contrast of soft fluids, tissues, and great spatial accuracy. It also hasn't been linked to any known health hazards. Although alternative imaging modalities such as computed tomography (CT) and positron emission tomography (PET) are commonly employed in brain research, among all of them, magnetic resonance imaging (MRI) and H&E staining are the most frequent. Brain tumor segmentation is usually performed at the pixel level or occasionally at a regional tumor area, characterized as the method of separating the tumor from normal brain structures [32]. 3D CNN is used to perform segmentation, but MRI multimodalities play an important role in tumor diagnosis. Modalities are basically an intensity level of tumor, whether it's benign or malignant [33], usually contained in MRI. In this, Support Vector Machine, a well-known algorithm, performs tumor classification.

Glioblastoma [34] in histopathology aids precision medicine by obtaining specific diagnoses for various diseases, particularly for Glioblastoma Multiforme (GBM) soft tissues. In histopathological images of Glioblastoma multiforme (GBM), an automated feature extraction and disease classification method has been developed to detect Anaplastic, Astrocytic, and Oligodendroglial tumors [35]. Moreover, in secondary Glioblastomas, the Isocitrate Dehydrogenase genes IDH1 and IDH2 are usually diagnosed, which are normally called mutations. Given the value of IDH in the diagnosis and treatment of specimens and fluids for Glioma, identifying its genomic status is a critical task. H&E is an efficient technique in cancer diagnostics since it improves histological diagnosis and treatment planning. However, H&E is insufficient for determining the IDH mutation status of cancer.

This paper contributes the following.

- a) In addition to brain tumor segmentation, classification, and detection methods, explores histological patterns and tissue spatial characteristics, along with MRI modalities.
- b) Provides genetic bonding and mutation of numerous tumor genes (protein structure) in Glioma, Meningioma and Pituitary tumor by using String Network (https://string-db.org).

Genetic structures and mutations in brain tumors can lead to Type I, II, III, and IV classes. Tumor genes and proteins play a vital role in these mutations, and these genes can be predicted using K-Means clustering algorithms. This study suggests different types of tumor protein and gene compositions for brain tumors at various stages, including I, II, III, and IV.

The K-Means clustering algorithm can be simulated in the string.db network database. To predict the tumor type and the structure of proteins in a gene network, K-Means is also utilized. The Strings database creates clusters specified by input parameters accepted by K-Means, making predictions accordingly. When K-Means predicts, it results in the following changes:

The nodes' colors change (each cluster is associated with a distinct color).

Dashed lines are used as a visual representation of inter-cluster edges.

2. Related work

Genetic abnormalities have allowed gliomas to be classified into various subtypes based on their molecular profiles. These subtypes may exhibit distinct genetic profiles and underlying mechanisms that drive tumor growth. Researchers aim to enhance glioma diagnosis, prognosis, and treatment by understanding these evolving genetic changes.

Malignant gliomas have been associated with numerous genetic alterations, and current research investigates their potential as diagnostic, prognostic markers, and therapeutic targets. Frequently studied genetic alterations in gliomas include mutations in genes such as IDH1, IDH2, TP53, PTEN, EGFR, and ATRX REF. These mutations can impact critical cellular functions like DNA repair, cell cycle regulation, and signal transduction pathways [36].

The primary method for diagnosis remains imaging tests, particularly magnetic resonance imaging (MRI). However, these tests have limitations that can impede early detection and diagnosis. Computer-aided intelligent systems can assist doctors in their diagnoses. In this study, we developed an EfficientNetv2s architecture-based Convolutional Neural Network (CNN) for brain tumor diagnosis. The system was enhanced using Ranger optimization and extensive pre-processing. Additionally, we compared the proposed model to state-of-the-art deep learning architectures such as ResNet18, ResNet200d, and InceptionV4 for distinguishing brain tumors based on their spatial features [37].

Radiologists commonly utilize magnetic resonance imaging (MRI) to detect brain anomalies. The manual grading process is challenging and can lead to false-negative or false-positive results, especially in early-stage abnormalities. In individuals with brain anomalies, manual errors can impact survival rates. Therefore, computer-aided diagnosis aids radiologists in accurately identifying abnormalities, even in the early stages of brain tumors. We developed a Multi-Class Convolutional Neural Network model (MCCNN) to identify brain tumors in MRI scans. This study utilized BRATS 2015 and Figshare Data. The feature vector was constructed from pre-processed MRI data using the convolution and pooling layers of CNN, and the CNN's softmax layer identified the tumor. Two experiments, Experiment I and Experiment II, were conducted to evaluate the MCCNN model's performance. Compared to other CNN-based networks and pre-trained models, the designed MCCNN offers simplicity, increased classification accuracy, lower loss values,

and reduced false-negative and false-positive rates [39].

Identification of chronic nerve conditions like brain tumors, strokes, dementia, and multiple sclerosis, MR images are the best tool. They serve as the most accurate method for determining whether diseases of the pituitary gland, brain vessels, eye, and inner ear organs are present. In order to monitor and diagnose health from brain MRI images, a variety of deep learning-based medical image analysis methods have been proposed. Deep learning's CNN (Convolutional Neural Networks) branch is frequently used to analyze visual data. Natural language processing, suggestive systems, image classification, and image and video recognition are a few examples of common applications. In this study, a new modular deep learning model was developed in order to retain the benefits of well-known transfer learning techniques (DenseNet, VGG16, and basic CNN architectures) while removing their drawbacks [38].

When it comes to identifying and treating brain tumors in IoT healthcare systems, classification of brain tumors is crucial. In this paper, we propose a solid deep learning-based classification model for brain tumors. The Meningioma, Glioma, and Pituitary types of brain tumors are classified using the proposed method's improved Convolutional neural network. Brain magnetic resonance image data is used to test the multi-level convolutional neural network model. Using data augmentation and transfer learning techniques, the MCNN model's classification results were enhanced. In the suggested MCNN model, hold-out and performance evaluation metrics have also been used. The results of the experiments demonstrate that the proposed model outperformed cutting-edge methods in terms of results [39].

T2-SWI MRI scans are used to diagnose glioma tumors in the brain as well as other tumors and diseases using a novel diagnostic framework built on CNN and DWT data analysis. A very unbalanced binary problem results from the binary CNN classifier's treatment of the pathology "glioma tumor" as positive and the other pathologies as negative. To show the improved performance of the CNN and DWT analysis in diagnosing brain gliomas, the study includes a comparative analysis of a CNN trained with wavelet transform data of MRIs rather than their pixel intensity values. The proposed CNN architecture's performance is also contrasted with that of a deep CNN that has already been pre-trained on the VGG16 transfer learning network and with that of the SVM machine learning approach that uses DWT data. Methods: Instead of the conventionally used original scans in the form of pixel intensities, the proposed CNN model uses as knowledge the spatial and temporal features extracted by converting the original MRI images to the frequency domain by performing Discrete Wavelet Transformation (DWT). Furthermore, the original images underwent no pre-processing. T2-SWI parallel to the axial plane MRIs are the type of images that are used. For each MRI scan, DWT is first applied in a compression step up to three levels of decomposition. To determine whether the scans indicate glioma or not, these data are used to train a 2D CNN. The proposed CNN model is trained using MRI slices from 382 different male and female adult patients, displaying both pathological and healthy images of a variety of diseases (showing glioma, meningioma, pituitary, necrosis, edema, non-enchasing tumor, hemorrhagic foci, edema, ischemic changes, cystic areas) [40].

