

## **Major nerve schwannomas vs intramuscular schwannomas**

**Shoji Shimose, MD, Takashi Sugita\*, MD, Tadahiko Kubo, MD, Toshihiro Matsuo, MD, Hiroo Nobuto\*, MD, Kumi Tanaka, MD, Koji Arihiro†, MD, and Mitsuo Ochi, MD**

Department of Orthopaedic Surgery, Graduate School of Biomedical Sciences,  
Hiroshima University, 1-2-3 Kasumi, Minami-Ku, Hiroshima 734-8551, Japan

\*Department of Orthopaedic Surgery, Hiroshima Prefectural Hospital, 1-5-54  
Ujinakanda, Minami-Ku, Hiroshima 734-8530, Japan

†Department of Pathology, Hiroshima University Hospital, 1-2-3 Kasumi, Minami-Ku,  
Hiroshima 734-8551, Japan

Running Title: Major Nerve and Intramuscular Schwannomas

Key words: Schwannoma, Major nerve, Intramuscular, Target sign, MRI, Tinel-like sign

Correspondence to:

Shoji Shimose, MD, 1-2-3 Kasumi, Minami-Ku, Hiroshima 734-8551, Japan

Telephone: +81 82 257 5232

FAX: +81 82 257 5234

E-mail: shimose @ hirosima-u.ac.jp

## **Abstract**

*Background:* A schwannoma is a benign peripheral nerve tumor. Predicting the involvement of a nerve on symptoms or MR findings is crucial to the diagnostic process.

*Purpose:* To compare symptoms, MR findings, and histological findings between major nerve schwannomas and intramuscular schwannomas.

*Material and Methods:* Thirty-four patients with 36 schwannomas (29 major nerve schwannomas and 7 intramuscular schwannomas) surgically excised and proven histologically were retrospectively reviewed.

*Results:* Frequencies of the Tinel - like sign, split-fat sign, entering and exiting nerve, and low-signal margin indicate the presence of the nerve and were significantly higher in major nerve schwannomas than in intramuscular schwannomas. In tumor morphological patterns (the target sign, inhomogeneous pattern, and homogeneous pattern), there were no significant differences between major nerve schwannomas and intramuscular schwannomas. Schwannomas showing the target sign histologically tended to be less degenerative. All major nerve schwannomas and 5 intramuscular schwannomas produce some characteristic symptoms and/or MR findings, but two intramuscular schwannomas didn't have any characteristic symptoms and findings.

*Conclusion:* In major nerve schwannomas, the Tinel - like sign, split-fat sign, entering and exiting nerve, and low-signal margin are commonly observed and useful for diagnosis. In intramuscular schwannomas, these characteristic findings are less common, which makes diagnosis difficult.

A schwannoma is a benign peripheral nerve tumor, usually formed in a peripheral nerve. The diagnosis of a schwannoma is often defined at surgery by its characteristic macroscopic appearance. A schwannoma should be separated from the affected nerve intraoperatively after incision of the epineurium to preserve the native nerve function. Partial resection can be performed to spare the nerve function, and recurrence is unusual. A preoperative correct diagnosis of a schwannoma is important for atraumatic management of the tumor.

Holdsworth and Kehoe reported that diagnosis of a peripheral nerve tumor is difficult when based on clinical assessment alone (7, 10). However, Hems and Ogoose reported that if a major nerve is involved, it is suspected on clinical grounds alone and the Tinel - like sign (paresthesia produced by percussing the tumor) is often observed (4, 6, 16). On the other hand, Kwon reported that clinical symptoms are rare in intramuscular schwannomas (12).

On MR images of schwannomas, the frequencies of characteristic findings such as the split-fat sign (fat tissue surrounding the involved nerve), entering and exiting nerve, low-signal margin (low signal rim surrounding the schwannoma), thin hyperintense rim (thin peripheral hyperintense rim on T2-weighted images), and the target sign (peripheral hyperintense rim and central low intensity on T2-weighted

images) have been reported variously (3, 8, 9, 15, 19). The morphologic features of tumors such as the target sign, inhomogeneous pattern, and homogeneous pattern have been generally indicated by T2-weighted images (11, 16). Little is known about the correlation between morphologic features and histological findings (18).

