Correlations of O^6-methylguanine DNA methyltransferase (*MGMT*) promoter methylation status with magnetic resonance imaging texture features and prognosis of glioblastomas

RUJIA WANG, ZHENGJUN SUN, JINGHUA SUN, MENHUA MA and HAIPING WANG

Department of Radiology, Tangshan Gongren Hospital, Tangshan, Hebei 063000, P.R. China

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Abstract. O6-methylguanine DNA methyltransferase (*MGMT*) promoter methylation is associated with the prognosis of patients with glioblastomas. With the aim of facilitating the discrimination of glioblastoma molecular phenotypes and improving the accuracy of molecular imaging diagnosis, the present retrospective study analyzed the association between *MGMT* promoter methylation and glioblastoma magnetic resonance imaging (MRI) texture features and prognosis. A total of 128 patients with pathologically diagnosed glioblastoma who had undergone preoperative MRI were enrolled. MRI texture features were extracted using 3D Slicer software and their relationship with *MGMT* promoter methylation was evaluated. In total, seven MRI texture features were significantly different between glioblastomas with methylated and unmethylated *MGMT* promoters-energy, entropy, uniformity, autocorrelation, and variance in gray level co-occurrence matrix, gray level non-uniformity and cluster shade. Glioblastomas with methylated and unmethylated *MGMT* promoters differed in tumor location, with the former predominantly located in the temporal lobe [Model I, area under the curve (AUC): 0.697]. Among MRI texture features, variance was significantly different between methylation groups (Model II, AUC: 0.838). Significant overall survival (OS) differences were noticed between patients with methylated and unmethylated *MGMT* promoters, between patients with preoperative Karnofsky performance status (KPS) scores ≥80 and <80, and among patients with glioblastoma who received radiotherapy, chemotherapy, or concurrent chemoradiotherapy. The seven MRI texture features may serve as independent predictors of prognosis for patients with glioblastoma with methylated *MGMT* promoters. MRI texture features demonstrated improved and more accurate diagnostic performance than MRI features regarding *MGMT* promoter methylation status prediction. For patients with glioblastoma with preoperative KPS scores ≥80, those with methylated *MGMT* promoters had significantly longer OS. Concurrent chemoradiotherapy had a significantly improved prognosis than either radiotherapy or chemotherapy alone. In summary, the present study provided a non-invasive, cost-effective method for detecting *MGMT* promoter methylation and can significantly contribute to personalized treatment planning for patients with glioblastoma, potentially improving their quality of life.

Correspondence to: Professor Zhengjun Sun, Department of Radiology, Tangshan Gongren Hospital, 27 Wenhua Road, Tangshan, Hebei 063000, P.R. China
E-mail: qq769183@163.com

Abbreviations: 95% CI, 95% confidence interval; AUC, area under the curve; CNS, central nervous system; FOV, field of view; GLCM, gray level co-occurrence matrix; GLN, gray level non-uniformity; HR, hazard ratio; KPS, Karnofsky performance status; MGMT, O^6-methylguanine DNA methyltransferase; MRI, magnetic resonance imaging; OR, odds ratio; OS, overall survival; T1WI, T1-weighted imaging; T1WI + C, contrast-enhanced T1WI; T2-FLAIR, T2-weighted fluid-attenuated inversion recovery; T2WI, T2-weighted imaging; TE, echo time; TR, repetition time

Key words: glioblastoma, IDH-1 mutation, MRI features, MGMT promoter methylation, texture analysisss

Introduction

Gliomas are the most common tumors of the central nervous system (CNS). The 2014 International Congress of Neuropathology added molecular findings to the diagnostic guidelines for brain tumors, whereas in 2016, the World Health Organization (WHO) classification standard introduced molecular features in the reclassification of CNS tumors (1). This included diffuse astrocytomas, oligodendrogliomas, ependymomas, choroid plexus tumors, neuronal and mixed neuronal-glial tumors, pineal region tumors and embryonal tumors (1). The 2021 edition of the classification standard highlighted the role of molecular diagnostics in the classification of CNS tumors (2). It integrated histological classification with molecular phenotypes, which included IDH-1, MGMT, 1p/19q, BRAF and ATRX. Glioblastomas are the most common malignant tumors of the CNS, accounting for 46% of all CNS tumors. Patients with glioblastomas have a relatively poor prognosis, with a five-year survival rate of <5% (3). Identifying specific molecular phenotypes is crucial for individualized treatment. One such molecular phenotype involves detecting methylation of the O6-methylguanine DNA methyltransferase (*MGMT*) promoter, which is associated with the glioblastoma prognosis (4-11). MGMT is

