European Review for Medical and Pharmacological Sciences 2022; 26: 8823-8831

Discriminating glioblastoma from solitary brain metastases on 3 Tesla magnetic resonance imaging: the roles of fractional anisotropy and mean diffusivity

D.-H. NGUYEN[1,2], T.-D. LE[2,3], H.-V. NGUYEN[1], V.-A. NGUYEN-THI[1], D.-H. NGUYEN[4], H. DONG-VAN[5], M.-D. NGUYEN[6]

[1]Department of Radiology, Hanoi Medical University, Hanoi, Vietnam
[2]Department of Radiology, Viet Duc Hospital, Hanoi, Vietnam
[3]Department of Radiology, VNU University of Medicine and Pharmacy, Vietnam National University, Hanoi, Vietnam
[4]Department of Radiology, Ha Dong General Hospital, Hanoi, Vietnam
[5]Department of Neurosurgery, Viet Duc Hospital, Hanoi, Vietnam
[6]Department of Radiology, Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam

Nguyen Duy Hung and Nguyen Minh Duc contributed equally to this article as co-first authors

Abstract. – OBJECTIVE: This study determined the diagnostic value of diffusion tensor imaging (DTI) sequences using fractional anisotropy (FA) and mean diffusivity (MD) for discriminating glioblastoma (GBM) from solitary brain metastases (SBM) using 3 Tesla magnetic resonance imaging (MRI).

PATIENTS AND METHODS: A retrospective study was conducted, including 40 patients who underwent biopsy or surgery and received a histological diagnosis of GBM or SBM between August 2020 and December 2021. All preoperative examinations were performed on 3 Tesla MRI using conventional and DTI sequences. Three regions of interest (ROIs) were placed to measure a solid tumor component, peritumoral edema, and the opposite normal white matter to evaluate FA and MD values. Parametric and nonparametric statistical tests were used to determine differences between GBM and SBM. The diagnostic value of significantly different parameters between the two tumor entities was analyzed using the receiver operating characteristic (ROC) curve.

RESULTS: The FA value for peritumoral edema (eFA) in GBM cases was significantly larger than that in SBM cases ($p < 0.05$), with no significant difference in MD values. The FA and MD values for the solid tumor component (sFA and sMD, respectively) and the ratio of the sFA value to the FA value of the opposite normal white matter (rFAs/n) in GBM cases were significantly larger than those in SBM cases ($p < 0.05$). Combining the sFA and sMD values provided the highest area under the ROC curve (AUC) value of 0.96, with a sensitivity, specificity, positive predictive value, and negative predictive value of 85.2%, 100%, 85.2%, and 87.1%, respectively, for distinguishing GBM from SBM.

CONCLUSIONS: MRI parameters, including sFA, sMD, eFA, and rFAs/n, are useful for differentiating between GBM and SBM. The combination of sFA and sMD may increase the diagnostic performance of MRI for these two tumor entities.

Key Words:
Diffusion tensor imaging, Glioblastoma, Solitary brain metastases, Magnetic resonance imaging, 3 Tesla.

Introduction

Glioblastomas (GBM) and brain metastases are the most common brain tumors identified in adults, with GBM accounting for 54% of gliomas and 16% of intracranial tumors and metastases accounting for approximately 20% of intracranial tumors[1]. Among brain metastases, 25%-30% are solitary masses[2]. GBM and solitary brain metastases (SBM) differ greatly in terms of tumor nature, clinical stage, treatment plan, and prognosis, and the correct differential diagnosis between these two tumor entities is crucial for developing an appropriate treatment strategy[3]. However, both tumor types typically present with nonspecific clinical manifestations, including focal neurological signs and intracranial hypertension. In addition, these two tumor types also share similar imaging characteristics on conventional magnetic resonance imaging (MRI), such as central necro-

Corresponding Author: Nguyen Minh Duc, MD; e-mail: bsnguyenminhduc@pnt.edu.vn

sis, irregular border enhancement, and extensive peritumoral edema[4], resulting in misdiagnosis in up to 40% of cases[5].

Diffusion tensor imaging (DTI) is a non-invasive technique for investigating anisotropic diffusion and the diffusion intensity of water molecules in axons. Quantitative metrics, including fractional anisotropy (FA) and mean diffusivity (MD), are influenced by microstructural changes in damaged brain tissue. Differences in the histopathological characteristics of the solid tumor components and peritumoral regions of GBM and SBM have been associated with differences in FA and MD values. Some studies[6] show that FA reflects the directional organization of microstructural components and glial cells that produce extracellular matrix, resulting in high anisotropy and increased FA values. The peritumoral region of GBM is characterized by both vasogenic edema and infiltration, whereas SBM is characterized by only vasogenic edema. In addition, SBM typically features reduced cell and blood vessel density compared with the normal brain parenchyma, allowing for an increase in the extracellular fluid volume, which can result in increased MD and decreased FA values[7]. DTI can also identify morphological changes in white matter tracts, which represents important information when planning the surgical approach for the resection of intraparenchymal tumors.

