### **REVIEW**

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## Predicting survival in malignant glioma using artificial intelligence



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### Abstract

Malignant gliomas, including glioblastoma, are amongst the most aggressive primary brain tumours, characterised by rapid progression and a poor prognosis. Survival analysis is an essential aspect of glioma management and research, as most studies use time-to-event outcomes to assess overall survival (OS) and progression-free survival (PFS) as key measures to evaluate patients. However, predicting survival using traditional methods such as the Kaplan–Meier estimator and the Cox Proportional Hazards (CPH) model has faced many challenges and inaccuracies. Recently, advances in artificial intelligence (AI), including machine learning (ML) and deep learning (DL), have enabled significant improvements in survival prediction for glioma patients by integrating multimodal data such as imaging, clinical parameters and molecular biomarkers. This study highlights the comparative effectiveness of imaging-based, non-imaging and combined AI models. Imaging models excel at identifying tumour-specific features through radiomics, achieving high predictive accuracy. Non-imaging approaches also excel in utilising clinical and genetic data to provide complementary insights, whilst combined methods integrate multiple data modalities and have the greatest potential for accurate survival prediction. Limitations include data heterogeneity, interpretability challenges and computational demands, particularly in resource-limited settings. Solutions such as federated learning, lightweight AI models and explainable AI frameworks are proposed to overcome these barriers. Ultimately, the integration of advanced AI techniques promises to transform glioma management by enabling personalised treatment strategies and improved prognostic accuracy.

Keywords Malignant glioma, Artificial intelligence (AI), Machine learning (ML), Deep learning (DL), Survival prediction approaches

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### Introduction

Malignant gliomas, including glioblastoma, are amongst the most aggressive primary brain tumours, known for their rapid progression and poor prognosis. Glioblastoma, the most common subtype, has a dismal 5-year survival rate of only about 5.6% [1]. Several studies suggest that overall survival in glioblastoma patients is closely linked to the tumour's anatomical location within the brain [2, 3]. A recent study by Osadebey et al. (2023) found that gliomas located in the hippocampus, thalamus, left insula and regions of the left lateral ventricle were associated with short survival [2] Gliomas in the frontal and temporal lobes are associated with



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intermediate survival, whilst tumours in the corpus callosum, right insula and regions of the right lateral ventricle are associated with long survival [2]. Other studies have also reported that central tumour location is associated with short survival, whilst survival is favourable according to the distance between the centre of the third ventricle and the contrast-enhancing tumour margin [3]. In addition, patients with gliomas in non-eloquent areas of the brain have been found to have favourable survival compared to patients with tumours in eloquent or neareloquent areas, irrespective of the extent of resection [4].

The management of gliomas has been challenging for decades due to difficulties in accurate diagnosis and tailored treatment. Early detection and accurate assessment of tumour progression are hampered by tumour heterogeneity, the variability of molecular markers and the limitations of current imaging techniques [5]. In addition, the highly infiltrative nature of gliomas, combined with the delicate structure of the brain, makes complete surgical resection difficult [6]. Standard treatment typically involves maximally safe surgical resection followed by radiotherapy and concurrent chemotherapy with temozolomide [7, 8]. However, despite these extensive interventions, median survival remains around 14 months, with progression-free survival (PFS) often limited to a few months [8].

Survival analysis is essential in clinical neuro-oncology research, as most studies use time-to-event outcomes to evaluate overall survival (OS) and progression-free survival (PFS) as key measures to assess patient prognosis after cancer diagnosis or recurrence [9]. However, the complex nature of gliomas has made accurate prediction of OS a major challenge for clinicians for decades. Recent developments have led to new technologies that can improve the accuracy of OS prediction, helping physicians to develop more comprehensive, personalised treatment plans that are best suited to individual patients. Historically, glioma survival has been predicted using traditional methods such as the Kaplan-Meier estimator and the Cox Proportional Hazards (CPH) model, which estimate survival probabilities and take into account prognostic factors [10]. Despite their widespread use, these methods have notable limitations, including the proportional hazards assumption and reduced power when applied to high-dimensional data, such as molecular biomarkers or complex imaging features [9]. In addition, these models struggle with non-linear interactions between variables and often require prior knowledge of the factors influencing outcomes [11]. Recent advances in artificial intelligence (AI) show promising potential to address these challenges by integrating complex datasets and generating personalised survival predictions. AI can handle large datasets, capture non-linear patterns and provide individualised risk assessments, achieving greater accuracy than traditional models [12].

This review aims to evaluate the application of AI and machine learning (ML) in predicting survival outcomes for glioma patients, to assess their performance relative to traditional statistical methods, and to explore their potential to improve clinical decision making in glioma management.

