

Prediction of Great Future Of Gliomas in Neurological Field: a Review

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Received: 📅 2026 June 10

Accepted: 📅 2026 June 29

Published: 📅 2026 July 17

Abstract

Despite all the limitations and challenges associated with the use of AI and the validity and general globalization of its results, the use of AI in glioma is promising, and the variety in the application predicts a great future. It is applied in various steps of care ranging from diagnosis, grading, the prediction of prognosis, and reaching to treatment and post-operative care. There is a need for international collaboration in this field to share knowledge and experience to overcome the faced challenges. The present review explored the uses of AI in glioma, providing valuable insight for a broad audience in the neurological field. Neurologists, neurosurgeons, imaging specialists, pathologists and other healthcare professionals may find the discussion of current advances in AI integration in glioma care informative for their practice and future research endeavors.

Keywords: Gliomas, Review, Learning Machine

Key Points

- Glioma is the most prevalent type of primary brain tumor in adults.
- The use of artificial intelligence (AI) in glioma is increasing and has exhibited promising results.

1. Introduction

Glioma is the most prevalent type of primary brain tumor in adults, which is responsible for >80% of malignant intracranial tumors [1-3]. Glioma tumors were categorized in the past into two categories based on their aggressiveness as follows: Low-grade glioma (LGG) and high-grade glioma (HGG) [4-6]. Some LGGs are benign tumors, whereas HGGs are malignant tumors [7,8]. However, the necessity for a new enhanced system arises as a result of rapidly increasing knowledge from clinical and molecular neuro-oncological research with high output. The fifth edition of the WHO Classification of Tumors of the Central Nervous System (CNS), published in 2021, focuses on the employment of intricate histological and molecular methods to determine the pathological diagnosis and grade of a tumor [9]. Some authors prefer to use the term cancerous glioma as opposed to the prior term LGG, as major revisions to the current WHO classification have increased the importance of molecular diagnostics in the classification of CNS tumors [10]. Currently, 'glial, glioneuronal, and neuronal tumors' are classified as a different family and are separated into

six categories as follows: i) Adult-type diffuse gliomas; ii) pediatric-type diffuse LGGs; iii) pediatric-type diffuse HGGs; iv) circumscribed astrocytic gliomas; v) glioneuronal and neuronal tumors; and vi) ependymal tumors [11].

To prevent tumor recurrence rates and develop effective treatments, it is imperative to leverage artificial intelligence (AI) to comprehend tumor heterogeneity [12]. This is based on 'radiomics', which typically consists of procedures and methods for extracting quantitative information from available imaging data [13]. The present systematic review discusses the uses of AI in glioma detection, grading, the prediction of the isocitrate dehydrogenase (IDH) genotype, O6-methylguanine-DNA-methyltransferase (MGMT) promoter methylation status, 1p19q codeletion, survival prediction, treatment response, pseudo-progression and progression, and the glioma functional network. IN THIS REVIEW THERE ARE NOT FIGURES AND TABLES.

Glioblastoma (GB), previously known as GB multiforme (GBM) is one of the most aggressive types of brain cancer, which is characterized by its rapid development, poor response to therapy and low rate of survival [12]. AI is used in glioblastoma detection, for the prediction of the overall survival (OS) rate, and for determining the MGMT promoter methylation status, which is a mutation positively associated with an improved prognosis and temozolomide treatment

response. AI is also used to determine tumor progression and pseudo-progression.

2. Data and Methods

The aim of the present study was to determine the trends of AI use in glioma and GB. For this purpose, a search is conducted in multiple databases including (Scopus, PubMed, Wiley and Google Scholar) using the keywords “machine learning”, ‘glioma’, ‘glioblastoma’, and ‘neurosurgery’. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. The included articles were full-text articles in the English language published from inception until June, 2022. The excluded articles were review articles, abstracts only, letters to the editor, commentaries, as well as non-human, non-glioma, non-GB and non-English articles. The duplicate articles were deleted. The articles were then retrieved, screened and then categorized according to the use of AI in glioma. Each article was subsequently reviewed individually, summarized and the results are presented in the Results section below. This type of study did not require approval from a research ethics committee. The PRISMA guidelines that were followed in the present study. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The guidelines used were according to the study by Page et al [67].