a DNA repair protein that reverses DNA damage caused by alkylating agents by removing the alkyl group from O^6-alkyl-guanine. When the *MGMT* promoter is hypermethylated, MGMT expression is silenced, leading to the absence of MGMT-mediated DNA repair. The alkylating agent temozolomide capitalizes on this lack of repair to improve the survival rates in patients with glioblastomas (12-15). However, the invasiveness of pathological biopsy and the high cost of detecting the methylation status of *MGMT* promoter, poses challenges for implementing individualized treatment in patients with glioblastomas. Glioblastomas with different genotypes exhibit vast heterogeneity on both genetic and histopathological levels, including intratumoral spatial variation in cellularity, angiogenesis, extravascular extracellular matrix and areas of necrosis (16-18). This high intratumoral heterogeneity of glioblastoma is an indicator of tumor malignancy, as it reflects areas of high cell density, necrosis, hemorrhage and mucoid degeneration. Intratumoral heterogeneity is also an important factor affecting prognosis and is related to tumor grade (19-21).

While glioblastoma heterogeneity cannot be discerned with the naked eye, MRI texture feature analysis is a valuable tool. In the present study, the 3D Slicer software was employed to analyze the magnetic resonance imaging (MRI) texture features of glioblastoma heterogeneity. The primary aim was to facilitate the discrimination of glioblastoma molecular phenotypes and improve the accuracy of molecular imaging diagnosis. This approach aims to provide patients with individualized treatment, predicting and improving their prognosis, and enhancing their quality of life.

Materials and methods

General information. A total of 128 patients who were pathologically diagnosed with glioblastoma at Tangshan Gongren Hospital (*Tangshan, China*) between June 2018 and September 2020 were enrolled in the *present* retrospective study. General clinical data included the age, sex, preoperative Karnofsky performance status (KPS) score, treatment method and overall survival (OS) *of patients*. Inclusion criteria were *as follows*: *i*) Patients with complete and reliable clinical, pathological and imaging data; *ii*) patients who did not undergo radiotherapy, chemotherapy, or other neoadjuvant therapies before surgery; and *iii*) patients pathologically diagnosed with glioblastoma after surgery. *The following* exclusion criteria were *applied*: *i*) Patients with a history of other malignant tumors; *ii*) patients with postoperative complications, such as intracranial hematoma or intracranial infection; and *iii*) patients who *succumbed due* to other causes. All biopsied specimens were tested for MGMT promoter methylation. In the study population, 79 patients had glioblastomas with methylated MGMT promoters, and 49 patients had glioblastomas with unmethylated MGMT promoters. All patients underwent conventional and contrast-enhanced MRIs. The Institutional Review Board of the Ethics committee at the Tangshan Gongren Hospital (Tangshan, China) granted an exemption to obtain informed consent due to the use of anonymous data (approval no. GRYY-LL-2020-44). The Ethics Committee exempted informed consent because of the retrospective nature of the present study.

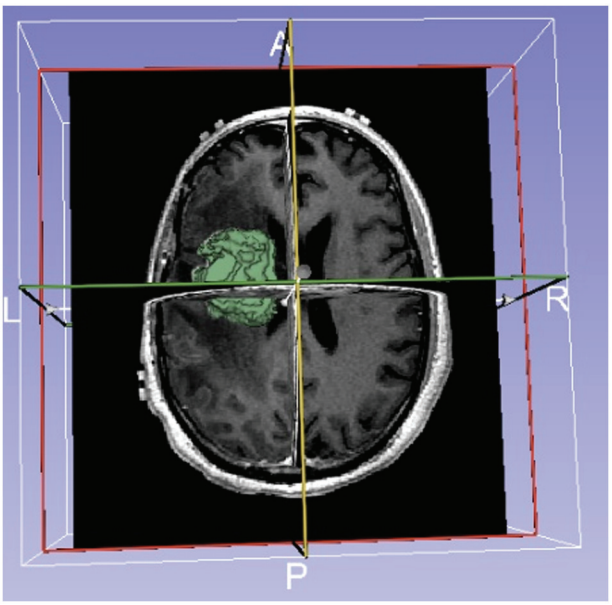

Figure 1. Schematic diagram of the 3D Slicer magnetic resonance imaging texture features for glioblastoma.