### Methods

This narrative review aims to establish a comprehensive framework for predicting survival in patients with malignant glioma using AI. To enhance methodological rigour, a comprehensive selection process was employed based on specific inclusion and exclusion criteria.

Only full-text articles published in English were included, and searches were conducted in several major databases, including PubMed/Medline, EMBASE, the Cochrane Library and Scopus. A wide range of targeted keywords such as "malignant glioma", "glioma", "glioblastoma", "brain tumour", "malignant brain tumour", "artificial intelligence", "machine learning", "deep learning", "imaging AI models", "non imaging AI models", "deep learning models", "machine learning models", "convolutional neural networks", "survival prediction approaches", "predictive modelling", "survival analysis", "non-multimodal neuroimaging", "multimodal imaging", "combined imaging", "MRI scan", "CT scan", "multimodal MRI", "multimodal PET" and "non-multimodal MRI" guided an exhaustive database search. In addition, references from recent reviews on related topics were manually screened to identify additional sources that could enrich the search strategy. The review included studies published between 2004 and 2024 to cover two decades of research progress on the topic. Studies included descriptive, preclinical/ animal model, cohort and observational research from clinical settings to provide a multidimensional understanding of the topic.

Exclusion criteria included stand-alone abstracts, conference proceedings, letters to the editor, editorials, perspectives and posters to focus on high quality and reliable studies. Studies that were not peer reviewed and not published in English were also excluded. A summary of the methodology, including inclusion and exclusion criteria, is provided in Table 1.

### Categories of survival prediction models for malignant gliomas

Malignant glioma survival prediction models use different types of data, including imaging and non-imaging data such as genomic and clinical parameters, to improve prediction accuracy. The following subsections categorise the types of models into ML, a subset of AI, Deep

### Table 1 Summary of methodology

Methodology steps	Description
Literature search	PubMed/MEDLINE, EMBASE, Scopus and the Cochrane Library
Inclusion criteria	Various study designs including experimental studies, randomised controlled trials, prospective and retrospective cohort studies Studies involving both paediatric and adult populations Studies providing raw data Full-text articles published in English
Exclusion criteria	Non-English and non-peer reviewed studies, stand-alone abstracts, conference proceedings, editorials, commentaries, and letters
Search terms	"malignant glioma", "glioma", "glioblastoma", "brain tumour", "malignant brain tumour", "artificial intelligence", "machine learning", "deep learning", "imaging Al models", "non imaging Al models", "deep learning models", "machine learning models", "convolutional neural networks", "survival prediction approaches", "predictive modelling", "survival analysis", "non-multimodal neuroimaging", "multimodal imaging", "combined imaging", "MRI scan", "CT scan", "multimodal MRI", "multimodal PET" and "non-multimodal MRI"
Additional search	A manual search was performed to include references from recently published procedure-specific and disease-specific reviews
Sample size requirement	No strict sample size requirement

Learning (DL), a subset of ML, and the statistical model, whilst briefly discussing how these methods thrive using imaging, non-imaging, and combined methods. The success of ML, DL and statistical models in predicting glioma OS is largely dependent on the integration of both imaging and non-imaging data. ML models excel at combining features from both MRI scans and clinical data, DL models excel with high-dimensional imaging data, and statistical models also excel at providing interpretability of survival probabilities [10, 13, 14]. Using these methods in combination, predictive models for glioma survival become more accurate and personalised, providing valuable insights for clinical decision making.

### **ML-based survival prediction models**

ML-based survival prediction models for malignant gliomas use both imaging and non-imaging data to improve prediction accuracy. Imaging-based models often use magnetic resonance imaging (MRI) scans, which can be non-multimodal (using a single type of imaging) or multimodal (combining multiple types of imaging, such as structural MRI and functional MRI). For example, recent systematic analyses have shown that the most commonly used ML algorithms are support vector machines (SVMs), random survival forests (RSFs), boosted tree methods and artificial neural networks (ANNs) [9, 13]. These algorithms have been successfully applied to radiological images, particularly MRI, to predict survival outcomes by extracting features such as tumour volume and shape [15]. Non-imaging models typically rely on clinical data such as patient age, genetic markers and treatment information to estimate survival. ML methods excel at integrating these features, improving the robustness of predictions and providing actionable insights in clinical settings [12]. Furthermore, models that combine imaging and non-imaging data have shown the best performance, as they integrate structural, functional and clinical features to provide personalised survival predictions [1].

