SCOPING REVIEW

Use of artificial intelligence and radio genomics in neuroradiology and the future of brain tumour imaging and surgical planning in low- and middle-income countries

Faiza Urooj[1], Aimen Tameezuddin[2], Zaira Khalid[3], Kiran Aftab[4], Mohammad Hamza Bajwa[5], Kaynat Siddiqui[6], Saqib Kamran Bakhshi[7], Hafiza Fatima Aziz[8], Syed Ather Enam[9]

Abstract

Brain tumour diagnosis involves assessing various radiological and histopathological parameters. Imaging modalities are an excellent resource for disease monitoring. However, manual inspection of imaging is laborious, and performance varies depending on expertise. Artificial Intelligence (AI) driven solutions a non-invasive and low-cost technology for diagnostics compared to surgical biopsy and histopathological diagnosis. We analysed various machine learning models reported in the literature and assess its applicability to improve neuro-oncological management. A scoping review of 47 full texts published in the last 3 years pertaining to the use of machine learning for the management of different types of gliomas where radiomics and radio genomic models have proven to be useful. Use of AI in conjunction with other factors can result in improving overall neurooncological management within LMICs. AI algorithms can evaluate medical imaging to aid in the early detection and diagnosis of brain tumours. This is especially useful where AI can deliver reliable and efficient screening methods, allowing for early intervention and treatment.

Keywords: Artificial Intelligence, Radiomics, Machine Learning, Genomics, Brain Neoplasms, Glioma, Biopsy

DOI: https://doi.org/10.47391/JPMA.S3.GNO-07

Introduction

CNS tumours can be fatal if diagnosis and intervention are not done at the right time. Currently, they are estimated to affect 7-11 persons per 100,000 person-years.[1] Although the incidence of brain tumours is fairly constant, significant resources are employed for the management of these patients which can often be a challenge, especially in lower-income countries.[1] Impoverished healthcare systems do not have access to timely standard diagnosis and treatment for many patients.[1] Brain tumour diagnosis involves assessing tumour size, type, location, grading, and biopsy and treatments include surgery, chemotherapy, and radiation therapy.[2] Imaging modalities such as magnetic resonance imaging (MRI) are excellent tools for initial assessment and monitoring the disease,[2] however, manual inspection of imaging to detect tumour features with disease characteristics is laborious, and performance varies depending on individual expertise. Distinction on visualized characteristics is difficult and predicated on minute changes that may not always be readily assessed. Differentiating pathologies is the key to guiding personalised management. Surgical biopsy can miss key molecular characteristics due to sampling error or tumour heterogeneity. Moreover, prognosticating requires a deeper, algorithmic model to assess all aspects of neuro-oncological intervention and care.

Recently, artificial intelligence (AI) technologies such as classical machine learning (ML) and deep learning (DL) have demonstrated advances in illness identification and categorisation. [2] Radiomics refers to the extraction of mineable data from medical imaging using image-processing techniques and using ML models to improve diagnosis, prognostication, and clinical decision support.[3] It is concerned solely with the imaging features or phenotype of the disease, whereas radio genomics combines and predicts both the imaging (phenotype) and genetic (genotype) aspects of the disorders.[4] The AI paradigm provides categorisation, detection, and segmentation for brain tumours, which has proven beneficial in terms of early identification, treatment, and survivability.[4] Based on genome-wide profiling and large-scale genomic analysis, molecular subtypes can be utilized to give diagnostic, prognostic, and therapeutic choices.5 MRI-derived texture characteristics have demonstrated to non-invasively predict tumour type,

---

[1]The Aga Khan Medical College and University, Karachi, Pakistan. [2]Ziauddin Medical College, Karachi, Pakistan. [3]Karachi Medical and Dental College, Karachi, Pakistan. [4,5-9]Department of Neurosurgery, The Aga Khan University, Karachi, Pakistan.

Correspondence: Syed Ather Enam **Email:** ather.enam@aku.edu

classification and behaviour. It important to note that radio genomic research is in early stages and large number of samples are required to create robust models with acceptable performance. [5] Companies can expedite testing and observation by employing virtual clinical trials, sequencing, and pattern identification.[6]

This review article will analyse the effectiveness of various machine learning models reported in literature and discuss how lower-income nations can potentially benefit from radio genomics for brain tumours to improve neurooncological management.

Methods

We conducted an extensive scoping review in March 2023, and identified 881 articles pertaining to the use of radiomics and radio genomics to assess imaging for different types of brain tumours. Fiftyfive articles were shortlisted after the title, abstract and full text review. Of these 7 manuscripts were not available. A total of 48 articles, published during 2020 onwards were included in this study. (Figure 1) We conducted and extensive literature review on PubMed and our search strategy was designed as follows (Radiomics OR Radio genomics OR Radiation Genomics OR Imaging Genomics) AND (Primary brain tumour [MeSH] OR Brain tumour [MeSH] OR Intracranial Neoplasm [MeSH] OR Malignant Brain Neoplasm [MeSH] OR Glioma [MeSH] OR Glioblastoma [MeSH] OR Astrocytoma [MeSH] OR Oligodendrogliomas [MeSH] OR neuroncology [MeSH]). [2] individuals conducted the title and abstract reviews independently and the finalised full texts were assessed for the type of tumour, sample size, study objectives, machine learning models used, and performance parameters.