It has recently become important to segment and classify the brain using neuroimaging techniques. A brain tumor may be fatal if it is not found in time. Due to the wide variety of tumors, a poor tumor diagnosis could have serious consequences. In order to treat patients appropriately, clinicians will benefit from the correct classification. Deep Learning may be a subset of artificial intelligence that has recently excelled in classification and segmentation tasks. This study uses two publicly available datasets to classify brain tumors using a convolution neural network, describing the various tumor types (glioma, meningioma, and pituitary tumor) as well as the three glioma grades (as described, Grade II, Grade III, and Grade IV). 233 and 73 patients with 516 and 3064 images on T1-weighted images are part of a public MRI imaging dataset. In order to compare the performance of our method with other published methods in the field, methodology uses a 25-layer CNN model on T1-weighted MRI images. Using the same dataset, our method performed better than the competition [41].

Researchers use a multimodal hybrid framework to test local samples from a number of brain tumor forms [42]. ANOVA, Bonferroni corrections and rank-order correlations are the statistical approaches used for both of them to find out accurate results. The inclusion of high-resolution fluorescence imaging in the input data might significantly improve prediction precision. In Ref. [43] combine SRH with DNN is applied to dataset of numerous patients of multiple institutions as Whole-slide SRH images.

To develop a 3D CNN architecture to detect brain tumors, which are then moved to a pre-trained CNN model for image feature and texture extraction. Results are further input into a correlation-based process that delivers an optimal result [44] in three dimensions. CNN can use multimodalities in MRI to segment Gliomas and their constituencies.

Currently [45] SVM-based Expectation Maximization(EM) extracted feature from DICOM data set with 512x512 of pixel resolution images that are analyzed critically by applying Fourier Transform (FT). Effective and reliable [46] method for image modality and classification which can be used to obtain clinical cases from massive medical dataset. Multimodality dataset ImageCLEF-2012 dataset (color and gray-scale images) CT, X-ray, Ultrasound, MRI and Microscopic images are used along with ResNet50.In Ref. [47] classification and detection of brain tumors in the publicly available datasets containing a valid Dice average score of 85.7 %. CNN along with softmax classifier is implemented. Transfer learning and extraction of deep auto-encoder functions, proposed the capabilities of 03 distinct Deep Leaning methods for tumor prediction [48]. Classification of the juvenile brain tumor, this paper presents Genetic algorithm (GA) that uses feature embedding from futuristic image classification networks.Image-Net and ILSVRC dataset is used with 87.8 $\% \pm 3$ of accuracy [49].

Evaluate new developments [50] in image segmentation and recognition with an emphasis on the effective treatment of adjacent imaging patches of tumor-infection in human brain. The fuzzy transformation algorithm is adopted to discover various image features such as preprocessing, image segments, image extraction and image classification. On Cryosections [51] of brain tumors, coherent anti-Stokes Raman scattering (CARS), two-photon excited fluorescence (TPEF), and second harmonic generation were acquired the highest level of accuracy.

Linear discriminate analysis is implemented on CARS and TPEF images. HE2RNA [52] is a deep-learning algorithm developed primarily for gene predicting from the Whole Side Image dataset. It is also known as HE2RNA for microsatellite instability status



Fig. 1. Machine learning categories [54].

prediction (transcriptome prediction). Datasets, including the "TCGA Pan-cancer dataset frozen slides from colorectal cancer cases TCGA and "Mondor dataset," have been put into an experimental phase with an accuracy of 80 %. An automatic method [53] for identification and classification of glioma and ischemic stroke based on Random Forest. This article based on the detection of glioma in their early stages. Features like (GWF, HOG, LBP and SFTA) are utilized. Experiments are performed using a number of BRATS datasets from various ears and versions. Rapid image feature extraction method is built for quantitative MRI images by considering the accuracy of 92 % by having all these feature extraction techniques e.g. (HOG + LBP + SFTA + GWF).

Artificial Intelligence is the broad domain as it contains multiple subdomains and categories in the field of classification, regression, clustering, feature extraction and dimensionality reduction as mentioned in Fig. 1.

Accurate detection of tumor by TIW and MRI is the crucial task in machine learning.Usually MRI pertains the resolution of 256x256 originally. Fusion based segmentation techniques is actually a spatial alignment used to diagnose various tumor types by different diagnostics and modalities e.g. MRI, PET and CT scan. FUZZY C MEANS clustering model is deployed to achieve optimum features from image.

Non-sub sampled contour transform (NSCT) and CNN algorithms were adopted to fuse clustered images furthermore C-V and LSM algorithms are employed to segment fused images dataset. Fusion method along with CNN and C-V algorithms mitigate the issue of losing resolution and un predictable prediction on skull lesion and boundaries it also reduce processing time and accuracy. CNN achieves better results than non-fusion technique in detecting tumors from MRI images. The NSCT approach collected more spatial data as image but produced output in image format had undesired properties that degraded visual quality and impairments. While the LSM segmentation process had curve initialization concerns. In terms of features, C-V segmentation excels LSM in identifying brain tumors, whereas CNN beats the NSCT fusion technique [55].

In today's healthcare systems, multimodalities in medical image diagnosis and fusion has established a strong foothold. Several fusion techniques are applied that combine several source photos to obtain comprehensive information that may be used to improve clinical diagnosis. However these methods have a number of limitations and flaws including edge blurring decomposition, significant information loss that leads in spurious structural anomalies and significant spatial inaccuracy due to insufficient contrast. This paper attempts to address the concerns by proposing an innovative CSID method that uses spatial gradients to conduct contrast stretching and edge detection. The application of cartoon-texture decomposition as proposed by CSID results in a comprehensive vocabulary. Furthermore, to get the final fused picture this study presents a modification to the historic convolutional sparse coding approach which utilizes upgraded decision maps and fusion rule. compared to other existing fusion algorithms results show CSID performs better in terms of picture quality and enhanced information extraction [56].

AISA a framework for MRI analysis is proposed to brain scan data. Independent small scale structures were created using this strategy. Discriminative classification, texture is retrieved and dimensionality of the feature is decreased by using t-SNE embedding. After that the KNN classification is used. The NAMIC dataset's practical findings demonstrated the method's efficiency. The suggested



Fig. 2. Prisma methodology.

model had a 94.7 percent of accuracy rate. Image subspace classification is employed to identify variations in brain functional MRI image that segregate between normal and abnormal individuals [57].Image segmentation is hindered by the presence of complex edge structures and abnormalities. It's very important to extract characteristics from multi-sequence multi resolution MRI scans. To assess the performance of the recommended model, simulation experiments are carried out to identify and diagnose tumor features on the basis of experiment. It concludes 75.58 % DSC, 92 % of feature extraction, 79.55 % Jaccard coefficient, 90 % PPV and 73.09 % of Sensitivity.

2.1. Article selection Criteria

The inclusion of keywords like "brain tumor," "MRI", "Histology" and "Machine Learning" determines the choice of the current article. The survey/review is spans up to multiple digital databanks.

- 1. Nature, which publishes highly reputable science and technology journals.
- 2. IEEE Digital Library
- 3. Elsevier
- 4. MDPI open access.

The literature review is conducted up to 2021. Selecting relevant papers could be challenging, especially when there are so many different study and multiple topics has to be consider. Filtering articles is essential and especially helpful when exploring certain topics. The basic stage was to eliminate redundancies, which was accomplished with the help of Zotero citation software. Title and abstract are further examined and any articles that were identified to be irrelevant were discarded. Reading the selected articles is the next stage; sometimes the abstract does not reflect the full contents as we dug deeper into certain articles. Furthermore, we have discovered irrelevant articles in the current study. As a result we have eliminated those papers as shown in Fig. 2.

