Diffusion-weighted magnetic resonance neurography for parapharyngeal schwannomas: preoperative determination of their originated nerves

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Aims and objectives

Introduction

Parapharyngeal space is an inverted pyramidal-shaped potential space extending down from the skull base on either side of pharynx. It is historically subdivided mainly by surgeons into two compartment: prestyloid and poststyloid compartment by tensor-vascular-styloid fascia. The component of poststyloid parapharyngeal space include internal of common carotid artery, internal jugular vein, cranial nerves # - #, and cervical sympathetic chain and gloms bodies, and this space has more recently been termed the carotid space, separated from the parapharyngeal space[1].

A schwannoma is a benign neoplasm originating from the Schwann cells of the nerve sheath, which surround peripheral, cranial, and autonomic nerves. Most extracranial schwannomas originate commonly from the neck sympathetic chain (SC) and vagus nerve (VN) and, on rare occasions, from other cranial nerves [2-4]. Most schwannomas can be explained to arise from not the parapharyngeal space but the carotid space, however, they are commonly discribed as "parapharyngeal space schwannoma" in the literature.

Resection of parapharyngeal schwannomas is an accepted treatment; however, postoperative neurological deficits often occur. Therefore, it is important to preoperatively determine the originating nerve, because neural complications differ between the SC and the VN: Horner's syndrome and first-bite syndrome for the SC and vocal cord paralysis and hoarseness for the VN [2,5,6].

Previous reports had indicated that the VN could be preoperatively discriminated from the SC as the origin of a schwannoma by analyzing the relationship of the tumor to the carotid sheath vessels, that is, the common or internal carotid artery (CA) and internal jugular vein (IJV) [2,5,7]. A vagal schwannoma tends to displace the CA and the IJV, with lateral separation of the IJV from the CA.

Recently, diffusion-weighted (DW) magnetic resonance neurography (MRN) (DW-MRN) was used to visualize peripheral nerves with suppression of the signal from the adjacent vessels [8,9]. Conventional MRN has been performed by using fat-suppressed T2-weighted imaging or short TI inversion recovery (STIR) and T1-weighted imaging [8,10,11] that have limitations related to visualizing the nerves in the neurovascular bundles because the signal intensities of vessels are often similar to those of the adjacent nerves, thus obscuring them.
The cervical SC and VN are fine structures and adjacent to the CA and IJV. Therefore, DW-MRN might be suitable for visualizing them, in comparison with conventional MRN. Actually, the use of conventional MRN for visualizing the parapharyngeal space has not yet been reported for the past 2 decades since the emergence of peripheral nerve examinations by MRN [10,11]. If DW-MRN could visualize the SC and the VN and their relationships to a schwannoma, it might support a diagnosis of the originating nerve.

The purpose of our study was to evaluate the feasibility of DW-MRN for visualizing the originating peripheral nerves of parapharyngeal schwannomas through a comparison of findings from conventional MR and surgery and to assess the potential role of these modalities to preoperatively determine the originating nerve.
Methods and materials

Patients

This study was approved by the ethics committee of our institution, and written informed consent was waived.

Since October 2010, DW imaging with AP unidirectional MPGs has been routinely performed for the assessment of neck tumors. This type of DW imaging had been reported to be applicable to DW-MRN for the brachial and sacral plexus [12,13]. Therefore, DW images of neck tumors that were acquired in our institution were considered to be available for DW-MRN. We retrospectively selected patients who were surgically and histopathologically confirmed to have a parapharyngeal schwannoma that had neck MR imaging including DW imaging in our institution, by searching through our pathological and radiologic records that were obtained between October 2010 and February 2013. Six patients (2 men and 4 women; age range, 22 to 69 years; mean, 43 years) met the inclusion criteria and were enrolled in our study. All 6 patients had unilateral masses. Of the 6 masses, 5 were located on the right side, while 1 was on the left side.

MR Imaging

MR imaging was performed by using one of two 1.5-T MR units (Signa HDxt, General Electric Medical Systems, Milwaukee, WI, or EXCELART vantage powered by Atlas, Toshiba Medical Systems, Tokyo, Japan) for 5 (case numbers 1, 2, 3, 5, and 6) patients and 1 (case number 4) patient, respectively. An MR unit was randomly selected for each patient. Images were acquired by using a phased array coil, composed of 8 channels with 18 elements (Neurovascular array coil, GE) or 16 channels with 20 elements (Atlas SPEEDER head + spine + body coil, Toshiba). The maximum gradient strength and slew rate were 33 mT/m and 120(Tm - 1)/s for GE and 33 mT/m and 200(Tm - 1)/s for Toshiba, respectively.

