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FULL PAPER

Differentiating spinal intradural-extramedullary schwannoma from meningioma using MRI T_2 weighted images

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Objective: Prior studies advocate the subjective visual differences between meningioma and schwannoma on T_2 weighted images, however objective measurement of signal intensity differences may be useful in certain cases. The aim of this study was to investigate whether an objective evaluation of SIs on T_2 weighted images would be useful to differentiate spinal schwannomas from meningiomas.

Methods: The patients with spinal MRIs demonstrating path proven and subsequently treated intradural extramedullary spinal tumors were selected between April 2008 and May 2017. Regions of interest (ROIs) were measured in the tumor and subcutaneous fat on the same image, and we calculated the SI ratio between tumor and fat ROIs.

Results: Twenty patients each with meningioma and schwannoma were enrolled. The SI ratios of schwannomas were significantly higher than those of meningiomas (both researcher 1 and 2: $p = 0.002$). The areas under the curve by researchers 1 and 2 were 0.780. The cutoff value of SI ratio by both of researchers 1 and 2 to differentiate between schwannomas from meningiomas was 0.420 (sensitivity: 80.0%, specificity: 70.0–75.0%).

Conclusion: The SI ratio, calculated from the SIs of the tumor and fat on T_2 weighted images, is useful for differentiating spinal schwannomas from meningiomas to obtain an accurate diagnosis.

Advances in knowledge: Signal intensity ratio of the spinal tumor and fat on T_2 weighted images is useful for differentiating schwannomas from meningiomas to obtain an accurate diagnosis.

INTRODUCTION

The diagnosis and treatment of spinal tumors has improved with the advances in diagnostic imaging and surgical techniques. CT myelography and MRI simplify diagnoses and accurate identification of both tumor location in the dura mater and its dural attachment prior to surgery.^{1,2} Using a contrast medium and high resolution, MRI may aid to characterize spinal tumors and determine their resectability and prognosis.³ Spinal tumors can be classified as extradural, intradural-extramedullary, and intramedullary. Intradural and extramedullary tumors, which include schwannomas, meningiomas, neurofibromas, teratomas, lipomas, and metastatic tumors,^{4–6} represent 60–70% of all spinal tumors and develop within the supportive cellular network around the spinal cord. Moreover, they cause spinal cord or nerve

root compression, which can result in pain, paresthesia, motor deficits, and sphincter disturbances. The majority of intradural-extramedullary spinal tumors are schwannomas or meningiomas. Approximately 90% of spinal schwannomas arise from Schwann cells of the dorsal nerve roots and sometimes extend along the nerve root to the extravertebral space.⁷ In contrast, meningiomas often appear as globular tumors that are usually located in the spinal canal and do not extend through the intervertebral foramen.^{7,8} Although most of spinal schwannomas and meningiomas are benign, an accurate diagnosis prior to surgery is important, as surgical procedures may vary by site of tumor origin.^{8,9}

In general, signal patterns on T_2 weighted images of schwannomas are hyperintense, whereas those of meningiomas are

iso- or hyperintense: both are hypo- or isointense on T_1 -weighted images.^{6,10,11} Thus, differences in the signal intensities (SIs) on T_2 weighted images may be useful to differentiate schwannomas from meningiomas. Prior studies^{8,10} have attempted differentiation by visual assessment on T_2 weighted images, however, differentiation of these tumors remains difficult.

Consequently, the aim of this study was to investigate whether an objective evaluation of SIs on T_2 weighted images would be useful to differentiate schwannomas from meningiomas.

METHODS AND MATERIALS

The institutional review board of our institution approved this retrospective analysis and waived the requirement for informed consent.

We retrospectively and consecutively selected patients with intradural extramedullary spinal tumors between April 2008 and May 2017 at our institution. All MR examination was performed prior to any treatment and surgery. The patients with spinal MRIs

demonstrating path proven and subsequently treated intradural extramedullary meningioma or schwannoma were selected. Among them, the patients were excluded due to an obvious cystic change on the T_2 weighted image, as determined by an experienced radiologist (Figure 1). The reason for this is that previous studies have reported that the characteristics of spinal schwannoma and meningioma were cystic degeneration.^{6,8,12,13}