Recent studies highlight how ML thrives when combining radiomics (from MRI scans) with molecular biomarkers or clinical data. The integration of radiomic features with non-imaging data in ML models has significantly improved the accuracy of predicting PFS in gliomas. By capturing complex interactions between diverse data types, ML methods demonstrate a high degree of adaptability to multimodal inputs, further enhancing their prognostic capabilities [6, 9]. ML models like RSF have also shown promise in predicting survival outcomes by handling mixed data types effectively [11]. However, ML methods are prone to overfitting, particularly when applied to small or unbalanced datasets, which complicates the extraction of clinically relevant information. Additionally, addressing challenges such as missing data and the integration of multimodal datasets-which includes clinical, imaging and molecular data-often necessitates the use of advanced preprocessing techniques [13].

### DL models for glioma survival prediction

DL models for glioma survival prediction rely heavily on imaging data. For example, convolutional neural networks (CNNs) can automatically learn features from structural MRI and multimodal imaging [16]. These DL methods are effective at integrating different types of data—imaging, genomic and clinical—and enable more accurate and reliable survival predictions by capturing complex patterns and relationships across modalities [13]. These DL approaches have demonstrated remarkable performance, particularly with high-dimensional imaging data, by recognising intricate patterns associated with glioma progression. Whilst DL models thrive primarily on imaging data, they can also incorporate non-imaging features, such as clinical or genetic data, to further improve survival predictions. DL-based models excel at integrating both imaging and clinical information, providing deeper insights into glioma characteristics and prognosis [17].

Holistic models that combine imaging with molecular data have led to improved predictive accuracy for glioblastoma survival [18]. For example, the integration of positron emission tomography (PET) imaging with histopathological features allows DL models to capture both physiological and molecular characteristics of tumours, providing more robust survival estimates [19]. In addition, advanced DL models, such as 3D CNNs, have proven particularly effective in identifying key brain regions that influence survival, providing clinicians with interpretable results [14].

### Statistical models

Statistical models, such as CPH and Kaplan–Meier estimates, have traditionally been used for survival analysis in gliomas. However, these models are often limited when it comes to handling complex, high-dimensional data. Despite this, they remain valuable for integrating clinical data (e.g., demographic features and treatment history) to generate survival estimates. Statistical methods, when combined with imaging or molecular data, can complement ML and DL models by adding interpretability and robustness to survival predictions [10]. These models are also useful in scenarios where simpler, more interpretable models are preferred over black-box methods like DL.

Recent advancements have demonstrated that integrating statistical approaches with ML and DL can enhance survival predictions. For example, hybrid models that combine statistical techniques with machine learning methods like support vector regression have provided better predictive performance by leveraging both clinical data and imaging features [20]. Moreover, statistical models like nomograms that incorporate both clinical and imaging data offer a more interpretable means of predicting survival, facilitating personalised treatment strategies [21]. Table 2 summarises the types of AI survival prediction models used for malignant gliomas.

### Survival predictions and outcomes based on imaging, non-imaging and combined AI models Imaging AI models

AI-based survival prediction in patients with malignant gliomas has leveraged both imaging techniques; non-multimodal and multimodal approaches that integrate clinical and molecular data.

Non-multimodal imaging methods, such as MRI and CT, have provided significant insights into patient prognosis. For example, a model using only MRI data from glioblastoma patients achieved a C-index of 0.78 by stratifying patients based on radiomic features from T1- and T2-weighted images [22]. MRI-derived radiomics has demonstrated an 83% accuracy in identifying biomarkers, such as tumour shape and texture, that correlate with survival [18]. Furthermore, the utilisation of post-radiotherapy MRI data achieved a high area under the curve (AUC) of 0.93 in predicting survival in glioblastoma patients, underscoring the potential of capturing imaging data at different treatment stages [23]. Similarly, CTbased models, with a C-index of 0.74, have highlighted tumour volume and enhancement patterns as key predictors of survival [17]. DL applied to histopathological images of glioma tissue achieved 87% accuracy, identifying nuclear pleomorphism and mitotic activity as indicators of poor prognosis [24]. Meanwhile, a DL model that focused on glioblastoma features like necrosis and oedema achieved 81% accuracy, strongly correlating with patient outcomes [2]. Furthermore, quantitative features from MRI scans can classify glioma patients into survival categories with up to 98% accuracy [25].

Non-multimodal scans provide detailed insights into tumour volume, texture, and intensity, beyond what clinical data alone can offer. These models provide a non-invasive alternative for prognostication, enabling clinicians to predict outcomes and tailor treatments effectively. Their high accuracy and specificity illustrate their potential to replace invasive methods, paving the way for broader applications in neuro-oncology. However, their reliance solely on imaging data limits their ability to capture systemic and molecular-level nuances that significantly influence survival [26, 27].

