RESEARCH ARTICLE

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Preoperative Evaluation of Tumor Adhesion to Adjacent Brain Tissue in Patients with Meningioma with BSMI Method and Its Comparison with the Width of Edema Around Tumor

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Abstract

Background: This study aims to investigate the ability of BSMI, to preoperative evaluation of tumor adhesion to adjacent brain tissue in patients with meningioma and comparing this method to the width of edema around tumor, using surgery findings as the reference standard. **Methods:** Thirty patients with meningioma brain tumor who underwent surgery at Loghman hospital were selected for the study between November 2016 and January 2018. The level of edema according to the classification of Ide et al., (u1995) was compared with the surgical findings with blinded results, and neurosurgeons made a qualitative assessment of tumor adhesion at the time of resection. The ability of BSMI and level of edema to predict the surgical assessment of adhesion was tested using the Fisher Exact Test. **Results:** BSMI method was conducted on patients with meningioma brain tumor, which judged 22 (73.3%) patients as adhesion (+) and 8 (26.66%) patients as adhesion (-). In this case, there was a significant relationship between BSMI judgment and surgical findings (p-value<0.0001). The sensitivity, specificity, precision and accuracy was high, at 91.30%, 85.71%, 95.45% and 90%, respectively. Using T2-Weighted SPACE sequence, of the 30 patients, 13 (43.3%) were judged as adhesion (+) and 17 (56.7%) as adhesion (-) from edema, whereas surgical findings evaluated 23 (76.7%) as adhesion (+) and 7 (23.3%) as adhesion (-).The sensitivity was moderate but the specificity was high, at 52.17% and 85.71%, respectively. Other criteria such as precision and accuracy were 62.31% and 60%, respectively. **Conclusions:** BSMI evaluated adhesion of the tumor to the adjacent brain tissue with high-accuracy prior to surgery. This method was more effective than Edema method in evaluating adhesion between meningioma and the brain.

Keywords: Tumor- meningioma- adhesion- magnetic resonance imaging- brain surface motion- preoperative surgery

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Introduction

Meningioma is one of the most common and primary tumors of the brain. This type of tumor grows from the middle layer of the meninges, called Arachnoid that covers the brain and spine (Yamashima et al., 1997). Successful treatment is achieved by complete tumor ablation; therefore surgery is recommended if possible (Yamada et al., 2015). Lack of tumor adhesion to the adjacent brain tissue is effective to the success of surgery (Ayerbe et al., 1999; Mirimanoff et al., 1985). Consequently, determining the presence or absence of adhesion between brain and meningioma before surgery can be very helpful in surgical success. MRI is the first choice in the surgical planning and evaluation of meningioma (İldan et al., 1999; Suzuki et al., 1994). In previous studies, common imaging methods including CT and MRI before surgery were used to determine the adhesion of tumor (İldan et al., 1999; Suzuki et al., 1994). The diagnosis of tumor adhesion using conventional magnetic resonance imaging has been rarely effective (Takeguchi et al., 2003). DSA is a successful method to determine the adhesion of tumor; however, it is an invasive procedure (Takeguchi et al., 2003). BSMI, a recently developed method, is empowered to predict the tumor-brain adhesion noninvasively and without the use of contrast agent (Yamada et al., 2015; Taoka et al., 2010). This technique uses the heavily T2 space sequence and as such, edema surrounding the tumor can also be examined (Taoka et al., 2010; Yamada et al., 2015). This study has also investigated the relationship between the adhesion of tumor and surrounding edema (Taoka et al., 2010; Yamada et al., 2015).

Materials and Methods

Patients

The researchers studied 30 patients with intracranial meningioma retrospectively according to previous MRI

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and CT scan images who underwent surgically tumor resection. The patients included 2 males and 28 females with a mean age of 48.97 (age range of 35-65 years). All patients underwent MRI prior to surgery and MR images were evaluated by radiologists with more than 10 years of experience in the field of neuroimaging. Radiological data included location of tumor, adhesion between tumor and brain and peritumoral brain edema.

Inclusion criteria included: 1) pathological diagnosis of meningioma after tumor surgery; 2) brain surface motion imaging before surgery; 3) patients with intracranial meningioma who should undergo surgery. All MR images in this study were performed with a 1.5T scanner (MAGNETOM Aera, Siemens AG,Healthcare Sector, Erlangen, Germany) using 20-channel head-neck coil. Images of cine phase contrast were obtained with the following parameters:

Repetition time (TR)/echo time (TE) =2345 ms/96 ms, flip angle=15°, field of view=230 mm, matrix=256×256, slice thickness=5mm, velocity encode=5 cm/s, ECG gated.