DW-MRN imaging

Before October 2010, we had performed DW imaging by using chemical shift selective suppression of fat and three-directional motion probing gradients (MPGs), in order to assess neck tumors in several patients. However, with these images, it was often difficult to assess lesions, because B1 inhomogeneity caused fat suppression to be unsuccessful, and blurring was severe because of different directional distortions from the source DW image with each unidirectional MPG. Therefore, we applied short TI inversion recovery (STIR) for fat suppression and altered three-directional MPGs into anterior-posterior (AP) unidirectional MPGs, and with these methods, these artifacts were reduced.
For DW-MRN, with the use of the GE MR unit in this study, the acquisition parameters were as follows: slice orientation, axial; sequence, spin-echo echo planar imaging (EPI); MPGs, AP; fat saturation, STIR; repetition time (TR)/echo time (TE)/inversion time (TI) (ms), 7800/minimum (71.9-74.8)/150; parallel imaging, ASSET 2, acquisition matrix (read out [RO] × phase encode [PE]), 98 × 128; reconstruction matrix, 256 × 256; acquisition pixel spacing (mm), 4.08 × 3.12; reconstruction pixel spacing (mm), 1.56 × 1.56; number of excitations, 7; slice thickness/gap (mm), 4/0; number of sections, 40; field of view (FOV; mm), 400 × 400; b-factor (s/mm²), 0, 900; and acquisition time (s), 218. For DW-MRN, with the use of the Toshiba MR unit, the acquisition parameters were as follows: slice orientation, axial; sequence, spin echo EPI; MPGs, AP; fat saturation, STIR; TR/TE/TI (ms) 13600/95/180; parallel imaging, SPEEDER factor 2; acquisition matrix (RO × PE), 128 × 96; reconstruction matrix, 308 × 192; acquisition pixel spacing (mm), 2.60 × 3.12; reconstruction pixel spacing (mm), 1.30 × 1.30; number of excitations, 4; slice thickness/gap (mm), 5/0; number of sections, 60; FOV (mm), 400 × 250; b-factor (s/mm²), 0, 900; and acquisition time (s), 234.

**Conventional MR imaging**

Conventional MR imaging that was used for this study was axial T1-weighted fast spin echo (T1W-FSE) imaging, axial and coronal T2-weighted fast spin echo (T2W-FSE) imaging. With the use of the GE unit, the acquisition parameters were as follows: (a) axial T1W-FSE imaging; sequence, FSE; fat saturation, non; TR/TE [ms], 440/7.5-8; parallel imaging, ASSET factor 2; matrix [RO × PE], 256 × 256; number of excitations, 3; slice thickness/gap (mm), 4/0.8 and (b) axial T2W-FSE imaging; sequence, FSE; fat saturation, non; TR/TE [ms], 4000/86.4-87.1; parallel imaging, ASSET factor 2; matrix [RO × PE], 256 × 224; number of excitations, 3; slice thickness/gap (mm), 4/0.8 and (c) coronal T2W-FSE imaging; sequence, FSE; fat saturation, chemical shift selective saturation (CHESS); TR/TE [ms], 4000/87.6-87.9; parallel imaging, non; matrix [RO × PE], 320 × 256; number of excitations, 2; slice thickness/gap (mm), 5/0.5. The acquisition parameters with the use of the Toshiba unit were: (a) axial T1W-FSE imaging: sequence, FSE; fat saturation, non; TR/TE [ms], 370/15; parallel imaging, SPEEDER factor 1.4 for axial, non-parallel for coronal; matrix [RO × PE], 228 × 224; number of excitations, 1; slice thickness/gap (mm), 5/1, (b) axial T2W-FSE imaging; sequence, FSE; fat saturation, non; TR/TE [ms], 3509.4-4086/90; parallel imaging, SPEEDER factor 1.4; matrix [RO × PE], 320 × 224; number of excitations, 2; slice thickness/gap (mm), 5/1 and (c) coronal T2W-FSE imaging; sequence, FSE; fat saturation, CHESS; TR/TE [ms], 4100/90; parallel imaging, non; matrix [RO × PE], 288 × 224; number of excitations, 2; slice thickness/gap (mm), 5/1.