Multimodal imaging, which combines MRI, CT, and PET, leverages the complementary strengths of radiomic features and clinical or molecular information. Multimodal AI overcomes the limitations of singlemodality approaches by providing greater accuracy and reliability, enabling comprehensive survival stratification and improved personalised treatment strategies. This integrated approach addresses the complexities of glioblastoma prognosis and represents a significant step forward in patient care [28, 29]. This extensive approach has further enhanced predictive accuracy. For example, an ML model applied to multiple imaging modalities achieved approximately 82% accuracy, outperforming traditional methods [20], whilst DL models integrating MRI and CT data have also achieved over 85% accuracy by identifying complex patterns across imaging types

Prediction model type	Data types	Methodology	Key features/outcomes
ML model			
Dynamic nomograms [21]	Molecular biomarkers, clinical parameters	Statistical modelling	Enables individualised predictions for personalised treatment decisions
Non-imaging models [12]	Clinical and molecular data	ML (CPH, Support Vector Machines)	Provides robust survival estimates through integration of demographic and clinical features
Radiomics-based methods [6, 9]	MRI-derived imaging features, clinical data	ML techniques	Achieves high accuracy in predicting PFS using feature extraction
DL model			
Imaging-based models [20]	MRI scans (structural, functional)	Neural networks	Utilises multimodal approaches com- bining resting-state fMRI and struc- tural MRI
Predictive performance models [15]	Radiology, pathology imaging	Ensemble regression, DL	Enhances predictive performance by integrating radiology and pathol- ogy images
Holistic models [19]	In vivo PET imaging, ex vivo histo- pathology	Integrated modelling	Captures physiological and molecular characteristics for improved survival predictions
3D convolutional neural net- works [2]	MRI scans, clinical data	DL (3D CNNs)	Provides interpretable outputs highlighting critical brain regions influencing survival predictions
Statistical model			
Traditional models (e.g. CPH, Kaplan–Meier estimates) [10]	Clinical data (demographics, treat- ment history)	Statistical survival analysis	Provides interpretable survival estimates but struggles with high- dimensional data
Hybrid statistical models (e.g. CPH combined with ML) [11]	Clinical and imaging data	Combination of CPH and ML techniques	Enhances predictive performance by integrating interpretability with non-linear data analysis
Nomograms [21]	Clinical and imaging data	Statistical modelling	Facilitates personalised predictions with interpretable survival prob- abilities

Table 2 Types of survival prediction models for malignant gliomas

MRI, Magnetic Resonance Imaging, fMRI, Functional Magnetic Resonance Imaging, PET, Positron Emission Tomography, ML, Machine Learning, 3D, 3-Dimensional, DL, Deep Learning, CNN, Convolutional Neural Networks, CPH, Cox Proportional Hazards, PFS, Progression-free Survival

[30]. An online survival prediction tool using multimodal imaging with WHO CNS5 data, along with models that integrate molecular and clinical information, has achieved a C-index of 0.75 [12].

In addition, quantitative radiomics features reflecting tumour heterogeneity and phenotype are extracted from imaging modalities such as multi-parametric MRI (mpMRI). Radiomics signatures derived from mpMRI are shown to stratify glioblastoma patients into survival groups with high accuracy. Imaging features have been integrated with clinical variables to further improve survival prediction using ML classifiers, such as ensemble learning models [31].

Imaging-based survival prediction has also benefited from DL techniques. Studies have proposed a multi-channel 3D DL architecture using multimodal neuroimaging data. The framework was built using contrast-enhanced T1 MRI, diffusion tensor imaging (DTI) and resting-state functional MRI (rs-fMRI) and achieved an accuracy of 90.66% in classifying survival outcomes. Such studies demonstrate the promise of DL for interpreting complex imaging datasets to improve clinical decision making [32].

Radiomics extracted from preoperative contrastenhanced MRI combined with linear discriminant analysis (LDA) had high predictive accuracy for 3- and 6-month survival in glioblastoma patients, with AUC values of 0.88 and 0.78, respectively [26]. Similarly, automated glioma grading using CNNs with high sensitivity and specificity allows survival stratification without invasive biopsy. These image-based approaches exploit spatial and textural information, laying the foundation for AI in non-invasive survival prediction [26, 27].

Whilst accurate and specific, imaging models may miss critical non-imaging factors such as genetic mutations or clinical history. Therefore, a combined approach that integrates imaging and non-imaging data is more promising, providing a more comprehensive framework for survival prediction and personalised treatment strategies.