3. Results

The majority of the articles were from the USA (n=18) followed by China (n=11). The number of articles increased annually, reaching the maximum number in 2022. The majority of the articles were investigating glioma as opposed to GB (grade IV glioma). The majority of the articles were about both LGG and HGG (n=23), followed by HGG/glioblastoma (n=13). Additionally, three articles were about LGG only, and one article was on HGG only; two articles not specify the grade. The article titled ‘Automatic assessment of glioma burden: A deep learning algorithm for fully automated volumetric and bidimensional measurement’ written by Chang et al had the highest sample size among the other included studies, reaching a sample size of 897 samples [14]. The most commonly used AI modality was deep convolutional neural networks (CNNs) alone or in combination with other methods.

The articles discussing the use of AI in glioma were classified into detection, grading, prediction of the IDH genotype, MGMT promoter methylation status (which is a mutation associated with an improved prognosis), 1p19q codeletion, survival prediction, treatment response, pseudo-progression and progression and the glioma functional network.

4. Detection

Since gliomas are frequently characterized by radiographic evaluation and magnetic resonance imaging (MRI), the precision of imaging-based tumor feature recognition has increased, since traditional machine learning algorithms use human-designed feature extraction to separate tumor characteristics [15]. Rajagopal used the feature optimization technique to distinguish glioma from non-glioma brain MRI

images using an optimum collection of features [16]. In order to identify the tumor areas in the brain MRI image and distinguish them from surrounding areas, the segmentation method was performed, and he achieved 96.5% specificity, 97.7% sensitivity, and 98.01% accuracy [16]. Another study employed the SegNet classification system on the HGG BRATS 2017 dataset and achieved 96.1% sensitivity, 96.5% specificity, and 96.4% tumor pixel segmentation accuracy [17]. One of the issues with glioma detection is the presence of noise, as well as low-sensitivity border pixels [18]. Mathiyalagan and Devaraj recognized and eliminated the noise content in the original brain MRI image using a ridge let filter and fuzzy logic was then used to detect the edges in the noise-removed image, and contrast adaptive local histogram equalization was applied to the edge-detected brain image to improve the edge pixels [19].

The suggested technique obtained 97.65% sensitivity, 97.8% sensitivity and 98.78% accuracy on the HGG brain MRI images in the BRATS 2017 dataset [19]. Another systematic review found that the most frequent type of algorithm used in glioma detection was neural networks. Algorithm accuracy varied from 0.75 to 1.00 (median, 0.96; 10 articles) [20]. The assessment of reporting quality using the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) criteria resulted in a mean individual TRIPOD ratio of 0.50 (standard deviation, 0.14; range, 0.37 to 0.85) (20). A standard MRI can make it challenging to distinguish between brain metastases and glioma, as imaging results in certain clinical circumstances can frequently be similar [21]. Jekel et al conducted systematic review and meta-analysis of a subset of qualifying studies that used machine learning models for the non-invasive distinction of glioma from brain metastases [21]. The average area under the receiver operating characteristic curve (AUC) from 17 studies was 0.916 ± 0.052 , while the average sensitivity (n=16) and specificity (n=15) were 0.868 ± 0.123 and 0.843 ± 0.235 , respectively [21]. In a different study, the ipsi- and contralesionally hemispheres of patients were compared using network measurements to identify structural connectivity deficits caused by gliomas [22]. The results were then linked to neurological testing. Both short- and long-range connection patterns were shown to be differentially impaired depending on the site of the lesion. In contrast to the contralesionally hemisphere, the ipsilesional hemisphere exhibited a reduced global and local efficiency, according to the network analysis, which is indicative of the degradation of information flow across various network areas [22].