Although previous studies[4,8-11] have examined the use of DTI using 1.5 Tesla MRI for the differential diagnosis of GBM from SBM, the results were controversial. Some studies suggest that the signal-to-noise ratio of 3 Tesla MRI is twice that of 1.5 Tesla MRI, resulting in smaller variance and higher accuracy when calculating FA and MD values[12]. Therefore, this study determined the differences in FA and MD values between GBM and SBM on 3 Tesla MRI.

Patients and Methods

Study Population

This retrospective study included 40 patients (27 men and 13 women) with histopathological confirmed GBM or SBM (based on surgery or biopsy samples) who were treated at Viet Duc Hospital, Hanoi, Vietnam, from August 2020 to December 2021. All patients are preoperatively examined using 3 Tesla MRI with conventional and DTI sequences. The patients were divided into two groups based on the pathological results: GBM (27 patients) and SBM (13 patients). Ethical clearance was obtained from the institutional ethics committee (Ref: 2682/QD-ĐHYHN dated 13 July 2021), and the informed consent of patients was waived. The study was in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013.

MRI Technique

All preoperative examinations were conducted on a 3 Tesla MRI (GE SIGNA Pioneer, GE Healthcare, Chicago, IL, USA) using a head coil with conventional sequences, including axial or sagittal T1-weighted image (T1W, repeat time [TR]/echo time [TE]: 2,325/25 ms), fluid-attenuated inversion recovery (FLAIR, TR/TE: 8,500/117 ms), axial T2 gradient echo (T2 GE), axial diffusion-weighted imaging (DWI, TR/TE: 5,202/78 ms, 116 × 116 matrix, 5 mm slice thickness) with apparent diffusion coefficient map reconstruction. Contrast agents were administered using a 0.1 mmol/kg dose, intravenously injected using an 18-20G needle, followed by 3-plane T1 imaging reconstruction.

The DTI sequence was performed using a single-shot echo-planar imaging sequence on the axial plane with the following parameters: 4 mm slice thickness; 0.4 mm slice space; number of excitations (NEX), 1; TR/TE, 7,000/84 ms; matrix 128 × 128; field of view (FOV) 260 × 260; 27 diffusion directions; and *b*-values of 0 and 1,000 s/mm^2. The acquisition time was 3 minutes.

Image Analysis

All images were transferred to Workstation 4.7 to generate FA and MD maps. On the FA map, using a *b*-values of 1000 s/mm^2, one of our radiologists with over 10 years of neurological experience who was blinded to the histopathological results created three regions of interest (ROIs, 15-30 mm^2) based on T1W pre- and post-contrast, T2 GE, and FLAIR images. The 3 ROIs were positioned on the solid tumor component, peritumoral edema, and opposite normal white matter. The first ROI was placed in a solid tumor region that appeared hypointense on T1W and hyperintense on T2-weighted imaging (T2W), with the strongest enhancement on T1W post-contrast images. Areas containing bleeding (which appear hyperintense on T1W and hypointense on T2 GE), calcifications (which appear hypointense on all sequences), cysts (which appear hypointense on T1W, hyperintense on FLAIR, with no contrast

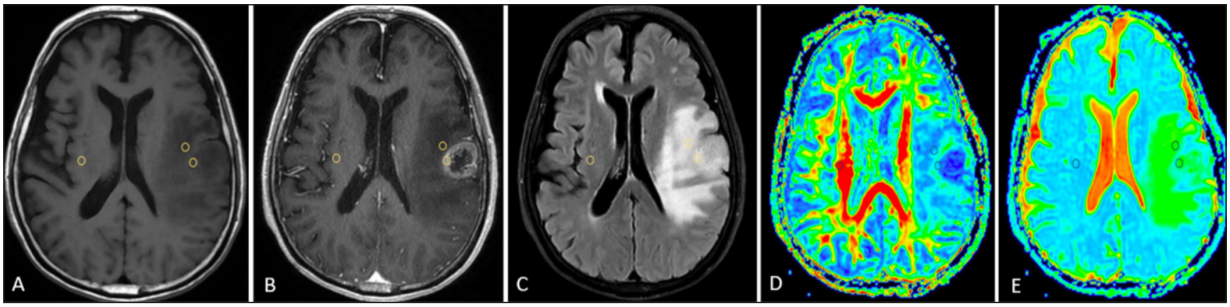

Figure 1. A 71-year-old man with a right frontal GBM. Pre-contrast T1-weighted T1W (**A**), post-contrast T1W (**B**), and axial fluid-attenuated inversion recovery (**C**) images show a heterogeneous tumor with central necrosis, ring enhancement, and peritumoral infiltration. Three regions of interest were placed in a solid tumor component, the peritumoral region, and the opposite normal white matter and measured using the FA (**D**) and MD maps (**E**).

