Quantitative assessment of the masticatory muscles in temporomandibular disorders using diffusion-weighted magnetic resonance imaging

MRI 拡散強調像による顎関節症の咀嚼筋の定量評価

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本論文は、

1) Diffusion-weighted magnetic resonance imaging of normal masticatory muscles in apparent diffusion coefficient

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2) Study of relationship between apparent diffusion coefficients of the masticatory muscles on magnetic resonance imaging and temporomandibular Joint disc displacement

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をまとめたものである。

Abstract

Purposes:

The purposes of this study were 1) to assess the apparent diffusion coefficient (ADC) values in normal masticatory muscles with magnetic resonance imaging (MRI), and 2) to evaluate relationships between ADC values of masticatory muscles on MRI and temporomandibular joint (TMJ) disc displacement.

Materials and Methods:

The university ethics committee approved in this study (EC15-12-009-1).

1) Twenty-seven healthy subjects (9 men and 18 women; age range, 21–77 years mean age, 53.7 years) who underwent MRI examination at Nihon University School of Dentistry at Matsudo from November 2015 to January 2017 were included in this study. Diffusion-weighted MR images were acquired using a 1.5 T unit with a b factor of 0 and 1000 s/mm^2, and ADC maps were generated. The ADC values were measured for healthy masticatory muscles. Regions of interest (ROIs) were drawn to completely include the right and left lateral pterygoid, medial pterygoid, and masseter muscles on a slice demonstrating the largest area of each muscle on the ADC maps.
2) Eighty patients with temporomandibular disorders with bilateral symptoms (16 men,

64 women, range 16–83 years, mean 49.2 years) who underwent MRI from November 2015 to January 2017 were included. These patients were diagnosed on the Diagnostic Criteria for Temporomandibular Disorders. MRI techniques used included axial diffusion-weighted imaging and short tau inversion recovery imaging through the neck to the skull base. Regions-of-interest were drawn that included the entire right and left lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles on a slice demonstrating the largest area of each muscle on an ADC map. Masticatory muscles involved in TMJ disc displacement on sides with reduction were compared with those on sides without reduction, and the effects of gender and age were analyzed.

Results:

1) The mean ADC values of the lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles were $1.21 \pm 0.31 \times 10^{-3}$ mm^2/s, $1.10 \pm 0.25 \times 10^{-3}$ mm^2/s, and $1.09 \pm 0.23 \times 10^{-3}$ mm^2/s, respectively. The ADC values of the lateral pterygoid muscles were significantly higher than those of the medial pterygoid muscles and masseter muscles.

2) ADC values of lateral pterygoid muscles and masseter muscles involved in TMJ disc displacement on sides without reduction were significantly higher than those on

sides with reduction (*$p < 0.05$). The respective mean ADC values of lateral pterygoid muscles on sides with and without reduction were $1.22 \pm 0.16 \times 10^{-3}$ mm^2/s and $1.28 \pm 0.15 \times 10^{-3}$ mm^2/s, for medial pterygoid muscles they were $1.18 \pm 0.14 \times 10^{-3}$ mm^2/s and $1.20 \pm 0.14 \times 10^{-3}$ mm^2/s, and for masseter muscles they were $1.20 \pm 0.15 \times 10^{-3}$ mm^2/s and $1.24 \pm 0.14 \times 10^{-3}$ mm^2/s.

Conclusion:

The study presented the ADC values of the masticatory muscles of healthy subjects in vivo. The ADC values of the lateral pterygoid muscles were significantly higher than those of the medial pterygoid and masseter muscles on healthy subject. In lateral pterygoid muscles and masseter muscles involved in disc displacement, ADC values of those on sides without reduction are higher than those on sides with reduction. These results suggested that quantitative assessment of the masticatory muscles in TMD using diffusion-weighted MR imaging could be very useful information in clinical situations.

Key Words:

apparent diffusion coefficient (ADC), healthy subject

magnetic resonance imaging (MRI), masticatory muscle, temporomandibular disorders (TMD)

Introduction

Temporomandibular disorders (TMD), which affect the temporomandibular joint (TMJ) and supporting structures, include symptoms such as limited mouth opening, clicking, pain, and tenderness in the pre-auricular area and masticatory muscles [1]. However, the etiology of these disorders is multifactorial and remains unknown. The four principal muscles involved in mastication are the medial and lateral pterygoid muscles, temporalis muscles, and masseter muscles. In previous studies, the evaluation of masticatory muscle function during jaw movement has been limited to electromyography (EMG) and palpation [2]. Recently, magnetic resonance imaging (MRI), with its high spatial resolution, has been used in muscular anatomical imaging [3]. Furthermore, functional MRI sequences, such as diffusion-weighted imaging (DWI), have been used to study muscular tissue function non-invasively [3].