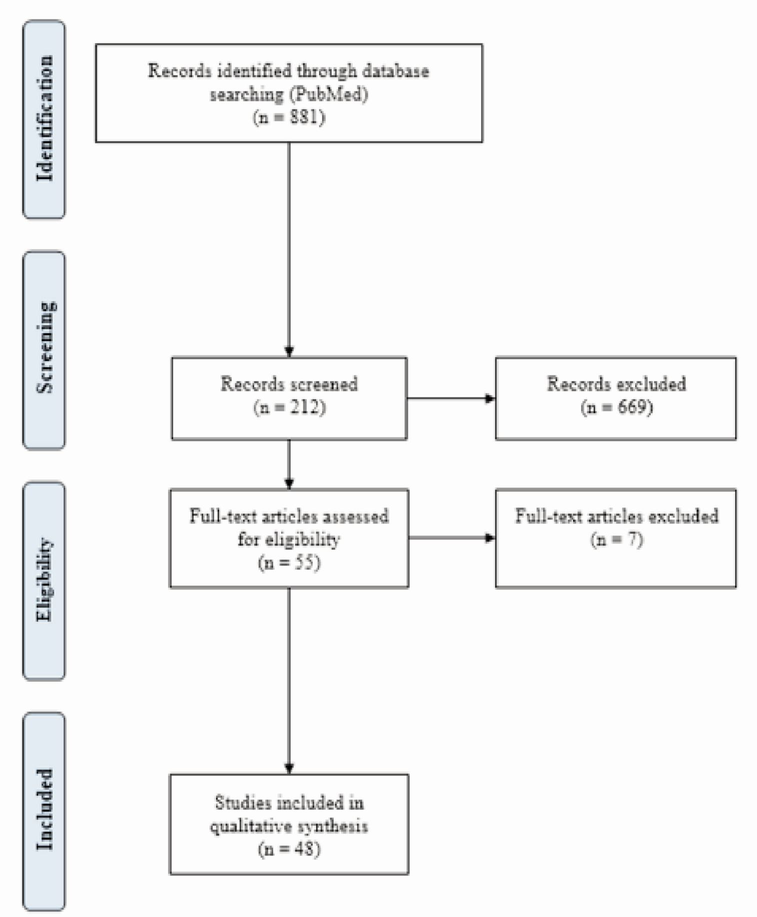

Figure-1: Literature search algorithm..

Results

Each article was reviewed, and the effectiveness of different ML models for brain tumour management has been summarised in tables 1 – 3.

Discussion

Artificial intelligence is a collection of technologies, most of which directly relate to various healthcare fields, but the specific processes and tasks they support vary. The commonest application of machine learning is in precision medicine, to predict which treatment protocols are favourable to a patient based on various patient attributes.[7] Our review analyses various machine learning models reported in literature to diagnose and assess disease outcomes in brain tumours and responses to treatments.

The following ML models were analysed:

1) Random Forest: A random forest is an ensemble learning method that combines multiple decision trees to make predictions by aggregating the results of each tree.

2) Support Vector Machine (SVM): SVM is a supervised learning model that analyses data and classifies it into different categories by finding an optimal hyperplane that maximally separates the data points of different classes.

3) Deep Learning: Deep learning is a subset of machine learning that involves training artificial neural networks with multiple layers to learn representations of data.

4) Cox Regression: Cox regression, also known as the proportional hazards model, is a statistical survival analysis model used to investigate the relationship between survival time and predictor variables. It allows for the estimation of hazard ratios and provides insights into the impact of

Table-1: Tumour Characterization and Grading.

Study	Type of tumour(n)	Objective	Machine Learning Model	Performance Parameters (Accuracy, AUC, DICE Coefficient, C-index/indices)
Choi et al. [9]2021	Glioma(1166)	Prediction of IDH status	CNN and binary classifier	Accuracy: 93.8, 87.9, 78.8 AUC: 0.96, 0.94, 0.86 DICE 0.86-0.92
Di Stefano et al.[17]2020	Gliomas(80)	Characterization and survival prediction of fibroblast growth factor receptor 3 (FGFR3) positive gliomas and features unique to IDH wildtype gliomas	Cox proportional hazards	Exploratory (AUC) = 0.87 Validation MRI (AUC) = 0.75, Predicted survival (C-index) = 0.75 Clinical, genetic, and radiomic data (C-index) 0.81
Bijari et al.[18]2022	GBM (50), Metastases (41)	Differentiating metastases from GBM using MRIs and comparing different machine learning models	MLP RF SVM LR DT Nb Knn Ada	Accuracy: AUC: 0.90 0.90 0:92 0.94 0:57 0.55 0.93 0.88 0.91 0.92 0.64 0.86 0.79 0.90 0.90 0.92
Dong et al.[19]2020	Glioblastoma and metastasis(120)	Differentiate supratentorial MET from GBM	Supervised learning category (decision tree, support vector machine, neural network, naiveBayes, and k-nearest neighbour	For the validation set Accuracy: 0.56 - 0.64 Sensitivity: 0.39 - 0.78 Specificity: 0.50 to 0.89
Hashido et al.2020	GliomaLGG: (15) HGG: (31)	1. Assess differences in glioma perfusion between arterial spin labelling (ASL) and dynamic susceptibility contrast (DSC) imaging2. Compare radiomic features of ASL and DSC imaging-derived cerebral blood flow (CBF)3. Assess radiomics-based classification models for low-grade gliomas (LGGs) and high-grade gliomas (HGGs)	Logistic regression models	AUC ASL-CBF: 0.888 DSC-CBF: 0.962
Jian et al. [20]2021	Gliomas (44) studies	Diagnostic accuracy of ML models in molecular subtyping gliomas on preoperative MRI.	Random forest and SVM werethe most common ML classifiers	AUC IDH Mutation Training: 0.92, Validation: 0.90 1p19q codeletion Training: 0.83, Validation: 0.75 MGMT methylation: Training dataset: 0.87

Continued on next page...

Continued from previous page...

Li et al [21]2020	Gliomas(51)	Identification of immunohistochemical typing, to achieve the image-indication of tumour progression, angiogenesis, proliferation, or invasion	Random ForestAndDeep Learning	Accuracy Ki-67: 66.0, S-100: 0.898, Vimentin: 0.738, CD34: 0.667 AUC Ki-67: 0.713, S-100: 0.92, Vimentin: 0.854, CD34: 0.745
Bae et al. [22]2020	Glioblastoma and Metastases(248)	Discriminating between glioblastoma and single brain metastasis.	Adaptive boosting and support vector machine	Deep Neural Network AUC: 0.956 Sensitivity: 90.6% Specificity: 88.0% Accuracy: 89% Traditional machine learning model AUC: 0.890 Human readers AUC: 0.774 and 0.904
Fan et al. [23]2022	Pineal tumours(134)	Distinguish germinoma and pineal blastoma before surgery and assist in individualized diagnosis of patients with pineal region tumours.	Fusion radiomic model was established based selectedradiomic features through support vector machine	Accuracy Clinic radiomic combined model: Training: 0.878, Validation: 0.909 AUC Fusion radiomic model: Training: 0.920, Validation: 0.880 Clinical model: Training: 0.900, Validation: 0.880 Clinic radiomic combined model: Training: 0.950, Validation: 0.940
Li et al. [24]2020	Ependymoma and Pilocytic astrocytoma (45)	Differentiated EP and PA using radiomics approach based on ML.	Support Vector Machine	Overall features set Texture: 0.82, Gabor transform: 0.75 Selected features set Selected texture: 0.80, Gabor transform based: 0.67, Wavelet transform: 0.73 AUC: Overall features set Texture: 0.81, Gabor transform: 0.73 Selected features set Texture: 0.78, Gabor transform based: 0.65, Wavelet transform: 0.72
Cao et al. [25]2022	Lung cancer Brain Metastasis: (53) Breast cancer Brain Metastasis: (25)	Differentiating BMs originated from primary lung cancer and breast cancer.	Binary logistic regression and support vector machine	Training (AUC) CT: 0.703 vs. 0.751 MRI: 0.718 vs. 0.754 CT and MRI: 0.781 vs. 0.803 Validation (AUC) CT: 0.708 vs. 0.763 MRI: 0.715 vs. 0.717 CT and MRI: 0.771 vs. 0.805
Chang et al.[26]2021	Medulloblastoma (38)	Multiparametric radiomics MRI analysis was conducted to reveal MB features since different MB subgroups have distinct patient	MR radiomics platform for feature extraction.	Accuracy: 71%AUCWNT: 0.82Group 3: 0.72Group 4: 0.78Prediction performance: 0.50

Continued on next page...