Detection of MGMT promoter methylation status. Nested methylation-specific polymerase chain reaction was performed to test the methylation status of the MGMT promoter. Assessment criteria were as follows: Samples with the corresponding fragments amplified using only the MGMT-U primer were unmethylated; samples with the corresponding fragments amplified using only the MGMT-M primer or both the MGMT-U and MGMT-M primers were methylated (22).

Testing methods. The Philips 3.0-T MRI scanner and 8-Channel Sense Head Coil were used on each patient to perform conventional and contrast-enhanced MRI including transverse T1-weighted (T1WI), transverse and sagittal T2-weighted (T2WI), transverse T2-weighted fluid-attenuated inversion recovery (T2-FLAIR), and contrast-enhanced T1WI (T1WI + C) imaging. Scan parameters were as follows. Transverse T1WI: repetition time (TR) 2,270 msec, echo time (TE) 20 msec, field of view (FOV) 196x196 mm, matrix 288x190, number of excitations 2, slice thickness 6 mm, interslice gap 1 mm. Transverse and sagittal T2WI: TR 2,500 msec, TE 90 msec, FOV 230x230 mm, matrix 420x306, number of excitations 2, slice thickness 6 mm, interslice gap 1 mm. Transverse T2-FLAIR: TR 8,000 ms, TE 120 msec, FOV 230x230 mm, matrix 304x216, number of excitations 2, slice thickness 6 mm, interslice gap 1 mm. T1WI + C: TR 200 msec, TE 2 msec, FOV 230x230 mm, matrix 256x256, number of excitations 2, slice thickness 6 mm, interslice gap 1 mm. For contrast-enhanced MRI, gadopentetate dimeglumine was injected intravenously at a dose of 0.1 ml/kg body weight and at a flow rate of 3 ml/sec.

Image processing. All patient MRI images were exported from the PACS workstation in DICOM format and imported into the 3D Slicer open-source software (version 4.4.0; available at: https://slicer.org/). First, three experienced neuroimaging experts extracted MRI texture features from the transverse

Table I. MRI texture analysis of *MGMT* promoter methylation status and glioblastoma heterogeneity.

A, MRI texture analysis of *MGMT* promoter methylation status and glioblastoma heterogeneity.

	MRI texture features	Methylated *MGMT* promoter (n=79)	Unmethylated *MGMT* promoter (n=49)	P-value
F1	Sphericity	0.372±0.106	0.391±0.116	0.505
F2	SRE	0.268±0.103	0.285±0.097	0.479
F3	RP	0.158±0.0470	0.173±0.054	0.227
F4	SRLGLE	0.268±0.103	0.285±0.097	0.479
F5	Surface Area mm^2	13969.933±9232.480	12279.785±7976.843	0.430
F6	Surface:Volume Ratio	0.497±0.208	0.538±0.266	0.474
F7	Compactness 1	30.676±13.806	29.745±17.756	0.807
F8	Maximum 3D Diameter	70.464±32.460	70.699±36.383	0.978

Data are presented as the mean ± standard deviation and were compared using the independent samples t-test. MGMT, O^6-methylguanine DNA methyltransferase; MRI, magnetic resonance imaging.

B, MRI texture analysis of *MGMT* promoter methylation status and glioblastoma heterogeneity.