**MR evaluations**
Two board-certified radiologists evaluated the parapharyngeal schwannomas with consensus on the conventional MR images and DW-MRN by using a DICOM viewer (OsiriX imaging software, version 5.6, Osirix foundation, Geneva, Switzerland). Conventional MR images were assessed for the following parameters on an affected side: (1) size of tumor (transverse, antero-posterior and craniocaudal diameters), (2) separation between the CA and the IJV, (3) CA displacement (medial, anterior, lateral, posterior, or oblique direction between them), and (4) tumor adjacent to the jugular foramen. DW-MRN images were evaluated for the following parameters on both sides: (1) visualization of the VN and SC, (2) level of visualization based on the vertebral body, and (3) nerve adjacent to the jugular foramen; as for an affected side: (1) tumor visualization, and (2) the relationship of a visualized nerve to the tumor, classified into either the connected or dislocated categories (Figure 1).

**Fig. 1:** DW-MRN classification of the relationship of the peripheral nerve to the parapharyngeal space schwannoma; (a) "connected" and (b) "dislocated."

**References:** Radiology, Tokyo Medical and Dental University - Tokyo/JP

On DW-MRN, signal intensities of the VN and SC were identified on the axial images according to the anatomy of the parapharyngeal space (Figure 2).
**Fig. 2:** An illustration of the parapharyngeal space. (a) normal anatomy; typical imaging of a sympathetic chain schwannoma (b) and a vagal schwannoma (c). The area surrounded by a solid black line encompasses both the prestyloid and poststyloid parapharyngeal space, and the broken white line is the post styloid parapharyngeal space, the carotid space (a). "Separation" between the internal carotid artery (ICA) and the internal jugular vein (IJV) is shown in a vagal schwannoma case (c). SC, sympathetic chain; VN, vagus nerve.

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We identified the vagus nerve if it was located in the posterior notch that was formed by the CA and IJV and identified the cervical sympathetic chain if it was located between the medial carotid space and lateral retropharyngeal space [14]. Fusion of axial T2W-FSE and DW-MRN images was performed by overlaying signals from a DW-MRN onto a T2W-FSE image and by correcting the misalignment of the DW-MRN manually. Reference to DW-MRN was performed by using the axial T2W- and T1W-FSE images in order to confirm whether the visible nerves were visualized as signal intensities, other than fat (that is, low-signal intensity on a T1W image and low to high signal intensity on a T2W image). Coronal and sagittal maximum intensity projection (MIP) images with DW-MRN were generated in order to evaluate the relationships of the visible nerves to the tumor. In addition, one of the radiologists placed a round-shaped region of interest (ROI) individually on the signal intensity of each nerve, created a three-dimensional (3D) ROI...
image by combining all the ROIs for each nerve and fusing these 3D ROI images into a 3D MIP of DW-MRN, in order to clearly show the range of visible nerves.

Predictions regarding the originating nerve were performed separately with the conventional method and DW-MRN. With the conventional method, we determined that a tumor showing "separation" originated from the VN and a tumor showing "no separation" originated from the SC. On DW-MRN, a nerve characterized as "connected" to the tumor was determined as the origin. These predictions were compared with the surgical results.

A pathologist re-evaluated the specimens of all 6 cases and searched for normal nerve fibers, other than those of the tumor. We summarized the relationships of the MR findings, surgical findings, and pathological findings with respect to normal nerve fiber and postoperative neural complications.
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## Results

A summary of the MR findings, as well as the surgical findings, is shown in Table 1.

<table>
<thead>
<tr>
<th>Patient Number/ Sex/Age (y)</th>
<th>MR Imaging Findings</th>
<th>Prediction of nerve origin</th>
<th>Surgical results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conventional MR imaging</td>
<td>DW-MRN&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Tumor size Separation of the CA and IJV</td>
<td>Direction of CA Displacement</td>
<td>Tumor adjacent to the Jugular foramen</td>
<td></td>
</tr>
<tr>
<td>1/M/69 31×42×59</td>
<td>No</td>
<td>Posterolateral</td>
<td>No</td>
</tr>
<tr>
<td>2/F/56 37×33×59</td>
<td>No</td>
<td>Posterolateral</td>
<td>No</td>
</tr>
<tr>
<td>3/F/22 26×39×48</td>
<td>Yes</td>
<td>Anteromedial</td>
<td>Yes</td>
</tr>
<tr>
<td>4/F/33 32×33×60</td>
<td>No</td>
<td>Posterolateral</td>
<td>No</td>
</tr>
<tr>
<td>5/M/39 36×52×55</td>
<td>No</td>
<td>Anterolateral</td>
<td>No</td>
</tr>
<tr>
<td>6/F/39 25×28×39</td>
<td>No</td>
<td>Posterolateral</td>
<td>No</td>
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</table>

**Table 1**: MR imaging findings and final diagnosis of the originating nerves in patients with a parapharyngeal schwannoma. MR, magnetic resonance; DW-MRN, diffusion-weighted magnetic resonance neurography; SC, sympathetic chain; VN, vagus nerve. 

