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MRI Radiomics for Predicting a Poor Prognosis in Patients with GBM

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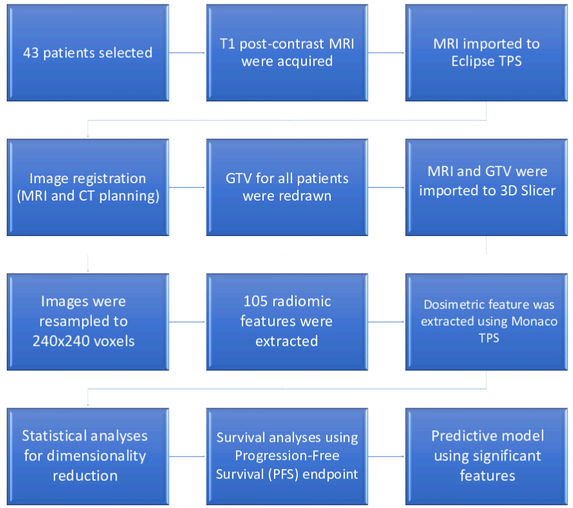
INTRODUCTION

Glioblastoma multiform (GBM) is the most common astrocyte brain tumor in adults, with an occurrence of two or three episodes by one hundred thousand habitants [1]. Its treatment is based on surgery (maximum resection of tumor) followed by radio and adjuvant chemotherapy cycles [2], and it has a very poor prognosis presenting high changes of recurrence and an average survival of 14 months [3]. This poor prognosis is related with its intra-tumoral heterogeneity characteristics that difficult the use of biopsies to extract detailed molecular information from it [4].
So, medical images – specifically Magnetic resonance images (MRI) – are being used to monitoring GBM, due to the possibility to extract information regarding pathology, biomarkers and genetics [5] through computational algorithms, such as radiomics features [6]. These characteristics can be correlated with disease prognosis creating predictive models of specific endpoints based on the extracted features.

AIM

Considering that MRI is used at the radiotherapy planning for delineating the clinical volumes of treatment, this study aims to present a methodology using the extraction of radiomics features from these structures and evaluate their significance for a poor prognosis. Also, a predictive poor prognosis model is presented.

METHODS



RESULTS

Table 1 presents general information for a sample of 43 patients. The sample had 26 male patients and 17 female patients. Their age varied from 34 to 85 years, with an average value of approximately 59 ± 11 years. The mean PFS was 13.5 ± 13.3 months, D95% varied from 67 to 100%, with a mean of 92.1 ± 5.4%, and lastly, the GTV volumes varied from 2.2 to 184.4 cc. Kaplan Meier survival curves for both groups studied are shown in figure 1.

After statistical analysis for PFS, 43 features presented a normal distribution, and among them, the only feature that could differentiate the two groups was kurtosis (table 2). The evaluation of kurtosis values distribution for all the patients indicate a possible threshold at 2.7 to separate the group of patients who had PFS lower and higher than 3 months (figure 2).

Thus, for the group of patients of this study, we evaluated the effect of using kurtosis equal to 2.7 as a rule in a PFS predictive model. This way, patients that presented kurtosis ≤ 2.7 were classified as having a PFS within 3 months and were labeled with endpoint class = 1, and patients with kurtosis > 2.7 were classified as having a PFS higher than 3 months and were labeled with endpoint class = 0.

The resulting confusion matrix of the predictive model indicates a global accuracy of 70%. The model can detect correctly all 6 patients with PFS within 3 months and 24 patients with PFS higher than 3 months. It missed 13 patients by providing false-positive results (table 3). The ROC curve presents an area under the curve (AUC) of 0.78 (figure 3).

As kurtosis was the feature able to differentiate the group of patients that presented PFS within 3 months of the group with higher PFS, we can infer that, using a threshold of 2.7, our data shows that poor prognosis GBM tumors are related to a heterogeneous tumor composed of a broad range of intensities in the MRI, but with a tendency of presenting almost the same number of voxels per intensity. Clinically it could be interpreted as a heterogeneous tumor composed of necrose, edema, and neoangiogenesis.