	MRI texture features	Methylated *MGMT* promoter (n=79)	Unmethylated *MGMT* promoter (n=49)	P-value
F9	Energy	39.38	28.97	0.033
F10	Entropy	39.37	28.95	0.032
F11	Uniformity	39.30	28.86	0.030
F12	Volume mm^3	36.17	33.84	0.585
F13	Volume cc	36.13	33.45	0.584
F14	Compactness 2	33.70	36.80	0.527
F15	Spherical Disproportion	33.98	36.41	0.618
F16	Autocorrelation	39.54	29.80	0.035
F17	Cluster Prominence	39.40	28.86	0.300
F18	Cluster Tendency	39.43	28.90	0.310
F19	Difference Entropy	39.45	28.86	0.370
F20	Energy (GLCM)	39.48	28.83	0.340
F21	Entropy (GLCM)	30.55	41.14	0.390
F22	Homogeneity 1	39.42	28.98	0.330
F23	Sum Average	39.46	28.80	0.350
F24	Sum Entropy	30.55	41.14	0.360
F25	Sum Variance	39.51	28.94	0.390
F26	Variance (GLCM)	39.49	28.50	0.031
F27	LRE	37.18	32.00	0.290
F28	GLN	39.50	28.79	0.029
F29	RLN	37.78	31.17	0.177
F30	LRLGLE	37.58	32.13	0.280
F31	Cluster Shade	30.58	41.10	0.032

Data are presented as mean values and were compared using the Mann-Whitney U test. GLCM, gray level co-occurrence matrix; GLN, gray level non-uniformity; MGMT, O^6-methylguanine DNA methyltransferase; MRI, magnetic resonance imaging.

T1WI + C images using the Editor module in 3D Slicer. The regions of interest were delineated manually on each slice to ensure that the tumor boundaries were delineated as accurately as possible, and the three experts reached a consensus for the reconstruction of the three-dimensional tumor model (Fig. 1). Second, the three experts used the Heterogeneity CAD extension module to extract the MRI texture features of the tumors. Subsequent analyses were performed only when the intraclass correlation coefficient of the region of interest delineated by the three experts was >0.75. Finally, first-order statistics on

Table II. Relationship between *MGMT* promoter methylation and tumor location.

Molecular phenotype	Temporal lobe (%)	Frontal lobe (%)	Other lobes (%)	χ^2	P-value
MGMT				6.649	0.039
Methylated *MGMT* promoter	41 (52)	18 (23)	20 (25)		
Unmethylated *MGMT* promoter	17 (35)	22 (45)	10 (20)	-	-

MGMT, O^6-methylguanine DNA methyltransferase.

Table III. Binomial logistic regression model of the MRI features and texture features of *MGMT* promoter methylation.

Model	Feature	OR (95% CI)	P-value	AUC (95% CI)
Model I: MRI features	Tumor location (frontal lobe/temporal lobe)	0.277 (0.1000-0.766)	0.013	0.679 (0.503-0.893)
Model II: MRI texture features	F26: Variance (GLCM)	1.68 (1.030-1.582)	0.005	0.838 (0.701-0.976)

AUC, area under the curve; CI, confidence interval; GLCM, gray level co-occurrence matrix; MGMT, O^6-methylguanine DNA methyltransferase; MRI, magnetic resonance imaging; OR, odds ratio.

the following four aspects of MRI texture features were calculated: Morphology, shape, texture: gray level co-occurrence matrix (GLCM), and texture: Gray level run-length matrix.

Follow-up. Follow-up was mainly conducted through medical records reviews and telephone interviews. The follow-up queries included the following: Inquiring about postoperative survival status (death or survival) of the patient; for patients who had survived, inquiring about their general condition following postoperative radiotherapy and chemotherapy; for patients who had succumbed, inquiring about the specific cause of death; other information was determined from the medical records of patient. OS was defined as the period from the date of surgery to the date of the last follow-up or death.

Statistical analysis. Statistical analysis was performed using SPSS 22.0 (IBM Corp.). Among the variables obtained through the 3D Slicer program, those that were normally distributed and demonstrating homogenous variance were subjected to the independent samples t-test. By contrast, those with non-normal distributions or non-homogenous variance were subjected to the Mann-Whitney test, to analyze the association between MGMT promoter methylation status and glioblastoma MRI texture analysis. The Chi square test was performed on the relationship between glioblastomas with the methylated MGMT promoter and MRI features and location. P<0.05 was considered to indicate a statistically significant difference. Binomial logistic regression analysis was then performed to further analyze the predictive power of MRI features and texture analysis heterogeneity for MGMT promoter methylation. Receiver operating characteristic curves were generated to compare the diagnostic performance between these two methods. In addition, Kaplan-Meier univariate survival analysis was performed to analyze the factors affecting glioblastoma prognosis. The corresponding survival curves were plotted, and the log-rank test was performed. Finally, multivariate analysis was conducted using the Cox proportional hazards model to further analyze the relationship of the relevant factors with prognosis.