Predicting the involvement of a nerve on symptoms or MR findings is crucial to the diagnostic process, but in intramuscular schwannomas, small nerves generally make the diagnosis difficult. The purpose of this study was to find useful diagnostic information from symptoms and MR findings, not only in major nerve schwannomas but also in intramuscular schwannomas. The findings between major nerve schwannomas and intramuscular schwannomas were compared, and the relationship between the MR morphologic findings and histological findings was also investigated.

## **Material and Methods**

Between January 1994 and December 2003, a consecutive series of thirty-six patients with 38 schwannomas surgically excised and histologically proven were retrospectively reviewed by five observers who were blinded to the results. Two patients, each with a subcutaneous schwannoma, were excluded from this study. Our institution approved the human protocol for this investigation and all investigations were conducted in

conformity with the ethical principles of research. There were 17 males and 17 females ranging from 26 to 71 years of age (mean 51 years). Two patients had surgical excisions for two schwannomas. MR imaging was performed using a system with a field strength of 1.5 T (Signa Horizon; GE Yokogawa Medical, Tokyo, Japan). Conventional scanning sequences consisted of T1-weighted (350-700/ 15-35) and T2-weighted (1800-3200/ 70-120) spin-echo sequences performed in at least two orthogonal planes. In all tumors, the contrast-enhanced T1-weighted spin-echo sequence was performed after administration of Gd-DTPA.

The medical records, MR images, and histological reports were available for all patients. Preoperative symptoms such as pain at rest, tenderness, the Tinel - like sign, sensory disturbance, and motor weakness were reviewed from the medical records by two experienced oncologists (T.S., K.T.). The Split-fat sign, entering and exiting nerve, and low-signal margin on T1 and T2-weighted images, and the thin hyperintense rim and target sign on T2-weighted images were reviewed by two experienced oncologists (T.K., T.M.) and decisions were reached by consensus. The reviewers classified a target sign when the central hypointense focus comprised less than three quarters of the lesion, and they classified a thin hyperintense rim when the rim was less than one quarter of the lesion's diameter (8). Additionally, central enhancement was necessary for classification

as a target sign. The correlation between the MR images and the histological findings were reviewed. The histological findings of all tumors were reviewed by an experienced pathologist (K.A.).

Twenty-nine schwannomas arose from a major nerve trunk and seven were intramuscular schwannomas (Table 1). The intervals between the onset of symptoms and surgical treatment were between one and 156 months with a mean of 26 months. Tumor sizes ranged from 1.5×1 cm to 12×5.5 cm (average, 4.4×3.1cm.). Needle biopsies were performed in five schwannomas (two major and three intramuscular schwannomas) and open biopsies in two (one major nerve and one intramuscular schwannoma).

Symptoms, MR findings, and histological findings between major nerve schwannomas and intramuscular schwannomas were compared. The morphologic features of the tumors on T-2 weighted images were correlated with the histological findings. Statistical analysis was performed using the chi-square test or Mann-Whitney's U test. For all statistical comparisons, significance was defined as a *p* value of less than 0.05.

## **Results**

For the clinical symptoms, pain at rest was noted in 10 schwannomas, tenderness in 15, the Tinel - like sign in 25, sensory disturbance in 7, and motor weakness in 2. Between major nerve schwannomas and intramuscular schwannomas, there was a significant difference only in the Tinel - like sign (Table 2). Two major nerve schwannomas and four intramuscular schwannomas didn't produce any characteristic symptoms. The average tumor size of the major nerve schwannomas was 4.1×2.9 cm and that of the intramuscular schwannomas was 5.6×3.9 cm. The average interval between the onset of symptoms and surgery in the major nerve schwannomas was 22± 6 months and that of intramuscular schwannomas was 44± 17 months. There were no significant differences in the size and the intervals.