MRIs were performed using a spine coil with a GE Signa HDx 1.5T (GE Healthcare, Milwaukee, WI). We analyzed slice of the center of the tumor with fast spin echo T_2 weighted cross-sectional images (TR: 4,000–5,000ms, TE: 100ms, FOV: 120–140mm, matrix: 256 × 192, slice thickness/gap: 4–5 mm/0.5–1 mm) of a central tumor slice that was obtained prior to surgery. Additionally, all images were obtained using a homogeneity correction. Regions of interest (ROIs) were measured in the tumor and subcutaneous fat on the same image, and we measured the mean values of the SI of the tumor (SI tumor) were measured in the ROIs. Furthermore, ROIs of the tumors were hand-drawn, and set with surrounding the tumor, whereas the

Figure 1. Flow chart of study selection for spinal schwannoma and meningioma.

Figure 2. Example of image analysis. In the T_2 weighted cross-sectional images, the two researchers set regions of interest (ROIs) of spinal tumor and subcutaneous fat and calculated signal intensity ratio of these lesions. (a) A 64-year-old male patient with schwannoma at the level of Th1. SI ratio; 0.96 (researcher 1) and 0.93 (researcher 2). (b.) A 41-year-old female patient with meningioma at the level of Th11/12. SI ratio; 0.30 (researcher 1 and 2).

ROIs of the subcutaneous fat were not standardized size, and set as three circle regions on the posterior side of the spinous process and on both pedicles; the mean value of the SI of the fat (SI fat) was calculated from those ROIs. An experienced research scientist (H.T.) and an experienced diagnostic radiologist (M.O.), blinded to the identification of the specimens, independently set the ROIs and measured the SI tumor and the SI fat. We calculated the SI ratio using the following formula;

$$\text{SI ratio} = \text{SI tumor} / \text{SI fat}$$

ROIs of the tumor and fat in all subjects were set by two researchers, and were shown with examples of ROI placement for comparison between the two researchers for the same lesion (Figure 2). The ratings from each researcher were pooled for statistical analysis.

Interclass correlation coefficients (ICCs) and Bland-Altman statistics were calculated as the inter rater reliability between the two researchers using MedCalc (v. 10.2.0.0; MedCalc Software, Ostend, Belgium). The 95%CI of the mean difference was used to determine systematic bias. If zero is included within the 95%CI, no significant systematic bias between measurements can be inferred.¹⁴ To investigate the presence of proportional bias, a regression equation was established from the Bland-Altman plot, and the significance of the regression was tested. If the regression was significant ($p < 0.05$), it was judged that proportional bias was present. Furthermore, we calculated coefficient of variation (CV) for evaluating the standard deviation in the tumor ROIs. The Mann-Whitney U test was used to test statistical significance for SI ratio and CV, which was set at a p

Table 1. Distribution of the examinees with regard to the gender, age and location of the spinal tumor

		Schwannoma	Meningioma
Gender	Female	7	16
	Male	13	4
Age (mean $\pm$ SD)		63.3 $\pm$ 11.1	63.3 $\pm$ 18.4
Location	Cervical	3	8
	Thoracic	10	11
	Lumbar	7	1

value of less than 0.05. Statistical analyses were performed using commercially available software (SPSS software, v. 20.0; IBM Corp., Armonk, NY). Furthermore, receiver operating characteristic (ROC) curve analyses were performed to determine the cutoff values of the SI ratios of the schwannomas and meningiomas. We calculated the cutoff values for the both tumors by ROC curve analyses using MedCalc (v. 10.2.0.0; MedCalc Software, Ostend, Belgium).

RESULTS

Finally, twenty patients each with spinal intradural-extra-medullary schwannoma and meningioma were enrolled. The details of subject characteristics are shown in the Table 1.