Then ROI was placed in the prepontine cistern of this prescan to obtain Time Intensity Curve, which detects delay time where CSF shows the highest and lowest signal intensity. Eventually, two volume sets of 3D heavily T2-weighted (SPACE) images were obtained in two different time delay (highest and lowest signal intensity) with the following parameters:

TR= 2R-R interval, TE=90, ETL=143, FOV=387, matrix=256×256, slice thickness=1.2, echo train duration=337, parallel acquisition acceleration factor=2.

Finally BSMI were obtained from Subtraction of these two volume sets.

Evaluation of MR imaging findings

Two experienced radiologists evaluated the preoperative tumor-brain adhesion based on BSMI. In this method, the presence of peritumoral band indicates there is no adhesion between the tumor and brain tissue while the absence of peritumoral band is reverse. We graded adhesion brain-tissue as: no adhesion, partial adhesion, and total adhesion. Peritumoral brain edema (PTBE) was measured from the T2 SPACE images. We graded peritumoral brain edema according to the classification of İldan et al., (1999) as: no edema,edema‹2cm in width, and edema›2cm in width (Enokizono et al., 2014).

Evaluation of surgical findings

Surgical findings on tumor adhesion to the adjacent brain tissue were evaluated by two neurosurgeons during surgery, without knowing the results of MR images. They also graded adhesion of tumor to the adjacent brain tissues in the same way as grading adhesion of the MR images: no adhesion, partial adhesion, and total adhesion. Finally, the results of surgery were compared with the results of MR imaging.

Statistical analysis

Statistical analyses of data considering specific variables (Edema, BSMI and surgical findings) were performed in R software version 3.4.1.

The Fisher Exact Test of Independence was used to determine if there is a significant relationship between Edema variable and Adhesion findings and also between BSMI variable and Adhesion findings. The significance was defined as $p< 0.05$. For each pair of variables (Edema-Adhesion and BSMI-Adhesion) some indices

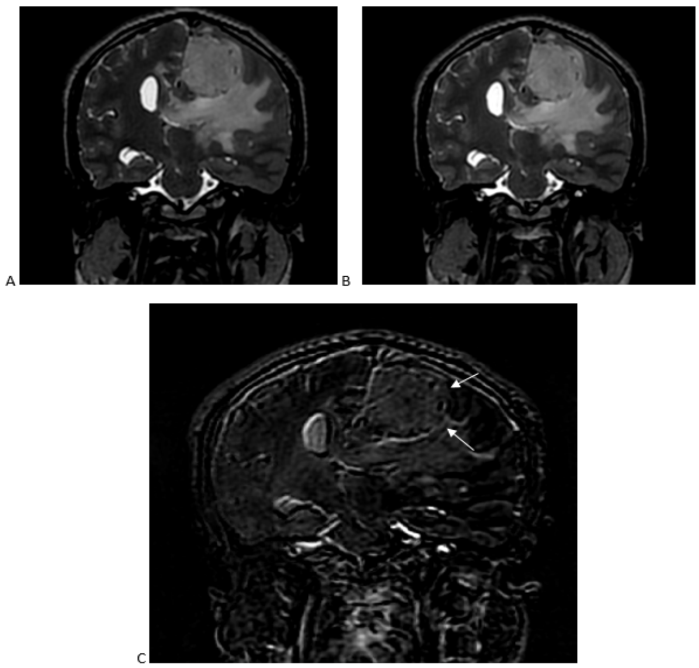

Figure 1. Images (A and B) show T2 SPACE images in systole and diastole. Image (c) shows the BSMI image, In this image, the strip margin around the tumor in areas clearly showed the adhesion of the tumor to the brain tissue around the tumor, and there were no stripes in the indicated areas (white arrow) to indicated that there is adhesion in this area. Case1. A 42-year-old man with a meningioma tumor with a history of dizziness and seizure and headache. A tumor was observed in the left parasagittal area. In this image the strip margin around the tumor in this area clearly indicated the adhesion of the tumor to the brain tissue around the tumor. There was no stripes in the indicated areas (white arrow) to indicate there is adhesion in this area. The width of edema in T2 images were more than 2 centimeters (figure 1).