DWI is able to measure water molecule diffusion and detect tissue microstructure in vivo. The quantitative metric derived from DWI is the apparent diffusion coefficient (ADC) [4], and many qualitative and quantitative DWI analyses have been utilized in numerous studies [5].

The most common TMJ disorder is disc displacement. Disc displacement can be categorized as anterior displacement with reduction, anterior displacement without

reduction, or posterior displacement [1]. In disc displacement with reduction, the disc is anterior to the condyle in the closed mouth position and returns to its normal position when the jaw is opened [1]. In disc displacement without reduction, the disc is anterior to the condyle in the closed mouth position, but does not return to its normal position when the jaw is opened [1]. A diagnosis of disc displacement associated with TMD is reached based the identification of clinical manifestations and confirmation through diagnostic imaging.

However, there is no report that evaluate the ADC values of normal masticatory muscles, and also in terms of DWI there is no report concerned with the question of whether the disc condyle relationship between the ADC values of the masticatory muscles on MR imaging and TMJ disc displacement.

The purposes of this study were 1) to assess the ADC values in normal masticatory muscles with MRI, and 2) to evaluate relationships between ADC values of masticatory muscles on MRI and TMJ disc displacement.

Materials and Methods

This prospective study was approved by the Institutional Review Board (EC15-12-009-1), and all subjects provided written informed consent prior to the MRI examination.

1) Diffusion-weighted magnetic resonance imaging of normal masticatory muscles in apparent diffusion coefficient

Subjects

The masticatory muscles (lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles) of 27 healthy subjects (9 men and 18 women; mean age, 53.7 years; age range, 21–77 years) who underwent MRI examination to evaluate brain and maxillofacial diseases as outpatients at the radiology department at Nihon University School of Dentistry at Matsudo from November 2015 to January 2017 were included in this study. The exclusion criteria were TMD patients, patients younger than 15 years old, patients with tumors around the TMJ, and imaging studies with severe artifacts. None of the subjects had a documented history of malignant or benign tumors or osteomyelitis. The inclusion criterion for the subjects was general good health. These subjects were diagnosed as healthy based on diagnostic criteria of the American Academy of Orofacial Pain [1].

MRI

MR imaging of the TMJ, which included the bilateral medial muscles, lateral pterygoid muscles, and masseter muscles, was performed using a 1.5-Tesla unit (Intera Achieva 1.5T, Philips Medical Systems, Best, The Netherlands) with a 5-channel phased array coil.

The first sequence was DWI, which was obtained using a spin-echo technique. DWI was acquired in the axial plane with the following parameters: TR, 5,800 ms; TE, 69 ms; matrix, 256×256; field of view, 28 cm: section thickness, 6.0 mm: intersection gap, 1.4 mm; imaging time, 3 min 29 s; b-values, 0 and 1000s/mm^2.

Image analysis

ADC values were calculated using the ADC visualization tool incorporated in a dedicated off-line workstation (Philips Medical Systems). Regions-of-interest (ROIs) were manually generated by tracing the contours of the bilateral lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles on b = 0 images that demonstrated the maximal area of each muscle in the postural position (**Figure 1**). Fascia, blood vessels, and fat were excluded from the ROIs. ROI placement was performed by two oral radiology specialists independently, then ADC calculation was performed. ADC values were measured for healthy masticatory muscles, and the effects

of gender and age were also analyzed. The temporalis muscles were not clearly demonstrated in many patients, therefore, the ADC of the temporalis muscles was not measured.

Statistical analyses

The relationship between the masticatory muscles and ADC values of each muscle were analyzed using the Kruskal-Wallis test. These analyses were performed using the statistical package SPSS, version 21.0 (SPSS Japan, Tokyo, Japan). *P-values <0.05 were considered statistically significant.