enhancement), or blood vessels were avoided when selecting the ROI. The second ROI was placed in the peritumoral edema (or adjacent to the tumor, in cases with no clear edematous area), which appears as hyperintense on FLAIR and hypointense on T1W with no enhancement on T1W post-contrast images. The third ROI was placed in the opposite normal white matter region on the same slice containing the lesion. All ROIs were placed on the FA map, which was synchronized with the MD map. The ratios of FA and MD values among the solid tumor region, the peritumoral edema region, and the opposite normal white matter region were calculated to obtain relative FA (rFA) and MD (rMD) values (Figures 1 and 2).

Statistical Analysis

Data were analyzed using SPSS 20.0 software (IBM Corp., Armonk, NY, USA). Qualitative parameters are presented as the number (n) and percentage (%), and quantitative parameters are presented as the mean ± standard deviation. The normal distribution of the variables was tested using the Shapiro-Wilk test, histograms, and boxplots. The Mann-Whitney U test and Student's *t*-test were used to compare differences between GBM and SBM for non-normally distributed and normally distributed variables, respectively. Significance was accepted at $p < 0.05$. Finally, combinations of significantly different variables were tested to determine the ability to combine parameters to increase diagnostic value.

The receiver operating characteristic (ROC) curve was analyzed for significantly different parameters and combinations of parameters to identify diagnostic cutoff points for distinguishing GBM from SBM.

Results

A total of 40 patients, including 27 diagnosed with GBM and 13 diagnosed with SBM (11 with lung metastases and 2 with unknown origins), were enrolled in this study. The study population included 27 men and 13 women,

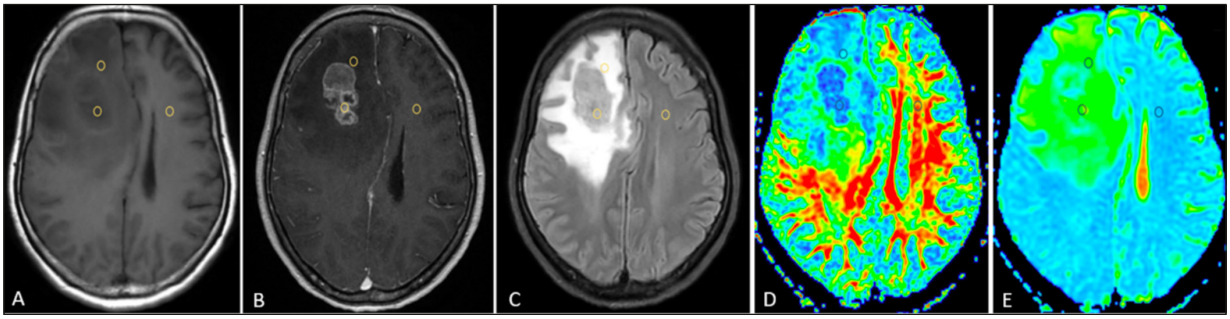

Figure 2. A 50-year-old woman with right frontal solitary brain metastases originating from lung cancer. Pre-contrast T1-weighted T1W (**A**), post-contrast T1W (**B**), and fluid-attenuated inversion recovery (**C**) images show a tumor with strong and heterogeneous enhancement and moderate peritumoral edema. Three regions of interest were placed in a solid component of the tumor, the peritumoral edema region, and the opposite normal white matter and measured using the FA (**D**) and MD (**E**) maps.

Table I. Patient characteristics.

Characteristics		Tumor		*p*-value
		GBM (n = 27)	SBM (n = 13)	
Age		58 (19–81)	59 (50–71)	0.732
Sex	**Male**	20 (74.1%)	7 (53.8%)	
	Female	7 (25.9%)	6 (46.2%)	0.284
	Total	27 (67.5%)	13 (32.5%)	

GBM, glioblastoma; SBM, solitary brain metastases. *p*-value for age determined by Mann-Whitney U test; *p*-value for sex determined by Fisher's exact test

aged 19 to 81 years, with a mean age of 59.50 ± 10.76 years.