Continued from previous page...

		demographics, clinical management, and disease outcomes.		
Jalalifar et al. [27]2020	BM40	The framework applied dissimilarities such as texture characteristics of tumour and enema to detect the tumour and lesion regions.	OC-SVM	DICE: QUANTITATIVE RESULTS OF SEGMENTATION FOR FIVE PATIENTS: 1. 0.88 ± 0.06 2. 0.84 ± 0.05 3. 0.88 ± 0.03 4. 0.80 ± 0.05 5. 0.82 ± 0.06
Dong et al.[28]2021	Ependymoma and Medulloblastoma (51)	To investigate the effectiveness of radiomics and ML techniques on multimodal MR images in EP and MB of childhood.	Multivariate logistic regression andRandom Forest	MLR and RF combined (AUC): 0.91
Chen et al.[29]2020	Lung cancer with Brain Metastasis (110)	To classify EGFR, ALK, and KRAS mutation status in patients with primary lung cancer	Random Forest	Accuracy: Clinical data and radiomic features: EGFR: 77.7%, ALK: 86.7%, KRAS: 96.7% EGFR mutation (AUC) Radiomic features: 0.847 Clinical data: 0.609 Combined 0.912 ALK alteration status (AUC) Radiomic features: 0.813 Clinical data: 0.603 Combined:0.915 KRAS mutation (AUC) Radiomic features: 0.938 Clinical data: 0.684 Combined: 0.985
Kandemirli et al.[30]2020	Grade II meningiomas with brain invasion (BI): 56 Grade I and IIMeningiomaswith no brain invasion (NBI): 52	Differentiating meningiomas with and without brain invasion based on histopathology demonstration.	Random Forest	Grade I and II with brain invasion (AUC) Training: 0.999, Validation: 0.81 Cross-validated AUC BI versus NBI: 0.67, BI versus grade I meningiomas: 0.78
Huang et al.[31]2021	Craniopharyngioma (164)	Discriminating the pathological subtypes of craniopharyngioma	Support vector machine recursive feature elimination (SVM-RFE)	Radiomic model (AUC) Training cohort: 0.899 Internal validation: 0.810 External validation: 0.920 Clinic radiological model (AUC) Training cohort: 0.677 Internal validation: 0.655 External validation: 0.671

Continued on next page...

Continued from previous page...

Jing et al. [32]2022	Recurrence: (75) Pseudo progression: (43)	Early differential diagnosis of recurrence versus pseudo progression.	Multivariate Logistic Regression	Accuracy: Training group: T1: 80.72, T2: 72.29, T1+T2: 77.11 Test group: T1: 80.00, T2: 77.14, T1+T2: 88.57 AUC: Training group T1 + T2: 0.831, T1: 0.815, T2: 0.745 Test group T1 + T2: 0.829, T1: 0.804, T2: 0.734
Han et al. [33]2021	Inflammation: (18) Glioma: (39)	Discriminating brain inflammation from grade II glioma.		Accuracy: Primary cohort T1W1: 0.795, T2W1:0.955, Combination: 0.955 Validation cohort T1W1: 0.615, T2W1: 0.846, Combination: 0.923 AUC: Primary cohort T1W1: 0.811, T2W1:0.980, Combination: 0.988 Validation cohort T1W1: 0.775, T2W1: 0.925, Combination: 0.950
Kim et al.[34]2020	LGG (155)	Predicting IDH mutation status and tumor grading	SVM and random forest algorithm	IDH mutation status (Accuracy): 65.3% IDH Mutation (AUC) Multiparametric MRI: Training set 0.795, Validation set 0.747 Conventional MRI: Training set 0.729, Validation set: 0.705 tumour Grading (AUC) Multiparametric MRI: Training: 0.932, Validation: 0.819 Conventional MRI Training: 0.555, Validation: 0.644
Hashido et al. [35]2021	Gliomas (52) LGG: (18) HGG: (34)	To evaluate various radiomics-basedmachine learning classification models using the apparent diffusion coefficient and cerebral blood flow maps for differentiating between low-grade gliomas and high-grade gliomas	1. Least absolute shrinkage and selection operator regularized logistic regression2. Random Forest3. Support vector machine with the radial basis function kernel4. SVM with the linear kernel	Training Set (AUC) LASSO-LR: 0.965 RF: 1.000 SVM-RBF: 0.979 SVM-L: 0.969 Test set (AUC) LASSO-LR: 0.883 RF: 0.917 SVM-RBF: 0.717 SVM-L: 0.917
Cheng et al.[36]2022	HGG(210) LGG(75)	Tumour grading and predictive performance of radiomic signature based on intratumorally, peritumoral features and their combinations	Minimum redundancy maximum relevance algorithm	Accuracy: ITV: 0.961, PTV: 0.856, IPTV: 0.933 AUC: ITV: 0.923 PTV: 0.877 IPTV: 0.954
Guo et al.[37]2021	Glioma (152)	Explore whether multiparametric magnetic resonance imaging	Least absolute shrinkage and	Differentiating between (AUC) Training:

Continued on next page...

Continued from previous page...

		(MRI)-based radiomics combined with selected blood inflammatory markers could effectively predict the gradeand proliferation in glioma patients.	selection operator (LASSO)	Low- and high-grade: 0.92 Grade III and grade IV: 0.91 Low Ki-67 and high Ki-67: 0.94 Validation Low- and high-grade: 0.94 Grade III and grade IV: 0.75 Low Ki-67 and high Ki-67: 0.82 67: 0.82

Table-2: Predicting Overall Survival and Treatment response.