<sup>a</sup> All the visualized nerves were found between jugular foramen and C2; 
<sup>b</sup> NA = not applicable

**References**: Radiology, Tokyo Medical and Dental University - Tokyo/JP

MR images of patients with cervical sympathetic chain schwannomas are shown in Figures 3 and 4.
**Fig. 3:** MR images of a 39-year-old woman with a sympathetic chain (SC) schwannoma (Case 6). (a) Axial T2-weighted image at the C3 level shows the ICA and IJV both displaced posterolaterally by the SC schwannoma, with no separation between them. (b) T2-weighted and (c) T1-weighted axial images through the C2 level, superior to (a), show the SC and vagus nerve (VN) are well delineated. (d) Axial fusion image of T2-weighted and DW-MRN data, at the level of (b) and (c), shows good correlation of conventional MR and DW-MRN data. Coronal (e) and sagittal (f) maximum intensity projection images of the DW-MRN data, with SC and VN depicted superior to the tumor at the C2 level, display the corresponding levels of the axial images (a-d). The SC is connected to the tumor, and the VN is displaced posterolaterally by the tumor. Reference lines of a sagittal or coronal MIP correspond to unmarked parallel lines on a coronal and sagittal MIP (e and f) and a fusion image (d). (g) Intraoperative photograph reveals the VN coursing downward between the ICA and the IJV, and laterally over the tumor. Specimen photomicrograph (h) shows the connected nerve fiber (white line, upper side), which is considered to be the SC, and tumor (lower side). ECA, external carotid artery.

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Fig. 4: Sympathetic chain schwannomas in a 33-year-old woman (case number 4). (a) Axial T2-weighted image at the C3 level shows the ICA and IJV both displaced anterolaterally by the SC schwannoma, with no separation between them. On coronal(b) and sagittal (c) MIP of the DW-MRN, both of the SC and the VN seem to connect to the tumor. (d) an intraoperative photograph revealed the VN coursing downward between the CA and the IJV.

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On conventional MR images, "separation" of the CA and IJV were demonstrated in 5 patients, whereas "no separation" was seen in 1 patient. Therefore, the conventional MR findings determined the originating nerve to be the SC for 5 patients and the VN for 1 patient.

With DW-MRN of the unaffected side, both the SC and the VN were visualized for all 6 patients. Meanwhile, with DW-MRN, on the affected side, both the SC and the VN were visualized in 4 patients, with the VN alone in 1 patient and neither in 1 patient. On the bilateral side, all visualized SC and VN were found between the level of jugular foramen and the lower end of the C2 vertebral body (Figure 5).
Fig. 5: Fusion images of the coronal MIP for the DW-MRN and 3D ROIs of the sympathetic chain (blue) and vagus nerve (red). (a) case 1, (b) case 2, (c) case 3, (d) case 4, (e) case 5, and (f) case 6. Case 2(b) fails to visualize the SC on the affected side, and case 3(c) fails to visualize the SC and the VN on the affected side.

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The portion of the SC adjacent to the jugular foramen was not seen in any case, on either side. The VNs adjacent to the jugular foramen was seen in 5 of 6 and 4 of 5 cases on the unaffected and affected sides, respectively. The schwannomas were revealed as a high-signal intensity and well-circumscribed mass with DW-MRN. On the basis of the relationships of the nerves to the tumor with DW-MRN, the originating nerves were determined to be the SC in 4 patients, undetermined in 1 patient, and not applicable in 1 patient.