Table I shows that no significant differences were found in age or sex distributions between GBM and SBM cases ($p > 0.05$).

Table II shows the absolute and relative FA and MD values in the solid tumor component, the peritumoral edema region, and the ratios of the values in these regions to the values measured in the normal white matter for both GBM and SBM. Table III shows the cutoff value, area under the curve (AUC), sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of the significantly different parameters between GBM and SBM.

No significant differences were observed between GBM and SBM for the MD of the peritumoral edema region (eMD), the ratio between the MD values of the solid tumor and the normal white matter (rMDs/n), the ratio between the FA values of the peritumoral edema region and the normal white matter (rFAe/n), or the ratio between the MD values of the peritumoral edema region and the normal white matter (rMDe/n).

A significant difference was found in the FA value of the solid tumor (sFA, $p < 0.001$) between GBM (0.162 ± 0.065) and SBM (0.069 ± 0.031). The AUC for sFA was 0.93 (Figure 3). A cutoff value of 0.108 was established as the threshold for differentiating between GBM and SBM, with Se, Sp, PPV, and NPV of 81.5%, 92.3%, 91.4%, and 83.3%, respectively.

A significant difference was found in the MD value of the solid tumor (sMD; $p = 0.043$) between GBM (1.114 ± 0.312) and SBM (0.910 ± 0.221). The AUC for sMD was 0.70 (Figure 3). A cutoff value of 0.990 was established for differentiating between GBM and SBM, with Se, Sp, PPV, and NPV of 70.4%, 61.5%, 64.6%, and 67.5%, respectively.

A significant difference was found for the mean FA value for the peritumoral edema region (eFA) between GBM (0.256 ± 0.112) and SBM (0.166 ± 0.061). The AUC for eFA was 0.75 (Fig-

Table II. The FA and MD values measured in solid tumor components, peritumoral edema regions, and opposite normal white matter in GBM and SBM.

Parameters	GBM	SBM	*p*-value
sFA	0.162 ± 0.065	0.069 ± 0.031	**<0.001***
sMD	1.114 ± 0.312	0.910 ± 0.221	**0.043***
eFA	0.256 ± 0.112	0.166 ± 0.061	**0.012***
eMD	1.373 ± 0.294	1.518 ± 0.259	0.137
rFAs/n	0.314 ± 0.184	0.135 ± 0.061	**<0.001***
rMDs/n	1.462 ± 0.439	1.233 ± 0.330	0.104
rFAe/n	0.479 ± 0.219	0.328 ± 0.138	0.052
rMDe/n	1.795 ± 0.403	2.044 ± 0.389	0.072

FA, fractional anisotropy; MD, mean diffusivity; GBM, glioblastoma; SBM, solitary brain metastases; sFA, solid tumor component FA value; sMD, solid tumor component MD value; eFA, peritumoral edema FA value; eMD, peritumoral edema MD value; rFAs/n, ratio of solid tumor FA value to normal white matter FA value; rMDs/n, ratio of solid tumor MD value to normal white matter MD value; rFAe/n, ratio of edema FA value to normal white matter FA value; rMDe/n, ratio of edema MD value to normal white matter MD value. MD is presented in 10^{-3} mm^2/sec. *significant difference ($p < 0.05$).

Table III. The diagnostic performance of significantly different parameters between GBM and SBM.

Parameters	Cutoff	AUC	Se (%)	Sp (%)	PPV (%)	NPV (%)
sFA	0.108	0.93	81.5	92.3	91.4	83.3
sMD	0.990	0.70	70.4	61.5	64.6	67.5
eFA	0.210	0.75	66.7	69.2	68.4	67.5
rFAs/n	0.182	0.90	85.2	84.6	84.7	85.1
sFA + sMD		0.96	85.2	100	85.2	87.1
sFA + sMD + eFA + rFAs/n		0.96	77.8	100	77.8	81.8

AUC, area under the receiver operator characteristic curve; Se, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; FA, fractional anisotropy; MD, mean diffusivity; sFA, solid tumor component FA value; sMD, solid tumor component MD value; eFA, peritumoral edema FA value; rFAs/n, ratio of solid tumor to normal white matter FA values.

ure 3). A cutoff value of 0.210 was established as the threshold for differentiating between GBM and SBM, with Se, Sp, PPV, and NPV of 66.7%, 69.2%, 68.4%, and 67.5%, respectively.

The mean ratio between FA values of the solid tumor and the normal white matter (rFAs/n) in GBM was 0.314 ± 0.184, whereas the mean rFAs/n in SBM was 0.135 ± 0.061, which was a significant difference ($p < 0.001$). The AUC of rFAs/n was 0.90 (Figure 3). A cutoff value of 0.182 was established as the threshold for differentiating between GBM and SBM, with Se, Sp, PPV, and NPV of 85.2%, 84.6%, 84.7%, and 85.1%, respectively.