2) Study of relationship between apparent diffusion coefficients of the masticatory muscles on magnetic resonance imaging and temporomandibular joint disc displacement

Patients

Eighty TMD patients with bilateral symptoms (16 men, 64 women, mean age 49.2 years, range 16–83 years) who underwent MRI from November 2015 to January 2017 were included in the study. All patients underwent MRI examination to evaluate brain and maxillofacial diseases as outpatients at the Department of Radiology at Nihon University School of Dentistry at Matsudo. These patients were diagnosed on the Diagnostic Criteria for Temporomandibular Disorders. Exclusion criteria were patients with joint effusion, patients aged younger than 15 years, patients with tumors around the TMJ, and imaging records with severe artifacts. None of the patients had documented malignant or benign tumors or osteomyelitis.

MRI

MRI of the TMJ, which included the bilateral medial muscles, lateral pterygoid muscles, and masseter muscles, was performed using a 1.5-Tesla unit (Intera Achieva 1.5T, Philips Medical Systems, Best, The Netherlands) with a 5-channel phased array coil.

The first sequence was DWI, which was obtained using a spin-echo technique. DWI was acquired in the axial plane with the following parameters: TR, 5,800 ms; TE, 69 ms; matrix, 256×256; field of view, 28 cm: section thickness, 6.0 mm: intersection gap, 1.4 mm; imaging time, 3 min 29 s; b-values, 0 and 1000s/mm^2.

Image analysis

ADC values were calculated using the ADC visualization tool incorporated in a dedicated off-line workstation (Philips Medical Systems). Regions-of-interest (ROIs) were manually generated by tracing the contours of the bilateral lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles on b = 0 images that demonstrated the maximal area of each muscle in the postural position (**Figure 2**). Fascia, blood vessels, and fat were excluded from the ROIs. ROI placement was performed by two oral radiology specialists independently, then ADC calculation was performed. The temporalis muscles were not clearly depicted in many patients, therefore the ADC values of the temporalis muscles were not measured in this study. Masticatory muscles involved in TMJ disc displacement on sides with reduction were compared with those on sides without reduction, and the effects of gender and age were also analyzed.

Statistical analyses

Relationships between TMJ disc displacement (with reduction and without reduction) and the ADC values of muscles were analyzed with the Mann–Whitney U test. These analyses were performed with the statistical package SPSS, version 21.0 (SPSS Japan, Tokyo, Japan), and $*p < 0.05$ was considered statistically significant.

Results

1) Diffusion-weighted magnetic resonance imaging of normal masticatory muscles in apparent diffusion coefficient

The ADC values of the lateral pterygoid muscles were significantly higher than those of the medial pterygoid and masseter muscles (*p<0.05) (**Figure 3**). The mean ADC values of the lateral pterygoid, medial pterygoid, and masseter muscles were 1.21 ± 0.31 × 10^{-3} mm^2/s (mean ADC ± SD), 1.10 ± 0.25 × 10^{-3} mm^2/s, and 1.09 ± 0.23 × 10^{-3} mm^2/s, respectively.

The comparison of ADC values of the masticatory muscles between healthy men and women subjects (**Table 1**). The ADC values of the men and women with regard to the lateral pterygoid muscles in healthy subjects were 1.17 ± 0.25 × 10^{-3} mm^2/s and 1.19 ± 0.32 × 10^{-3} mm^2/s, respectively. The ADC values of the medial pterygoid muscles in healthy men and women subjects were 1.08 ± 0.24 × 10^{-3} mm^2/s and 1.11 ± 0.25 × 10^{-3} mm^2/s, respectively. The ADC values of the masseter muscles in healthy men and women subjects were 1.06 ± 0.24 × 10^{-3} mm^2/s and 1.11 ± 0.23 × 10^{-3} mm^2/s, respectively.

The ADC values of healthy subjects according to age groups by decade (**Table 2**).

2) Relationships between apparent diffusion coefficients of the masticatory

muscles on magnetic resonance imaging and temporomandibular joint disc displacement

The ADC values of lateral pterygoid muscles and masseter muscles involved in TMJ disc derangement on sides without reduction were significantly larger than those on sides with reduction (*$p < 0.05$) (**Figure 4**). The respective mean ADC values of lateral pterygoid muscles on the sides with and without reduction were $1.22 \pm 0.16 \times 10^{-3}$ mm^2/s and $1.28 \pm 0.15 \times 10^{-3}$ mm^2/s. The respective mean ADC values of medial pterygoid muscles on the sides with and without reduction were $1.18 \pm 0.14 \times 10^{-3}$ mm^2/s and $1.20 \pm 0.14 \times 10^{-3}$ mm^2/s. The respective mean ADC values of masseter muscles on the sides with and without reduction were $1.20 \pm 0.15 \times 10^{-3}$ mm^2/s and $1.24 \pm 0.14 \times 10^{-3}$ mm^2/s.