### Non-imaging AI models

AI applications for predicting survival outcomes in malignant gliomas are increasingly utilising non-imaging approaches, focusing on clinical data and histopathological features. For instance, an online tool that combines traditional statistical methods with ML uses variables such as Karnofsky Performance Status (KPS) and patient demographics to improve survival predictions in glioblastoma patients [33].

The inclusion of inflammatory biomarkers has also proven beneficial, with models incorporating these markers achieving a C-index of 0.78, surpassing the accuracy of traditional methods [34]. Furthermore, integrating quality-of-life assessments into survival models has reduced the mean absolute error to 3.4 months, demonstrating the value of patient-reported outcomes in enhancing predictive accuracy [35]. Alternative studies have achieved similar results using WHO CNS5 data, demonstrating high predictive accuracy with AUC values of 0.849, 0.835, and 0.821 for 1, 3, and 5-year overall survival predictions, and identified key prognostic factors like age, IDH1, and CDKN2A alterations [21]. Additionally, when clinical and demographic data were incorporated into a DL model, it achieved 85% accuracy in predicting 1-year survival outcomes [36].

Whilst imaging remains critical, non-imaging data such as genetic, molecular and clinical parameters provide complementary insights. Studies have highlighted the importance of multi-type genetic data, including mRNA expression, DNA methylation and microRNA profiles, to address cancer heterogeneity. A DL approach effectively captured common and specific genetic features and outperformed conventional methods in survival prediction accuracy [37]. Similar studies have also investigated the use of ML techniques such as ANNs and SVMs in analysing small, heterogeneous glioma datasets. The results showed that these techniques outperformed traditional statistical methods, and that the inclusion of demographic and clinical variables was critical for more nuanced survival predictions. Such non-imaging approaches highlight the importance of AI in harnessing diverse data to accurately predict patient outcomes [38].

Transformer-based models have been introduced for glioblastoma survival prediction by integrating clinical and molecular pathology data. These models achieved consistent performance across multiple datasets, highlighting their generalisability and reliability. Using highdimensional data integration, this approach provides insights into survival determinants beyond anatomical imaging [14]. Another important development is the use of ML algorithms to investigate non-imaging variables such as age, performance status and genetic mutations. The combination of clinical features such as Ki-67 and P53 mutation status with ML algorithms improves survival prediction beyond traditional statistical methods [39].

AI-driven non-imaging approaches using clinical, genetic and molecular data improve glioma survival prediction. Techniques such as ML, ANN and transformers outperform traditional methods by integrating variables such as KPS, biomarkers and genetic mutations, highlighting their accuracy and value in complementing imaging data.

### Combined AI models: a combination of imaging and nonimaging

Predicting glioma survival with AI by integrating both imaging features with clinical data has further improved prognostic accuracy. For example, adding MRI-based radiomic features to clinical parameters (age, performance status) reduced the mean absolute error in survival prediction to 4.5 months [40]. A similar study found that radiomics-based AI models further improved predictions by extracting quantitative features from MRI scans, with random forests achieving 92.27% accuracy for PFS. Texture-based features were key to stratifying patients [35]. Another approach achieved 90% accuracy in predicting 1-year survival in glioblastoma patients by combining radiomic and clinical data, demonstrating the value of incorporating patient-specific features for personalised survival estimates. Comparative studies showed that RSFs outperformed other models, with a concordance index of 0.72 for OS prediction. Important features included MGMT promoter methylation and extent of resection [22]. In addition, adding radiomic features to clinical and genetic data significantly improves survival prediction for low-grade gliomas [41].

Studies have created a nomogram that combines radiomics signatures from MRI, genetic markers such as IDH mutation, and clinical factors such as age [42]. This combined model showed improved accuracy in predicting overall survival compared to models using imaging or non-imaging data alone. In addition, CNNs have been shown to simultaneously process histological images and genomic biomarkers. By exploiting adaptive feedback, the models achieved unprecedented accuracy in predicting glioma survival outcomes, highlighting the potential of multimodal AI frameworks. Such combined approaches are leading the way to precision oncology by providing holistic and individualised survival predictions [43].