Author	Type of Tumor (n)	Machine Learning Model	Objective	Performance Parameters (Accuracy, AUC, DICE Coefficient, C-index/indices)
Geraghty et al.[38] 2022	IDH-Wildtype Glioblastoma Multiforme(235)	Linear Regression	Explore the role postoperative radiation planning MRI – based radiomics to predict the outcomes, with features extracted from the gross tumour volume and clinical target volume	Combined radiomics and clinical model (AUC): 0.632. GTR subgroup (AUC): 0.604 STR subgroup (AUC): 0.523 Biopsy subgroup (AUC): 0.632.
Computer et l.[8] 2021	Glioblastoma Multiforme(218)	Cox Regression	Prognostic value of Computed Tomography radiomics for overall survival.	Clinical Prognostic Score: 0.63-0.65, Volume-based Score: 0.52-0.61 Complex Radiomics Prognostic Score: 0.57-0.64 Clinical + Radiomics model: 0.59-0.71
Fathi Kazerooni et al. [39]2022	Glioblastoma Multiforme(516)	Multivariate Cox-PH	To predict progression free survival (PFS) and overall survival (OS)	OS (AUC); Clinical: 0.623, Genetic: 0.588, Radiomics: 0.649, Combined: 0.725 PFS (AUC); Clinical: 0.582, Genetic: 0.587, Radiomics: 0.616, Combined: 0.670
Choi et al. [40] 2020	Low Grade Glioma(296)	Random Forest	Evaluate whether MRI-based radiomic features could improve the accuracy of survival predictions for lower grade gliomas over clinical and IDH status.	Clinical and IDH status (AUC): 0.627 Clinical + radiomic features (AUC): 0.709
Garcia Ruiz et al. [41]2021	Primary Glioblastoma Multiforme (GBM)(144)	Multivariate Logistic Regression	1. Quantification of the enhancing residual tumourthrough computational image analysis and assessment of correlation with survival2. Pathological enhancement thickness on post-surgical MRI correlated with survival	Prognostic capacity for predicting long and short survival (AUC): 0.72
George et al. [42]2022	Glioblastoma Multiforme(154)	Random Forest	Prediction of progression free survival and overall survival in patients with glioblastoma on PD-L1 inhibition immunotherapy	Predictive value for OS and PFS: C-index = 0.472–0.521 Predictive value for first on-treatment MR imaging: C-index = 0.692–0.750 (OS)and 0.680–0.715 (PFS)
Choi et al. [43]2021	Glioblastoma Multiforme(120)	k-Nearest Neighbours (kNN), Naïve Bayes, Random Forest and Support vector machine (SVM)	Prognostic value of multivariate models in glioblastoma	Accuracy Transcriptome subtypes: Classical (70.9), Mesenchymal (73.3), Neural (88.4), Perineural (88.4) AUC Transcriptome subtypes: Classical (0.711), Mesenchymal (0.763), Neural (0.745), Perineural

Continued on next page...

Continued from previous page...

				(0.854)
Dasgupta et al.[44]2021	Low Grade Glioma: 34Brain Metastasis: 29	Support Vector Machine	Region's indicative of infiltrative tumours was correlated to the future areas of radiological disease recurrence	Accuracy of 0.92 and 0.79 in the training and test set, respectively (LGG vs. BM
Li et al.[21]2020	Gliomas(51)	Random ForestAndDeep Learning	Identification of immunohistochemical typing, to achieve the image-indication of tumour progression, angiogenesis, proliferation or invasion.	Accuracy Ki-67: 66.0, S-100: 0.898, Vimentin: 0.738, CD34: 0.667 AUC Ki-67: 0.713±0.073, S-100: 0.92±0.0381 Vimentin: 0.854±0.0579, CD34: 0.745±0.077
Beig et al. [45]2020	Glioblastoma Multiforme(203)	Cox Regression Model	1. Create a survival risk-score using radiomic features from the tumour habitat on routine MRI to predict progression-free survival in Glioblastoma2. Obtain a biological basis for prognostic radiomicfeatures, by studying radio-genomic associations with molecular signaling pathways	Combination of Radiomic Risk Score with clinical (age, gender) and molecular features (MGMT, IDH status) resulted in a concordance index of 0.81 ($p < 0.0001$) on training and 0.84 ($p = 0.03$) on the test set
Jiang et al. [46]2022	Brain Metastasis with lung cancer (LCBM)(137)	Random forest with five-fold cross validation	Predicting the posttreatment response of LCBM to Gamma Knife Radiosurgery, facilitating the adjustment in treatment strategy	AUC RFTC+RFPE: 0.852 0.848, RFTC: 0.750 CBV map: 0.714, ADC map: 0.598 Post-contrast T1WI: 0.557 T2-FLAIR: 0.704, T1WI: 0.656, T2WI: 0.725 RF Score (AUC): 0.848
Ari et al. [47]2022	High Grade Primary tumours (131)	Generalized Boosted Regression Model	Predicting pseudo progression in a representative patient cohort diagnosed with high grade adult-type diffuse gliomas (WHO grade 3 and 4).	Occurrence of pseudo progression with an AUC, mean sensitivity, mean specificity and mean accuracy of 91.49%, 79.92%, 88.61% and 84.35% in the full development group 78.51%, 66.26%, 78.31% and 72.40% in the testing group 72.87%, 71.75%, 80.00% and 76.04% in the independent validation sample
Jing et al. [32]2022	Gliomas118	SMOTE and un sampling algorithms were employed.	Early differential diagnosis of recurrence versus pseudo progression.	Accuracy Training group: T1: 80.72, T2: 72.29, T1+T2: 77.11 Test group: T1: 80.00, T2: 77.14, T1+T2: 88.57 AUC Training group; T1 + T2: 0.831, T1: 0.815, T2: 0.745 Test group: T1 + T2: 0.829, T1: 0.804, T2: 0.734

Table-3: Predicting mutations and biomarker status.

Author	**Type of tumour (n)**	**Machine Learning Model**	**Objective**	**Performance Parameters (Accuracy, AUC, DICE Coefficient, C-index/indices)**
Choi et al. [9]2021	Glioma1166	CNN and binary classifier	Prediction of IDH status and characterization of gliomas.	Accuracy:93.8, 87.9, 78.8AUC:0.96, 0.94, 0.86DICE:0.86-0.92

Continued on next page...

Continued from previous page...