The ADC values of masticatory muscles involved in disc displacement on sides with and without reduction in men and women patients. (**Table 3**).

The ADC values of lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles involved in disc displacement on sides with reduction in different age groups (**Table 4**).

The ADC values of lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles involved in disc displacement on sides without reduction in different

age groups (**Table 5**).

Discussion

1) Diffusion-weighted magnetic resonance imaging of normal masticatory muscles in apparent diffusion coefficient

The present study measured the diffusion coefficients of normal masticatory muscles using diffusion-weighted MRI. The ADC values of the lateral pterygoid muscles were significantly higher than those of the medial pterygoid muscles and those of the masseter muscles. The present study speculate that the lateral pterygoid muscles is one of the most important muscles involved in mastication functions, and it participates in the control of jaw movements [6].

While DWI has become more widespread, the relative value of DWI sequences, in addition to or as alternatives to conventional MR sequences, is equivocal for many conditions [7-9].

Muscles can be divided into three types, striated muscles, smooth muscles, and cardiac muscles. The masticatory muscles are striated muscles, as are the dorsi flexor and spinal column erector muscles. Concretely, Yanagisawa et al.[10] reported that the $ADC^{b0–50}$ and $ADC^{b50–750}$ values were 2.64×10^{-3} mm^2/s and 1.44×10^{-3} mm^2/s in the ankle dorsiflexors and 3.02×10^{-3} mm^2/s and 1.49×10^{-3} mm^2/s in the erector spinae muscles, respectively. The study results of healthy subjects revealed that the mean ADC

values of the normal ankle dorsiflexors and erector spinae muscles were significantly higher than those of the masticatory muscles in healthy subjects. The difference in ADC values between the masticatory muscles and muscles of the foot (ankle dorsiflexors, erector spinae muscles) may be attributed to differences in the composition of the muscle architecture[11], as the muscles of the feet and masticatory muscles are functionally different.

The ADC values of the masticatory muscles in healthy women subjects were higher than those of men subjects. However, there was no relationship found among the ADC values of the masticatory muscles in terms of sex. These sex differences may be attributed to differences in the motor units and constituent muscle fibers between men and women [12]. Furthermore, these findings showed that water molecules within the muscles diffused more easily in women subjects than in men subjects.

On the other hand, Galbán et al.[13] used DWI to show that DWI of the skeletal muscles generally decreased with aging. However, this was not shown in our study. The present study speculate that the masticatory muscles might become less fatigued than the muscles of the feet as they only control mandibular movements for mastication and are involved in speech and facial expressions.

These results suggest that the difficulties in using palpation alone to study

temporomandibular disorders may be circumvented by employing the ADC values as an alternative method for studying masticatory muscles.

2) Relationships between apparent diffusion coefficients of the masticatory muscles on magnetic resonance imaging and temporomandibular joint disc displacement

In this study, ADC values of lateral pterygoid muscles and masseter muscles involved in TMJ disc displacement on sides without reduction were significantly higher than those on sides with reduction.

DWI utilizes water diffusion characteristics. These are dependent on multiple factors including cell membrane integrity, cell density, viscosity of extracellular fluid, and vascularity[14]. ADC values can be calculated from DWI parametric maps. The structural condition of muscles as determined using ADC values depends on Brownian motion of water molecules. These movements are quantified using a coefficient known as the ADC [10, 15]. ADC mapping can yield useful quantitative information pertaining the cellularity of musculoskeletal lesions[16].

In the present study, the ADC values of masticatory muscles on sides without reduction were higher than those on sides with reduction. Repetitive muscle contractions cause a temporal increase in intramuscular microcirculation, elevated

capillary pressure and permeability, increased osmotic pressure due to metabolite accumulation in the extravascular space, or a combination of these factors, which can increase extravascular water within an exercised muscle[17]. In a previous study, Katzberg et al.[18] reported that the severity of disc displacement without reduction was greater than that of disc displacement with reduction.

No significant gender differences were observed between the ADC values of each muscle type in this study. Muscle fiber composition is relatively similar in men and women patients, and it is related to the capillary density within a muscle. There were also no significant differences between the ADC values associated with TMJ disc displacement in different age groups.

In a study reported by Galbán et al.[13] using DWI, water diffusion in skeletal muscles generally decreased with age. Masticatory muscles may become less fatigued than the muscles of the feet, because they only control mandibular movements for mastication and are also involved in speech and facial expressions.