The combination of all four significantly different metrics (sFA, sMD, eFA, and rFAs/n) resulted in an AUC of 0.96 (Figure 3). The Se, Sp, PPV, and NPV of this combinatio n were 77.8%, 100%, 77.8%, and 81.8%, respectively.

When the two metrics, sFA and sMD, were combined, the AUC was 0.96 (Figure 4). The Se, Sp, PPV, and NPV of this combination were 85.2%, 100%, 85.2%, and 87.1%, respectively.

Discussion

DTI evolved from DWI, which obtains the direction and magnitude of water movements to estimate the structural integrity of white matter fibers in the central nervous system. FA is a measurement of the anisotropic tendency of water to diffuse and ranges from 0 (isotropy) to 1 (anisotropy in normal neurons), whereas MD is the mean diffusion coefficient in all directions[13]. Damage to axonal membranes may affect both FA and MD values. Several studies[8,10] have shown significant decreases in FA values and increases in MD values in solid tumor regions compared with those in normal white matter.

sFA may be higher in GBM than in SBM because FA is directly proportional to tumor cellularity and vascularity, and GBM cells produce specific extracellular matrix components, leading to high anisotropy and increasing the FA value[8]. Wang et al[14] reported that the solid tumor regions of GBM displayed significantly increased FA compared with those in SBM ($p < 0.001$), with an AUC of 0.784. In a separate study, Wang et al[15] also measured FA values in 4 tumoral regions: a center region, an enhancing region, an immediately peritumoral region, and a distant peritumoral region, which showed that FA values in GBM measured in areas of tumor enhancement were approximately 34% higher than those for similar regions of SBM, with an AUC of 0.9. In a third study, Wang et al[16] defined an FA cutoff value of 0.13 for the tumor enhancement region, which resulted in an AUC of 0.84, with Se, Sp, PPV, and NPV of 80%, 76%, 80%, and 73%, respectively, for distinguishing between GBM and SBM. Our study showed that the sFA had the highest AUC of 0.93 using a cutoff value of 0.108, which resulted in Se, Sp, PPV, and NPV of 81.5%, 92.3%, 91.4%, and 83.3%, respectively, for distinguishing between GBM and SBM.

The MD value characterizes the diffusion of water molecules in the tissue, often associated with changes in cell density. Our study showed that the sMD of GBM was significantly higher than that of SBM, with mean values of 1.114 ± 0.312 and 0.910 ± 0.221, respectively. A cutoff value of 0.990 for this parameter allowed for the differentiation between GBM and SBM with a Se of 70.4% and a Sp of 61.5%. This result was similar to the study reported by Byrnes et al[9], who found sMD values for GBM and SBM of 1.220 ± 0.284 and 0.980 ± 0.188, respectively. Byrnes et al[9] stated that the presence of degenerative microcysts in GBM, featuring varying degrees of ne-