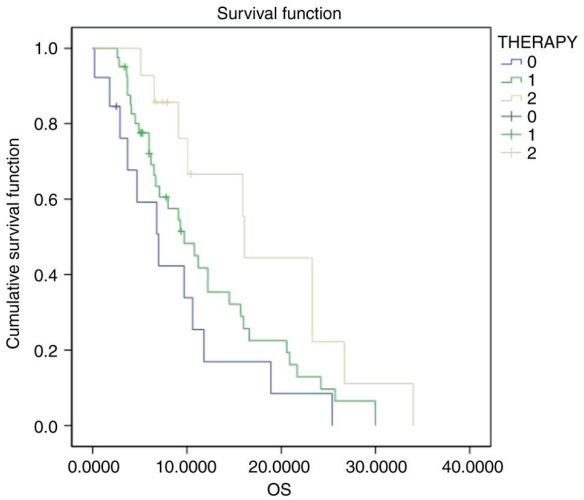

Figure 2. Comparison of the two models (O^6-methylguanine DNA methyltransferase promoter methylation). OS, overall survival.

Results

Relationship between MGMT promoter methylation status and glioblastoma MRI texture features. Comparisons were made between glioblastomas with methylated and unmethylated MGMT promoters using 31 texture features extracted with 3D Slicer. Among those, seven texture features showed statistically significant differences between the two groups (P<0.05): Energy, Entropy, Uniformity, Autocorrelation, Variance (GLCM), Gray Level Non-Uniformity (GLN), and Cluster Shade (Table IA and B).

Table IV. Factors affecting glioblastoma prognosis.

Factors	Number of patients	Median survival	SE	95% CI	χ^2	P-value
MGMT promoter						
Methylated	79	11.8	1.656	11.131-17.264		
Unmethylated	49	9.3	1.367	7.732-13.090	4.019	0.045
Age, years						
<60	52	9.1	2.063	8.557-16.644		
≥60	76	10.8	1.334	10.287-15.515	0.231	0.631
Sex						
Female	58	9.7	1.324	8.954-14.145		
Male	70	12.2	1.920	10.383-17.910	1.103	0.294
Preoperative KPS score						
≥80	54	24.2	1.617	20.914-27.255		
<80	68	7.1	0.727	6.583-9.433	34.163	<0.001
NA	6					
Treatment method						
Radiotherapy	33	7.0	2.120	4.587-12.897		
Chemotherapy	26	9.7	1.369	9.446-14.814		
Concurrent chemoradiotherapy	69	16.1	2.85	12.550-23.720	6.706	0.035

The results of the Kaplan-Meier univariate survival analysis are shown. CI, confidence interval; KPS, Karnofsky performance status; MGMT, O^6-methylguanine DNA methyltransferase; NA, not applicable; SE, standard error.

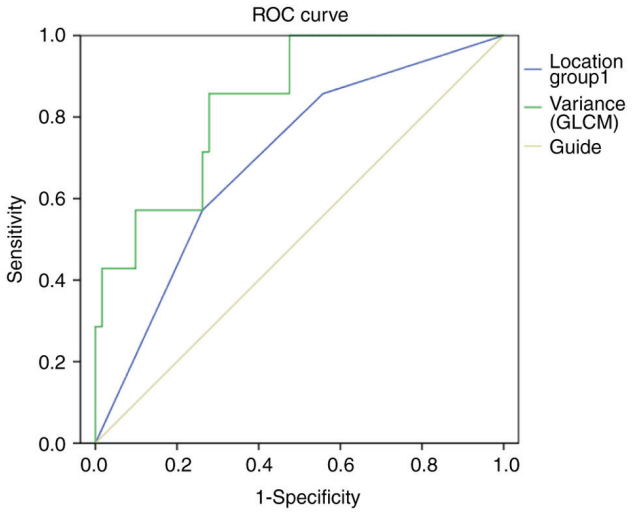

Figure 3. Survival curves according to *MGMT* promoter methylation. Patients with glioblastoma with methylated *MGMT* promoters have significantly longer overall survival than those with unmethylated *MGMT* promoters. MGMT, O^6-methylguanine DNA methyltransferase; ROC, receiver operating characteristic; GLCM, gray level co-occurrence matrix.