The study has some limitations. First, the present study was not able to detect the temporalis muscles because of low resolution images on DWI. Second, the present study was not able to measure ADC values in patient with severe image distortions from susceptibility artifact.

Conclusion

The study presented the ADC values of the masticatory muscles of healthy subjects in vivo. The ADC values of the lateral pterygoid muscles were significantly higher than those of the medial pterygoid and masseter muscles on healthy subject. In lateral pterygoid muscles and masseter muscles involved in disc displacement, ADC values of those on sides without reduction are higher than those on sides with reduction. These results suggested that quantitative assessment of the masticatory muscles in TMD using diffusion-weighted MR imaging could be very useful information in clinical situations.

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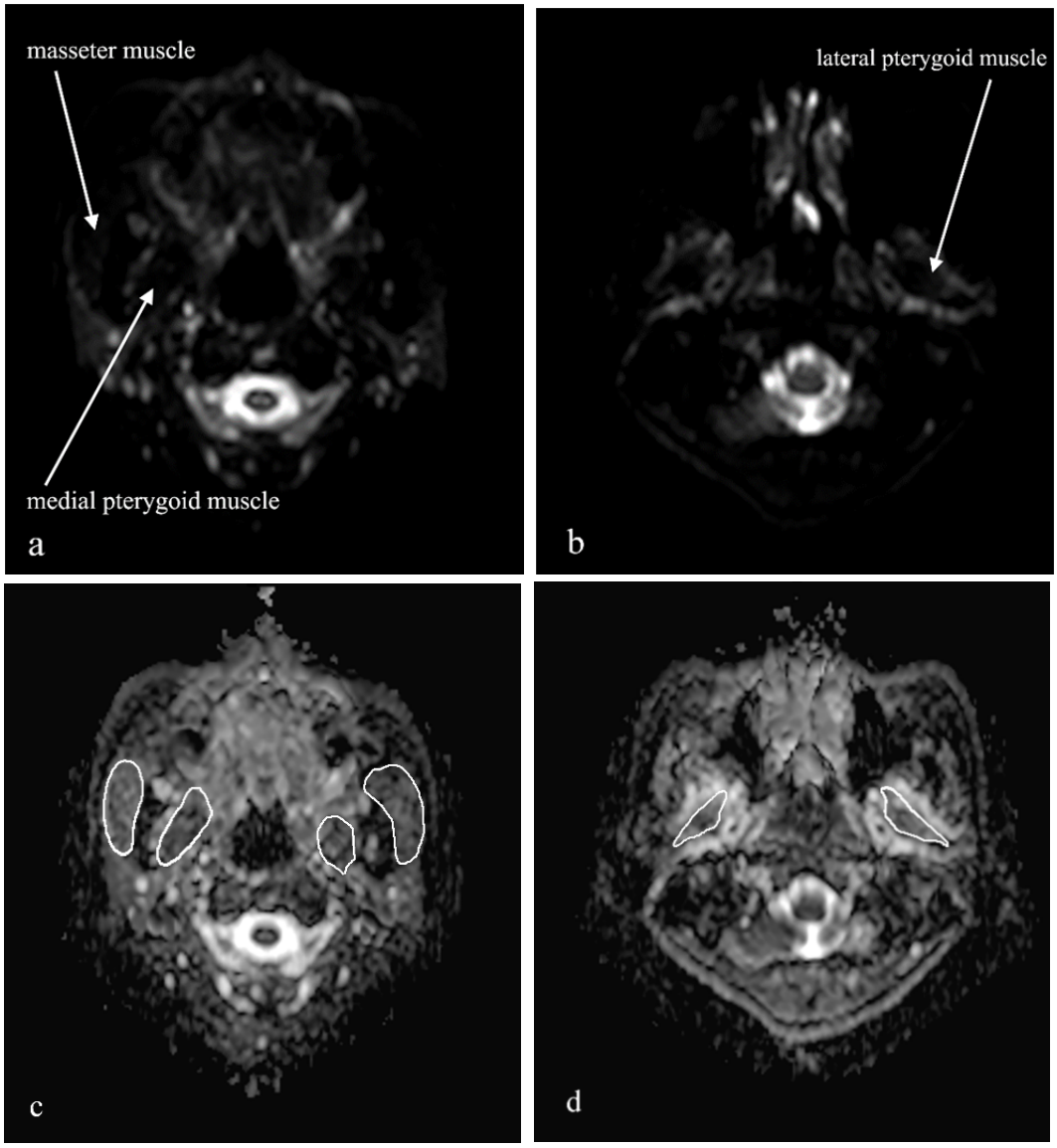
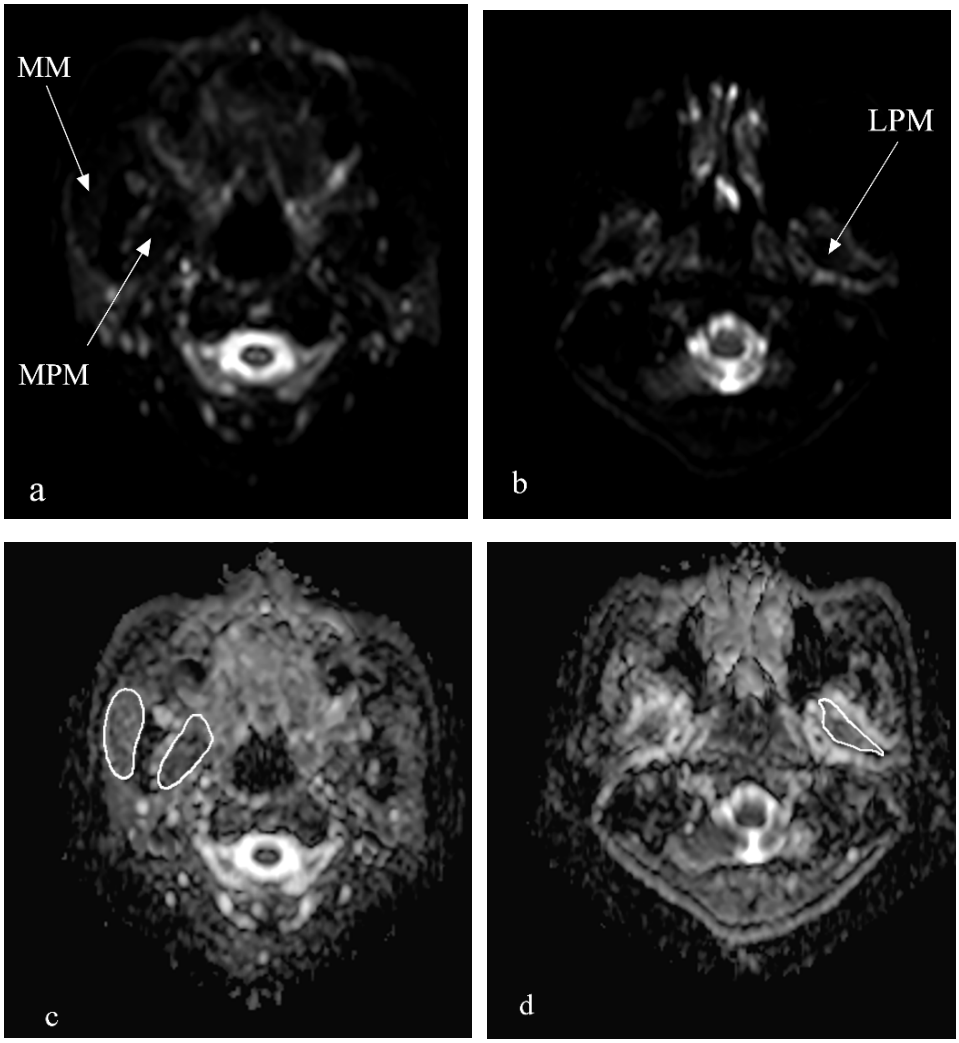
Figure 1. ADC map of the masticatory muscles of the present study (normal subjects)