The integration of imaging and non-imaging data represents a paradigm shift in survival prediction. A dual graph neural network (GNN) combining radiomic and clinical features has been developed using transformer decoders, achieving a classification accuracy of 0.586 on the BraTS20 dataset [29]. By combining complementary

data modalities, this approach outperforms stand-alone imaging or clinical models. Similarly, ensemble classifiers have been used to predict overall survival, IDH mutations and other molecular features from a combination of radiomic and clinical data. Here, ensemble methods were shown to consistently outperform individual classifiers [28]. This demonstrates the potential of combined models to improve predictions and guide treatment strategies. This was further illustrated by evaluating the synergy of multimodal data by incorporating tumour location and radiomic features to further improve survival prediction accuracy. The results indicate that combined models not only improve predictive performance, but also provide a more complete picture of the factors influencing glioblastoma outcomes [44]. Table 3 summarises the strengths and limitations of different parameters used to predict glioma survival.

### Comparison of the efficacy of imaging, non-imaging and combined AI methods for glioma survival prediction

Imaging-based models are adept at capturing the fine details of tumour characteristics including shape, texture, and growth patterns and have high predictive accuracy. For instance, post-radiotherapy MRI-derived radiomics have been shown to have an AUC of up to 0.93 in predicting glioblastoma survival outcomes [23]. In contrast, non-imaging models are highly accessible and cost effective, using readily available clinical and molecular data such as age and KPS to achieve substantial accuracy with minimal resources [33]. However, whilst imaging models demand advanced technologies and expertise that may not be accessible in all clinical settings, non-imaging models lack the ability to capture critical tumour-specific insights, such as spatial and textural features, which can limit their predictive accuracy.

Multimodal imaging has been shown to synergise multiple imaging modalities such as MRI, CT, and PET to achieve accuracies of around 82% [20]. By combining anatomical, functional, and metabolic insights, a comprehensive understanding of glioma behaviour is achieved. On the other hand, non-imaging models use a variety of data types, including molecular biomarkers and quality of life metrics, to improve patient centric predictions and add substantial value in resource-limited settings [34]. However, whilst multimodal imaging requires substantial computational infrastructure to integrate these complex data sources, non-imaging approaches are limited by their inability to directly assess tumour physiology or structural progression, reducing their predictive robustness.

Interpretable outputs of DL imaging models, including 3D CNNs, identify critical brain regions that affect survival, which are essential for personalised treatment strategies [2]. Meanwhile, non-imaging models using patient-reported outcomes, such as quality-of-life data, add a human dimension to survival predictions, addressing patient-specific concerns often overlooked in imaging models [34]. However, DL imaging models often operate as a "black box" of many algorithms, the hidden layers in neural networks, significantly reducing the interpretability of a potentially powerful predictive model, making its decision-making process opaque to clinicians and limiting trust and widespread adoption [45]. On the other hand, whilst patient-reported outcomes add context to survival estimates, they may introduce subjectivity and variability that can affect model accuracy and

Finally, combined models that integrate imaging with clinical and molecular data demonstrate the greatest potential by leveraging the strengths of both approaches. As an example, combining MRI-derived radiomics with clinical data has reduced the mean absolute error in survival predictions to 3.4 months [35]. These models can provide stratification of patients into more precise survival categories so that patients can be treated more personally. Although combined models achieve better accuracy and prediction power, they require large computational and logistical resources to integrate and manage different data types [30]. Non-integrated models, whether imaging-based or non-imaging-based, are easier to implement but lack the nuanced insights necessary for advanced treatment planning.

consistency.

Overall, the most promising approach is the combined method, but practical challenges related to data integration and computational demands need to be overcome for widespread clinical application.

# Discussion; general limitations and probable solutions for using AI models to predict glioma survival

A major challenge of using AI for glioma survival prediction is the existence of data heterogeneity which stems from variations in the patients' characteristics, treatments and performance status [43]. This variability limits the model generalisation, particularly when used across different populations. Furthermore, the combination of multiple data types, including histopathological features and molecular signatures, poses a problem due to the limited sample size and sparsity of the data, increasing the risk of overfitting [31, 43, 46]. To overcome this limitation, there is a need to create multi-institutional and common datasets to increase data variability and generalisation. The solution to this problem can be found in federated learning, which allows for model training across institutions whilst keeping patient data private.