ICCs were calculated between the two researchers for the SI tumor [$r = 0.980$, 95% CI (0.962–0.989)], the SI fat [$r = 0.978$, 95% CI (0.958–0.988)], and the SI ratio [$r = 0.981$, 95% CI (0.965–0.990)]. Moreover, mean difference $\pm$ 1.96SD with Brand-Altman statistics were on the SI tumor [5.92 $\pm$ 63.1, 95% CI (–14.3 to 26.1)], the SI fat [–6.30 $\pm$ 86.2, 95% CI (–3.9 to 21.3)], and the SI ratio [0.012 $\pm$ 0.042, 95% CI (–0.002 to 0.025)] (Figure 3). No significant systematic bias between measurements were indicated because of including zero within the 95% CI. Moreover, the regression was not significant, and no proportional bias was present. The SI ratios of schwannomas and meningiomas were 0.61 $\pm$ 0.25 and 0.38 $\pm$ 0.13 (researcher 1), 0.59 $\pm$ 0.24 and 0.38 $\pm$ 0.13 (researcher 2), respectively. The SI ratios of schwannomas were significantly higher than those of meningiomas (researcher 1: $p = 0.002$, researcher 2: $p = 0.002$). Meanwhile, the CV in the tumor ROIs of schwannoma and meningioma were not significantly different (Figure 4). The results of the ROC curve analysis for each researcher are shown in Figure 5. The areas under the curve by both of researchers were 0.780 (95%CI: 0.621 to 0.895). The cutoff value of the SI ratio to differentiate schwannomas from meningiomas by both of researchers were 0.420 on most accurate point from ROC curve [researcher 1; sensitivity: 80.0%, specificity: 75.0%, positive predictive value (PPV): 76.2%, negative predictive value (NPV): 78.9%, and researcher 2; sensitivity: 80.0%, specificity: 70%, PPV: 72.7%, NPV: 77.8%]. Meanwhile, the cutoff value on the highest specificity were 0.31 (researcher 1; sensitivity: 35%, specificity: 90%, PPV: 77.8%, NPV: 58.1%) and 0.30 (researcher 2; sensitivity: 30.0%, specificity: 90%, PPV: 75%, NPV: 56.2%) (Figure 5).

Figure 3. Intraclass correlation coefficients (ICCs) and Brand-Altman analysis of each SI between the two researchers. (a) ICCs were excellent reliability, and zero was included within the 95% CI, the regression was no significant for SI tumor ($p = 0.7652$). (b) ICCs were excellent reliability, and zero was included within the 95% CI, the regression was no significant for SI fat ($p = 0.0537$). (c) ICCs were excellent reliability, and zero was included within the 95% CI, the regression was no significant for SI ratio ($p = 0.1492$).

DISCUSSION

Previous studies on the differential diagnoses of such tumors have focused on gender, tumor location, and findings from CT and MRI.⁸ Schwannomas are more common in males, and meningiomas are more common in females,^{15,16} presumably because of the influence of female sex hormones on specific tumor development.² Additionally, spinal meningiomas are primarily located in the thoracic region of the spine.⁸ In this study, schwannomas were also more common in males, and meningiomas were more common in females; these findings are consistent with the results of previous reports.^{2,8,15,16} Schwannomas tend to have an SI that is equal to or less than that of the spinal cord on T_1 -weighted images and a mild to marked hyperintensity on T_2 weighted images. Focal areas of even greater hyperintensity on T_2 weighted images often correspond to cystic regions, whereas hypointensity may represent hemorrhage, dense cellularity, or collagen deposition.^{8,17} In contrast, meningiomas can show a decreased SI on T_2 weighted images, because of intratumoral calcification in approximately 20–30% of cases.^{18,19} Meanwhile, previous studies have reported that intracranial meningiomas is rarely to occur cystic change.^{12,13} Thus, we considered it might be helpful to know the standard deviation in addition to the average signal intensity. However, there were no significant difference with CV

between schwannoma and meningioma due to excluding the cystic change.

Intradural-intramedullary and -extramedullary tumors account for 20 and 80% of all spinal tumors, respectively.^{20,21} Furthermore, two-thirds of all intradural extramedullary tumors are schwannomas or meningiomas (approximately 60%).²² Schwannomas are solitary, well-circumscribed, encapsulated tumors, which are located eccentrically on peripheral nerves or spinal nerve roots. In contrast, spinal meningiomas are typically small, single, discrete, round or oval intradural tumors,^{8,9} which may cause spinal cord or nerve root compression and can result in pain, paresthesia, motor deficits, and sphincter disturbances.²¹ The surgical treatment of schwannomas requires incision of both the dura mater and arachnoid membrane, because the tumors reside in the subarachnoid space. To prevent postoperative leakage of cerebrospinal fluid (CSF), the dura mater and arachnoid membrane are sutured to produce a watertight dural closure. Meanwhile, meningiomas reside intradurally in the extra arachnoid space. With regard to their surgical treatment, the attachment site of the meningioma to the dura mater must be resected with the tumor to remove any residual tumor cells; thus, preservation

Figure 4. Comparison of SI ratios and CV with schwannoma and meningioma. (a) The coefficient of variation (CV) of schwannoma and meningioma in the ROIs were not significantly different. (b) The mean values of the SI ratios of schwannomas and meningiomas were significantly different ($p = 0.002$).

of the arachnoid membrane helps prevent postoperative CSF leakage.^{2,7,23} Therefore, an accurate preoperative diagnosis that differentiates a spinal schwannoma from a meningioma is important.