Even for radiologists, radiomics has proven to be useful in identifying differential diagnoses that were challenging to make. Furthermore, research has evaluated the added value of radiomics compared to the eyes of radiologists [23]. Multiple research projects set up AI approaches to distinguish glioblastomas from single-brain metastases. A previous study which employed support vector machine (SVM) data classification and post-contrast 3D T1W gradient-echo sequence radiomics, revealed an accuracy of 85% and

an AUC of 0.96 [24]. Another study using multiple feature selection and classification techniques, including SVM and Lasso, along with contrast-enhanced images, obtained a good accuracy and an AUC performance of 0.90. Moreover, the best classifiers outperformed expert neuroradiologists in terms of clinical performance [25]. Primary CNS lymphoma (PCNSL) may exhibit heterogeneous contrast enhancement and internal necrosis, similar to glioblastoma behavior [23]. A previous study found that radiomics were able to discriminate PCNSL from glioblastoma based on the apparent diffusion coefficient with optimal performance on both internal (AUC, 0.984) and external (AUC, 0.944) validation sets [26]. Glioblastomas were distinguished from tumefacien multiple sclerosis by another study that used dynamic texture parameter analysis to extract features from the first pass of the contrast phase of dynamic susceptibility contrast-enhanced perfusion maps [27]. AI can be used to differentiate between four molecular subtypes of glioblastoma: Neural, proneural, mesenchymal and classical by using the transcriptomic profiling tool [28]. Research based on standard MRI sequences that used SVM obtained an accuracy of 71% in distinguishing the four subtypes [29].

5. Glioma Grading

Glial tumor grading is critical for patient care. It has a major impact on the extent of surgical resection, the need for adjuvant therapy and overall patient outcomes [30]. Zhuge et al used the deep convolutional neural networks method for glioma grading [31]. The suggested approaches were tested using 5-fold cross-validation on The Cancer Imaging Archive (TCIA) LGG data and the Multimodal Brain Tumor Image Segmentation (BraTS) Benchmark 2018 training datasets and they achieved sensitivity of 0.935, a specificity of 0.972 and an accuracy of 0.963 for the 2D Mask R-CNN based method, and sensitivity of 0.947, specificity of 0.968 and an accuracy of 0.971 for the 3DConvNet method [31]. Another study used radiomics for distinguishing between grades II, III and IV; that study retrieved radiomics characteristics using conventional, diffusion and arterial spin labeling perfusion MRI [32]. That study utilized an SVM classifier and achieved a high AUC of 0.97 and an accuracy of 98% [32]. Another study used SVM in the grading of gliomas in 120 individuals. These researchers used SVM with the synthetic minority over-sampling technique (i.e., over-sampling the abnormal class and under-sampling the normal class) and achieved 94-96% accuracy in diagnosing both HGGs and LGGs [33]. In a different study, three distinct classification techniques, including random forest (RF), K-nearest neighbor and SVM were compared [34]. After pre-processing, the tumor area was extracted from post-processed images using the fuzzy C-means segmentation approach. Texture, local binary pattern and fractal-based characteristics were obtained using MATLAB software. Subsequently, using the grasshopper optimization algorithm, they found that the RF performed better than the other classification techniques, with an accuracy of 99.09% [34]. This finding is supported by another study that found that the RF-derived optimum feature set offered higher grading outcomes than previous methods utilizing the SVM classifier [35]. Hsu et al merged

the whole slide imaging (WSI) and multiparametric magnetic resonance imaging (mpMRI) data guided by a confidence index [36]. Experiments conducted on the validation dataset for the CPMRadPath 2020 competition revealed that combined judgments from both modalities performed better in glioma classification than either WSI or mpMRIs used alone [37].

