RESEARCH ARTICLE

Diffusion tensor imaging of the inferior alveolar nerve using 3T MRI: a study for quantitative evaluation and fibre tracking

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Objectives: Diffusion tensor imaging (DTI) can provide structural information and objective values for nerves. The aims of this study were to perform quantitative evaluation and fibre tracking of the normal inferior alveolar nerve (IAN) using DTI on 3.0-T MRI.

Methods: DTI was applied to 92 IANs of 46 healthy volunteers. Circular regions of interest (ROIs) were placed on three different positions at the mandibular foramen, second molar and mental foramen of each nerve on apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps, and the ADC and FA of each ROI were measured. Differences in the values arising from the nerve positions were evaluated. Furthermore, fibre tracking of the IANs was performed by tractography, and the quality of visualization was evaluated.

Results: There were no significant differences in the ADC and FA between the right and left sides regardless of the anteroposterior positions. Regarding differences arising from the anteroposterior measurement positions, the ADC and FA showed no significant differences ($p > 0.017$), except for the ADCs between the positions at the mandibular foramen and mental foramen in the left side ($p = 0.0068$). Overall, 70 (76%) of the 92 IANs could be visualized fully or partially by tractography.

Conclusions: The ADC and FA of the IAN were successfully obtained from healthy volunteers using DTI and were confirmed to be symmetrical regardless of the measurement positions. DTI is a feasible technique for the quantitative evaluation and visualization of the IAN.

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Introduction

The inferior alveolar nerve (IAN) is one of the branches of the mandibular nerve and runs in the mandibular canal, extending from the mandibular foramen to the mental foramen of the mandible. An injury to the IAN during dental treatment, including impacted tooth extraction, dental implant placement and osteotomy, may cause prolonged paraesthesia or paralysis of the lower

lip and mental region.^{1–3} Paraesthesia can also be caused by traumatic injury, osteomyelitis and pressure from intrabony mass lesions. When an IAN injury occurs, subjective methods based on patient complaints are commonly used to assess the severity of the neurosensory deficit.⁴ Thus, it is essential to develop precise and quantitative evaluation methods for damage to the IAN and its recovery after treatment.

Several imaging techniques, including multidetector CT and cone-beam CT, have been widely used for the

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assessment of the mandibular canal containing the IAN bundle.^{5,6} Although these images can delineate the course of the mandibular canal at high spatial resolutions, they cannot directly visualize the IAN itself. Recently, several studies have evaluated the mandibular canal using MRI.^{7–9} Among these, some researchers reported that changes to the neurovascular bundle including IAN could be evaluated on the basis of T_1 - and T_2 -related signal intensities on high-quality MR images.

Diffusion tensor imaging (DTI) is a relatively new MRI technique that reflects the physiological function of biological tissues. DTI can provide tissue contrast based on the diffusivity and anisotropy of microscopic water motion within biological tissues.^{10,11} According to previous studies, nerve bundles and muscle fibres can be evaluated quantitatively and visualized directly using DTI. On DTI, the indices of the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) are commonly used for quantitative evaluation. The ADC is a measure of the mean diffusivity of microscopic water motion. The FA is a measure of microscopic water anisotropy and ranges from 0 (perfect isotropy) to 1 (total anisotropy). DTI has mainly been applied to the functional analysis and diagnosis of diseases in the central nervous system. Recently, this technique has also been applied to several peripheral nerves, namely the median nerve,¹² tibial nerve^{13,14} and lumbar plexus.¹⁵ Those studies demonstrated that the ADC and FA could reflect the pathological conditions of peripheral nerves. To date, only a few studies reported the application of DTI to the IAN.^{16–18} In particular, to our knowledge, there has been only one study that has quantitatively evaluated the physiological function of the IAN using the FA and diffusivity.¹⁸ Accordingly, DTI of the IANs has not been well covered in the literature and still requires systematic assessment.