Kim et al.[34]2020	LGG155	SVM and random forest algorithm	Predicting IDH mutation status and tumour grading	IDH mutation status:(Accuracy): 65.3% IDH Mutation (AUC) Multiparametric MRI: Training set 0.795, Validation set 0.747 Conventional MRI: Training set 0.729, Validation set: 0.705 Tumour Grading (AUC) Multiparametric MRI: Training: 0.932, Validation: 0.819 Conventional MRI Training: 0.555, Validation: 0.644
Le et al.[10]2021	GBM120	XGBoost algorithm	Classification of GBM transcriptome sub types	Accuracy Classical: 70.9% Mesenchymal: 73.3% Neural: 80.4% Perineural 80.4%
Cao et al. [48]2021	LGG102	Random forest	Characterize the IDH1 mutation status in LGGs.	Accuracy: Training: 0.70 to 0.76 Validation: 0.56 to 0.64
Bhandari et al. [49]2021	LGG1655	SVM + Deep Learning	Classifying IDH and 1p19q status using MR imaging radiomics	Best classifier of IDH status (AUC)= 0.95. The best classifier of 1p19q status (AUC): 0.96.
Casale et al.[50]2021	LGG209	Random Forest	Predicting the 1p/19q status of LGG from MRI images using texture analysis as an alternative to surgical biopsy	Accuracy Training Cubic interpolation: 0.86, Linear interpolation: 0.76 Validation Cubic interpolation: 0.72 Linear interpolation: 0.72 AUC: Training Cubic interpolation: 0.86 Linear interpolation: 0.82 Validation Cubic interpolation: 0.87 Linear interpolation: 0.77
Choi et al.[11]2020	Grade IV Glioblastoma136		Compare IDH mutation status predictive performances between manual and fully automatic deep-learning segmentations	Accuracy: Manual: 86.8 % V-net: 75.8 % Development set: 73.3 % AUC: Manual: 0.904 V-net: 0.857 Development set: 0.771
Ahn et al. [51]2020	Lung cancer with Brain Metastasis(210)	Random Forest,	Predicting EGFR mutation status in primary lung cancers	Identifying EGFR mutation (AUC): 86.81 Subgroup analyses revealed that small brain metastasis had the highest AUC: 89.09 The diagnostic performance for large BMs was lower than that for small brain metastasis (AUC): 78.22
Calabrese et al. [52]2020	Glioblastoma199	Random Forest	Predicting genetic biomarker status in glioblastomas using preoperative imaging	AUC: TRX: 0.97 IDH: 0.95 7/10 aneuploidy: 0.93 CDKN2: 0.85 EGFR: 0.70

Continued on next page...

Continued from previous page...

				TERT: 0.65 PTEN: 0.64 TP53: 0.57 MGMT: 0.55
Kandemirli et al.[12]2021	Gliomas(109)	Extreme gradient boosting algorithm(XGBoost)	Predict H3K27M mutation in midline gliomas	Accuracy: 72.7% AUC Training: 0.791 Validation:0.737
Kocak et al.[53]2020	LGG(107)	Adaptive boosting, k-nearest neighbours, naive Bayes, neural network, random forest, stochastic gradient descent; and support vector machine	Predicting the 1p/19q codeletion status of LGGs	Accuracy: Adaptive boosting: 75.2. k-nearest neighbours: 74.4, Naive Bayes: 80.3, Neural network: 83.8 Random Forest: 84.0, Stochastic gradient descent: 80.1, Support vector machine: 81.1 AUC: Adaptive boosting: 0.717, k-nearest neighbours: 0.751, Naive Bayes: 0.829, Neural network: 0.869 Random Forest: 0.840, Stochastic gradient descent: 0.769, Support vector machine: 0.838
Li et al. [54]2022	Brain Metastasis(186)	Random Forest	Identifying EGFR and ALK mutation status in brain metastasis and exploring which MR sequence is most predictive.	Training (AUC) T2-FLAIR: 0.991 T1-CE: 0.954 T2WI: 0.880 Testing T2-FLAIR: 0.950 T1-CE: 0.867 T2WI: 0.731
He et al. [55]2022	Glioma81	Multivariate Logistic Regression	Explored clinical and MRI imaging characteristics to predict four kinds of glioma molecular biomarkers (IDH, MGMT, TERT, 1p/19q)	Clinical model (AUC) IDH: 0.88; MGMT: 0.78; TERT: 0.66; 1p/19q: 0.66 Radiomics model (AUC) IDH: 0.87, MGMT: 0.83, TERT: 0.72, 1p/19q: 0.68

covariates on the survival outcome.

We found Cox regression and Random Forest algorithms as the most common methods being used when building a model to predict overall survival rates and tumour prognostication analysis. A Cox regression is commonly useful when evaluating the time to an event, therefore was found to be a common method when evaluating OS using selected features. Computer et al, in their study used age and WHO performance status as predictors to build the regression with a clinical prognostic score of 0.63-0.65. [8] However, a Cox regression is limited by its assumption of potential hazards - the assumption that the hazard function remains constant over time and is only a function of the explanatory variables. To counter this limitation, we found multiple studies, opting for the use of a random forest trained model to predict OS based on radiomic features, clinical profile, and IDH mutation status. A RF model is able to handle interactions of hundreds of radiomics features, not limiting itself to selected specialized explanatory variables such as in a Cox regression. This allows the use of MRI based radiomic features, leading to an increased accuracy of progression free survival predictions. Choi et al.[9] conducted a cohort study of LGG patients and found that MRI based radiomics features improved accuracy of the model from 0.627 to an AUC reading of 0.709.[9] Other studies using RF models also saw increased accuracy in their predictions thereby confirming the benefits of using the model in radiomic phenotyping.

Traditionally, identification of biomarkers in brain tumours has been done through labour-intensive and time-consuming methods of DNA sequencing and PCR, prone to errors with limited sensitivity. The financial cost associated with this traditional method is extremely high and unaffordable for most patients therefore, not all molecular testing is available within LMICs. This severely limits the application of new, established markers within our regions which impacts patient selection, survival, and treatment protocols. Our review found that machine learning models, using radiomic features, are increasingly being proven to be effective in predicting the presence of these key biomarkers. Our review shows that various models are being used but RF and Support Vector Machine (SVM) prevailed as the most common due to their relative better performance in handling large complex data sets, tumour classifications and predicting patterns in comparison to traditional statistical classifiers. Cao et al 2021,[10] was able to use VASARI features extracted from conventional MRI's and selected through RMR (Relevance Minimum Redundancy) as an input to their trained RF to create a model to predict the presence of the IDH/IDH1 mutation. The model achieved an area under ROC curve (AUC) of 0.779 for the training cohort and 0.849 for the validation cohort. The accuracy was further improved when further radiomics features were added thereby confirming the validity of using RF to create a predictive model for the presence of the IDH1 mutation. In addition to predicting IDH mutations, random forest algorithm is also used to predict EFGR mutation status. According to Ahn et al, a model trained with RF to identify an EGFR mutation presented an AUC of 86.81. RF was also effective in the identification of the 1p19q gene in tumours.[11] However, we also found support Vector Machine (SVM) coupled with a deep learning machine to be highly accurate and precise. According to Kocak et al, the accuracy of random forest model for predicting 1p19q mutation status was 84.0, while SVM remained almost equally as accurate at 81.1. [12] CNS tissue samples are difficult to obtain and preoperative localization of mutations and molecular characteristics of brain tumours using radio genomics can open up avenues for neo-adjuvant therapy and personalized medicine.