Surgeries that were performed on the parapharyngeal schwannomas revealed that their originating nerves were the SC for 5 patients and the VN for 1 patient. With the conventional MR images findings, we were able to correctly predict the originating nerves in all patients, whereas with DW-MRN, we correctly predicted the originating nerves in only 4 of 6 patients with SC schwannomas.
In 2 SC schwannomas (Figures 3 and 4), a small amount of nerve fiber was found attached to the tumor capsule in a pathological specimen. Following surgery, these 2 (case 4 and 6) patients, as well as the other 2 of 3 patients (case 2 and 5) with an SC schwannoma developed Horner's syndrome and first-bite syndrome, and 1 patient (case 3) with a vagal schwannoma had unilateral vocal cord paralysis.
Table 1: MR imaging findings and final diagnosis of the originating nerves in patients with a parapharyngeal schwannoma MR, magnetic resonance; DW-MRN, diffusion-weighted magnetic resonance neurography; SC, sympathetic chain; VN, vagus nerve. a, All the visualized nerves were found between jugular foramen and C2; b, NA = not applicable

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Conclusion

Discussion

To our knowledge, this is the first study to demonstrate a cervical SC and VN by using DW-MRN, as well as the potential role of DW-MRN for determining the originating nerves of a cervical schwannoma preoperatively.

With DW-MRN, portions of the SCs were consistently visualized between the level of jugular foramen and the lower end of the C2 vertebral body. As an overview of this region, 3 ganglia anatomically are located in the cervical SC [3]. Regarding these 3 ganglia, the superior one is the largest and usually often found between the levels C2 and C4, with a diameter of 5.3 (± 0.6 mm). The middle one is the smallest and is usually located around C6. The inferior one is variable in position, and it often fuses with the first thoracic ganglion to form the stellate ganglion. Therefore, the SC that was visualized with DW-MRN was considered to be consistent with the superior sympathetic ganglion.

The VN was also visualized with DW-MRN only at the level of C2. This could be because visualization of the peripheral nerve depends on the diameter of the nerve fiber bundle [8]. The diameter of the proximal portion of the VN might be larger than that of the distal portion. Moreover, the VN passes through the jugular foramen, accompanied by the glossopharyngeal and accessory nerves, and descends into the carotid space with these nerves. Separation of these nerves occurs at the nasopharyngeal level or at C2 level [14,15]. These nerves are intimately related, forming intercommunicating branches between them [14-16]. These characteristics might contribute to the visualization of the peripheral nerve in the parapharyngeal space at the level of C2 with DW-MRN.

During this study, some nerves were not visualized, and in fact, a nerve could present as a false positive, or seemed to be "connected" to a tumor. In a patient with a vagal schwannoma, which extended to the jugular foramen, neither the SC nor the VN was visualized on the side. These nerves must have been masked by tumor compression or replacement of these nerves. In another case, the VN was falsely shown to be "connected" to the tumor in a patient with an SC schwannoma that was displacing the CA and IJV anterolaterally (Fig 4 and table 1), whereas the VNs were precisely shown as "dislocated" in all four patients with an SC schwannoma that had posterolateral displacement. A "connected" sign might not be necessary to indicate the originating nerve, because both the SC and the VN could be in close contact with a parapharyngeal space tumor.

We chose AP unidirectional MPG for DW-MRN. It seemed to overcome the weakness of using multidirectional MPGs because of distortion in the direction of each unidirectional
MPG [12,13]. The distortion was increased with B1 inhomogeneity. In the neck region, B1 inhomogeneity was relatively strong. In addition, the positioning of AP unidirectional MPGs, which are approximately perpendicular to the course of the VN, is effective for visualizing the VN because nerve fibers have anisotropic diffusion, that is, water diffusion is predominant in the large dimension of the nerve axis. If unidirectional MPGs are used, the signal of the nerve fiber is highest if those directions are perpendicular to the nerve, or in the short dimension of nerve.

Previous studies have reported that the analysis of the separation pattern of the CA and IJV had a high accuracy for discriminating VN from SC as a origin of parapharyngeal schwannoma, however, rarely failed to diagnose [3,5,17]. In the future, DW-MRN may becomemantary to the conventional MR imaging.

This study had some limitations. First, there were a small number of patients with schwannomas. Our study included only 1 vagal schwannoma. A second limitation was that the spatial resolution was low with DW-MRN. Optimization of the MR acquisition parameter is necessary to improve sensitivity for the detection of peripheral nerves. However, the stretched and thinned originating nerve might be hard to track.

In conclusion, DW-MRN is a feasible approach for visualizing the cervical sympathetic chain and vagus nerve and for determining the originating nerve of a parapharyngeal schwannoma preoperatively.
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