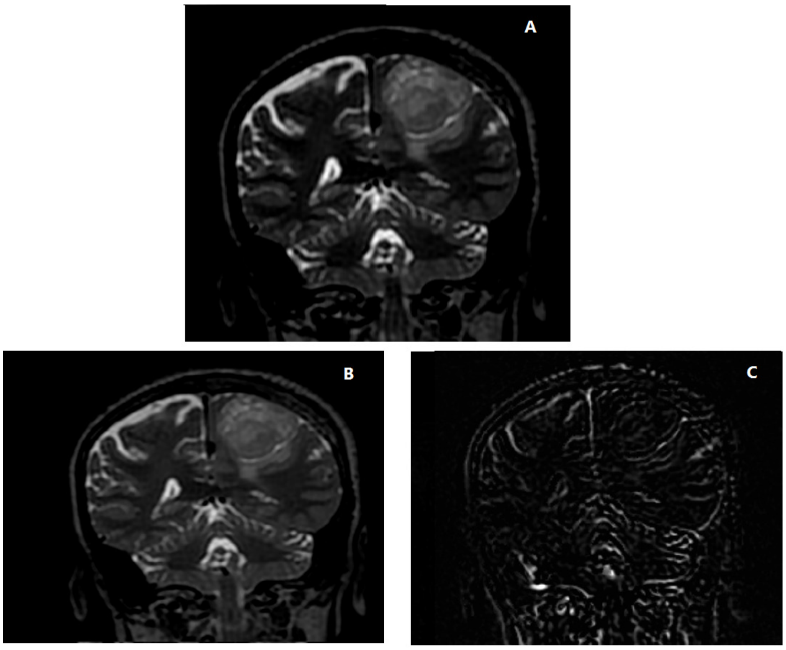

Figure 2. BSMI(c) Demonstrated no Apparent Stripes Around the Tumor that Indicates There is no Adhesion in This Area. The width of edema in T2 images is less than 2 centimeters. Case 2. A 56-year-old woman with a history of headache who had a tumor in the left parietal region. In this image, the strip margin around the tumor clearly indicated that the tumor does not adhere to the brain tissue around the tumor. The width of edema in T2 images were less than 2 centimeters (figure2).

Table 1. Patients' Clinical Characteristics

characteristics	Number (%)
Mean age in years (range)	48.97 (35-65)
Gender	
Male	28 (93.3%)
Female	2 (6.7%)
Location	
Parasagital	10 (33.3%)
Posterior Fossa	5 (16.37%)
Temporal Lobe	2 (6.7%)
Foramen Magnum	2 (6.7%)
Convexity	5 (16.7%)
Parieto-Occipital Lobe	2 (6.7%)
Sella Turcica	4 (13.3%)

were evaluated such as sensitivity, specificity, positive and negative predictive value and accuracy.

Results

Thirty Patients with meningioma brain tumor at Loghman hospital entered the study between November 2016 and January 2018. The mean age of patients was 48.97 (age range of 35-65 years), 28 of which (93.3%) were female and 2 male (6.7%) as can be observed in Table1.

BSMI was conducted on all patients. Using T2-W SPACE sequence, of the 30 patients, 13 (43.3%) were judged as adhesion (+) and 17 (56.7%) as adhesion (-) from edema, whereas surgical findings evaluated 23 (76.7%) as adhesion (+) and 7 (23.3%) as adhesion (-). According to Fisher Exact Test of Independence, there was not any significant relationship between Edema judgment and surgical findings (p-value=0.104); however, when Edema was positive, the number of positive adhesion of surgical findings was significantly more than the negative ones based on Binomial Test (p-value=0.006). The sensitivity was moderate while the specificity was high at 52.17% and 85.71%, respectively. Other criteria such as precision and accuracy were 62.31% and 60%, respectively (Table 2). Also, the BSMI method was conducted on patients with meningioma brain tumor, which judged 22 (73.3%) patients as adhesion (+) and 8 (26.66%) patients as adhesion (-). In this case, there was a significant relationship between BSMI judgement and surgical findings (p-value<0.0001). The sensitivity, specificity, precision and accuracy were high, at 91.30%,

Table 2. Results and Comparisons of the Adhesion between the Judgment of Edema and the Surgical Findings

	Surgical Findings		
	Adhesion (+)	Adhesion (-)	Predictive and Negative predictive value
Edema			
Adhesion (+)	12	1	0.9231
Adhesion (-)	11	6	0.3529
Sensitivity/Specificity	0.5217	0.8571	