6. Prediction of the IDH Genotype

An enzyme involved in the Krebs cycle and the energy metabolism of the cell is termed IDH. Alpha-ketoglutarate is typically accumulated from isocitrate in IDH wild-type gliomas; however, in cases of IDH mutation, isocitrate transforms into 2-hydroxyglutarate [30]. The prognostic and predictive significance of IDH mutation renders it one of the most significant molecular markers, with the prognosis and treatment sensitivity being better for the IDH mutant subtype [37]. The WHO classification of Tumors of the CNS was updated in 2016 to include molecular status for identifying diffuse gliomas, such as IDH gene mutation and chromosomal 1p/19q codeletion [9]. A previous study used short echo time (TE) proton MR spectroscopy (1H-MRS) at 3T to classify IDH and TERTp mutation-based subsets of gliomas [38]. They achieved an accuracy of 88.39%, a sensitivity of 76.92% and a specificity of 94.52% for a TERTp mutation in primary IDH wild-type gliomas, and an accuracy of 92.59%, a sensitivity of 83.33% and a specificity of 95.24% for a TERTp mutation in primary IDH wild-type gliomas [38]. Another study used 3D-CNN in 94 cases of IDH mutation to associate multiparametric imaging characteristics with glioma IDH mutations, and 120 wild-type gliomas exhibited a higher effectiveness, attaining 98% sensitivity, 97% specificity and an AUC of 99% [39]. Nalawade et al assessed three CNN models (Inception-v4, ResNet-50 and DenseNet-161) using T2-weighted (T2w) MRI data from 120 individuals diagnosed with HGGs and 140 individuals diagnosed with LGGs [40]. The highest-performing model with minimum preprocessing steps was determined to be DenseNet-161 with a 5-fold cross-validation. That study achieved a mean slice-wise accuracy, sensitivity and specificity of 90.5, 83.1, and 94.8%, and subject-wise accuracy, sensitivity and specificity of 83.8, 83.5, and 83.5%, respectively [40]. Another study that employed the voxel-wise clustering method examined 69 patients with treatment-naïve diffuse glioma using diffusion-weighted imaging, fluid-attenuated inversion recovery, pH-sensitive amine chemical exchange saturation transfers MRI, and contrast-enhanced T1-weighted imaging at 3 T [37]. The 10-class clustering method performed best in predicting IDH mutation status, with a mean AUC, accuracy, sensitivity and specificity of 0.94, 0.91, 0.90, and 0.91%, respectively [37].

7. MGMT Promoter Methylation Status

When the MGMT promoter, an enzyme involved in DNA damage and dealkylation, undergoes hypermethylation, there is a positive association between this mutation and improved treatment outcomes with temozolomide [41]. Previous studies have used radiomics to non-invasively determine the methylation status of the MGMT promoter. Levner et al used artificial neural networks (ANN) in

conjunction with two-dimensional discrete orthonormal Stockwell transform (2D-DOST) to perform a texture analysis of T2, fluid attenuated inversion recovery (FLAIR) and T1 post-contrast MR images to predict 59 patients with newly diagnosed glioblastoma regarding their MGMT promoter methylation status [42]. An 87.7% accuracy rate was attained in that study, which was obtained by the 2D-DOST in combination with ANN [42]. The study by Korfiatis et al tested and assessed three different residual CNNs without any prior tumor segmentation pre-processing to predict the MGMT status on 155 brain MR scans [43]. ResNet50 (50 layers), ResNet34 (34 layers) and ResNet18 (18 layers) achieved an accuracy of 94.90, 80.72, and 76.75%, respectively [43]. In addition, Chang et al (44) used the MRIs of 259 glioma patients and a CNN model to predict the methylation status of the MGMT promoter. The model attained a level of accuracy of 83.0% [44]. Another study combined IDHmut and MGMTmet to establish a significant prognostic molecular marker for gliomas [45]. That study analyzed 162 individuals with gliomas, comprising 58 patients with IDHmut and MGMTmet co-occurrence and 104 patients with other statuses. The effectiveness of the models produced by the tree-based pipeline optimization tool was evaluated using the AUC. Using shape and textual features from the Laplacian-of-Gaussian-filtered Gd-3DT1, the gradient boosting classifier was trained and performed best in 4-fold cross-validation (average sensitivity, 81.1%; average specificity, 94%; average accuracy, 89.4%; average kappa score, 0.76; average AUC, 0.951) [45].