Against these backgrounds, the aims of this study were to perform quantitative evaluation and fibre tracking of the IANs in a large number of healthy volunteers using DTI on 3.0-T MRI and to discuss the feasibility and clinical usefulness of this technique.

Methods and materials

This prospective study protocol was approved by our institutional review board (No. 1096), and written informed consent was obtained from all participants before the MRI examination.

Subjects

46 healthy volunteers were included in this study (21 males and 25 females; mean age, 25 years; age range, 20–36 years). None of the volunteers had any history of neuropathy, trauma or surgery of the IAN.

MRI techniques

All MRI examinations were performed with a 3.0-T MRI scanner (Magnetom Spectra; Siemens Healthcare,

Erlangen, Germany) with a 16-channel head and neck coil. DTI was performed using spin echo-based single-shot echoplanar imaging (EPI) with fat suppression by short tau inversion recovery (STIR). The imaging parameters were as follows: repetition time/echo time/inversion time, 15,000/80/250 ms; field of view, 230 × 230 mm; matrix, 128 × 128; slice thickness, 1.8 mm with no intersection gap; and number of signals averaged, 3. A total of 30 axial slices were obtained with parallel imaging acceleration (GRAPPA with iPAT factor of 3). In addition, a bipolar scheme was applied. Motion-probing gradients (MPGs) were applied in 12 directions with two b -values (0 and 600 s/mm²). The total scan time for DTI was 11 min 30 s. Before DTI, three-dimensional T_1 weighted (3D T1W) images were obtained using magnetization-prepared rapid gradient echo. The imaging parameters were as follows: repetition time/echo time/inversion time, 1800/2.2/800 ms; flip angle, 10°; field of view, 210 × 210 mm; matrix, 256 × 256; slice thickness, 0.8 mm with no intersection gap; and number of signals averaged, 1. A total of 178 sagittal slices were obtained. The total scan time for 3D T1W imaging was 4 min 44 s.

Image analysis

After the MRI examination, DTI data including ADC and FA maps were automatically computed using the console computer of the MRI system. The DTI data were based on the methods of a monoexponential model. Quantitative evaluation and tractography were performed with an advanced visualization system (syngo.via; Siemens Healthcare) and the application software associated with the system (syngo.MR Neuro 3D Engine).

For the quantitative evaluation, the ADC and FA maps and 3D T1W images were displayed in triplanar views on the visualization system. To measure the ADC and FA of the IAN, circular regions of interest (ROIs) were placed at three different positions on the left and right IANs on the coronal view of ADC and FA maps, with reference to the triplanar views of 3D T1W images (Figure 1). The positions of the ROIs were as follows: mandibular foramen (m_1); second molar (m_2); and mental foramen (m_3). The ROIs were placed on the coronal view of ADC and FA maps. The ROIs were slightly smaller than the sections of the IAN in the same location on the coronal view of 3D T1W images, so that they did not include the surrounding bone marrow. The appropriateness of the placed ROIs was determined by consensus between the two authors (with more than 3 and 10 years' MRI experience). Subsequently, the former author measured the ADC, FA and ROI size.

To visualize the IAN three-dimensionally, fibre tracking was performed by tractography. The fibre-tracking approach is dependent on the deterministic tractography. After the location of the inferior alveolar neurovascular bundle was confirmed on the 3D T1W images, an ROI, as the seed point for fibre tracking, was placed at the mandibular foramen. The ROI was

Figure 1 Region-of-interest (ROI) settings for the measurement of the inferior alveolar nerves using the triplanar views of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps: (a) triplanar views of the reference three-dimensional T_1 weighted (3D T1W) images and ADC map. Image scrolling and planar setting could be synchronized between the two images. The ROIs were placed on the coronal view of the ADC map, and ADC values were measured. FA values were measured by copying and pasting the ROIs for ADC. (b) The coronal and oblique sagittal views of the ADC map. The positions of the ROIs are the mandibular foramen (m_1); second molar (m_2); and mental foramen (m_3).

slightly larger than the section of the bundle on the 3D T1W images to avoid underestimation. The parameters for fibre tracking of the IAN were set as follows: FA threshold, 0.2; angle threshold, $\pm 40^\circ$; and minimum fibre length, 35 mm. One author performed fibre tracking in all cases and another author evaluated the quality of the IAN visualization using a three-point rating scale: good, full-length visualization of the IAN from the mandibular foramen to the mental foramen; fair, partial-length visualization of the IAN; poor, very short or no visualization of the IAN.