On the MR images, the split-fat sign was detected in 29 schwannomas, entering and exiting nerve in 27, low-signal margin in 25, and thin hyperintense rim in 7. The entering and exiting nerves were situated peripherally in 20 schwannomas and centrally in 7. In the split-fat sign, entering and exiting nerve, and low-signal margin, there were significant differences between the major nerve schwannomas and intramuscular schwannomas. The target sign was observed in 9 major nerve schwannomas (31%) and in 2 intramuscular schwannomas (29%). One major nerve schwannoma and two intramuscular schwannomas did not show any characteristic MR findings. The two

major nerve schwannomas with no characteristic symptoms showed the split-fat sign, entering and exiting nerve, and low-signal margin. In the four intramuscular schwannomas with no characteristic symptoms, one had the split-fat sign and low-signal margin (Fig. 1), one had the fascicular sign, and two had no characteristic MR findings. Ultimately, for symptoms and MR findings, some characteristic findings were observed in all major nerve schwannomas and in 5 intramuscular schwannomas, but no characteristic findings were observed in two intramuscular schwannomas.

The morphological features on the T2-weighted MR images could be classified as the target sign (n= 11), inhomogeneous pattern (n= 17), and homogeneous pattern (n= 8). The target sign corresponded to more cellular Antoni A regions centrally and more myxoid Antoni B areas peripherally in 6 of 11 schwannomas (Fig. 2) and was also observed by contrast between the central cellular area and the peripheral more loosely arranged tissue area, with water content in the other five schwannomas. The inhomogeneous pattern corresponded to irregular distribution of Antoni A and Antoni B combined with variable degrees of degenerative changes including cyst formation, hemorrhage, myxoid degeneration, and hyaline degeneration. The homogeneous pattern corresponded to inhomogeneous degenerative changes with various amounts of Antoni A and Antoni B components in 5 schwannomas and to homogeneous extensive myxoid,

hyaline degeneration, or marked peripheral myxoid degeneration with a large cystic space in the other three. The thin hyperintense rim corresponded to the peripheral myxoid Antoni B area or peripheral myxoid degeneration was observed in both inhomogeneous and homogeneous patterns. In the three patterns, there were no significant differences between the major nerve schwannomas and the intramuscular schwannomas. However, the interval from onset to surgery was significantly shorter with the target sign ( $10 \pm 5$  months) than with the other patterns ( $33 \pm 8$  months). The findings after Gd-DTPA could be classified as inhomogeneous enhancement (n= 16), homogeneous enhancement (n= 3), central enhancement (n=11), and marginal enhancement (n=6). The T2-weighted images had little correspondence with the findings of contrast medium enhancement (Table 3).

## **Discussion**

The frequencies of symptoms caused by schwannomas have been reported variously (1, 5, 6, 10, 16, 18). The frequency of the Tinel - like sign has been reported as being between 43.8 % and 94.5 % (1, 9, 14, 16). In our series, it was 69.4% which is significantly higher than that of the intramuscular schwannomas. Major nerve schwannomas usually produce some symptoms, because major nerves usually consist of

many bundles of sensory and motor nerve fibers, whereas intramuscular schwannomas seldom produce symptoms, because they usually consist of few bundles of motor nerve fibers.

On MR findings, the major nerve schwannomas usually showed the split-fat sign, entering and exiting nerve, low-signal margin and occasionally showed the target sign and thin hyperintense rim. Identification of the entering and exiting nerve is the most useful finding for the diagnosis of a neural tumor (6, 9, 13, 17). It has been reported that the split-fat sign represents fat tissue surrounding the involved nerve (15) and that low-signal margin represents epineurium surrounding the schwannoma (3, 9). These findings denote the presence of the nerve and are more easily detectable in major nerves than in small nerves. On the other hand, the target sign and thin hyperintense rim represent characteristic findings of the tumor itself rather than of the nerve.

Morphologically, three patterns could be identified on T2-weighted MR images. The frequencies of these three patterns in schwannomas have been reported as being between 4 % and 46.2 % for the target sign, between 45.5 % and 77.5 % for the inhomogeneous pattern, and between 13.3 % and 55.5 % for the homogeneous pattern (1, 8, 11, 16, 19). The correlation between the target sign and histological findings has been reported variously (2, 14, 19). In only six of 11 schwannomas, the target sign

corresponded to Antoni A regions centrally and Antoni B areas peripherally. The target sign tended to be observed in schwannomas which histologically showed less degeneration and had shorter intervals from onset to surgery. The schwannomas which show the target sign are never very old. Microscopic findings in tumors with irregular distribution of Antoni A and Antoni B with varying degrees degenerative changes commonly showed an inhomogeneous pattern and occasionally showed a homogeneous pattern on MR images. When moderate degenerative changes extended to a whole tumor, MR images showed a homogeneous pattern.