Precision medicine, in which the course of treatment is tailored to the individual genetic profile and epigenetic signature of each tumor, is within reach when phenotypic, genotypic and epigenetic features are combined in glioblastoma diagnostics [46]. The MGMT promoter's methylation status has key therapeutic implications in predicting response to alkylating chemotherapy. As a result, studies have used radiomics to determine the methylation status of the MGMT promoter [46]. An example is a study that used conventional MRI in order to anticipate the MGMT promoter methylation status in patients with glioblastoma. A subset of six features was used by the final random forest classifier and achieved an AUC of 0.88 [47]. Another study used a subset of 36 characteristics, in both the validation and test datasets, the final model achieved diagnostic accuracy of 87 and 80%, respectively [48]. In addition, another study took advantage of positron emission tomography (PET) scans of 107 patients by the extraction of >1,500 features; it made use of a support vector machine classifier. In training, the model achieved an AUC of 0.94, and in testing, it reached 0.86 [49].

8. 1p19q Codeletion

Oligodendroglioma is defined by IDH mutant gliomas containing 1p19q codeletion. Astrocytomas are the term for non-codeleted 1p19q tumors, whether or not they have an IDH1/2 mutation [50]. Chang et al achieved a 92% accuracy in predicting 1p19q codeletion status using a

2D/3D hybrid [44]. Shofty et al used 152 radiomics variables from conventional MRI to create an ensemble bagging tree classifier that identified a chromosomal 1p/19q co-deletion and obtained an accuracy of 87% following 5-fold cross-validation [51]. Ge et al augmented the data and employed contrast-enhanced T1 and T2-weighted MRs to obtain an accuracy of 89.39% on a cohort of 159 patients using a unique multistream deep CNN (a 7-layer 2D CNN) [52]. Han et al developed a radiomics signature from 277 patients with WHO grade II and III gliomas using conventional MRI using a RF classifier [53]. In the training cohort, the final model had an AUC of 0.89 while in the test cohort, it had an AUC of 0.76. They found that a combination model that included radiomics and clinical characteristics did not enhance the prediction of the chromosomal 1p/19q co-deletion [53]. Akkus et al used a multiscale CNN in 159 cases, they could predict the 1p19q codeletion status with an accuracy of 87.70% [54].

9. Survival Prediction

The prediction of the survival of patients with glioma has also been proposed using deep learning-based radiomics models. Chen et al developed a machine-learning model for patients with HGG by obtaining eight clinical variables and 39 dose-volume histogram parameters [55]. Their study used Cox proportional hazards, SVM and random survival forest (RSF) models. The RSF model outperformed the other two models, where the concordance indices of the training and testing sets were 0.824 and 0.847, respectively [55]. The AUCs of the testing set for 1-, 2- and 3-year survival were 92.4, 87.7 and 84.0%, respectively. They demonstrated that with this approach, overall survival could be predicted and patients with HGG could be categorized into high- and low-risk groups [55]. Another study combined an SVM technique with a deep learning architecture [56]. A three-dimensional CNN was used in this deep learning architecture to extract distinguishing characteristics of brain tumors that already existed in conjunction with SVM; the two-step technique predicted the OS of 69 individuals with gliomas of high grade with an accuracy of 89% [56].

Recently, OS has been demonstrated to be predicted by radiomic models in patients with glioblastoma using radiomics features and clinical non-imaging data, such as age, resection status and the survival duration of patients [57]. A previous study employed the bioinspired optimization approaches, genetic algorithms (GA) and particle swarm optimization (PSO) algorithms, to a fused feature set in the prediction of patient survival (OS) duration for the survival groups in the two and three classes [58]. The technique obtained an AUC of 0.66 when using fusion feature + SVM + GA (3-class group) and 0.70 when using fused feature + SVM + PSO (2-class group) [59]. Another study used radiomics nomograms along with radiomic signatures, ependymal and pia mater involvement (EPI), and age for the prediction of OS and dividing up patients with GBM into long-term vs. short-term survival [59]. The nomogram, radiomic signature, age, and EPI accuracy for the external validation

