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Evaluation of Radiomic Analysis over the Comparison of Machine Learning Approach and Radiomic Risk Score on Glioblastoma

Accurate patient prognosis is important to provide an effective treatment plan for Glioblastoma (GBM) patients. Radiomics analysis extracts quantitative features from medical images. Such features can be used to build models to support medical decisions for diagnosis, prognosis, and therapeutic response. The progress of radiomics analysis is continuously improving. The aim of this research is to extract standardised radiomic features from MRI scans of GBM patients, perform feature selection, and compare radiomic-based risk score (RRS) and machine learning (ML) approaches for the risk stratification of GBM patients. We have also tested the generalisability of these models which is crucial for clinical implementation. Our work demonstrates that a stratification model based on logistic regression generalised better than the RRS method when applied to new unseen datasets.

Keywords:
Glioblastoma, radiomics, brain tumour, overall survival.

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INTRODUCTION

Glioblastoma (GBM) is a malignant and lethal brain tumour [1]. Grade IV gliomas exhibit the highest level of aggression and rapid progression. After initial diagnosis, the median survival time for GBM patients is 15 months [2]. The poor prognosis for GBM can be related to genetic heterogeneity between patients and at intratumor level [3].

In clinical practice, brain tumours are evaluated for their diagnosis and prognosis by utilising magnetic resonance imaging (MRI) techniques. The location of tumours is detected in three dimensions via non-invasive MRI technology. In contrast to X-ray and CT imaging, MRI gives high resolution with better soft tissue contrast without the use of ionising radiation [4].

Biopsies are an invasive procedure to diagnose, grade and characterise brain tumours [5]. Due to having genetic differences in sub-regions of a tumour, biopsies can provide only limited information with a sample of small section from tumour tissue [6]. Other assessment methods including quantitative image analysis, which is non-invasive and evaluate the entire tumour tissue, can support biopsy as additional assessment. Image analysis utilising radiomics features has the potential to replace biopsies when they are infeasible or risky [7].

Radiomics analysis is a rapidly growing field of medical imaging involving the extraction of large amounts of quantitative data from medical images [8], [9]. This approach seeks to reveal hidden patterns and features that are imperceptible by the naked eye in order to provide patients with more personalised and precise care. To extract radiomic features from medical images, radiomics analysis employs advanced image processing techniques that can characterise tumour heterogeneity [10] and microenvironment [11]. Radiomic imaging features can be then used to train a model to stratify patients in different risk groups. This is achieved using statistical methods and machine learning (ML) techniques as outlined in the literature [9].

N. Beig et al. proposed a Radiomics-based Risk Score (RRS) for GBM tumour habitat [12]. However, a comparison with alternative methods including machine learning (ML) approaches was not performed. In this work, we investigate the best model to risk-stratify GBM patients including RRS, and a range of ML approaches applied to a large dataset of clinical MRI images and clinically defined contours.

MATERIALS AND METHODS

In this research we used two GBM datasets: (1) the publicly available BraTS 2020 including 236 cases [13]–[15] and (2) a local dataset STORM_GLIO including 53 eligible cases. Both datasets included overall survival (OS) information. The MRI sequences included in the datasets were: T1-weighted (T1), T1-weighted contrast-enhanced (T1ce), T2 weighted (T2), and T2 Fluid attenuated inversion recovery (T2-FLAIR). All scans included in the STORM_GLIO dataset were acquired between April 2014 - April 2018 in Wales.

Sixty six percent of the BraTS dataset was used as training cohort with the remaining 33% used in the testing cohorts together with the STORM_GLIO dataset. Image pre-processing techniques similar to those used for the curation of the BraTS2020 dataset were implemented in this work. They included the following steps: (1) skull stripping, which was carried using HD-BET algorithm [16] (2) rigid registration of all sequences was applied to the dataset based on T1ce modality (3) an intensity normalisation algorithm implementing Z-score normalisation was applied to all datasets.

The BraTS2020 challenge [17], included three annotated regions: enhancing tumour (ET), tumour core (TC; enhancing tumour and necrotic) and whole tumour (WT; enhancing tumour, necrotic and edema). On the other hand, the STORM_GLIO dataset included Gross Tumour Volume (GTV) segmentation which is defined as the gross palpable or visible/demonstrable extent and location of malignant growth [18]. For the purpose of this study, we considered GTV and TC equivalent volumes where to perform radiomics analysis in Fig.1. We have demonstrated the equivalence of these two volumes in previous work [19].

For each patient, 143 imaging features were extracted from each scan. The radiomics analysis was performed using SPAARC Pipeline for Automated Analysis and Radiomics Computing (SPAARC) [20], [21] which is an IBSI compliant software package [22] written in MATLAB (The MathWorks, Natick USA).

The study was designed to investigate the ability of radiomics features based on MRI scans to risk-stratify on GBM patients. The integration of radiomics-based risk stratification within the oncology landscape carries profound implications for transforming clinical decision-making and achieving significant advancements in patient outcomes. Radiomic feature selection was carried out using the LASSO Cox regression method. Selected features were then used on the training cohort to build a stratification model. An RRS, was constructed by linearly combining the features chosen with LASSO technique within the training cohort and multiplying them with their corresponding coefficients [12]. The median value of the RRS was used as a fixed cut-off for stratifying low-risk and high-risk groups. Additionally, we used a range of machine learning (ML) techniques to build alternative risk stratification models and compared their performance with the RSS model. The ML techniques used in this work were: Logistic Regression, Support Vector Machine, Decision Tree, Random Forest and Neural Networks. For both ML approach and RSS method, the precise evaluation of the expected overall survival was tested by implementing the Kaplan–Meier (KM) survival analysis and log-rank test. The KM curve is a graphical representation of the estimated probability of survival over time, and it is frequently used in survival analysis to evaluate the results of medical research. KM plots were used to compare survival times across low-risk and high-risk groups on both training and testing cohorts for T1, T1ce, T2 and T2-FLAIR modalities. P-values < 0.05 were accepted as significant. For ML models, the low-risk and high-risk stratification was based on grid search to determine a cut-off on overall survival (OS). This method searches the optimum cut-off which is OS in month by trying to reach the minimum P-value.