Figure 5. A receiver-operating characteristic (ROC) curve between schwannomas and meningiomas for each researcher. Area under the ROC curve (AUC) of the two researchers were 0.780 [95% CI (0.621–0.895)]. Researcher 1: The cutoff value of SI ratio to differentiate between schwannomas from meningiomas was 0.420 on most accuracy point from ROC curve. Moreover, the cutoff value with the highest specificity were 0.31. Researcher 2: The cutoff value of SI ratio to differentiate between schwannomas from meningiomas was 0.420 on most accuracy point from ROC curve. Moreover, the cutoff value with the highest specificity were 0.30.

Previous studies⁸ have differentiated schwannomas from meningiomas using T_2 weighted images, reporting sensitivity and specificity values of 36.1 and 87.0% cases in which a meningioma with a comparable SI to the spinal cord was diagnosed, and 55.4 and 97.2% in cases in which a schwannoma with a comparable SI to CSF was diagnosed. From these results, it can be said that differentiating schwannomas from meningiomas by comparing their SIs with those of other tissues, such as the spinal cord and CSF, on T_2 weighted images is difficult.^{7,8,24} Thus, we measured the SI values of the tumors and fat objectively and calculated the SI ratio. The results showed good reliability in differentiating between the tumors: The sensitivity of the differential diagnosis was 80% and the specificity was 70–75%. Therefore, we consider that this can provide the additional information for identification of these tumors using this technique.

The SI of an MR image is not an absolute value due to the effect of various factors, including signal detection and signal amplification.^{25,26} Thus, in the present study, we measured the SI fat and calculated the SI ratio, because the fat was constantly distributed within the same cross-sectional images with the spinal tumors. Although we considered the CSF, spinal cord, and muscle as control tissues for measuring the SI ratio for these tumors, we decided not to use the SIs of these tissues, because of the variability of the SI of the CSF due to flow artifacts, the limited positioning of the ROIs in the compressed spinal cord, and the

fatty degeneration of skeletal muscles due to age and obesity. Furthermore, most of the tumors were sized with spinal canal space occupying lesion and compression of spinal cord because surgical cases. Therefore, we considered that the effect of volume averaging with adjustment CSF and spinal cord were limited. Therefore, we suggest that it is possible to reflect the signaling characteristics of tumors by calculating the SI ratio between spinal tumors and subcutaneous fat. Furthermore, the current study is useful because of simple and high inter rater reliability.

The present study has several limitations that should be addressed. First, the number of subjects included in the study was small. The frequency of meningioma occurrence is reportedly similar to that of schwannomas in western countries.^{21,22} On the contrary, the frequency of meningioma occurrence is less than that of schwannomas in Japan. Therefore, the total number of subjects is less than in major reports, making the number of subjects with schwannomas or meningiomas relatively equal. Additionally, the T_2 weighted images used in the current study were obtained only at our institution. We have not confirmed

whether evaluations of SI ratios on T_2 weighted images obtained at other institutions show the same results. However, we believe that it is possible to apply the current method for T_2 weighted images obtained at other institutions, although the MR scanner and scan technique differ because ratio of SI was used. Further, using homogeneity correction for the images is essential because the SIs of various tissues are affected by differences in the distance from the receiver coil. Furthermore, it is unclear whether this technique can be applied to intracranial tumors and other spinal tumors. However, intracranial schwannoma and meningioma are generally bigger in size than spinal lesions. Therefore, intracranial lesions easy often to indicate characteristics of inhomogeneous signal (e.g. cystic and calcific change) or contrast effect than spinal lesion. We hope to analyze other spinal tumors in the future.

In conclusion, the SI ratio, calculated from the SIs of the tumor and fat on T_2 weighted images, is useful for differentiating schwannomas from meningiomas to obtain an accurate diagnosis.

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