Both traditional classifiers and deep learning have their strengths and weaknesses, and the choice between the two approaches depends on the nature of the task and availability of resources. Traditional classifiers have their strength in interpretability and efficiency for certain tasks and smaller datasets, while deep learning excels in handling complex data, large datasets, and tasks where feature engineering is challenging. The choice between the two approaches depends on the specific problem, available data, and implementation details.[13,14]

Low- and Middle-Income Countries (LMICs) face several challenges in translating radio genomic and artificial intelligence technologies into clinical practice. High expenses for hardware, software, maintenance and limited access to advanced medical infrastructure, including high-quality imaging equipment and computing resources limit their widespread adoption. Lack of large and high-quality datasets limit development and validation of robust models' radio genomic and AI-based systems. Successful implementation of these systems requires a skilled workforce with expertise in both radiology and data science. In LMICs, there is a shortage of trained professionals, making it challenging to develop, validate, and implement these technologies effectively.

Furthermore, integrating AI into clinical practice raises ethical concerns pertaining to patient privacy, data security, and potential biases in the algorithms. In LMICs, there may be limited regulations and guidelines specific to AI in healthcare, leading to uncertainty and hesitancy in adopting these technologies. In some regions, there may be cultural or societal barriers to accepting AI technologies and patients and healthcare providers may be hesitant to trust automated systems over traditional human expertise. Many AI models are developed and validated on datasets from high-income countries, which may not fully represent the diverse populations and diseases prevalent in LMICs. This lack of external validation can limit the generalizability and accuracy of AI systems in these settings.[15,16]

Conclusion

AI-driven solutions and ML models are a non-invasive and low-cost technology for diagnostics compared to surgical biopsy and histopathological diagnosis. Radiomics and radio genomic models have proven to be useful in various steps of brain tumour management including diagnosis, grading, subtyping of tumours, survival prediction and treatment planning. Use of AI in conjunction with healthcare behaviours, socioeconomic factors and education can result in greater chances of improving overall neurooncological management within LMICs.

Disclaimer: None.

Conflict of Interest: None.

Funding Disclosure: None.

References

1. Mohammadi E, Ghasemi E, Azadnajafabad S, Rezaei N, Saeedi Moghaddam S, Ebrahimi Meimand S, et al. A global, regional, and national survey on burden and Quality of Care Index (QCI) of brain and other central nervous system cancers; global burden of disease systematic analysis 1990-2017. PLoS One 2021;16:e0247120. doi: 10.1371/journal.pone.0247120.
2. Jena B, Saxena S, Nayak GK, Balestrieri A, Gupta N, Khanna NN, et al. Brain Tumor Characterization Using Radiogenomics in Artificial Intelligence Framework. Cancers (Basel) 2022;14:4052. doi: 10.3390/cancers14164052.
3. Shur JD, Doran SJ, Kumar S, Ap Dafydd D, Downey K, O'Connor JPB, et al. Radiomics in Oncology: A Practical Guide. Radiographics 2021;41:1717-32. doi: 10.1148/rg.2021210037.
4. Yi Z, Long L, Zeng Y, Liu Z. Current Advances and Challenges in Radiomics of Brain Tumors. Front Oncol 2021;11:732196. doi: 10.3389/fonc.2021.732196.
5. Bodalal Z, Trebeschi S, Nguyen-Kim TDL, Schats W, Beets-Tan R.

Radiogenomics: bridging imaging and genomics. Abdom Radiol (NY) 2019;44:1960-84. doi: 10.1007/s00261-019-02028-w.