Statistical analysis

A paired t -test was used to evaluate the differences in the ADC and FA at each position of the IANs between the right and left sides. Values of $p < 0.05$ were considered statistically significant. Furthermore, a paired t -test with a Bonferroni correction was used to evaluate the differences in the ADC and FA of the IANs among the three measurement positions of the nerve on each

side. In this analysis, Bonferroni-corrected values of $p < 0.017$ ($0.05/3$) were considered statistically significant. In addition, Bland–Altman plot was performed for evaluating the distribution of differences in ADC and FA values at each position between the right and left sides. All statistical analyses were performed with statistical software Prism 5 for Mac OS X (GraphPad Software Inc, San Diego, CA).

Results

Quantitative evaluation of the inferior alveolar nerve using diffusion tensor imaging data

DTI data were successfully obtained for all of the 46 healthy volunteers. Three cases were excluded from this quantitative evaluation because all of the six ROIs could not be placed on their ADC maps. Therefore, a total of 258 ROIs in 43 cases were placed to measure the ADC and FA values. The mean values for the

Table 1 Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) of the inferior alveolar nerves

Measurement position		ADC ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	FA	ROI (mm^2)
m ₁	Right	0.981 $\pm$ 0.244 (0.905–1.06)	0.401 $\pm$ 0.109 (0.368–0.435)	6.77
	Left	1.02 $\pm$ 0.247 (0.904–1.09)	0.425 $\pm$ 0.0865 (0.398–0.452)	6.23
m ₂	Right	0.971 $\pm$ 0.283 (0.884–1.06)	0.413 $\pm$ 0.103 (0.381–0.444)	7.02
	Left	0.961 $\pm$ 0.321 (0.862–1.06)	0.419 $\pm$ 0.0950 (0.390–0.449)	6.88
m ₃	Right	0.865 $\pm$ 0.400 (0.742–0.988)	0.439 $\pm$ 0.134 (0.398–0.480)	6.72
	Left	0.848 $\pm$ 0.368 (0.735–0.962)	0.424 $\pm$ 0.128 (0.384–0.463)	6.23

ROI, region of interest.
m₁, mandibular foramen; m₂, second molar; m₃, mental foramen.
Data in parentheses are 95% confidence intervals.

ADC, FA and ROI size are shown in Table 1, and the scatter plots of the ADC and FA values are shown in Figure 2. Regardless of the measurement positions, there were no significant differences in the ADC and FA between the right and left IANs ($p > 0.05$). Regarding differences arising from the anteroposterior measurement positions, the ADC and FA showed no significant differences ($p > 0.017$), except for the difference of ADCs between m₁ and m₃ in the left side ($p = 0.0068$).

Bland–Altman plots for the distribution of differences in ADC and FA values are shown in Figure 3. The visual inspection indicated that no systematic bias was present in each plot. The intrasubject variabilities in ADC between the right and left [right ADC- left ADC/average ADC (%)] at positions m₁, m₂ and m₃ were -55.9 to 57.6% [95% confidence interval (CI): -11.9 to 4.69%], -172 to 57.6% (95% CI: -9.88 to 13.5%) and -65.7 to 81.1% (95% CI: -10.2 to 11.8%), respectively. Also, those in FA were -82.8 to 39.0% (95% CI: -16.2 to 1.82%), -104 to 66.7% (95% CI: -12.7 to 8.34%) and -91.4 to 100% (95% CI: -8.85 to 16.5%), respectively.