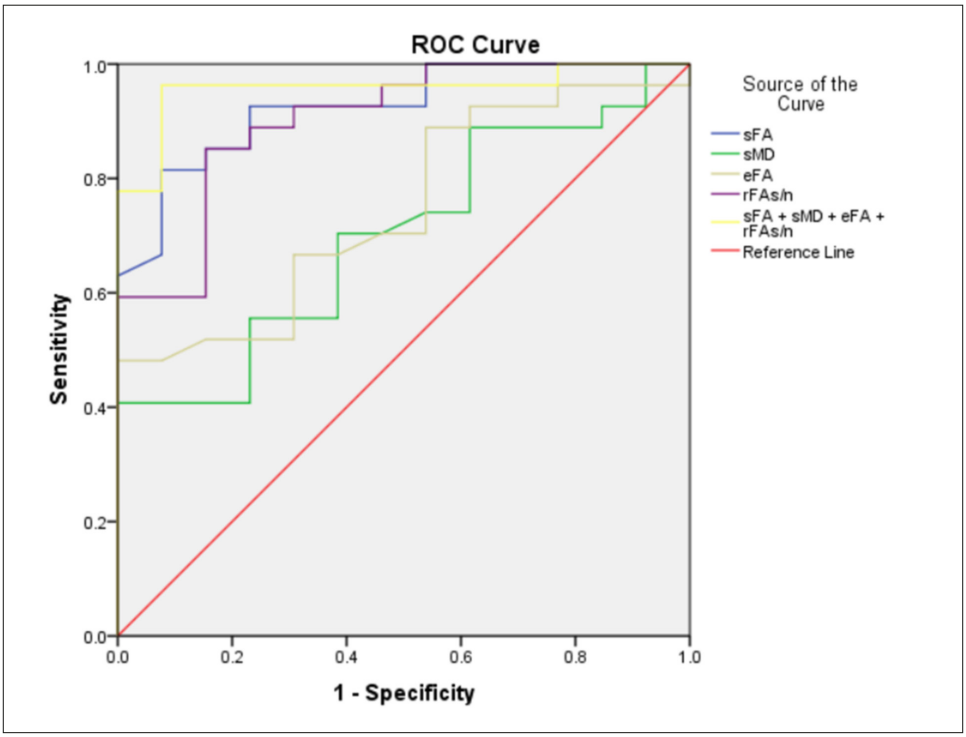

Figure 3. Receiver operating characteristic curve using FA value of the solid tumor (sFA), MD value of the solid tumor (sMD), FA value of the peritumoral edema (eFA), the ratio of FA values between the solid tumor and the normal white matter (rFAs/n), and the combination of these parameters for differentiating between glioblastoma (GBM) and solitary brain metastases (SBM).

crosis or hemorrhage, could be responsible for the difference between these two tumors. By contrast, some studies did report significant differences in MD values between tumor types[4,6,16-18].

Tumors can be found in various locations of the brain parenchyma, including the gray matter, subcortical white matter, and deep white matter, leading to changes in FA and MD values. Therefore, we calculated the relative ratios of FA and MD measured in the tumor and peritumoral regions compared with the opposite normal white matter to reduce inaccuracies. Our results showed that rFAs/n of GBM was significantly higher than that of SBM, with an AUC of 0.9, and a cutoff value of 0.182 resulted in a Se of 85.2% and a Sp of 84.6% for distinguishing between these two tumor types. GBM showed a significantly increased sMD value compared with that of SBM ($p = 0.043$), but no significant difference in rMDs/n was observed between the two tumors ($p = 0.104$). Tan et al[18] also demonstrated a change in the diagnostic accuracy for the peritumoral edema MD value alone and when reported relative to the normal white matter, with p-values of 0.057 and 0.042, respectively.

Some studies have focused on the peritumoral edema region to differentiate between GBM and SBM, as this area is thought to be associated with tumor cell infiltration in GBM, whereas the peritumoral region of SBM is thought to consist of pure edema, with no tumor cell infiltration[19]. However, controversial results have been reported for both eFA and eMD values, likely due to differences in how the peritumoral edema region is defined, which affects the placement of ROIs across studies[9]. Tumor cell infiltration in GBM can cause the destruction of nerve fiber tracts, leading to increased anisotropy and resulting in higher eFA in GBM than in SBM. The studies by Byrnes et al[9] and Wang et al[15] showed eFA values in GBM were significantly higher than those in SBM ($p < 0.005$). We also found a significantly higher mean eFA in GBM than in SBM, and a cutoff value of 0.210 allowed for the distinction between GBM and SBM with a Se of 66.7% and a Sp of 69.2%. However, some studies reported no significant difference in eFA between the two tumor groups[10,14,17,18]. El-Serougy et al[4] reported that the eFA of high-grade glioma was significantly lower than that of SBM ($p = 0.008$). Byrnes et al[9] and Lu et al[10] showed

that SBM had significantly higher eMD than GBM. According to Lu et al[10], increased eMD in SBM can be explained by increased extracellular water due to vasogenic edema in the peritumoral area, whereas in GBM, tumor infiltration disrupts the extracellular matrix structure, leading to increased water diffusion[10,20]. By contrast, eMD was significantly higher in GBM than in SBM, with an AUC of 0.89, a Se of 77%, and a Sp of 95% in the study reported by Skogen et al[6]. Our study results were similar to those reported by Skogen et al[6], with a higher eMD in GBM than in SBM, but this difference was not significant in our study.

The combination of different parameters to improve the ability to differentiate between GBM and SBM has been investigated in several previous studies, which generally showed that combinations could improve diagnostic values[6,15]. Wang et al[15] demonstrated that the combination of MD and FA improved diagnostic accuracy compared with the MD value alone (the AUC increased from 0.57 to 0.96). The authors also found that the combination of MD, FA, and the planar anisotropy coefficient in the tumor enhancing region was the best predictor for differentiating between GBM and SBM, with an AUC of 0.98, a Se of 92%, and a Sp of 100%. Our study showed that the combination of sFA and sMD provided an AUC of 0.96, with Se, Sp, PPV, and NPV of 85.2%, 100%, 85.2%, and 87.1%, respectively. However, the further combination of all 4 significantly different parameters, including sFA, sMD, eFA, and rFAs/n, did not improve diagnostic accuracy.