Parameter type	Significant contribution	Lesser contribution
Imaging features [17, 20, 22–26, 30, 32]	MRI-based radiomics (e.g. tumour volume, texture) achieving high accuracy (AUC: 0.93) for survival prediction	CT imaging with tumour enhancement patterns achieving moder- ate C-index (0.74)
	Multimodal imaging (MRI, CT, PET) achieving ~ 82% accuracy	Single-modality imaging (MRI) with lower predictive accuracy (C-index: 0.78)
	Post-radiotherapy MRI significantly improves prognostic out- comes	Histopathological imaging with 87% accuracy in specific features
	Longitudinal MRI data integration further refining survival predic- tions	Reliance on non-multimodal imaging methods limits systemic insights into tumour biology
	Preoperative contrast-enhanced MRI radiomics predicting short-term survival with AUC of 0.88 for 3 months and 0.78 for 6 months	
	Multi-channel 3D DL integrating multimodal MRI achieving 90.66% accuracy for survival classification	
	Quantitative imaging features identifying survival categories with up to 98% accuracy	
Clinical parameters [12, 33, 35, 40]	Integration of age, KPS, and performance metrics improving predictions	Standalone clinical data often results in reduced predictive accuracy compared to integrated approaches
	Incorporating quality-of-life metrics reducing mean absolute error in survival predictions to 3.4 months	Inconsistent data reporting limits standalone clinical models' generalisability
	Demographic features like age and treatment history enhance predictive accuracy	
Molecular parameters [21, 22, 30, 33, 37]	Incorporating biomarkers like IDH1 mutations and CDKN2A alterations enhancing multimodal models	Isolated molecular markers without integration yielding inconsistent results
	Using MGMT promoter methylation status for stratifying glioblas- toma patients	Limited utility of single-gene analysis in survival prediction due to tumour heterogeneity
	Multi-omics integration of mRNA, DNA methylation, and micro- RNA profiles improving model adaptability to glioblastoma heterogeneity	
	PET-based molecular features enabling survival stratification	
Combined approaches [29, 30, 35, 40, 41, 44]	Combined imaging and clinical data yielding reduced error in survival predictions (mean absolute error:~ 3.4 months)	Models lacking sufficient integration showing lower reliability in prediction outcomes
	Addition of radiomic features to clinical and genetic data improv- ing prediction for lower-grade gliomas	Partial integration approaches with lower multimodal complexity
	Holistic models combining PET imaging, histopathology, and clinical data for robust survival predictions	
	Ensemble learning combining radiomics, genomics, and clinical features achieving 92.27% accuracy for progression-free survival prediction	
	Incorporation of tumour location into combined models improv- ing accuracy in glioblastoma predictions	
	Transformer-based multimodal integration achieving classifica- tion accuracy of 0.586 on BraTS20 dataset	
	Combined radiomics and clinical features reduced survival prediction error to 4.5 months	
Al and ML models [11, 15, 16, 20, 28]	3D CNNs and ensemble regression models excelling in multi- modal setups	CPH models struggle with high-dimensional data unless comple- mented by ML approaches
	Federated learning enables multi-institutional data use whilst preserving privacy	Standalone statistical approaches without ML showing reduced utility for complex datasets
	Explainable AI methods like SHAP and Grad-CAM improving interpretability	Overfitting risks in ML models when applied to small or unbal- anced datasets
	Random survival forests handle mixed data types effectively	
	Neural networks combining structural and functional MRI out- performing classical statistical models Ensemble classifiers consistently outperform single models for multimodal glioma survival predictions	

### **Table 3** Parameters contributing to survival prediction in malignant glioma

MRI, Magnetic Resonance Imaging; fMRI, Functional Magnetic Resonance Imaging; PET, Positron Emission Tomography; ML, Machine Learning; 3D, 3-Dimensional; DL, Deep Learning; AI, Artificial Intelligence; CNN, Convolutional Neural Networks; CPH, Cox Proportional Hazards; PFS, Progression-free Survival; DNA, Deoxyribonucleic

### Table 3 (continued)

Acid; RNA, Ribonucleic Acid; PET, Positron Emission Tomography; 3D, Three Dimensional; AUC, Under the Curve; Grad-CAM, Gradient-Weighted Class Activation Mapping; SHAP, Shapley Additive exPlanations; MGMT, O6-methylguanine-DNA Methyltransferase; KPS, Karnofsky Performance Status; IDH, Isocitrate dehydrogenase

Programs like the ReSPOND consortium show how multi-institutional databases can corroborate and extend the applicability of AI algorithms. These efforts indicate the effectiveness of collaborative frameworks in addressing data heterogeneity and enhancing AI performance in clinical settings [47].