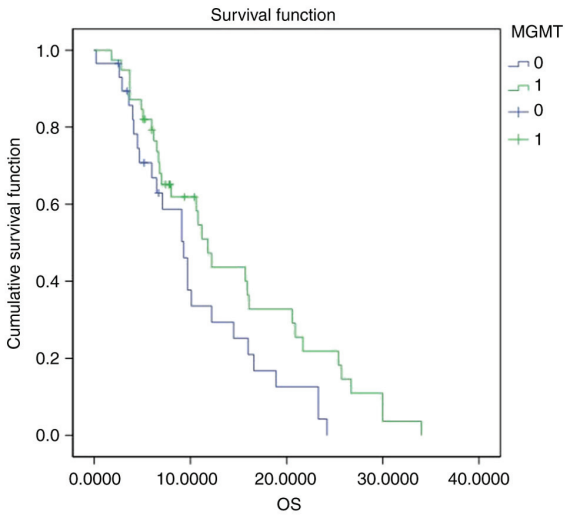

Figure 4. Survival curves according to preoperative KPS score. Patients with preoperative KPS scores ≥80 have significantly longer OS. KPS, Karnofsky performance status; OS, overall survival; MGMT, O^6-methylguanine DNA methyltransferase.

Relationship between MGMT promoter methylation and tumor location. The analysis revealed that glioblastomas with methylated MGMT promoters were predominantly located in the temporal lobe (Table II), with significant differences in the tumor location between the two groups (P=0.039).

Binomial logistic regression model and receiver operating characteristic (ROC) curve analysis. In the logistic regression model, glioblastomas with methylated MGMT promoters were primarily located in the temporal lobes [Model I, odds ratio (OR): 0.277, 95% confidence interval (95% CI): 0.100-0.766, P=0.013], which showed an area under the curve (AUC) of 0.679 (95% CI: 0.503-0.893). MRI texture analysis showed a significant difference in Variance (GLCM) (Model II, OR: 1.68, 95% CI, 1.030-1.582, P=0.005), with an AUC of 0.838 (95% CI, 0.701-0.976). Consequently, Model II demonstrated

Table V. Factors affecting glioblastoma prognosis.

Factors	n (%)	HR (95% CI)	P-value
MGMT promoter			
Methylated	79	References	
Unmethylated	49	1.630 (0.474,5.608)	0.439
Age, years			
<60	52	References	
≥60	76	1.901 (0.991, 3.648)	0.053
Sex			
Male	58	References	
Female	70	0.698 (0.377,1.292)	0.252
Preoperative KPS score			
<80	54	References	
≥80	68	2.315 (1.075,4.987)	0.032
NA	6	-	-
Treatment method			
Radiotherapy	33	References	
Chemotherapy	26	2.010 (0.930,4.344)	0.076
Concurrent chemoradiotherapy	69	2.817 (1.086,7.306)	0.033

The results of multivariate survival analysis based on the Cox proportional hazards model are shown. CI, confidence interval; HR, hazard ratio; KPS, Karnofsky performance status; MGMT, O^6-methylguanine DNA methyltransferase; NA, not applicable.