6. Javaid M, Haleem A, Singh RP, Suman R, Rab S. Significance of machine learning in healthcare: Features, pillars and applications. Int J Intell Netw 2022;3:58-73. doi:.10.1016/j.ijin.2022.05.002.
7. He J, Ren J, Niu G, Liu A, Wu Q, Xie S, et al. Multiparametric MR radiomics in brain glioma: models comparation to predict biomarker status. BMC Med Imaging 2022;22:137. doi: 10.1186/s12880-022-00865-8.
8. Compter I, Verduin M, Shi Z, Woodruff HC, Smeenk RJ, Rozema T, et al. Deciphering the glioblastoma phenotype by computed tomography radiomics. Radiother Oncol 2021;160:132-9. doi: 10.1016/j.radonc.2021.05.002.
9. Choi YS, Bae S, Chang JH, Kang SG, Kim SH, Kim J, et al. Fully automated hybrid approach to predict the IDH mutation status of gliomas via deep learning and radiomics. Neuro Oncol 2021;23:304-13. doi: 10.1093/neuonc/noaa177.
10. Le NQK, Hung TNK, Do DT, Lam LHT, Dang LH, Huynh TT. Radiomics-based machine learning model for efficiently classifying transcriptome subtypes in glioblastoma patients from MRI. Comput Biol Med 2021;132:104320. doi: 10.1016/j.compbiomed.2021.104320.
11. Choi Y, Nam Y, Lee YS, Kim J, Ahn KJ, Jang J, et al. IDH1 mutation prediction using MR-based radiomics in glioblastoma: comparison between manual and fully automated deep learning-based approach of tumor segmentation. Eur J Radiol 2020;128:109031. doi: 10.1016/j.ejrad.2020.109031.
12. Kandemirli SG, Kocak B, Naganawa S, Ozturk K, Yip SSF, Chopra S, et al. Machine Learning-Based Multiparametric Magnetic Resonance Imaging Radiomics for Prediction of H3K27M Mutation in Midline Gliomas. World Neurosurg 2021;151:e78-85. doi: 10.1016/j.wneu.2021.03.135.
13. Krizhevsky A, Sutskever I, Hinton GE. ImageNet classification with deep convolutional neural networks. Commun ACM 2017;60:84–90. Doi: 10.1145/3065386.
14. Ribeiro MT, Singh S, Guestrin C. “Why Should I Trust You?”: Explaining the Predictions of Any Classifier. In: Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining. San Francisco California, USA: Association for Computing Machinery (ACM) Inc, 2016; pp 1135–44. [Online] 2016 [Cited 2023 September 08]. Available from URL: https://dl.acm.org/doi/10.1145/2939672.2939778
15. Hosny A, Parmar C, Quackenbush J, Schwartz LH, Aerts HJWL. Artificial intelligence in radiology. Nat Rev Cancer 2018;18:500-1. doi: 10.1038/s41568-018-0016-5.
16. Mollura DJ, Culp MP, Pollack E, Battino G, Scheel JR, Mango VL, et al. Artificial Intelligence in Low- and Middle-Income Countries: Innovating Global Health Radiology. Radiology 2020;297:513-20. doi: 10.1148/radiol.2020201434.
17. Di Stefano AL, Picca A, Saragoussi E, Bielle F, Ducray F, Villa C, et al. Clinical, molecular, and radiomic profile of gliomas with FGFR3-TACC3 fusions. Neuro Oncol 2020;22:1614-24. doi: 10.1093/neuonc/noaa121.
18. Bijari S, Jahanbakhshi A, Hajishafiezahramini P, Abdolmaleki P. Differentiating Glioblastoma Multiforme from Brain Metastases Using Multidimensional Radiomics Features Derived from MRI and Multiple Machine Learning Models. Biomed Res Int 2022;2022:e2016006. doi: 10.1155/2022/2016006.
19. Dong F, Li Q, Jiang B, Zhu X, Zeng Q, Huang P, et al. Differentiation of supratentorial single brain metastasis and glioblastoma by using peri-enhancing oedema region-derived radiomic features and multiple classifiers. Eur Radiol 2020;30:3015-22. doi: 10.1007/s00330-019-06460-w.
20. Jian A, Jang K, Manuguerra M, Liu S, Magnussen J, Di Ieva A. Machine Learning for the Prediction of Molecular Markers in Glioma on Magnetic Resonance Imaging: A Systematic Review and Meta-Analysis. Neurosurgery 2021;89:31-44. doi: 10.1093/neuros/nyab103.
21. Li J, Liu S, Qin Y, Zhang Y, Wang N, Liu H. High-order radiomics features based on T2 FLAIR MRI predict multiple glioma immunohistochemical features: A more precise and personalized gliomas management. PLoS One 2020;15:e0227703. doi: 10.1371/journal.pone.0227703.
22. Bae S, An C, Ahn SS, Kim H, Han K, Kim SW, et al. Robust performance of deep learning for distinguishing glioblastoma from single brain metastasis using radiomic features: model development and validation. Sci Rep 2020;10:12110. doi: 10.1038/s41598-020-68980-6.
23. Fan Y, Huo X, Li X, Wang L, Wu Z. Non-invasive preoperative imaging differential diagnosis of pineal region tumor: A novel developed and validated multiparametric MRI-based clinicoradiomic model. Radiother Oncol 2022;167:277-84. doi: 10.1016/j.radonc.2022.01.005.
24. Li M, Wang H, Shang Z, Yang Z, Zhang Y, Wan H. Ependymoma and pilocytic astrocytoma: Differentiation using radiomics approach based on machine learning. J Clin Neurosci 2020;78:175-80. doi: 10.1016/j.jocn.2020.04.080.
25. Cao G, Zhang J, Lei X, Yu B, Ai Y, Zhang Z, et al. Differentiating Primary Tumors for Brain Metastasis with Integrated Radiomics from Multiple Imaging Modalities. Dis Markers 2022;2022:5147085. doi: 10.1155/2022/5147085.
26. Chang FC, Wong TT, Wu KS, Lu CF, Weng TW, Liang ML, et al. Magnetic resonance radiomics features and prognosticators in different molecular subtypes of pediatric Medulloblastoma. PLoS One 2021;16:e0255500. doi: 10.1371/journal.pone.0255500.
27. Jalalifar A, Soliman H, Ruschin M, Sahgal A, Sadeghi-Naini A. A Brain Tumor Segmentation Framework Based on Outlier Detection Using One-Class Support Vector Machine. Annu Int Conf IEEE Eng Med Biol Soc 2020;2020:1067-70. doi: 10.1109/EMBC44109.2020.9176263.
28. Dong J, Li L, Liang S, Zhao S, Zhang B, Meng Y, et al. Differentiation Between Ependymoma and Medulloblastoma in Children with Radiomics Approach. Acad Radiol 2021;28:318-27. doi: 10.1016/j.acra.2020.02.012.
29. Chen BT, Jin T, Ye N, Mambetsariev I, Daniel E, Wang T, et al. Radiomic prediction of mutation status based on MR imaging of lung cancer brain metastases. Magn Reson Imaging 2020;69:49-56. doi: 10.1016/j.mri.2020.03.002.
30. Kandemirli SG, Chopra S, Priya S, Ward C, Locke T, Soni N, et al. Presurgical detection of brain invasion status in meningiomas based on first-order histogram based texture analysis of contrast enhanced imaging. Clin Neurol Neurosurg 2020;198:106205. doi: 10.1016/j.clineuro.2020.106205.
31. Huang ZS, Xiao X, Li XD, Mo HZ, He WL, Deng YH, et al. Machine Learning-Based Multiparametric Magnetic Resonance Imaging Radiomic Model for Discrimination of Pathological Subtypes of Craniopharyngioma. J Magn Reson Imaging 2021;54:1541-50. doi: 10.1002/jmri.27761.
32. Jing H, Yang F, Peng K, Qin D, He Y, Yang G, et al. Multimodal MRI-Based Radiomic Nomogram for the Early Differentiation of Recurrence and Pseudoprogression of High-Grade Glioma. Biomed Res Int 2022;2022:e4667117. doi: 10.1155/2022/4667117.
33. Han Y, Yang Y, Shi ZS, Zhang AD, Yan LF, Hu YC, et al. Distinguishing brain inflammation from grade II glioma in population without contrast enhancement: a radiomics analysis based on conventional MRI. Eur J Radiol 2021;134:109467. doi: 10.1016/j.ejrad.2020.109467.
34. Kim M, Jung SY, Park JE, Jo Y, Park SY, Nam SJ, et al. Diffusion- and perfusion-weighted MRI radiomics model may predict isocitrate dehydrogenase (IDH) mutation and tumor aggressiveness in