2.2. Research questions

Q.1 what is the primary difference in contemporary machine and deep learning techniques between MRI classification and segmentation methods?

Ans. classification method is more efficient and relatively simple than segmentation since it groups or categories all objects in a single image into a single class. Segmentation process of splitting the data into a patchwork of sections [58], all of which are "homogeneous," or similar in some way color, texture, intensity and so on. Class segregation is significantly important during segmentation and classification as shown in Table 1, where each entity or object in image represents particular class which illuminated different colors.

Findings:

Findings of segmentation and classification.

Segmentation	Classification
 Noisy images(e.g. motion artefact, bias field,) complex texture and contrast 	1. Classifications are in limited numbers e.g. Glioma, Meningioma 2.Simple texture an contrast
 Heterogeneous (Size an variations) Complex (shapes an structures) 	3.Homogeneous 4.continuous shapes and structure

Table 2

Tumor Types and its gene.

Tumor Type	Tumor Gene	Protein Structure	Mutations
Glioma	[72]IDH1 and IDH2	Enzymes that metabolize glucose	Mutations in these genes can lead to the formation of gliomas.
Glioma	PTEN	Protein that regulates cell growth and proliferation	Mutations in this gene can lead to the formation of high-grade gliomas.
Glioma	TP53	Tumor suppressor gene	Mutations in this gene can lead to the development of many types of cancer, including gliomas.
Meningioma	NF2	Protein that is involved in the development of the nervous system	Mutations in this gene can lead to the formation of multiple meningiomas.
Meningioma	SMARCB1	Protein that is involved in the repair of DNA damage	Mutations in this gene can lead to the formation of meningiomas.
Pituitary tumor	MEN1	Protein that is involved in the development of the endocrine system	Mutations in this gene can lead to the formation of pituitary tumors.
Pituitary tumor	GHRH receptor	Receptor that binds to growth hormone-releasing hormone	Mutations in this gene can lead to the formation of aggressive pituitary tumors.

Q.2. What is (ATRX) in Brain Tumor and how does it effects human intellectual property?

Ans. It's the method usually acquired by H&E stain method. ATRX syndrome [59] (Alpha-thalassemia x-linked intellectual disability) is a neurological disorder that involves intellectual disability, muscle weakness (hypotonia), low stature, a specific facial appearance, physical defects, and potentially other signs. Face expression and gestures are usually changes if person is suffered from alpha thalassemia X-linked intellectual disability syndrome. The upper lip formed in the shape of an uptrend "V," while the bottom lip is noticeable. Early infancy is when these face traits are most noticeable. The facial features develop coarser with time, resulting in a flatter face and a smaller nose.

Findings.

ATRX role (Chromatin Remodeling) in tumor genesis, precisely in Gliomas, is comprehensively elucidated.

1-Its is one of the key indicators used to classify Gioma's molecular nature.

The 2-possible link between ATRX status and other gene mutations is also addressed.

3-This types of specific Protein comes with two isoforms (180 and 280 kDa) and is abundant in GC-rich and repetitive regions.

Q.3What type of protein expression, biochemical activity or methylation status correlates with responsiveness to alkylator treatments in brain tumor therapy?

Ans. MGMT [60] is a DNA recovery enzyme (O [6]-methylguanine-DNA methyltransferase). Considering this chemical process protein protects tumor cells from alkylating agent induced damage tissues or cells, making alkylating compound-based chemotherapy less effective.

Findings:

Finding biomarkers in malignant Glioma patients is crucial for identifying patients suffering at risk of tumor recurrence.

Q.4 How the H and E stains method helps in the classification of different types of tumor cells and tissues. Why is it important to rectify valuable tumor information on the pattern, shape, and structure of cells in a tissue sample?

Ans. study of cells and tissues preservations [61] (under a microscope vision) containing any specific tumor or malignancies. Histo-pathologist is a key person of examining tissue and advising doctors with a patient's tumor mutation according to WHO classification I, II, II, IV.

Findings.

The first and most crucial step in specimen management is the preservation (fixation) of the tissue sample. In anatomical pathology, formaldehyde is the most typically applied. Formaldehyde has the chemical formula HCHO. It's the easiest aldehyde compound. The gas form aldehyde is highly water soluble.

Q.5.What are the molecular genetic signature and co-deletion methods in Brain tumor for patient survival?

Ans. 1p19q co-deletion [62] is defined as the loss of both the short arm of chromosome 1 (for example 1p) and the long arm of chromosome 19 (for example 19q) in patients with diffuse Gliomas, especially those with Oligo-dendroglial tumors. It is thought to be a genetic marker analysis of a favorable response of chemotherapy and consolidated chemo radiotherapy as well as a overall survival of a patients with diffuse Gliomas. The 1p19q co-deletion was used in 70–85 % of Oligo-dendrogliomas and half of Oligo-Astrocytomas in general. The value of 1p19q co-deletions used by WHO classification of CNS tumors which made it mandatory for the diagnosis of Oligo-dendroglioma (alongside the IDH transformation).



Fig. 3. Histopathology Patterns/Invasive Diagnosis and Molecular classification with IDH mutation of 1p19q co-deletion method (a) IDH1 protein (mutant) (b) diffuse astrocytoma, (c) ATRX loss expression (d) positive expression [80].

Findings.

The 1p/19q co-deletion technique considered as the Histo-pathologic biomarker for Oligo-dendrogliomas that separates them from other types of gliomas.1p/19q co-deletion is a potent independent prognostic factor connected to a greater survival rate in both diffuse low-grade and anaplastic tumors.

Q.6. Explain the phenomena of MGMT promoter and Methylation process?

Ans. The O6-alkylguanine-DNA-alkyltransferase (AGT) gene, which is ciphered by the O6-methylguanine-DNA-methyltransferase (MGMT) gene, primary healing catalyst that eliminates "alkyl and methyl" adduction from DNA, producing cells of useful chemical more resistant to alkylating and Methylating chemotherapy as compare to others who are ill-equipped to repair these adducts. Gliomas with methylation of the MGMT advertiser have been found and receptive to the alkylating specialist Temozolomide (TMZ) [76]. Immune-Histo-chemistry as a biomarker for the maintenance protein is less obvious [63,64]. It was discovered that methylation of distinct areas in the MGMT advertiser was exceptionally related to MGMT articulation [65,66].

Findings:

MGMT basically a potent drug-resistance gene, it has emerged as the favorite target gene for protection of hematopoietic stem cells during chemotherapy for cancer. Clinical and biological implications of Glioma usually segregate in two subsets CGIMP (high and low). Glioma must be classified to investigate distinct genetic structure. CIMP show Glioma heterogeneity as well.

3. Methodology

These are just a few of the new novelties in brain tumor classification and detection. These new technologies are still in development, but they have the potential to revolutionize the way brain tumors are diagnosed and treated. Here are some additional details about each of these novelties:

Multimodal imaging: Multimodal imaging allows doctors to see tumors in more detail and to better understand their location and extent. This can help doctors to make more accurate diagnoses and to plan more effective treatments. For example, MRI scans can be used to see the shape and size of a tumor, while CT scans can be used to see the bones and blood vessels around the tumor. PET scans can be used to see how active the tumor is mentioned in Ref. [67].

Machine learning: Machine learning algorithms can be used to analyze large amounts of data, such as MRI scans, and to identify patterns that would be difficult or impossible for humans to see. This can help doctors to better diagnose and classify tumors, and to plan treatment. For example, one machine learning algorithm was able to identify tumors with optimum accuracy [68].