Fibre tracking of inferior alveolar nerves

70 (76%) of the 92 IANs could be visualized fully or partially by tractography. The results related to the quality of the IAN visualization are shown in Table 2. There was no difference in the IAN visualization quality between the right and left sides. In 7 (7.6%) of the 92

IANs rated as poor, no nerve fibres could be visualized by tractography. Representative cases of IAN rated as each category (good, fair, poor) are shown in Figure 4.

Discussion

Previously, there have been several studies on MRI assessment of the inferior alveolar neurovascular bundle that were based on T_1 - and T_2 -related signal intensities on conventional MR images.^{7–9} While on the other hand, the IAN was evaluated quantitatively using DTI and was visualized three-dimensionally by tractography in the present study. DTI can provide quantitative data based on the diffusivity and anisotropy of microscopic water motion within nerve fibres, and the nerve fibres can be visualized three-dimensionally.

In our study, the ADC and FA of the IAN were successfully obtained from 43 (93%) of the 46 healthy volunteers, and no significant differences were found in these values between the right and left IANs regardless of the measurement positions. Manoliu *et al*¹⁸ initially reported the quantitative evaluation of the IAN using DTI data in a small number of healthy volunteers. Our study showed that FA values of the IANs ranged from 0.37 to 0.49, which were similar to the results in their study.¹⁸ Our study also showed that the 95% CIs of intrasubject variabilities in ADC and FA were within a narrow range. According to several previous studies

Figure 2 Scatter plots of the apparent diffusion coefficient (ADC) (a) and fractional anisotropy (FA) (b) among the three measurement positions: m₁ (mandibular foramen); m₂ (second molar); and m₃ (mental foramen). Regarding the measurement positions, the FA shows no significant differences ($p > 0.017$), except for the ADCs at positions between m₃ and m₁ in the left side ($p = 0.0068$). The asterisk is showing significant differences.

Figure 3 Bland–Altman plots for the distribution of differences in apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values at each position between the right and left sides: (a–c) ADC at the measurement positions: m_1 (mandibular foramen) (a); m_2 (second molar) (b); and m_3 (mental foramen) (c). (d–f) FA at the measurement positions: m_1 (mandibular foramen) (d); m_2 (second molar) (e); and m_3 (mental foramen) (f).

that evaluated DTI of the peripheral nerves, the FA of an injured nerve became significantly lower than that of the normal nerve.^{19–21} Furthermore, the use of DTI parameters on the contralateral side as an internal control was recommended for the evaluation of unilateral peripheral neuropathy.²² These studies strongly indicate that differences in the condition of the IAN, such as normal and damaged regions, can be evaluated by comparisons of the values between the right and left IANs at the same positions.

Dental treatment including mandibular molar extraction and dental implant placement may incidentally cause damage to the IAN that leads to prolonged sensory dysfunctions.^{1–4} For such patients, it is necessary to quantitatively evaluate the severity of the damage and its recovery after treatment. However, at present, there are no purely objective clinical neurosensory testing

modalities for the evaluation of the IAN.⁴ We believe that this study is one of the few early-phase trials to indicate the feasibility of DTI in evaluating the normal conditions of the IAN quantitatively.

The bilateral symmetry of the ADC and FA for the IAN in our results might be due to the recent MRI innovations such as increasing the magnetic field strength and coil sensitivity. Furthermore, we performed several optimizations of DTI to obtain high-quality images. Regarding fat-suppression techniques for DTI, the STIR method was applied in our study. In the head and neck region, fat suppression by the chemical shift-selective method is often inadequate because of the magnetic field inhomogeneity caused by the irregular shape of the head down to the neck and the presence of anatomical air spaces. In contrast, the STIR method is less sensitive to magnetic field inhomogeneity than the chemical shift-selective method and has been widely used as a fat-suppression technique in the head and neck region.^{23,24} Regarding the number of MPG directions for DTI, 12 directions were applied to improve the directional resolution and signal-to-noise ratio in our study, whereas previous studies on the head and neck region applied 6 MPG directions.^{16,17} The IAN runs through the mandibular canal, which is surrounded by the bone marrow, and its nerve fibre size is sufficient for the application of DTI. In addition, its course is simple, in contrast to the central nervous system nerves that have crossing fibres. Therefore, even six directions may be usable for the visualization for the IAN, similar