diffuse lower grade glioma. Eur Radiol 2020;30:2142-51. doi: 10.1007/s00330-019-06548-3.
35. Hashido T, Saito S, Ishida T. Radiomics-Based Machine Learning Classification for Glioma Grading Using Diffusion- and Perfusion-Weighted Magnetic Resonance Imaging. J Comput Assist Tomogr 2021;45:606-13. doi: 10.1097/RCT.0000000000001180.
36. Cheng J, Liu J, Yue H, Bai H, Pan Y, Wang J. Prediction of Glioma Grade Using Intratumoral and Peritumoral Radiomic Features From Multiparametric MRI Images. IEEE/ACM Trans Comput Biol Bioinform 2022;19:1084-95. doi: 10.1109/TCBB.2020.3033538.
37. Guo J, Ren J, Shen J, Cheng R, He Y. Do the combination of multiparametric MRI-based radiomics and selected blood inflammatory markers predict the grade and proliferation in glioma patients? Diagn Interv Radiol 2021;27:440-9. doi: 10.5152/dir.2021.20154.
38. Geraghty BJ, Dasgupta A, Sandhu M, Malik N, Maralani PJ, Detsky J, et al. Predicting survival in patients with glioblastoma using MRI radiomic features extracted from radiation planning volumes. J Neurooncol 2022;156:579-88. doi: 10.1007/s11060-021-03939-9.
39. Fathi Kazerooni A, Saxena S, Toorens E, Tu D, Bashyam V, Akbari H, et al. Clinical measures, radiomics, and genomics offer synergistic value in AI-based prediction of overall survival in patients with glioblastoma. Sci Rep 2022;12:8784. doi: 10.1038/s41598-022-12699-z.
40. Choi YS, Ahn SS, Chang JH, Kang SG, Kim EH, Kim SH, et al. Machine learning and radiomic phenotyping of lower grade gliomas: improving survival prediction. Eur Radiol 2020;30:3834-42. doi: 10.1007/s00330-020-06737-5.
41. Garcia-Ruiz A, Naval-Baudin P, Ligero M, Pons-Escoda A, Bruna J, Plans G, et al. Precise enhancement quantification in post-operative MRI as an indicator of residual tumor impact is associated with survival in patients with glioblastoma. Sci Rep 2021;11:695. doi: 10.1038/s41598-020-79829-3.
42. George E, Flagg E, Chang K, Bai HX, Aerts HJ, Vallières M, et al. Radiomics-Based Machine Learning for Outcome Prediction in a Multicenter Phase II Study of Programmed Death-Ligand 1 Inhibition Immunotherapy for Glioblastoma. AJNR Am J Neuroradiol 2022;43:675-81. doi: 10.3174/ajnr.A7488.
43. Choi Y, Nam Y, Jang J, Shin NY, Lee YS, Ahn KJ, et al. Radiomics may increase the prognostic value for survival in glioblastoma patients when combined with conventional clinical and genetic prognostic models. Eur Radiol 2021;31:2084-93. doi: 10.1007/s00330-020-07335-1.
44. Dasgupta A, Geraghty B, Maralani PJ, Malik N, Sandhu M, Detsky J, et al. Quantitative mapping of individual voxels in the peritumoral region of IDH-wildtype glioblastoma to distinguish between tumor infiltration and edema. J Neurooncol 2021;153:251-6. doi: 10.1007/s11060-021-03762-2.
45. Beig N, Bera K, Prasanna P, Antunes J, Correa R, Singh S, et al. Radiogenomic-Based Survival Risk Stratification of Tumor Habitat on Gd-T1w MRI Is Associated with Biological Processes in Glioblastoma. Clin Cancer Res 2020;26:1866-7. doi: 10.1158/1078-0432.CCR-19-2556.
46. Jiang Z, Wang B, Han X, Zhao P, Gao M, Zhang Y, et al. Multimodality MRI-based radiomics approach to predict the posttreatment response of lung cancer brain metastases to gamma knife radiosurgery. Eur Radiol 2022;32:2266-76. doi: 10.1007/s00330-021-08368-w.
47. Ari AP, Akkurt BH, Musigmann M, Mammadov O, Blömer DA, Kasap DNG, et al. Pseudoprogression prediction in high grade primary CNS tumors by use of radiomics. Sci Rep 2022;12:5915. doi: 10.1038/s41598-022-09945-9.
48. Cao M, Suo S, Zhang X, Wang X, Xu J, Yang W, et al. Qualitative and Quantitative MRI Analysis in IDH1 Genotype Prediction of Lower-Grade Gliomas: A Machine Learning Approach. Biomed Res Int 2021;2021:e1235314. doi: 10.1155/2021/1235314.
49. Bhandari AP, Liong R, Koppen J, Murthy SV, Lasocki A. Noninvasive Determination of IDH and 1p19q Status of Lower-grade Gliomas Using MRI Radiomics: A Systematic Review. AJNR Am J Neuroradiol 2021;42:94-101. doi: 10.3174/ajnr.A6875.
50. Casale R, Lavrova E, Sanduleanu S, Woodruff HC, Lambin P. Development and external validation of a non-invasive molecular status predictor of chromosome 1p/19q co-deletion based on MRI radiomics analysis of Low Grade Glioma patients. Eur J Radiol 2021;139:109678. doi: 10.1016/j.ejrad.2021.109678.
51. Ahn SJ, Kwon H, Yang JJ, Park M, Cha YJ, Suh SH, et al. Contrast-enhanced T1-weighted image radiomics of brain metastases may predict EGFR mutation status in primary lung cancer. Sci Rep 2020;10:8905. doi: 10.1038/s41598-020-65470-7.
52. Calabrese E, Villanueva-Meyer JE, Cha S. A fully automated artificial intelligence method for non-invasive, imaging-based identification of genetic alterations in glioblastomas. Sci Rep 2020;10:11852. doi: 10.1038/s41598-020-68857-8.
53. Kocak B, Durmaz ES, Ates E, Sel I, Turgut Gunes S, Kaya OK, et al. Radiogenomics of lower-grade gliomas: machine learning-based MRI texture analysis for predicting 1p/19q codeletion status. Eur Radiol 2020;30:877-86. doi: 10.1007/s00330-019-06492-2.
54. Li Y, Lv X, Wang B, Xu Z, Wang Y, Gao S, et al. Differentiating EGFR from ALK mutation status using radiomics signature based on MR sequences of brain metastasis. Eur J Radiol 2022;155:110499. doi: 10.1016/j.ejrad.2022.110499.
55. He J, Ren J, Niu G, Liu A, Wu Q, Xie S, et al. Multiparametric MR radiomics in brain glioma: models comparation to predict biomarker status. BMC Med Imaging 2022;22:137. doi: 10.1186/s12880-022-00865-8.