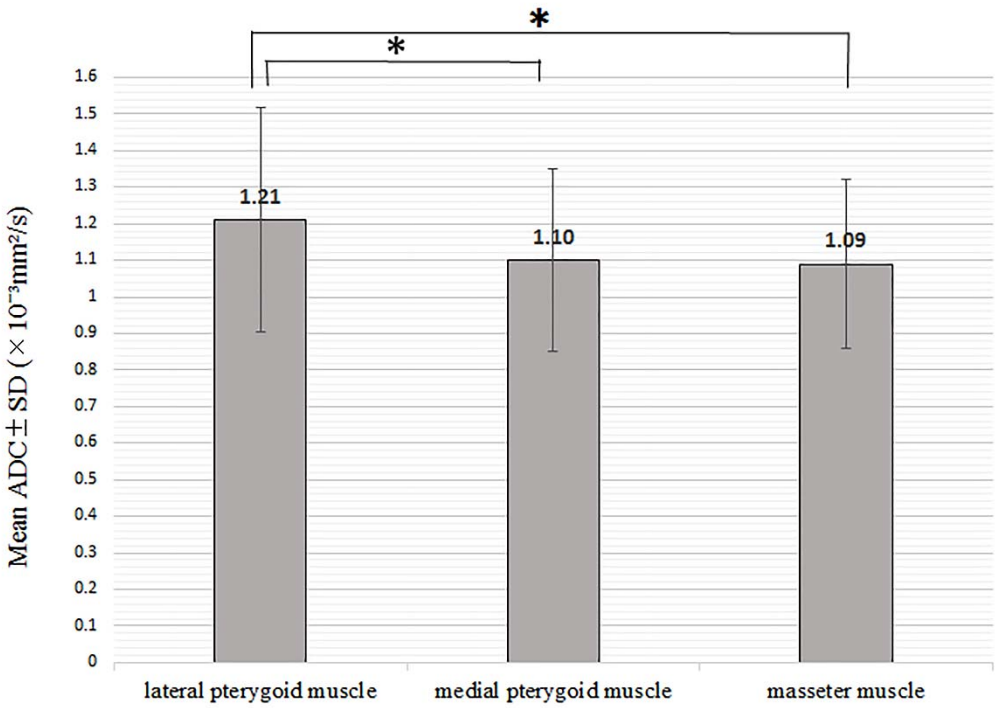
DWI (*b*=0) images (a, b) and ADC maps (c, d) of a representative subject.
The ROIs were manually placed on ADC maps by tracing the contours of the bilateral lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles on *b*=0 images that demonstrated the maximal area of each muscle in the postural position.