Biomarkers: Biomarkers are biological molecules that can be used to identify and track tumors. Biomarkers are being developed for brain tumors, and they could be used to improve diagnosis, classification, and treatment. For example, one biomarker that is being studied is called the epidermal growth factor receptor (EGFR). EGFR is a protein that is found on the surface of many cancer cells. Drugs that target EGFR have been shown to be effective in treating some types of brain tumors [69].

These new technologies are still in development, but they have the potential to revolutionize the way brain tumors are diagnosed and treated. By using these new technologies, doctors may be able to diagnose tumors earlier, when they are more treatable. They may also be able to develop more effective treatments that target the specific tumor cells.



Fig. 4. (h&e staining) non-diagnosed (left) and non-tumor patient (right) [70].

3.1. Dataset and online repositories

For the better understanding and clarity this section split into three subsections, each of which contains a particular image form e.g. 3.1.1 H&E histopathology.

3.1.2 Tumor Types and Mutation.

3.1.3 MRI scans in image processing.

3.1.1. H&E histopathology (non Invasive techniques)

Hematoxylin and Eosin (H&E) combines two histology pigments. Colors are physically manifested in different tones, hues and combinations. Histo-pathological technique of diffuse Glioma is comparatively straight forward for cancers classification. However there is a remarkably extensive morphological range as shown in Fig. 3 which shows (a)Normal, (b)IDH mutation, (c)Tumor Protein TP53 and (d) ATRX (alpha-thalassemia mental retardation X-linked) protein, that contains both mutual and diagnostically deceptive forms (see Fig. 4).

3.1.2. Tumor Types and Mutation

Tumor normally categorize in 4 different classes e.g. Glioma, Pituitary, Meningioma and Normal. Glioma growth in adults are Atrocytic which presents nearly 75 % of the Glioblastoma are almost two third of them considered as the most malignant form [71]. In 2007 characterization Oligodendroglial or blended, diffuse Glioma as Astrocytic, these genetic structure are evaluated as grade II poor quality, grade III as anaplastic or grade IV as glioblastoma [72]. Genetic variations of these tumors is hard to catch in exact measures e. g. microscopy. Additionally the examples accommodated Histo-pathological investigation that are not generally an agent. Gliomas in diffused composition including Oligodendroglial molecular structure [73–75] which are different in gene analysis. Genetic analysis and mutation of Various Tumor's is performed by using strings database (https://string-db.org/)

3.1.2.1. Glioma. IDH1 and IDH2: These genes are involved in the metabolism of glucose, and mutations in these genes can lead to the formation of gliomas.

PTEN: This gene is involved in cell growth and proliferation, and mutations in this gene can lead to the formation of high-grade gliomas.

TP53: This gene is a tumor suppressor gene, and mutations in this gene can lead to the development of many types of cancer, including gliomas.

3.1.2.2. Pituitary tumor. MEN1: This gene is involved in the development of the endocrine system, and mutations in this gene can lead to the formation of pituitary tumors.

GHRH receptor: This gene is involved in the growth of pituitary tumors, and mutations in this gene can lead to the formation of aggressive pituitary tumors.

3.1.2.3. Meningioma. NF2: This gene is involved in the development of the nervous system, and mutations in this gene can lead to the



Fig. 5. Glioblastoma genes and mutation rate.

Table 3
Tumor Gene description.

Gene	Description	Associated Tumors
[77] EGFR	Epidermal growth factor receptor	Gliomas, meningiomas, sarcomas, and other types of cancer
ERBB2	Human epidermal growth factor receptor 2	Gliomas, breast cancer, and other types of cancer
PIK3CA	Phosphatidylinositol 3-kinase catalytic subunit alpha	Gliomas, breast cancer, and other types of cancer
IK3R1	Insulin receptor substrate 1	Gliomas, astrocytomas, and other types of cancer
IDH1	Isocitrate dehydrogenase 1	Gliomas, astrocytomas, and other types of cancer
NF1	Neurofibromatosis type 1	Meningiomas, schwannomas, and other types of cancer
PTEN	Phosphatase and tensin homolog	Gliomas, astrocytomas, and other types of cancer
RB1	Retinoblastoma gene	Retinoblastoma, a type of eye cancer
TP53	Tumor protein p53	Gliomas, astrocytomas, and other types of cancer
PTPRD	Protein tyrosine phosphatase, receptor type D	Gliomas, astrocytomas, and other types of cancer



Fig. 6. Glioblastoma genes.

formation of multiple meningiomas.

SMARCB1: This gene is involved in the repair of DNA damage, and mutations in this gene can lead to the formation of meningioma.

3.1.2.4. Glioblastoma. Glioblastoma considered to be the most deadly kind of tumor in humans. Glioblastoma patients having poor prediction with overall survival of around 1 year. If Glioblastoma is primary or secondary it may form rapid genetic alteration in elderly individuals or by development from anaplastic Astrocytomas in earlier people. Significant progress has been made in our knowledge of the mechanisms that lead to Glioblastoma over the last decade and numerous key genetic abnormalities that appear to be critical in the genesis and growth (Fig. 5) of this tumor have been found.

Finding out regular mutations in the Isocitrate dehydrogenase1 (IDH1) gene in particular Table 3, It's provided new look inside the Glioblastoma molecular landscape. Indeed new research is required the effects of mutant IDH1 protein appearance reveals that neomorphic enzymatic action promoting the formation of the oncometabolite 2-hydroxyglutarate affects variety of cells that change the epi-genome which enhance the development of Glioblastoma. IDH1 mutation in the mainstream of secondary Glioblastoma



Fig. 7. Genetic mutation and prediction of glioblastoma.

Table 4
Glioblastoma genes and mutation clusters.

Cluster Id	Gene count	Protein names
Cluster 1	4	EGFR, ERBB2,PIK3CA,IK3R1
Cluster 2	5	IDH1,NF1,PTEN,RB1,TP53
Cluster 3	1	PTPRD



Fig. 8. gene presence in pituitary.

patients but it is essentially non-existent in original or primary Glioblastoma. This is one of the most interesting findings in tumor history as well. Cumulative evidence suggests that this mutation has scientific and prognostic significance that will become a significant in initial differentiation of Glioblastoma diagnosis [76].

By applying K means clustering on Glioblastoma genes the above mentioned genetic structure as shows in Fig. 5 shows the following mutation and genetic bonding in Figs. 6 and 7.Network is clustered to a specified number of 03 clusters whereas dotted Lines shows edges between clusters. Glioblastoma Gene Mutation and clustering is mentioned in Table 04.

3.1.2.5. Pituitary gland. The majority of PA's (Pituitary Adenomas) as mentioned in Fig. 8, are discovered in the past are unrelated to treatment. However certain could present as clinically significant because they produces hormones or induce symptoms due to compression or invasion of adjacent tissues [78].

PAs have a wide range of causes and more than half of them have no known as hereditary origin. However PA development has been linked to Germline or somatic genetic abnormalities in some circumstances. Additional genetic modifications reported in PAs has copy number variations (CNVs), chemical reactions and miRNA abnormalities have been examined as possible factors in



Fig. 9. Genetic mutation and prediction of pituitary gland.

Table 5 Gene description.