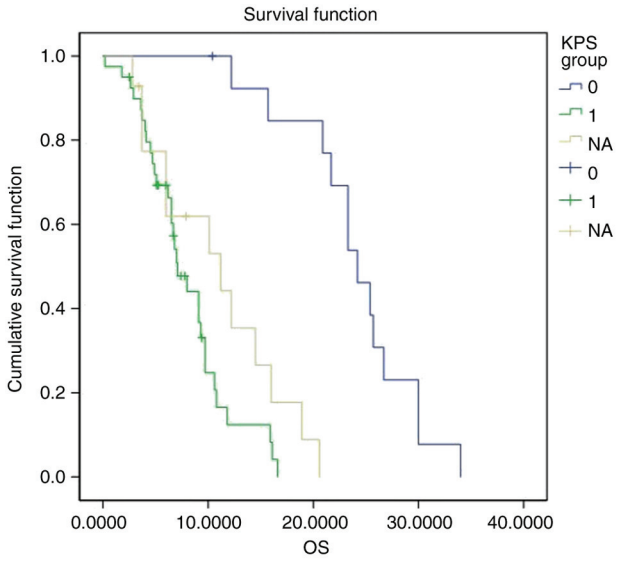

Figure 5. Survival curves according to treatment methods. Patients who received concurrent chemoradiotherapy have a significantly longer OS than those who received either radiotherapy or chemotherapy alone. OS, overall survival; KPS, Karnofsky performance status.

significantly improved diagnostic performance than that of Model I (Fig. 2, Table III).

Factors affecting glioblastoma prognosis. Kaplan-Meier univariate survival analysis results are shown in Table IV. Briefly, a significant difference in OS between glioblastomas with methylated and unmethylated MGMT promoters was noticed (P=0.045; Fig. 3). The median survival for patients with methylated MGMT promoters was 11.8 months, whereas for patients with the unmethylated MGMT promoters the median survival time was 9.3 months. Thus, glioblastoma with methylated MGMT promoters had a significantly longer OS. When comparing patients with preoperative KPS scores ≥80 to those with scores <80, the median survival was 24.2 months for the former and 7.1 months for the latter, with a statistically significant difference (P<0.001). Thus, patients with preoperative KPS scores ≥80 had a longer OS (Fig. 4). Among the treatment groups, 33 patients received radiotherapy, 26 received chemotherapy, and 69 received concurrent chemoradiotherapy. The differences in OS among the three groups were statistically significant (P=0.035), with a median survival of 7.0 months for radiotherapy, 9.7 months for chemotherapy and 16.1 months for concurrent chemoradiotherapy. Thus, patients who received concurrent chemoradiotherapy had a significantly longer OS than those who received either radiotherapy or chemotherapy alone (Fig. 5). No significant differences in OS were found based on age, sex, or glioblastoma subtype.

Multivariate survival analysis. Multivariate survival analysis using the Cox proportional hazards model (Table V) showed the following results: The difference in OS between patients with preoperative KPS scores ≥80 and <80 was significant (P=0.032), with a hazard ratio (HR) of 2.315 and a 95% CI of 1.075-4.987. The OS among patients receiving different postoperative adjuvant therapies (radiotherapy, chemotherapy, or concurrent chemoradiotherapy) also showed a significant difference (P=0.033), with an HR of 2.817 and a 95% CI of 1.086-7.306. Patients receiving concurrent chemoradiotherapy had a significantly longer OS than that of patients receiving

only radiotherapy or chemotherapy. No significant differences in glioblastoma prognosis were observed based on MGMT promoter methylation, age and sex.

Discussion

Owing to the extremely high malignancy and high invasiveness of glioblastoma, it has been difficult to achieve satisfactory outcomes using radiotherapy, chemotherapy, or concurrent chemoradiotherapy. Using the 3D Slicer, a visualization and data analysis tool used in MRI studies, the MRI texture features of glioblastoma with methylated and unmethylated MGMT promoters were compared. The present results identified seven MRI texture features [Energy, Entropy, Uniformity, Autocorrelation, Variance (GLCM), GLN and Cluster Shade] that showed significant differences between the two groups.

MGMT has been shown to be closely linked to glioblastoma (4-11). Different molecular phenotypes of glioblastoma can reflect the different biological states and processes of the body (23). Current literature suggests that the location of intracranial gliomas is related to the origin of the tumor cell genetic phenotype, and hence there is some correlation between tumor location and molecular phenotype (24). The current findings revealed a significant difference in tumor location between glioblastomas with methylated and unmethylated *MGMT* promoters, with the former mostly located in the temporal lobe. This observation is consistent with the results obtained by Li *et al* (25) and may be related to the origin and genetic alterations of mutations in *MGMT* promoter methylation. It mainly refers to texture features on T2-weighted images assessed by the space-frequency analysis, which were significantly different between methylated and unmethylated cases by Drabycz *et al* (26). The present retrospective study analyzed the correlation of MGMT promoter methylation with glioblastoma MRI texture features and prognosis. Although there are similarities between these two studies, there are still some differences.