Macroscopically, a schwannoma is a shiny and greyish smooth ovoid mass and is surrounded by a true capsule consisting of the epineurium, since it occurs within the nerve sheath. Because the diagnosis of a schwannoma can be easily defined at the time of surgery by its characteristic macroscopic appearance, a biopsy can be prevented if the preoperative diagnosis is a schwannoma. Although biopsies were performed in three major nerve schwannomas and in four intramuscular schwannomas, we could have avoided this by careful examination of the characteristic symptoms and of the MR findings (except for two intramuscular schwannomas which had no characteristic symptoms and MR findings).

In conclusion, the Tinel - like sign, split-fat sign, entering and exiting nerve, and

low-signal margin are commonly observed in major nerve schwannomas and less commonly in intramuscular schwannomas. Although frequencies of target sign are only about 30% both in major nerve schwannomas and intramuscular schwannomas, the sign is useful for diagnosis because of a unique finding which denotes the tumor itself. In intramuscular schwannomas, these characteristic findings are less common, which makes diagnosis difficult. Biopsies could be avoided by careful examination of these findings in all major nerves schwannomas and in most intramuscular schwannomas.

## References

1. Artico M, Cervoni L, Wierzbicki V, D'Andrea V, Nucci F. Benign neural sheath tumors of major nerves: characteristics in 119 surgical cases. *Acta Neurochir (Wien)* 1997; 139: 1108- 1116.
2. Bharagava R, Parham DM, Laster OE, Chari RS, Chen G, Fletcher BD. MR imaging differentiation of benign and malignant peripheral nerve sheath tumors: use of target sign. *Pediatr Radiol* 1997; 27: 124- 129.
3. Cerofoloni E, Landi A, DeSantis G, Maiorana A, Canossi G, Romagnoli R. MR of benign peripheral nerve sheath tumors. *J Comput Assist Tomogr* 1991; 15: 593- 597.
4. Davis EN, Chung KC. The Tinel sign: A Historical Perspective. *Plastic and Reconstructive Surg* 2003; 114: 494- 499.
5. Donner TR, Voorhies RM, Kline DG. Neural sheath tumors of major nerves. *J Neurosurg* 1994; 81: 362- 373.
6. Hems TEJ, Burge PD, Wilson DJ. The role of magnetic resonance imaging in the management of peripheral nerve tumours. *J Hand Surg Br* 1997; 22: 57-60.
7. Holdsworth BJ. Nerve tumours in the upper limb. A clinical review. *J Hand Surg* 1985; 10B: 236- 238.
8. Jee WH, Oh SN, McCauley T, Ryu KN, Suh JS, Lee JH, et al. Extraaxial

neurofibromas versus neurilemmomas: Discrimination with MRI. *Am J Roentgenol* 2004; 183: 629- 633.

9. Kang H. J., Shin S. J., Kang E.S. Schwannomas of the upper extremity. *J Hand Surg Br* 2000; 25B: 604- 607.

10. Kehoe NJS, Peid R, Semple JM. Solitary benign peripheral-nerve tumours: review of 32 years' experience. *J bone Joint Surg Br* 1995; 77: 497-500.

11. Ko SF, Ng SH, Lee TY, Lin WL, Chen WJ, Hsieh MJ, et al. MR imaging of thoracic neurilemmomas. *Magnetic Resonance Imaging* 1997; 15: 525- 533.

13. Lin J, Martel W. Cross-section imaging of peripheral nerve sheath tumors: Characteristic signs on CT, MR imaging, and Sonography. *Am J Roentgenol* 2001; 176: 75- 82.

14. Manabe J, Kawaguchi T, Amino K, Matsumoto S, Kitagawa T, Machinami M, et al. A clinico-pathological study on 105 cases of schwannoma developed in the peripheral nerve. *Rinsho Seikei Geka Clin Orthop Surg* 1987; 22: 1035- 1046.

15. Murphey MD, Smith WS, Smith SE, Kransdorf MJ, Temple HT. From the archives of the AFIP. Imaging of musculoskeletal neurogenic tumors: radiologic-pathologic correlation. *RadioGraphics* 1999; 19: 1253- 1280.