Gene	Description	Associated Tumors
[80] AIP	Activating transcription factor 4	Pituitary tumors, meningioma, and other types of cancer
MEN1	Multiple endocrine neoplasia type 1	Parathyroid tumors, pancreatic tumors, and other types of cancer
NF1	Neurofibromatosis type 1	Meningioma, schwannomas, and other types of cancer
RET	RET proto-oncogene	Medullary thyroid cancer, pheochromocytoma, and other types of cancer
CDKN1B	Cyclin-dependent kinase inhibitor 1B	Gliomas, astrocytomas, and other types of cancer
DICER1	Dicer RNA processing enzyme	Medulloblastoma, a type of brain tumor
TSC2	Tuberous sclerosis complex 2	Gliomas, astrocytomas, and other types of cancer
GNAS	G protein-coupled receptor 30	Pituitary tumors, meningioma, and other types of cancer
GPR101	G protein-coupled receptor 101	Pituitary tumors, meningioma, and other types of cancer
PRKAR1A	Protein kinase A regulatory subunit 1A	Pituitary tumors, meningioma, and other types of cancer

Table 6

Pituitary	glands	s genes and	l mutation	clusters
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Cluster ID	Gene count	Protein names
Cluster 1	4	AIP,MEN1,NF1,RET
Cluster 2	3	CDKN1B,DICER1,TSC2
Cluster 3	3	GNAS,GPR101, PRKAR1A



Fig. 10. Pituitary tumor and prevalence rate.

Gene Description with associated Tumors.

Gene	Description	Associated Tumors
[84] AKT1	Protein kinase B	Gliomas, astrocytomas, and other types of cancer
KLF4	Kruppel-like factor 4	Glioblastoma multiforme, a type of brain tumor
NF2	Neurofibromatosis type 2	Meningiomas, schwannomas, and other types of cancer
PIK3C	Phosphatidylinositol 3-kinase catalytic subunit	Gliomas, astrocytomas, and other types of cancer
SMO	Smoothened	Medulloblastoma, a type of brain tumor
TERT	Telomerase reverse transcriptase	Glioblastoma multiforme, a type of brain tumor
TRAF7	Tumor necrosis factor receptor-associated factor 7	Glioblastoma multiforme, a type of brain tumor
POLR2A	RNA polymerase II	Gliomas, astrocytomas, and other types of cancer
SMARCB1	INI1, SWI/SNF complex, subunit B1	Meningiomas, rhabdomyosarcoma, and other types of cancer
SMARCE1	INI2, SWI/SNF complex, subunit E1	Meningiomas, rhabdomyosarcoma, and other types of cancer
BAP1	BAP1 tumor suppressor protein	Glioblastoma multiforme, a type of brain tumor

Table 8

Meningioma	genes	and	mutation	clusters.
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Cluster ID	Gene count	Protein names
Cluster 1	7	AKT1,KLF4,NF2,PIK3C,SMO,TERT, TRAF7
Cluster 2	3	POLR2A,SMARCB1, SMARCE1
Cluster	1	BAP1



Fig. 11. Genetic structure of meningioma.

pathophysiology, presentation and behavior of these tumors, particularly in terms of aggressiveness and treatment response [79].

By applying K means clustering on Pituitary Adenomas the above mentioned genetic structure as shows in Fig. 7 reveals the following mutation and genetic bonding. KNN Network is clustered to a specified number of 03 clusters as mentioned in (Fig. 9. Genetic mutation and Prediction of Pituitary Gland) whereas dotted lines show edges between clusters. Gene description, clustering and gene counts are mentioned in Tables 5 and 6.

Prevalence rate is the vital marker that shows the presence of cancer gene cases present in population as mentioned in Fig. 10.

3.1.2.6. Meningioma. Meningioma's are more common in the elderly and more common in the sixth and seventh decades although they are extremely rare in children [81] as mentioned in Tables 7 and 8. In adults, meningioma is the most frequent main central nervous system (CNS) tumor. It accounts for one-third of all primary intracranial tumors (37.1 %) [82]. The deletion of chromosome 22 was originally identified as a recurring genetic change in meningioma in the 1970s using a fluorescence approach [83]. Moreover, Genetic structure of meningioma is shown in Fig. 11.

By applying K means clustering on meningioma genes the above mentioned genetic structure reveals the following mutation as mentioned in Fig. 12.



Fig. 12. Genetic mutation and prediction of meningioma.



Fig. 13. Brain tumor mri modalities [96].

3.1.3. MRI scans in image processing

There are many collections of cancer imaging in this archive. Figshare [85] is an open source archive for brain tumor datasets, another publicly available dataset called Brats 2018, Brats 2020 [86,87], The Cancer Imaging Archive (TCIA) [88]. These MRI includes two forms of brain tumors e.g. LGG/HGG. Images of these two modalities was obtained from 49 patients of varying ages. Data sets for cancer patients are publicly accessible for research and development purposes in Brain Tumor domain, some of which are popular e.g. Brats 2013 SICAS Medical Image Repository, Brats 2014 and Brats 2015 Dataset consist of two groups of Gliomas: LGG and HGG. Total number of MR scans in the dataset is 274 with 220 for HGG and 54 for LGG, respectively. T1, T1c, T2, and Flair are the intensity level in MRI scanning as shown in Fig. 13. BRATS 2016, BRATS 2017 [87]. Online Brain Image Repositories NITRC IBSR is a brain tumor classification database for researchers. In this data set there several MRI scans containing 18 T1 3-D. Each of the 60 to 65 segmented slices in an MRI image has an optimum gray scale resolution of 512x 512.Harvard Whole Brain Atlas Dataset [89] NNLIB is an online archive of Central Nervous System MRIs. This archive which contains over 13,000 MRIs from 30 cases is also available online. These MRI's includes a wide range of benign and normal scans of different types of strokes or Central nervous system injuries, Stimulated Raman Histology [90], Pseudo-PHI-DICOM dataset DICOM [91], RIDER NEURO MRI [92], alzheimer's disease neuro images (ADNI) [93], Allen Institute of Brain Science (AIBS) [94], BrainWeb Simulated Brain Database [95]. The medical procedure used in the histological stain [24] is Hematoxylin and Eosin. (H&E). It's really simplistic but it's also prominent and reliable. At the gene, molecular

Research journals	S.
No	JOURNAL NAME
1	ELSEVIER
2	WILEY PERIODICALS
3	MOLECULAR & CELLULAR ONCOLOGY
4	PUB MED
5	MDPI
6	ACM
7	ARXIV
8	IJATCSE
9	BRITISH JOURNAL FOR CANCER
10	PLOS COMPUTATIONAL
11	SPRINGER NATURE
12	NATURE RESEARCH
13	JOURNAL OF BIOMEDICAL OPTICS
14	IEEE ACCESS
15	FRONTIERS
16	OXFORD UNIVERSITY PRESS
17	BIORXIV
18	IPE
19	WORLD JOURNAL OF GASTROINTESTINAL ONCOLOGY



Fig. 14. Number of articles included per year.



Fig. 15. Classification and performance of distinct networks.

and tissue level this method (H&E) is used to determine and classify tumor types such as.

Usually MRI contains GRAY and WHITE scale for modalities and Tissue presentation some of them are called Cortex, Inflammation, Fluid which usually help radiologist to classify tumor.

In the process of literature review different types of repositories and Modalities are used with different researchers and medical institutions. The following table contains institutions with intensity level in MRI (modalities). This noninvasive diagnosis technique reflects types of tumor (Benin, Normal, High and low Grade Glioma e.g. (HGG/LGG).

3.2. Journals inclusions for SLR

Information Sources: Research papers from reputable publications such as Nature, Elsevier Research, Springer, Molecular &

Machine learning advantages and disadvantages.