Figure 2. ADC map of the masticatory muscles of the present study



DWI (b = 0) images (a, b) and ADC maps (c, d) of a representative subject.
The ROIs were manually generated by tracing the contours of the bilateral lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles on b = 0 images that exhibited the maximal area of each muscle in the postural position.
LPM indicates lateral pterygoid muscle. MPM indicates medial pterygoid muscle. MM indicates masseter muscle.

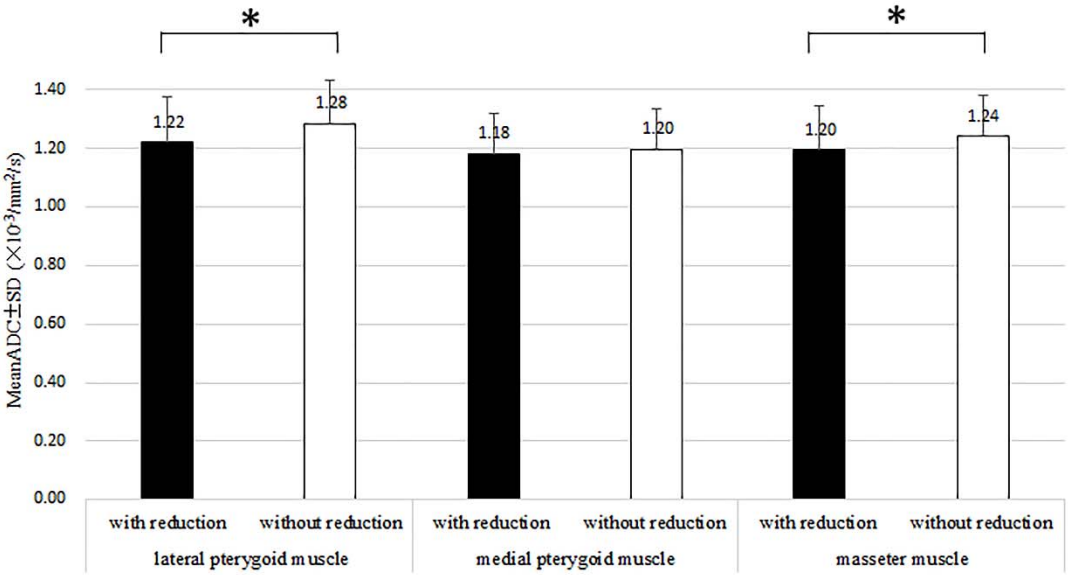
Figure 3. Comparison the ADC values of the masticatory muscles in healthy subjects



The ADC values of the lateral pterygoid muscles were significantly higher than those of medial pterygoid muscles and masseter muscles (* p<0.05).