Table 2 Results of the three-point rating scale for visualization of the inferior alveolar nerves (IANs) by tractography (number of cases)

Quality	Right	Left	Total
Good	23	26	49
Fair	11	10	21
Poor	12	10	22
Total	46	46	92

Good, full-length visualization of the IAN from the mandibular foramen to the mental foramen.

Fair, partial-length visualization of the IAN from the mandibular foramen to the mental foramen.

Poor, very short or no visualization of the IAN from the mandibular foramen to the mental foramen.

Figure 4 Cases of inferior alveolar nerve (IAN) visualization rated as each rating category—red: horizontal direction; green: anteroposterior direction; and blue: vertical direction. (a) Good case of an IAN on the left side in a 26-year-old male. The full-length IAN is clearly visualized from the mandibular foramen to the mental foramen. (b) Fair case of an IAN on the left side in a 21-year-old female. A partial length of the IAN is visualized. (c) Poor case of an IAN on the left side in a 27-year-old female. A very short length of the IAN is visualized.

to the previous studies. However, our optimization might lead to high spatial resolution on the axis, through application of the thinner slice thickness of 1.8 mm in comparison with the previous studies. There is a trade-off between the number of MPG directions and the scan time. Specifically, an increase in the number of directions prolongs the scan time. Therefore, 12 directions might be the optimal number of MPG directions for the IAN with consideration of the scan time. Regarding the improvement in the magnetic field homogeneity that leads to reduced susceptibility artefacts, manual localized shimming was always performed before DTI.

We obtained a success rate of 76% in the 3D visualization of healthy IANs by tractography. Mori *et al*¹⁶ applied tractography to the IAN of healthy volunteers using a 1.5-T MRI scanner. Concerning the post-processing technique for ROI setting as the seed point, they used a multiple ROI technique, in which the full-length nerve bundle from the mandibular foramen to the mental foramen can be tracked and visualised. However, for peripheral nerves, the size of the visualized nerve bundle can differ from the actual size.^{25,26} Thus, we applied a single ROI technique for the fibre tracking, in common with other previous studies on DTI of the peripheral nerves.^{12,15,19}

Our study had several limitations. First, our case series involved only healthy volunteers, and their age group was relatively young. Although changes in the FA of the peripheral nerves caused by ageing have been reported,²¹ these changes may not be very important because of the bilateral symmetry of the FA for the IAN. However, further studies are needed to confirm such changes in the IAN. Second, there were potential

image distortions on the diffusion tensor images, regardless of how the optimizations for DTI were performed. Hence, there were mild position gaps between the diffusion tensor and 3D T1W images. In our study, the reconstructed ADC map in the coronal plane was carefully matched with the 3D T1W image and the ROIs for measurement of the FA were copied from that of the ADC. The DTI and 3D T1W images were superimposed manually with focus on the IAN in the tractography to reduce the position gaps. These potential distortions might be reduced by the latest MRI techniques for diffusion-weighted imaging, such as zoomed diffusion-weighted EPI and readout segmented EPI.^{18,27,28} In the future, more precise DTI data will be provided with the advent of innovative MRI techniques and devices.

Conclusions

The ADC and FA maps of the IAN were successfully obtained from all of the healthy volunteers and were proved to be symmetrical regardless of the measurement positions. DTI is a feasible technique for the quantitative evaluation and visualization of the IAN. We hope that DTI will be applied to neurological disorders of the IAN and that comparative studies between normal and damaged IANs will be carried out in the future.

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