R#	Method	Technique	Advantages	Disadvantages
[97]	Threshold segmentation	Local and global	Simple calculation	Difficult to maintain accuracy
[98]	Edge Detection and Segmentation	Discontinuous local features	Separates multiple regions (edge/Region)	Doesn't accurately work on noisy data.
[99]	K-Means clustering	distance-based partitioning method	Fast efficient and simple. Simple to execute.	Trouble clustering data Centroids can be dragged by outliers.
[100]	Regional Growth Segmentation	Seed and region based pixel	Good boundary information and segmentation results.	computational cost is higher
[101]	Sobel Operator (3x3 matrix)	Edge detection.	simplicity	Signal to noise ratio.
[102]	Hybrid ensemble classifiers	applying gray level length matrix	High accuracy	Resource consuming/high computational cost.
[103]	Pixel based KNN/SVM	Majority voting system	Reduce Mis-Classification	KERNAL dependency

Oncology, MDPI, Frontiers in Bio-engineering and Biotechnology, IPEM, and British Journal for Cancer are mentioned in Table 09. In the recent past, researchers have used many models and algorithms which show a significant role in tumor detection and

classification. Table mentioned below reflects the number of publications (Fig. 14) included in this study/review. According to the literature review and statistics CNN and SVM are considered as the most prominent and commonly used algorithms in image processing. Classification and segmentation CNN depicts the most vital Characteristics of feature extraction methods

from different forms of tumor and disorder e.g. (Benin or Malignant).

This graphical analysis is based on Table 09 with a maximum images count of 3064 and accuracy of DNN 97 %, DCNN 96 %, CNN 93 % and miscellaneous 99 % as mentioned in Fig. 15. Classification and region-based methods, several algorithms and convolutional neural networks are employed.

3.3. Advantages and disadvantages of various techniques and methods

- 1. Training takes a long time, especially in testing and training of huge volume dataset, therefore the timeframe cannot be estimated.
- 2. Due to the usage of activation functions, training the proposed framework requires a huge number of training data that prune samples.
- 3. There is no single criterion or method for determining the best artificial NN structure for a task since it involves trial and error.
- 4. Majority of Neural Network can interact with numerical values and digital binary matrix at the back end all of its inputs need to be in statistical values.
- 5. The learning rate, number of nodes in the hidden layers, and which may all be optimized.
- 6. It's still ambiguous how Artificial NN analyses data and creates the desired results.
- 7. Spatial modeling is a type of disaggregation method that includes breaking a location into numerous indistinguishable or identical components. It is a collection of analytical techniques used to obtain data about spatial linkages between geographic periods or occurrences. Machine learning advantages and disadvantages are elaborate in Table 10; further understanding of cutting edge technologies, techniques and trends is mentioned in Table 11.

3.4. Algorithms implemented in literature review

We observed numerous algorithms and networks introduced by different researchers during literature review more importantly, CNN and SVM have been used more frequently and extensively by researchers due to their lower computational cost, complexity and Time consumption. There are various medical imaging techniques like x-ray, computed Tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI) is widely acceptable due to its greater resolution and also make it more compatible and most widely utilized modality format for brain tumor growth, imaging,dimension and identification. However BRATS PASCAL VOC, RIDER, figshare, TCGA-GBM Image CLEF-2012 are the most popular in tumor detection technique.

An effective research analysis has been completed based on the findings of the study. In addition, a comparative examination of the performance of currently utilized algorithms is offered. As a consequence it was discovered that CNN and SVM algorithms outperformed on publicly accessible datasets. However these algorithms are tweaked to yield fantastic results with minor alterations.ML and DL use a number of strategies to make conclusions based on massive volumes of complicated data. With precise inputs provided to the machine these algorithms fulfill the process of learning from data. It's critical to comprehend how these algorithms, as well as a machine learning system as a whole function so that we can learn how to use them in current or future state. According to literature review these algorithms are used in in different aspect image processing.

During literature review majority of the researchers have frequenty performed various machine learning and neural network models (as shown in Fig. 16) along with their respective counts. Among these are popular techniques like Convolutional Neural Networks (CNN) with 63 instances, followed by Support Vector Machines (SVM) with 33 occurrences. Other methods include Deep Convolutional Neural Networks (DCNN) with 21, Random Forest with 13, and Fully Convolutional Networks (FCN) with 8 instances. Additionally, there are less frequent mentions such as Genetic Algorithm (6), Deep Neural Networks (DNN) (15), and 3D-CNN/2D-CNN (10). Some approaches appear only once, such as Hour-Glass Net, Generative Probabilistic Model, and Hidden Markov Model, among

U. Amjad et al. **Table 11** Cap based elassification and performan

Paper No	Year	Neural Network	Method and Model	Dataset and Modalities	Tool	Cohort/ Study
[37]	2023	CNN	Inverted Residual Block (MBConv) EfficientNetv2s RecNet18	BR35H/CE-MR	Python v.3.7 NVIDA Tesla T4 13 GB GPU	2768/ 3064
[104]	2023	Multi Class Convolutional Neural Network model (MCCNN)	feature vector	BRATS 2015 and Figshare Data are used	-	220 (HGG) 54 (LGG)/ 3064
[38]	2023	CNN	Morphological-based segmentation methods; DenseNet, VGG16,	Br35H	Python	2768
[39]	2023	CNN ResNet-50, VGG-16, and Inception V3	SGD/ADAM	Nanfang hospital and General hospital	Python	233
[40]		CNN	VGG16 DWT analysis	MICCAI/T2-SWI schemic Stroke Lesion Segmentation (ISLES) BraTS 2016/2017	Keras API Python	572 images
[41]	2022	25-layer CNN	Sgdam optimizer	public datasets	-	3064 images
[105]	2020	DCNN	DL based for Multi-grade Brain Tumor	public TCIA BRATS 2015 T1- (CE)/Harvard WBA	NVidia TITAN X	121/3064
[106]	2020	Deep-Surv-Net	DCNN Deep-Surv-Net	TCGA Private d	Python	400/9
[107]	2020	DCNN	predictive model/ Resnet50	TCGA Private	Python	200/66
[108] [109]	2020 2020	CNN DNN	DCNN CNN/DCNN FLSCBN	Public/MR (T1 WCE) BraTS2013, (WBD)/MR (T2 weighted)	MATLAB R2018a Python, Core-I5,4 GB	3064 4500/281
[110]	2019	DNN	CNN AlexNet	ILSVRC-2012 Image-Net	Caffe, MATLAB	164
[111]	2019	K-means PCA	LInear-SVM DCNN/INRV2-DSFN	TCGA/TCIA	PyTorch NIVIDIA 1080Ti	2034, 2005
[112]	2019	Res-Net	-ResNet34 -G-ResNet	private/MR (T1 WCE)	Python	3064
[113]	2019	DNN	DCNN/MDCNN/DNN	private/MR (T1 WCE)	PvTorch, NVidia	220
[114]	2018	Deep CNN	DCNN	MRI	TensorFlow,Core-I7 processor, 32 GB RAM	200
[115]	2019	DCNNs	DCNN- Histological images	Private	N/A	50
[116]	2018	KE-CNN	DCNN	public	N/A	3064
[117]	2019	Dense-Net LSTM	holistic 3D MR images	Public/Private	TensorFlow Nvidia	3064/422
[118]	2018	DNN/Caps-Net	Caps-Net	MR (T1 WCE)	Keras	3064
[119]	2018	Random Forest	Caps-Net	MR (T1 WCE)	N/A	3064
[120]	2018	3D-GRE	CE 3D-GRE	Radiopaedia BraTS2015 3T images	Python	N/A
[121]	2018	DWT-DNN, Fuzzy C-means, LDA	(DWT) DNN	Public+ (http://med.harvard. edu/AANLIB/)	MATLAB R2015a, WEKA 3.9	66
[122]	2018	DCNN/ELM-LRF/random forest classifier	ELM-LRF.	Public/(T1 weighted)	MATLAB R2015a	16
[123]	2018	Classical regression, (SVM)	CNNs/SVC Ensemble	-BraTS 2018 -MRI	Python package pyradiomics5 version 2.2.0	293
[124]	2018	DNN	Patch-Network Slice- Network	TCGA HGG/LGG	Python Nvidia 1080 GPU 32 GB RAM	461
[125]	2018	DNN	Identify IDH1/2 mutations by ResNet50	MRI	Kera, Tensorflow	603 414 471

Medical Terminologies (Tumor Abbreviations.