In addition to the retrospective design of this study, other potential limitations of our study include the small number of patients, inconsistencies in ROI size and the location of ROI placement, and the separation of FA values in the normal white matter between cases. Studies with larger sample sizes should be conducted in the future. The combination of MRI with other advanced techniques, such as magnetic resonance spectroscopy and perfusion, should also be investigated for the potential to increase diagnostic performance.

Conclusions

This study suggested that DTI represents a non-invasive technique that is able to provide useful information for differentiating between

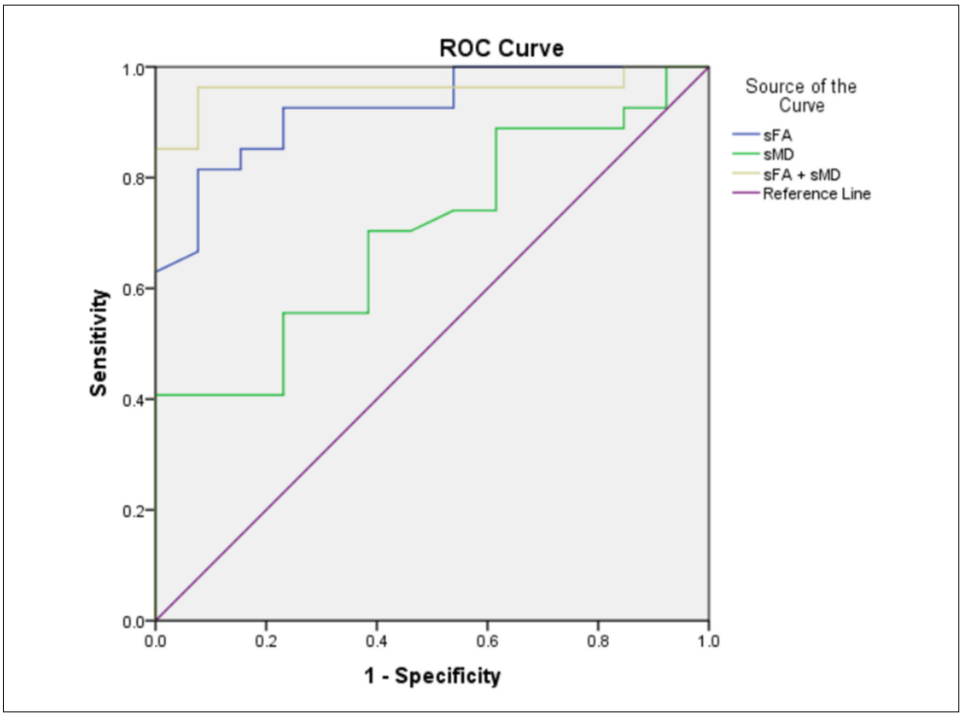

Figure 4. Receiver operating characteristic curve using FA value of the solid tumor (sFA), MD value of the solid tumor (sMD), and a combination of these parameters for differentiating glioblastoma (GBM) and solitary brain metastases (SBM).

GBM and SBM. This result was achieved using FA and MD values in the solid tumor component and assessing the infiltration of the tumor into the peritumoral white matter, causing edema. Furthermore, the combination of sFA and sMD further enhanced the discrimination ability between GBM and SBM, with increased Se and Sp compared with either single parameter analysis.

Conflict of Interest

The authors declare no competing interests.

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request.

Authors' Contributions

D.-H. Nguyen and M.-D. Nguyen contributed equally to this article as first authorship. D.-H. Nguyen and M.-D. Nguyen: designed and conducted research, analysed data, wrote, and reviewed paper; D.-H. Nguyen and M.-D. Nguyen: reviewed paper and has primary responsibility for the final version of manuscript. All authors read and approved the manuscript.

Ethics Approval

The institutional review board of Hanoi Medical University approved this retrospective study (Ref: 2682/QD-ĐHYHN dated 13 July 2021).

Informed Consent

Due to the retrospective nature of this study, the requirement for informed consent was waived by institutional review board of Hanoi Medical University.