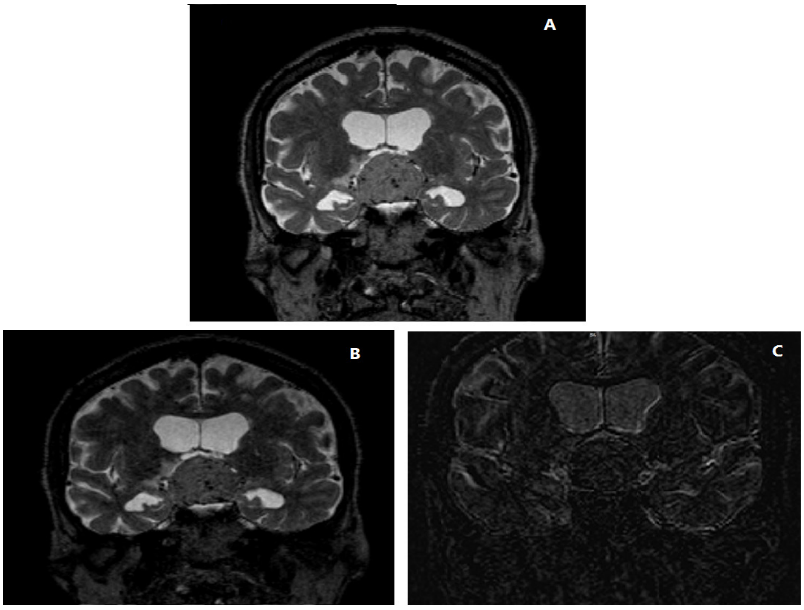

Figure 3. Images (A and B) show coronal view of T2 SPACE images in systole and diastole. Image (c) shows the BSMI image and indicates that no adhesion around the tumor has been observed. Case 3. A 65-year-old male with meningioma tumor with a history of headache with unilateral vision reduction. A tumor was recognized in the tuberculum sellae area. In this image, the strip margin around the tumor clearly indicated that the tumor does not adhere to the brain tissue around the tumor. The width of edema in T2 images were less than 2 centimeters. In this case, the patient has moved a little (Figure 3).

Table 3. Results and Comparison of the Adhesion between the Judgment of BSMI and the Surgical Findings

	Surgical Findings		
	Adhesion (+)	Adhesion (-)	Predictive and Negative predictive value
BSMI			
Adhesion (+)	21	1	0.9545
Adhesion (-)	2	6	0.75
Sensitivity/Specificity	0.913	0.8571	

85.71%, 95.45% and 90%, respectively (Table3).

In current study, the researchers added a “partial” category to BSMI levels. In this case, the BSMI method judged 4 (13.33%) patients as adhesion (+), 18 (60%) patients as partial adhesion and 8 (26.66%) patients as adhesion (-). The relationship between BSMI and surgical levels were significant according to Fisher Exact Test of Independence (p-value<0.0001).

Illustrative cases

Case1. A 42-year-old man with a meningioma tumor with a history of dizziness and seizure and headache. A tumor was observed in the left parasagittal area. In this image the strip margin around the tumor in this area clearly indicated the adhesion of the tumor to the brain tissue around the tumor. There was no stripes in the indicated areas (white arrow) to indicate there is adhesion in this area. The width of edema in T2 images were more than 2 centimeters (Figure 1).

Case 2. A 56-year-old woman with a history of headache who had a tumor in the left parietal region. In this image, the strip margin around the tumor clearly indicated that the tumor does not adhere to the brain tissue around the tumor. The width of edema in T2 images were less than 2 centimeters (Figure 2).

Case 3. A 65-year-old male with meningioma tumor

Table 4. Results and Comparison of the Adhesion between the Judgment of BSMI with Three Levels and the Surgical Findings

	Surgical Findings		
	Adhesion (+)	Adhesion (-)	Predictive and Negative predictive value
BSMI			
Total adhesion (+)	4	0	--------
Partial adhesion	17	1	--------
No adhesion (-)	2	6	--------
Sensitivity/Specificity	-------	--------	

with a history of headache with unilateral vision reduction. A tumor was recognized in the tuberculum sellae area. In this image, the strip margin around the tumor clearly indicated that the tumor does not adhere to the brain tissue around the tumor. The width of edema in T2 images were less than 2 centimeters. In this case, the patient has moved a little (Figure 3).

Discussion

One of the critical factors that causes surgical difficulty of the intracranial meningeal tumors is adhesion of tumor to the adjacent brain tissue. According to the previous studies (Takeguchi et al., 2003; Yamada et al., 2015; Vaz et al., 1998), MRI and DSA are two important imaging methods to evaluate the tumor adhesion before surgery based on peritumoral brain edema, shape, presence of the strip margin around the tumor and tumor blood supply status. In addition, PTBE is one of the other problems which occur in about 40-70% of meningiomas (Mattei et al., 2005).