set were represented by the ROC curves as follows: 0.858, 0.826, 0.664 and 0.66(57). Another study used single feature class models, such as 'clinical', 'pathological', 'MRI-based' and 'FET-PET/CT-based' models and combinations, as well [60]. The results of that study revealed that the MRI-based model improved performance over all single-feature class models and provided the optimal OS prediction performance when all features were combined. Adding treatment information improved prognostic performance even further, reaching C-indices of 0.73 (0.62-0.84) and 0.71 (0.60-0.81) on the validation set [60]. Kickingeder et al demonstrated the utility of radiomics in addition to the well-established prognostic indicators of age, surgical extent, Karnofsky performance score and the methylation status of the MGMT gene [61]. When paired with clinical data, radiomic analysis enhanced progression-free survival and OS prediction using standard-of-care imaging (C-index increased from 0.637 to 0.696) [61].

10. Treatment Response

Neuro-oncology specialists frequently manually calculate tumor size using the two-dimensional diameters of the growing tumor. However, this method is only limited to interobserver variability and is time-consuming [14]. Chang et al created an automated algorithm that segments FLAIR hyperintensity and contrast-enhancing tumors, measuring tumor volumes and generating the largest bidimensional diameters possible in order to satisfy the Response Assessment in Neuro-Oncology (RANO) requirements (AutoRANO). The intraclass correlation coefficient for the FLAIR hyperintensity volume, contrast-enhancing tumors volume and RANO measures were used to compare longitudinal changes in tumor burden that were computed manually and automatically, respectively, 0.917, 0.966 and 0.850 [16].

11. Glioma Functional Network

In order to determine the functional network of gliomas, Xiang et al attempted to create a systematic method for combining information with high throughput CRISPRCas9 tests for screening using machine learning techniques [62]. They demonstrated that the network highly enhanced different biological pathways and may contribute to the development of gliomas. They also identified 12 putative Wnt/-catenin signaling pathway targeted genes, such as AARS1, HOXB5, ITGA6, LRRC71, MED19, MED24, METTL11B, SMARCB1, SMARCE1, TAF6L, TENT5A and ZNF281, from densely coupled glioma functional modules [62]. The overall survival prognosis of gliomas was highly associated with Cox regression modeling using these targets. Additionally, TRIB2 was identified as a glioma neoplastic cell marker by single-cell RNA-seq analysis of GBM samples [62].

12. Tumor Progression and Pseudo-Progression

True progression and pseudo-progression are difficult to reliably distinguish by MRI, and this continues to be a challenging issue in patient care despite the use of several methods, such as MR perfusion and watchful waiting. It is more challenging to identify pseudo-progression from

true progression, as inflammatory responses with complex signal features have evolved with the emergence of novel immunotherapies [30]. Since distinguishing glioblastoma tumor progression and pseudo-progression is difficult for the radiologist's view, a multivariate study demonstrated radiophenotypic signals differentiating between the two groups [63]. In a leave-one-out cross-validation, the proposed signature predicted pseudo-progression with an accuracy of 87% (AUC, 0.92) and true progression with an accuracy of 84% (AUC, 0.83) [63].

13. Discussion

The results of the reviewed studies demonstrate that, in comparison to other high-performing algorithms, deep learning methods can be dominant. Therefore, it is reasonable to believe that deep learning will survive and its product line will continue to grow. Future developments with deep learning indicate greater promise in various medical domains, particularly in the area of medical diagnosis. However, it is currently unclear whether deep learning can take the place of clinicians or doctors in the diagnosis of medical conditions [65]. Studies on gliomas and glioblastomas have demonstrated a marked increase in the use of AI over the past few years for a variety of purposes, including diagnosis, grading, the prediction of molecular markers such as IDH genotype and MGMT promoter methylation status, prediction of survival, response to treatment, and even understanding functional networks. Each phase of the process of caring for patients with gliomas, including intraoperative tissue analysis, outpatient and oncology care, the post-operative acute phase, and intraoperative workflow analysis, could be completely transformed by artificial intelligence. AI can also improve brain tumor research and therapy and impact national guidelines and policies [65]. AI models have successfully associated multiparametric imaging features with IDH mutations with high sensitivity and specificity, providing useful information for prognostic and treatment decisions. Moreover, the methylation status of the MGMT promoter must be known in order to assess the treatment efficacy. AI-based radiomics techniques have demonstrated efficacy in accurately estimating the methylation status, thereby facilitating customized treatment planning and the assessment of therapeutic outcomes.