ORCID ID

Nguyen Minh Duc: 0000-0001-5411-1492

References

1) Ostrom QT, Gittleman H, Farah P, Ondracek A, Chen Y, Wolinsky Y, Stroup NE, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2006-2010. Neuro Oncol 2013; 15: ii1-56.
2) Schiff D. Single Brain Metastasis. Curr Treat Options Neurol 2001; 3: 89-99.
3) Campos S, Davey P, Hird A, Pressnail B, Bilbao J, Aviv RI, Symons S, Pirouzmand F, Sinclair E, Culleton S, Desa E, Goh P, Chow E. Brain metastasis from an unknown primary, or primary brain tumour? A diagnostic dilemma. Curr Oncol 2009; 16: 62-66.
4) El-Serougy LG, Abdel Razek AAK, Mousa AE. Differentiation between high grade gliomas and metastatic brain tumors using Diffusion Tensor Imaging metrics. Egypt J Radiol Nucl Med 2015; 46: 1099-1104.
5) Csutak C, Ștefan PA, Lenghel LM, Moroșanu CO, Lupean RA, Șimonca L, Mihu CM, Lebovici A. Differentiating High-Grade Gliomas from Brain Metastases at Magnetic Resonance: The Role of Texture Analysis of the Peritumoral Zone. Brain Sci 2020; 10: 638.
6) Skogen K, Schulz A, Helseth E, Ganeshan B, Dormagen JB, Server A. Texture analysis on diffusion tensor imaging: discriminating glioblastoma from single brain metastasis. Acta Radiol 2019; 60: 356-366.
7) Pekmezci M, Perry A. Neuropathology of brain metastases. Surg Neurol Int 2013; 4: S245-255.
8) Tsuchiya K, Fujikawa A, Nakajima M, Honya K. Differentiation between solitary brain metastasis and high-grade glioma by diffusion tensor imaging. Br J Radiol 2005; 78: 533-537.
9) Byrnes TJ, Barrick TR, Bell BA, Clark CA. Diffusion tensor imaging discriminates between glioblastoma and cerebral metastases in vivo. NMR Biomed 2011; 24: 54-60.
10) Lu S, Ahn D, Johnson G, Cha S. Peritumoral diffusion tensor imaging of high-grade gliomas and metastatic brain tumors. AJNR Am J Neuroradiol 2003; 24: 937-941.
11) Yang G, Jones TL, Barrick TR, Howe FA. Discrimination between glioblastoma multiforme and solitary metastasis using morphological features derived from the p:q tensor decomposition of diffusion tensor imaging. NMR Biomed 2014; 27: 1103-1111.
12) Alexander AL, Lee JE, Wu YC, Field AS. Comparison of diffusion tensor imaging measurements at 3.0 T versus 1.5 T with and without parallel imaging. Neuroimaging Clin N Am 2006; 16: 299-309.
13) Abdullah KG, Lubelski D, Nucifora PG, Brem S. Use of diffusion tensor imaging in glioma resection. Neurosurg Focus 2013; 34: E1.
14) Wang W, Steward CE, Desmond PM. Diffusion tensor imaging in glioblastoma multiforme and brain metastases: the role of p, q, L, and fractional anisotropy. AJNR Am J Neuroradiol 2009; 30: 203-208.
15) Wang S, Kim S, Chawla S, Wolf RL, Zhang WG, O'Rourke DM, Judy KD, Melhem ER, Poptani H. Differentiation between glioblastomas and solitary brain metastases using diffusion tensor imaging. Neuroimage 2009; 44: 653-660.

16) Wang S, Kim SJ, Poptani H, Woo JH, Mohan S, Jin R, Voluck MR, O'Rourke DM, Wolf RL, Melhem ER, Kim S. Diagnostic utility of diffusion tensor imaging in differentiating glioblastomas from brain metastases. AJNR Am J Neuroradiol 2014; 35: 928-934.

17) Toh CH, Wei KC, Ng SH, Wan YL, Lin CP, Castillo M. Differentiation of brain abscesses from necrotic glioblastomas and cystic metastatic brain tumors with diffusion tensor imaging. AJNR Am J Neuroradiol 2011; 32: 1646-1651.

18) Tan Y, Wang XC, Zhang H, Wang J, Qin JB, Wu XF, Zhang L, Wang L. Differentiation of high-grade-astrocytomas from solitary-brain-metastases: Comparing diffusion kurtosis imaging and diffusion tensor imaging. Eur J Radiol 2015; 84: 2618-2624.

19) Jiang R, Du FZ, He C, Gu M, Ke ZW, Li JH. The value of diffusion tensor imaging in differentiating high-grade gliomas from brain metastases: a systematic review and meta-analysis. PLoS One 2014; 9: e112550.

20) Morita K, Matsuzawa H, Fujii Y, Tanaka R, Kwee IL, Nakada T. Diffusion tensor analysis of peritumoral edema using lambda chart analysis indicative of the heterogeneity of the microstructure within edema. J Neurosurg 2005; 102: 336-341.