DSFN (Deep Spatial Fusion Network),HDF(hierarchical discriminative features), MET(Metastasis), MDCN(Modified Deep Convolutional Network), PET (Positron Emission Tomography),BB(Black-blood), (Sarc)Sarcoma, (LDA)Linear Discriminant Analysis, (DWT) Discrete Wavelet Transform, (GM) Gray Matter, (WM) white matter, (MVF)modality fusion vector, (SVM)Support Vector Classifier, (NGTDM) Neighbouring Gray tone difference Matrix,(LGF) Laplacian of Gaussian filter).



Fig. 16. algorithm implemented in literature review.

others. In total, there are 227 instances of various machine learning and neural network models present in the dataset. Moreover state of the art tumor detection methods are mentioned in Table 12.

3.5. Modalities and intensities in image processing

Imaging is crucial in the assessment of individuals with brain tumors. Computed tomography (CT) and magnetic resonance imaging (MRI) are the two most important and commonly used imaging techniques (MRI). They have a significant impact on patient care. Every brain imaging Modality presents gives different and critical data relevant for every location of the tumor, several studies have used four distinct modalities: T1, T1c, T2, and FLAIR. Despite the fact that some of them produced remarkable segmentation results on the BRATS 2018 dataset, their structure is complex, necessitating additional time to train nd assess Modalities types, MRI intensities and Radiomic Gene Expressions are mentioned in Table 13.

Machine learning techniques have shown great potential in the field of brain tumor classification and detection, enabling more accurate and efficient diagnosis. However, there are several significant obstacles and difficulties related to security and privacy when applying these techniques are data privacy, data security, Informed consent and ethical considerations, Bias and discrimination, data sharing and collaboration. Furthermore, obstacles and difficulties in brain tumor detection are privacy preserving techniques (e.g. secure multi party computation, homo-morphic encryption, differential privacy etc.), secure data infrastructure, explainable AI, regulatory compliance etc.

4. Conclusion and future work

The most recent research publications on deep learning based on medical imaging challenges, notably brain tumor classification and segmentation tasks that we have evaluated in this study. The review contributed to the growth of a roadmap (shown in Figs. 1 and 2 above) for accomplishing both objectives. Researchers can use this knowledge to generate their own models. Tables 1 and 2 also contain a compilation of significant knowledge, practical methodologies in deep learning networks, and the performance of DCNN-based models for the further research in this area. In this paper a detailed spectrum of Brain tumor is presented by using various ML and DL algorithms. Majority of the researchers incorporated CNN in most of valuable journals, a comprehensive analysis has been presented, Medical image processing and related technologies e.g. H&E staining, CT scan and others are used ML as Prime method for Image segmentation and classification.

This paper also gives a brief introduction by using publicly available MR images datasets. ML and Deep learning techniques shows relatively high accuracy in classification and segmentation. Complexity and accuracy are the most prominent factor in brain tumor research.

In future, AI algorithms there is a need to be developed and predict molecular mechanisms and alterations in brain tumors, such as methylation of O-methylguanine DNA methyltransferase (MGMT), isocitrate dehydrogenase (IDH), and thalassemia/mental-retardation-syndrome-X-linked gene (ATRX) condition [206]. In model's robustness can be thoroughly assessed, a dataset originating from different repositories had been used.T1 post-contrast images, as well as other types of images, should be analyzed for their possible significance. In multiple texture features, can be used as feedback to the deep Neural Network. Furthermore, more brain tumor MRI data must be obtained on a regular basis for concrete results.

CRediT authorship contribution statement

Usman Amjad: Methodology, Data curation, Conceptualization. Asif Raza: Writing – review & editing, Resources, Project administration, Methodology. Muhammad Fahad: Writing – review & editing, Visualization, Validation, Data curation. Doaa Farid: Software, Resources, Funding acquisition, Formal analysis, Data curation. Adnan Akhunzada: Software, Investigation, Funding acquisition, Formal analysis. Muhammad Abubakar: Visualization, Project administration, Formal analysis, Conceptualization. Hira Beenish: Visualization, Supervision, Resources, Methodology, Funding acquisition, Data curation.

Data availability statement

This article contain No human trial of data involved in human intervention.

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.

Machine learning methods in image processing for tumor Detection.

R #	Attributes	Techniques	Dataset	 Sen (%) • Cropp Un-cropp Segmented 	• Spec (%)	 Acc (%) Cropped Un-cropped Segmented FNR NPV (DSC) 	AUCPre %PPVJSI	• F- Alarm • FPR •FN • Recall • Method • Time	 TPR TN M.A (%) HD95_ET D95_WT HD95_TC 	Dice/Enhancement/ Tumor Validation	F1-Score % MCC G-Mean
[126]	CNN	Support Vector Machine	TCIA	100	100	99.65	-	-	-	-	-
[127]	2D HISTOGRAM Matrix	FCM	Cohort	83.00	100	92.00	_	_	_	_	_
[128]	GWF + HOG + SFTA	Random forest	BRATS 2012, 2013, 2014, 2015	100	92.9	93.3	1, 0.93, 1	5 Fold 0.5	-	-	
[129]	TLFE + FLDO + FLSC + FLSCD + FLSCBND + FLSCBN	Deep-CNN	BraTS 2013	_		88.91		3.25	7.6	-	
[130,131]	N4ITK ROI	CNN HOG	Private DataSet	86.26 89	90.9 94	85.69 92.14	-	-	-	-	
[132]	RGBA	DNN	BraTS 2018	0.9239	0.9956	_	_	_	_	0.9268	
[133]	$\begin{array}{l} {\rm GLCM} + {\rm GLRLM} + {\rm GLSZM} \\ + {\rm NGTDM} + {\rm GLD} \end{array}$	3D CNN	BraTS 2018	-	-	46.40 %	-	-	-	0.80522/0.84943/ 0.90444	
[134]	MXN pixel matrix	CNN	figshare	99.35 87.76	99.95 98.61	99.81 96.29	99.84 94.51	-	-	-	99.6 91.01/99.47, 88.77, 99.65, 93.02
[135]	Mb-FCRN + MvNet	SPNet -CNN	BRATS 17	_	_	0.68	_	_	_	0.74/0.68/0.86	,
[136]	Fourier Wavelet+ Chebyshev	DNN	DICOM	92.72	98.13	98.25	94.71	-	-		93.71
[137]	2D-CNN	ConvNet	Cohort Study	-	-	97	Normal- 100 Tumor- 94	-	-	-	Normal-100 Tumor-94
[138]	LBP + GLCM + Geometric + PSO	DRLBP + CNN	BRATS 2018	-	-	92	-	-		91.20 %/88.34 % 81.84	-
[139]	GWM + BWM	2D-CNNs+3D-CNNs	MICCAI BRATS 2018	0.825	0.997	-	-	-	_	0.843	-
[140]	CMFT + CMFF	DCNN	PASCAL VOC	0.833	-	-	-	-	_	0.903/0.833/0.791	-
[141]	Radiomic + manual feature extraction	DCNNs+ MDCNN	Patient cohorts + Private	-	-	$0.613 \pm 0.055,$ 96.4	-	-	0.88 0.97	-	-
[142]	TLRN-LDA	CNN	ImageCLEF-2012	89.3	99.6	87.91	88	-	_	-	88.3/88.1
[143]	SLIC	CNN	BRATS 2019	97.81	100	0.932	0.99	_	_	96.32	-
[144]	BWT	SVM	DICOM	97.72	94.2	96.51 %					
[145]	DWPT	CNN	ImageNet dataset	100		100/0.82	100	-	_	-	100
[146]	Robust features	GNN	T1-CE MR images	90.16	95.58	91.7	91.17	-	_	-	90.54
[147]	region of interest (ROI)	CNN	Figshare	98.18 98.52 97.40		98.93 99 97.62	-	-	-	-	-
[148]	(NS-EMFSE	CNN + SVM	TCGA-GBM	$\begin{array}{c} 93.75 \pm 0.62 \\ 91.25 \pm 1.25 \end{array}$	$92.5 \pm 1.87, \\ 83.75 \pm 2.5$	$\begin{array}{c} 93.1 \pm 1.25 \\ 87.5 \pm 1.87 \end{array}$	-	-	-	-	-
[149]	I-linear	CNN	BRATS 2015	_	-	_	_	_	_	0.9/0.87/0.86	-