16. Ogose A, Hotta T, Morita T. Tumors of peripheral nerves: correlation of symptoms,

clinical signs, imaging features, and histologic diagnosis. *Skeletal Radiol* 1999; 28: 183-188.

17. Rettenbacher T, Sogner P, Springer P, Fiegl M, Hussl H, Nedden Dz. Schwannoma of the brachial plexus: cross-sectional imaging diagnosis using CT, sonography, and MR imaging. *Eur Radiol* 2003; 13: 1872- 1875.

18. Suh JS, Abenzoa P, Galloway HR, Everson LI, Griffiths HJ. Peripheral (extracranial) nerve tumors: correlation of MR imaging and histologic findings. *Radiology* 1992; 183: 341- 346.

19. Verma DGK, Mouloupoulos A, Sara AS, Leeds N, Kumar R, Kim E, et al. MR imaging of extracranial nerve sheath tumors. *J Comput Assist Tomogr* 1992; 16: 448-453.

## Figure legends

### Figure 1

T2-weighted MR images of an intramuscular schwannoma involving biceps femoris in a 41-year-old female. A sagittal image shows an oval mass with low-signal margin (black arrow) and the surrounding fat (fat-split sign) (white arrow) (A). An axial image shows a round mass in the biceps femoris (B).

### Figure 2

Sciatic nerve schwannoma in a 58-year-old male. An axial T2-weighted MR image shows the target sign with entering and exiting sciatic nerve (white arrows) (A). A sagittal T2-weighted image shows the target sign with low-signal margin (B). A photomicrograph (original magnification,  $\times 50$ ; hematoxylin-eosin stain) shows more cellular Antoni A regions centrally and more myxoid Antoni B areas peripherally (C).



Fig. 1 A

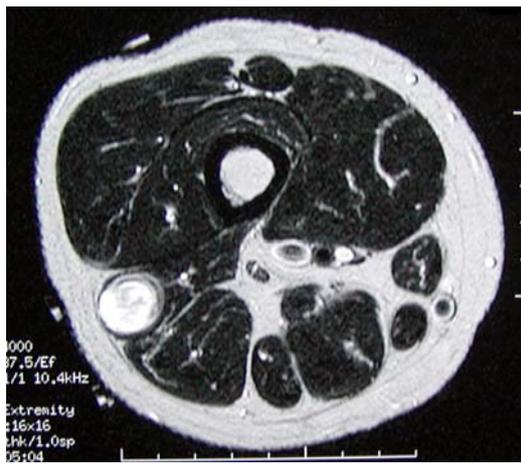


Fig. 1 B



Fig. 2 A



Fig. 2 B



Fig. 2 C

Table 1. Sites of 36 schwannomas

<b>Major nerve schwannoma</b>	<b>29</b>	<b>Intramuscular schwannoma</b>	<b>7</b>
Sciatic nerve	9	Gluteus maximum	2
Brachial plexus	6	Infraspinatus	1
Tibial nerve	5	Extensor carpi ulnaris	1
Peroneal nerve	3	Longissimus thoracis	1
Musculocutaneous nerve	2	Tensor fascia lata	1
Median nerve	2	Biceps femoris short	1
Ulnar nerve	2		

Table 2. Symptoms and MR findings of 36 schwannomas

<b>Symptoms and MR findings</b>	<b>Major nerve (n= 29)</b>	<b>Intramuscular (n= 7)</b>	<b>P value</b>
Pain at rest	9	1	0.6518
Tenderness	14	1	0.2003
Tinel-like sign	24**	1	0.0014
Sensory disturbance	7	0	0.3029
Motor weakness	2	0	0.4746
Split-fat sign	26*	3	0.0164
Entering and exiting nerve	26**	1	0.0003
Low-signal margin	23*	2	0.0180
Thin hyperintense rim	6	1	0.6924
Target sign	9	2	
Inhomogeneous pattern	13	4	0.8031
Homogeneous pattern	7	1	

\* $P < 0.05$ , \*\*  $P < 0.01$

Table 3. Correlation between T2-weighted images and enhanced images

<b>Enhancement</b> <b>T2-weighted images</b>	Inhomogeneous	homogeneous	Central	Marginal
Target sign (n=11)	2	0	8	1
Inhomogeneous pattern (n=17)	11	0	2	4
Homogeneous pattern (n=8)	3	3	1	1