The mean ADC values of the lateral pterygoid, medial pterygoid, and masseter muscles were 1.21 ± 0.31 × 10^{-3} mm^2/s (mean ADC ± SD), 1.10 ± 0.25 × 10^{-3} mm^2/s, and 1.09 ± 0.23 × 10^{-3} mm^2/s, respectively.

Figure 4. Comparison between ADC values on MRI and disc displacement on sides with and without reduction



The ADC values of the lateral pterygoid muscles and masseter muscles involved in TMJ disc displacement on sides without reduction were significantly higher than those on sides with reduction (*$p < 0.05$).

Table 1. Comparison of the ADC of the masticatory muscles between healthy men and women subjects

	lateral pterygoid muscles	medial pterygoid muscles	masseter muscles
men(n=9)	1.17±0.25	1.08±0.24	1.06±0.24
women(n=18)	1.19±0.32	1.11±0.25	1.11±0.23

Values are shown as mean± S.D. ($\times 10^{-3}$ mm^2/s).

Table 2. The ADC values with healthy subjects (lateral pterygoid muscles, medial pterygoid muscles and masseter muscles) according to age groups

age groups	lateral pterygoid muscles	medial pterygoid muscles	masseter muscles
20-29(n=4)	1.13±0.27	1.08±0.24	1.14±0.30
30-39(n=2)	1.22±0.42	0.98±0.33	1.09±0.18
40-49(n=3)	1.10±0.30	1.01±0.26	1.02±0.26
50-59(n=6)	1.11±0.29	1.21±0.21	1.14±0.22
60-69(n=8)	1.14±0.28	1.14±0.26	1.07±0.24
70-79(n=4)	1.20±0.26	1.15±0.22	1.10±0.22

Values are shown as mean± S.D. ($\times 10^{-3}$ mm^2/s).

Table 3. Comparisons of ADC values of masticatory muscles involved in disc displacement on sides with and without reduction in men and women patients

	lateral pterygoid muscles		medial pterygoid muscles		masseter muscles	
	with reduction	without reduction	with reduction	without reduction	with reduction	without reduction
men (n=16)	1.22±0.09	1.23±0.15	1.19±0.10	1.15±0.16	1.17±0.08	1.26±0.16
women （n=64)	1.22±0.16	1.30±0.16	1.18±0.13	1.21±0.14	1.20±0.15	1.26±0.15

The values shown represent the mean ± standard deviation ($\times 10^{-3}$ mm^2/s).

Table 4. ADC values of lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles involved in disc displacement on sides with reduction in different age groups

age groups	lateral pterygoid muscles	medial pterygoid muscles	masseter muscles
16-19(n=6)	1.21±0.25	1.23±0.17	1.33±0.23
20-29(n=11)	1.20±0.13	1.23±0.11	1.15±0.13
30-39(n=6)	1.15±0.20	1.10±0.20	1.17±0.23
40-49(n=19)	1.18±0.15	1.16±0.13	1.17±0.15
50-59(n=8)	1.22±0.08	1.18±0.11	1.20±0.12
60-69(n=18)	1.25±0.24	1.19±0.17	1.20±0.22
70-79(n=10)	1.32±0.14	1.19±0.11	1.23±0.10
80-89(n=2)	1.20±0.10	1.08±0.10	1.12±0.09

The values shown represent the mean ± standard deviation ($\times 10^{-3}$ mm^2/s).

Table 5. ADC values of lateral pterygoid muscles, medial pterygoid muscles, and masseter muscles involved in disc displacement on sides without reduction in different age groups

age groups	lateral pterygoid muscles	medial pterygoid muscles	masseter muscles
16-19(n=6)	1.23±0.16	1.10±0.14	1.28±0.13
20-29(n=11)	1.26±0.19	1.23±0.20	1.25±0.17
30-39(n=6)	1.35±0.13	1.18±0.09	1.36±0.13
40-49(n=19)	1.32±0.17	1.26±0.14	1.22±0.17
50-59(n=8)	1.24±0.13	1.22±0.12	1.14±0.12
60-69(n=18)	1.30±0.15	1.15±0.16	1.23±0.15
70-79(n=10)	1.24±0.21	1.20±0.14	1.31±0.17
80-89(n=2)	1.26±0.08	1.16±0.09	1.17±0.06

The values shown represent the mean ± standard deviation ($\times 10^{-3}$ mm^2/s).