RESULTS

In Table 1, the performance of the RRS method for all available modalities in the datasets is reported. The table includes the P-value for tests carried out with both BraTS and STOMR_GLIO datasets. The data indicate that the model based on the T2 modality provides significantly higher performance for risk stratification while its application generalises well an unseen dataset (STORM_GLIO).

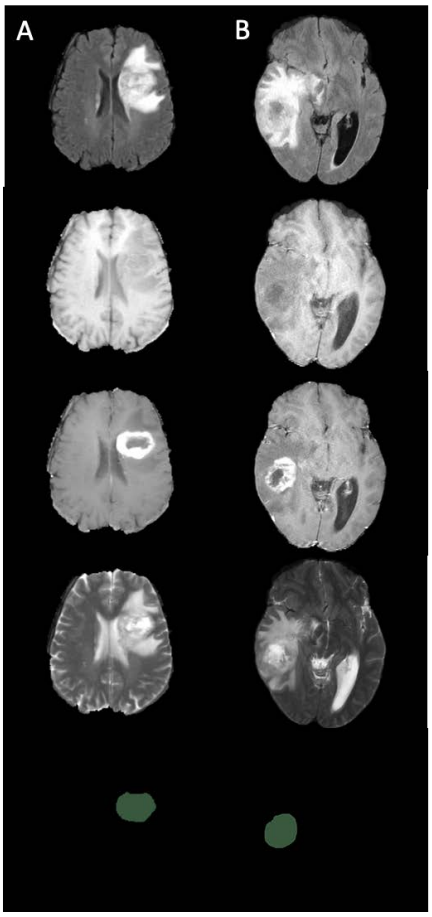

Fig. 1. Example of A) TC delineation from the BraTS dataset and B) GTV delineations from the STORM_GLIO dataset. From top to bottom modalities; T1, T1ce, T2 and T2-FLAIR and Reference contour.

Modality	BraTS Testing	STORM_GLIO
T1	0.01	0.22
T1ce	0.14	0.86
T2	0.0007	0.001
T2-FLAIR	0.003	0.94

Table 1. Performance of the RSS method for BraTS and STORM_GLIO dataset (P-value < 0.05 is significant).

Method	BraTS Testing	STORM_GLIO Testing
RRS	0.0007	0.001
Logistic Regression	0.01	5.75x10-5
Decision Tree	0.26	0.91
Random Forest	0.046	0.002
Support Vector Machine	0.01	0.0016
Neural Networks	0.007	0.75

Table 2. Performance of RRS and ML models for T2 modality (P-value < 0.05 is significant)

Fig. 2 shows KM curves of Logistic Regression and RRS method for STORM_GLIO dataset. The survival probability of RRS remained constant along the X-axis at a value of 0.2 from 5-month of OS to over 15-month of OS. On the other hand, that of Logistic Regression in the same figure remained constant at a less value than 0.2 which resulted in a significantly better P-value in Table 2.

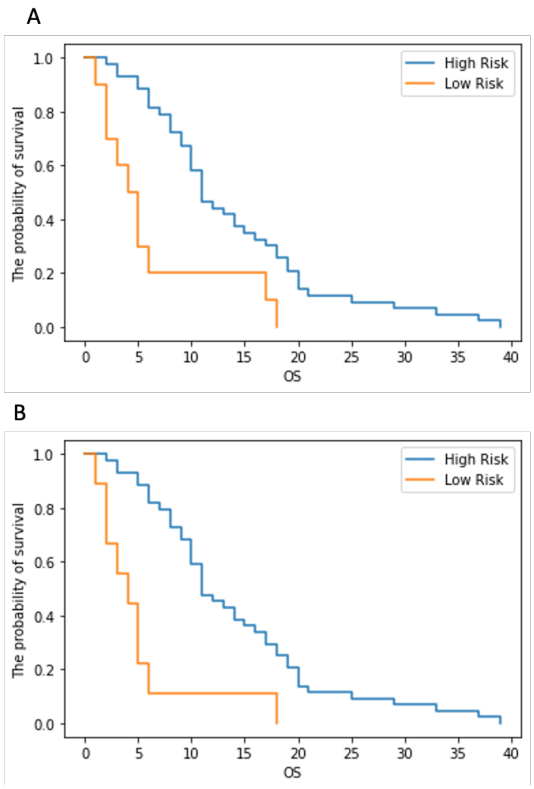

Fig. 2. The KM curve of T2 modality for A) RRS score with a median cut-off and B) Logistic Regression (The blue line represents high-risk group and the orange line represents low-risk group).

DISCUSSION

To the best of our knowledge, this is the first time that RRS and ML approaches are compared in their ability to risk-stratify on GBM patients. Although the performance of ML approaches used in the BraTS dataset was inferior to RRS, our results suggest that they can be considered as an alternative method for risk stratification based on overall survival information. The generalisability of stratification models is an important factor for clinical implementations and the logistic regression model performed well when tested on local MRI scans of GBM.

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Conflicts of interest
The authors declare no conflict of interest.

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