***Table 1:** Demographics information of the 43 patients. AVG means average; SD means standard deviation and Min/Max corresponds to the minimum and maximum values, respectively.*

Demographics	Values
Age on Diagnosis (AVG / SD / Min / Max in years)	58.9 / 11.2 / 34 / 85
Gender (M / F)	26 / 17
PFS (AVG / SD / Min / Max in months)	13.5 / 13.3 / 0 / 52
D95% (AVG / SD / Min / Max) (%)	92.1 / 5.4 / 67 / 100
GTV volumes (AVG / Min / Max in cc)	71.4 / 2.2 / 184.4

***Table 2:** Normal distribution features found on the Shapiro-Wilk test and significant features selected at the t-test.*

PFS (3 months)	
Gaussian feature	42
Significant feature	**p-value**
Kurtosis	0.02

***Table 3:** Confusion Matrix and its evaluation parameters for the predictive model based on the threshold of the kurtosis value.*

Data	Confusion matrix			Evaluation parameters		Accuracy
Classification Model	True Label	Predicted Label		Precision	Recall	0.70
		0	1			
	0	24	13	1.00	0.65	
	1	0	6	0.32	1.00	

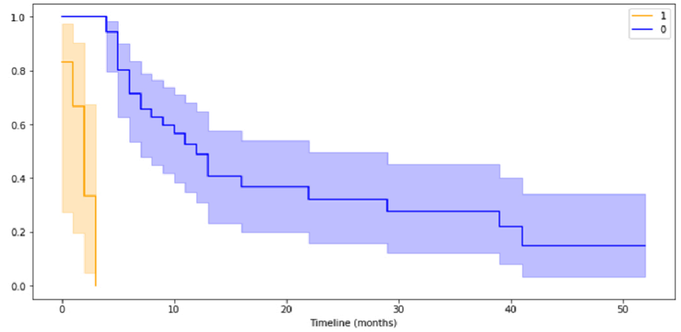


***Figure 1 –** Kaplan Meier survival curves for both groups evaluated in this study. Patients grouped as endpoint class = 1 (orange line) had the PFS within 3 months, and patients with PFS higher than 3 months were labeled with endpoint class = 0 (blue line).*

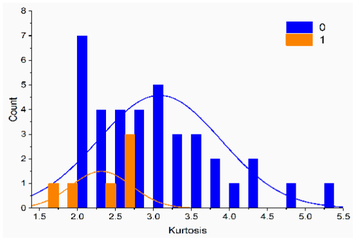


***Figure 2:** Kurtosis values distribution for PFS within 3 months: histogram (a) and kurtosis versus class value plot (b).*

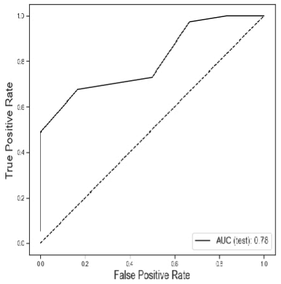


***Figure 3 -** Receiver Operating Characteristic (ROC) Curve for the proposed predictive model.*

CONCLUSIONS

This study presented a Radiomics analysis of MRI images to predict GBM's poor prognosis (PFS < 3 months). We used statistical analysis to assess that kurtosis can identify GBM patients with a poor prognosis using the intensities from T1 post contrast MRI. Kurtosis works as a marker of short term for tumor progression, capturing significant differences in the heterogeneous intensities distributions of the residual tumor in the MRI. A predictive model with a global accuracy of 70% and ROC AUC of 0.78 was developed based on a kurtosis threshold value. Although a large sample and the standardization of MRI acquisition protocol images could improve the statistical significance of the results, this study provided an insight into the understanding between Radiomics features and survival outcomes, that may help physicians in the clinical management of the patient.

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