Vascular supply observed by DSA was significantly correlated with the degree of tumor brain adhesion; however, DSA is an invasive method (Takeguchi et al., 2003). İldan et al., (1999) demonstrated that the degree of adhesion of the tumor to the surrounding brain tissue, which was tested by MRI, was significantly high in cases of severe edema. researcher also demonstrated that the degree of adhesion of the tumor and brain was significantly higher in a group with very severe edema around the tumor (Takeguchi et al., 2003). The results of this study showed a significant relationship for adhesion prediction between T2-W MRI findings and the findings of surgery in the case of severe edema. In total (no edema, edema less than 2 centimeters and edema more than 2 centimeters), there was no significant relationship between edema and tumor adhesion in this study. Edema-inducing factors include tumor size, tumor location, histological differentiation and maybe hormonal receptors that founded in meningeal tumoral cells (Mattei et al., 2005). The type of arterial tumor supply is also an effective factor for the creation edema around the tumor (Takeguchi et al., 2003; Mattei et al., 2005).

The presence of edema around the tumor by CT and MRI is a simple way to predict pre-surgical tumor adhesion (İldan et al., 1999; Suzuki et al., 1994; Takeguchi et al., 2003; Yamada et al., 2015). Vascular endothelial growth factor (VEGF) is one of the most important angiogenesis regulators that has been reported is increased in the meningeal tumors with severe edema (Piazza et al., 2017; Pistolesi et al., 2004; Otsuka et al., 2004). In the presence of edema, the MMP_2 and MMP-9 degrading enzymes play an important role in infiltrating invasive meningeal tumor cells adjacent to brain tissue (Reszec et al., 2015). When VEGF expression is high and MMP expression is low, edema develops even in cases with a weak adhesion. Therefore, the development of edema in the surrounding brain tissue does not necessarily indicate a strong adhesion (Piazza et al., 2017; Pistolesi et al., 2004; Bitzer et al., 1997). A new technique known as BSMI with high sensitivity, specificity, precision and accuracy can assess the presence or absence of tumor-brain adhesion (Taoka et al., 2010; Yamada et al., 2015; Taoka et al., 2012).

This study showed a significant relationship between BSMI findings and surgical findings (p-value<0.0001). Also, BSMI provides a noninvasive method to evaluate tumor-brain adhesion before surgery. The sensitivity, specificity, precision and accuracy of BSMI were high, at percentages of 91.30, 85.71, 95.45 and 90, respectively. Evaluation of tumor-brain adhesion in BSMI is based on the characteristic relationship between the tumor and adjacent brain mobility under heartbeat. As previously mentioned, meningeal tumors originate from the meningeal layer (Yamashima et al., 1997; Bondy and Ligon, 1996). The presence of sub-arachnoid space around the tumor demonstrates that there is no adhesion between the tumor and the surrounding tissues, and the accumulation of this space causes the infiltrating of tumor to the brain tissue and finally causes tumor-brain adhesion. After any heartbeat, pulsatile motion of brain is triggered and a motion gap is created where a subarachnoid space is present. Therefore, this motion gap is seen as a form of light or dark band surrounding the tumor in the BSMI technique. Light bands area demonstrate the brain is replaced by CSF in that area with pulsatile motion while black bands are the reverse. BSMI images are obtained by subtracting images (3D heavily T2 SPACE) in two delay times (systole and diastole) which determine the motion gap status (Taoka et al., 2010; Yamada et al., 2015; Taoka et al., 2012). This method not only determines the presence or absence of adhesion but also determines the adhesion sites. The surgeon's surgical program determines the severity of post-operative complications for the patient so that if the surgeon can obtain preoperative information about the infiltrating tumor adjacent to brain tissue, he can change his surgical schedule in order to reduce the incidence of complications. BSMI is a non-invasive method and its time is low. No contrast material is used in this technique. In this study, ECG gating was used for more precision compared to pulse gating used in a recent study (Yamada et al., 2015). To our knowledge, in ECG gating, its sensors use the electrical signals generated by heart activity directly. Pulse gating is less accurate than ECG due to the long and unpredictable delay between myocardial contraction and arrival of the pulse wave to the finger(Lanzer et al., 1985). In addition, 3D motion correction has been used in 3D SPACE images in this study.

Study limitations

There were several limitations in this study. The patients' number was relatively small and the reference standard of this study was the qualitative assessment of tumor brain adhesion by the surgeons during resection, while using an image guided neurosurgery navigation system increases precision. Despite these limitations, BSMI has demonstrated potential usefulness in providing surgeons preoperatively with the degree of tumor brain adhesion.

In conclusion, BSMI evaluated adhesion of the tumor to the adjacent brain tissue with high-accuracy prior to the surgery. BSMI therefore appears to be useful for planning surgical strategy and evaluating surgical risks. The BSMI method was more effective than evaluating the width of edema in predicting adhesion between meningioma and the brain.

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