Previously, Kickingereder *et al* (27) demonstrated the correlation between MRI texture features and molecular characteristics. However, the reliability and accuracy of software analysis used in such studies still require further improvement. In fact, only a few MRI studies have analyzed glioblastoma heterogeneity, and currently, there is no uniform standard among the software used. Currently available software includes OsiriX, MaZda and 3D Slicer. Among these, OsiriX is proprietary software dedicated to the Apple system, with special requirements for the imported data type and device model. Although MaZda is open-source software, it can only extract tumor information on a two-dimensional level and delineate tumor information layer by layer on images stored in the BMP format, which inevitably leads to loss of tumor information. 3D Slicer is one such open-source, freely available software used in the analysis and interpretation of medical imaging data. Over the past 20 years, the US National Institutes of Health (NIH) has allocated multiple grants for the creation of 3D Slicer, with the aim of achieving powerful medical image processing capabilities. This visualization and data analysis tool is extensible and has powerful plug-in capabilities, enabling the addition of algorithms and application programs. 3D Slicer is able to reconstruct the tumor volume in three-dimensional space, thereby capturing all available information about the tumor and minimizing the loss of tumor information. Egger *et al* (28) found that using the 3D Slicer semi-quantitative segmentation tool can improve the reliability of glioblastoma segmentation, overcoming the effects of human factors, and enabling the quantification of texture parameters while also yielding more intuitive and accurate values. By utilizing the Heterogeneity CAD extension module of 3D Slicer, 31 texture features of tumor heterogeneity were extracted. A total of seven MRI texture features with significant differences were identified between glioblastomas with methylated and unmethylated *MGMT* promoters. These features included Energy, Entropy, Uniformity, Autocorrelation, Variance (GLCM), GLN and Cluster Shade. *MGMT* promoters with variance showed particularly strong diagnostic performance. Glioblastomas with methylated *MGMT* promoters were frequently found in the temporal lobe. The present study also found that patients with higher preoperative KPS scores and those receiving concurrent chemotherapy have improved OS. Such findings raise the hope that texture features extracted using 3D Slicer can facilitate determining the *MGMT* promoter methylation status in patients with glioblastomas. The main texture features commonly used in clinic are energy, entropy and autocorrelation. Among them, energy is mainly related to the differences in the heterogeneity of tumor cells, which mainly reflects the arrangement of tumor cells. Entropy is a widely used texture feature in clinical practice and plays an important role in the diagnosis and treatment of various malignant tumors. Texture analysis based on T1WI-enhancement is expected to provide some help in identifying the methylation status of *MGMT* promoter in patients with GBM. By understanding the texture characteristics of magnetic resonance, the limitations of human eyes in evaluating tumors are overcome. At the same time, the results of texture analysis were quantified by quantitative extraction of parameters related to tumor heterogeneity.

Overall, the findings of the present study suggested that MRI texture analysis is a valuable, non-invasive, less-expensive method for detecting *MGMT* promoter methylation and personalizing treatment, potentially improving patient outcome. Despite providing such valuable information, this was a single-center study with a small sample size. Therefore, selection bias cannot be ruled out. Future studies should involve multicenter cooperation to verify the results of the present study.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

RW collected and analyzed data, post-processed imaging data, performed literature review and follow-up, and wrote the manu-

script. ZS and HW confirm the authenticity of all the raw data, designed the project and revised the manuscript. JS and MM analyzed imaging data and performed statistical analysis. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The Institutional Review Board of the Ethics committee at the Tangshan Gongren Hospital (Tangshan, China) granted an exemption to obtain informed consent due to the use of anonymous data (approval no. GRYY-LL-2020-44). The Ethics Committee exempted informed consent because of the retrospective nature of the present study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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