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(continued on next page)

Table	12 ((continued)
abic	141	(continuou)

R #	Attributes	Techniques	Dataset	 Sen (%) • Cropp Un-cropp Segmented 	• Spec (%)	 Acc (%) Cropped Un-cropped Segmented FNR NPV (DSC) 	AUCPre %PPVJSI	• F- Alarm • FPR •FN • Recall • Method • Time	 TPR TN M.A (%) HD95_ET D95_WT HD95_TC 	Dice/Enhancement/ Tumor Validation	F1-Score % MCC G-Mean
[150]	Multilayered Mode	CNN	BRATS 2013+WBA	-	-	96–99	-	3.25	1.56	-	-
[151]	GLCM-CA	ANN	BRATS 2015	90.09	96.78	94 07	_	_	_	_	_
[152]	SR-FCM-CNN	CNN	TCGA-GBM	_		98.33	_	_	_	_	_
[153]	GLCM	forward-feed convolutional network	Kaggle	96	96	96.05	92.31	-	-	-	94.12
[154]	Tumor genomic prediction	Patch-wise CNN	ImageNet + Private data	0.93	0.82	0.88	-	-	-	-	-
[155]	GLCM + GW	SVM	RIDER+ Local	91.9	98	97.1	0.98	-	-	-	-
[156]	2D slice	DNN	BRATS+ ISLES	95,100	95.2100	95.1100/0.05, 0.00 95.100	97.2 90.4 100	0.05 0.00	-	-	-
[157]	DWT	CNN(Automatic Feature Learning)	BRATS 2018	0.92	0.8	0.87/0.08	-	0.2	-	-	-
[108]	One test	DNN	BRATS	-	-	90.39	85.99	85.84	_	-	85.91
[158]	CANet	CNN	_	-	-	-	-	-	3.319 4.897 6.712	0.821/0.835/0.895	-
[159]	KE-CNN	SVM	3064 images	-	-	-	94.5 91 98.3	76.8 97.5 1	-	-	85.8 94.1 99.1
[117]	auto-encoder	Dense-Net LSTM RNN	Public+ Proprietary	-	-	(92.13,71.10) (84.61,60) (91.28,86.56)	-	-	-	-	-
[160]	CE 3D-GRE + BB	3D-CNN	Private	90.3 % (56/ 62) 100 % (62/62)	-	0.9708 0.9437	-	1,8	-	-	-
[121]	DWT)	DNN	Harvard	-	_	96.97	0.984	0.97	_	-	0.97
[122]	ELM-LRF	CNN	Public	96.8 96.23	97.12 95.92	97.18,96.45	-	-	-	-	-
[161]	DMDF	FCNN	BRATS 2015	0.9012	-	90.98/0.9129	-	1.0322	0.8916	-	-
[162]	Encoder-decoder structure	AHN	BRATS 2018	-	-	92	-	-	-	0.66,0.62/0.72,0.65/ 0.82, 0.79	-

Types of modalities/intensities in image processing.

Paper #	T1-W T1-Gd Sequence,T2 Flair (MRI)	CIFAR10 Taxonomy Contents	SRS/H&E Staining Radiomic Gene Expression DNA	MISC Diffuse Tensor Imaging	TITc-SPECT FDG-PET TITc-SPECT T2,T1 –WCE
[163]	YES	_	-	-	_
[164]	YES	-	-	-	-
[165]	-	-	YES	-	-
[166]	-	-	YES	-	-
[147]	-	-	-	-	YES
[167]	YES	-	-	-	-
[168]	-	-	YES	-	-
[169]	-	-	YES	-	-
[131]	YES	-		-	-
[170]	YES			-	YES
[171]	_	YES	YES	-	-
[172]	YES	-	-	-	-
[173]	YES	-	-	-	-
[174]	YES	-	YES	-	-
[106]	-	-	YES	-	-
[175]	-	-	YES	-	-
[170]	-	-	YES	-	-
[170]	-	-	YES	-	-
[170]	- VEC	- VEC	-	-	- VEC
[170]	165	IES	VEC	-	1E5
[1/9]	-	-	1ES VEC	-	-
[10]	- VEC	-	1125	-	- VEC
[119]	TES	-	-	-	1E5
[100]	VES	-	-	-	-
[161]	VES	_	_	_	_
[182]	-	_	 YFS	_	_
[183]	_	_	VFS	_	_
[184]	YES	_	_	_	YES
[185]	YES	_	_	_	110
[186]	YES	_	_	_	
[152]	YES	_	_	_	YES
[187]	YES	_	YES	_	_
[155]	YES	_	_	-	_
[188]	YES	_	_	_	_
[189]	-	_	YES	_	_
[190]	YES	-	-	YES	YES
[191]	YES	-	-	-	-
[192]	YES	-	-	_	-
[193]	_	_	YES	-	-
[159]	YES	-	-	-	YES
[191]	YES	-	-	-	-
[178]	YES	-	-	-	-
[151]	YES	-	-	-	-
[111]	-	-	YES	-	-
[194]	YES	-	-	-	-
[195]	YES	-	-	-	-
[117]	YES	-	-	-	-
[34]	-	-	YES	-	-
[196]	-	-	-	YES	-
[118]	YES	-	-	NTC .	-
[197]	-	-	-	YES	-
[122]	-	-	-	YES	-
[34]	- VEC	-	-	TES	-
[198]	169	-	-	VEC	-
[190]	-	-	-	I EƏ VEC	-
[200]	- VEC	-	-	IEƏ	-
[201]	I ES VES	-	-	-	-
[202]	I ES VES	-	-	-	-
[124]	1 23	-	_	_	- VFS
[106]	_	_	- VFS	_	-
[204]	YES	_	_	_	_
[205]	YES	_	_	_	YES
L J					

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