One of the biggest issues with advanced AI models, especially those based on DL methods, is that they are often 'black boxes'. This lack of transparency and interpretability makes it difficult for clinicians to comprehend and rely on the outcomes yielded by these tools, hampering their clinical implementation [13, 48]. Lack of well-defined decision-making procedures is still a factor that hinders the adoption of AI in practice. Better model interpretability requires using frameworks like SHapley Additive exPlanations (SHAP), Locally Interpretable Model-agnostic Explanations (LIME), and Gradient-weighted Class Activation Mapping (Grad-CAM) to explain the decision-making process [48, 49]. SHAP employs cooperative game theory to evaluate the contribution of each feature to the model's output. In contrast, LIME generates locally faithful explanations by modifying data and analysing changes in predictions. Grad-CAM provides visual insights into neural network decision-making, primarily in image classification, by producing heat maps that highlight key regions influencing class predictions. [48, 49]. Furthermore, providing clinicians with information regarding how these models are used can help to overcome the gap between technicality and usability. Large-scale prospective studies with standardised protocols are needed to confirm the potential of AI tools in clinical practice. Increasing international partnerships might also improve external recognition and the use of interpretable AI in various clinical contexts.

Whilst models like the RSF and CPH have been shown to be effective in terms of predictive performance, challenges still remain. RSF performs well in handling nonlinear interactions but the interpretation of the results is less straightforward when compared to CPH. On the other hand, CPH models are interpretable but may not work as well in complex data processing situations [11]. Recently, there's a development in the creation of mixed models that would inherit the interpretability of CPH along with the data processing capabilities of RSF for increasing the predictive accuracy. It is such integrated approaches that could provide clinicians with both decision support and accurate prognosis, thereby ensuring the applicability of the approaches in various clinical contexts [11].

In low-resource settings, there is a major challenge in terms of the available computational power to support the use of AI [50]. Large-scale cloud platforms and high resource requirements of conventional AI models pose accessibility challenges in resource-scarce environments. The recent emergence of light-weight AI models that are designed to work in environments with limited resources can be seen as a solution [49]. Accessibility can also be improved using cloud-based platforms that can scale to deliver the computational resources required for innovative AI applications. Such innovations are essential for the implementation of AI in clinical practice across the world to make these technologies available to everyone. Post-training mathematical optimisation can mitigate this issue. Techniques that streamline AI models reduce their memory footprint and latency whilst maintaining accuracy. These optimisations enable the deployment of AI tools on standard consumer-grade CPUs, making them more accessible in resource-limited clinical environments [51].

Current glioma survival prediction models are plagued by small datasets with low geographical variability, lack of external validation, and absence of large-scale prospective studies; rendering them non-generalizable to other clinical applications [52]. To solve these problems, we need to increase international collaborations and datasets, use federated learning to increase the diversity of the data (whilst maintaining privacy), and use self-supervised learning to extract useful features from unannotated data. For instance, the addition of longitudinal MRI data and clinical variables has increased the accuracy of survival predictions for glioma patients [16, 53, 54]. Moreover, the complexity of large datasets often masks important predictors. Studies have demonstrated that of the 1265 extracted features, only 29 were significant for survival prediction, indicating the necessity of effective feature selection. Recursive feature elimination and correlation based selection can be used to reduce data noise, improve predictive power and refine clinical relevance **[40]**.

Finally, as with all AI applications in oncology, the use of patient data to train AI models is a major ethical and legal issue. It is crucial to protect patient privacy when using such information. These issues can be addressed through the use of standard operating procedures for data management and the use of effective anonymisation techniques. In addition, increased clarity in data use agreements promotes trust in the application of AI in healthcare [55].

### Conclusion

By integrating complex data sources and providing individualised risk assessments, AI and ML techniques have the potential to significantly improve survival predictions for patients with malignant gliomas. Although AI models predict more accurately than traditional methods, problems of data heterogeneity, model interpretability and the need for large, diverse datasets remain. Overcoming these limitations is essential for the clinical adoption of AI-driven tools and provides a pathway to more precise and personalised treatment strategies that may lead to improved patient outcomes in neuro-oncology.

### Abbroviations

Al	Artificial intelligence
ML	Machine learning
DL	Deep learning
MRI	Magnetic resonance imaging
CT	Computer tomography
3D	3-Dimensional
OS	Overall survival
PFS	Progression-free survival
CPH	Cox proportional hazards
RSF	Random survival forest
C-index	Concordance index
SVM	Support vector machines
CNN	Convolutional neural network
AUC	Area under the curve
DNA	Deoxyribonucleic acid
RNA	Ribonucleic acid
PET	Positron emission tomography
3D	Three dimensional
SHAP	Shapley Additive exPlanations
Grad-CAM	Gradient-Weighted Class Activation Mapping
MGMT	O6-methylguanine-DNA Methyltransferase
KPS	Karnofsky performance status
IDH	lsocitrate dehydrogenase
ANN	Artificial neural network

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### Author contributions

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### Data availability

No datasets were generated or analysed during the current study.

### Declarations

Ethics approval and consent to participate Not applicable.

### **Consent for publication**

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### **Competing interests**

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