It should be mentioned that accurate generalizability estimation requires the validation of studies in independent, representative and clinically applicable datasets [21]. In addition, the description of algorithm fine-tuning using data that is distinct from the training data should be saved for validation. Testing is the term for the objective assessment of an algorithm with data that is not included in the training or validation sets. Each study provided training and testing data; however, according to Subramanian et al, a number of them mislabeled testing as validation [20]. Numerous studies are conducted based on small sample sizes or small databases. A related issue with small datasets is the well-documented ability of a multimillion-parameter deep learning algorithm to overfit to a single training cohort, leading to artificially inflated algorithm accuracy. With the

comparatively small number of carefully selected datasets that are currently used in radiography research, a number of limitations may interfere with the clinical implantation of AI in the clinical setting [15].

The adoption of the system depends on how well it fits into the radiologist's workflow, which includes the dictation software, picture archiving and communication system, and electronic medical records. Furthermore, manual intervention and the application of a range of tools are necessary for many segmentations and radiomic methods. To increase the generalizability of the performance of an algorithm across various imaging sites, acquisition parameters and patient populations, bigger and more diverse data sets may be required [15,66]. Furthermore, there may be discrepancies in the current analysis of retrospective data obtained during standard clinical care. Ultimately, even with the ability to aggregate large cohorts from multiple hospitals, annotation remains a laborious process requiring a high degree of skill. Future developments of tailored semi-automated labeling tools and iterative re-annotation strategies may offer an efficient solution as manual annotations are frequently time-consuming [15]. Finally, it has been noted that datasets from different global locations exhibit significant heterogeneity due to regional differences as there are different patient populations and pathologies in tertiary or academic medical centers, small hospitals and outpatient practices, and other diverse healthcare settings [57].

13. Limitations

As regards limitations, even though applying AI methodologies to imaging analysis has produced positive results, there are still issues that need to be taken into account. These include the various imaging platforms, the various protocols and parameters used to obtain the images, the various patient classification criteria, and the variety of patient demographic and treatment data [64].

14. Conclusions

Glioma is the most prevalent type of primary brain tumor in adults. The use of artificial intelligence (AI) in glioma is increasing and has exhibited promising results. The present study performed a systematic review of the applications of AI in glioma as regards diagnosis, grading, prediction of genotype, progression and treatment response using different databases. The aim of the present study was to demonstrate the trends (main directions) of the recent applications of AI within the field of glioma, and to highlight emerging challenges in integrating AI within clinical practice. A search in four databases (Scopus, PubMed, Wiley and Google Scholar) yielded a total of 42 articles specifically using AI in glioma and glioblastoma. The articles were retrieved and reviewed, and the data were summarized and analyzed. The majority of the articles were from the USA (n=18) followed by China (n=11). The number of articles increased by year reaching the maximum number in 2022. The majority of the articles studied glioma as opposed to glioblastoma. In terms of grading, the majority of the articles were about both low-grade glioma (LGG) and high-grade

glioma (HGG) (n=23), followed by HGG/glioblastoma (n=13). Additionally, three articles were about LGG only; two articles did not specify the grade. It was found that one article had the highest sample size among the other studies, reaching 897 samples. Despite the limitations and challenges that face AI, the use of AI in glioma has increased in recent years with promising results, with a variety of applications ranging from diagnosis, grading, prognosis prediction, and reaching to treatment and post-operative care.

Acknowledgements

None

Funding

Funding: No funding was received.

Availability of Data and Materials

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the current study.

Ethics Approval and Consent to Participate

Not applicable.

Patient Consent for Publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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