Quantitative analysis of age-related changes in the tongue and jawbone marrow using diffusion-weighted magnetic resonance imaging

（MRI 拡散強調像を用いた舌および顎骨骨髄における加齢変化の定量解析）

日本大学大学院松戸歯学研究科

放射線学

近藤　匠

（指導：　金田　隆　教授）

本論文は、

1) Quantitative analysis of tongue changes with aging using diffusion-weighted magnetic resonance imaging

Oral Science International (https://doi.org/10.1002/osi2.1167　令和 4 年 11 月発行)

2) Quantitative assessment of age-related changes in the mandibular bone marrow using apparent coefficient value

Oral Radiology (第 38 巻 1 号　令和 4 年 1 月発行)

をまとめたものである。

1. Abstract

Purposes:

The purposes of this study were to 1) quantitatively assess the changes in the apparent diffusion coefficient (ADC) value of the tongue with aging using diffusion-weighted imaging (DWI) and, 2) to quantitatively assess the age-related changes in ADC values of the normal jawbone marrow using DWI.

Materials and Methods:

This study was approved by the Institutional review board (EC19-18-002-1, EC19-011).

1) This retrospective cohort study comprised all patients who underwent magnetic resonance imaging (MRI) between January 2018 and February 2020 at the Nihon University Hospital at Matsudo. A total of 480 participants (230 men, 250 women), aged 20- 89 years (mean age 53.66 years), were included in the study. The Mann-Whitney *U* test was performed with the ADC value as the explanatory variable and the sex as the criterion variable. Moreover, calculated the Spearman's correlation coefficient with age as the criterion variable and ADC value as the explanatory variable. $P<0.05$ was considered statistically significant.

2) This retrospective cohort study comprised all patients who underwent panoramic radiography and MRI between April 2018 and November 2020 at the Nihon University

Hospital at Matsudo. A total of 351 participants (140 men, 211 women), aged 15- 89 years (mean age 46.01 years), were included in the study. Spearman's correlation coefficients were calculated using age groups as the criterion variable and the ADC values as the explanatory variables. $P<0.05$ was considered statistically significant.

Results:

1) A significantly positive correlation was found between age and ADC values of the tongue in the men and women groups ($P<0.001$, r=0.40, and $P<0.001$, r=0.27, respectively). No significant differences were observed between the sex and the ADC values of the tongue ($P=0.19$).

2) A significantly negative correlation was found between age and the ADC values of the jawbone marrow in each sex group ($P<0.001$).

Conclusion:

ADC values of the tongue and jawbone marrow were significantly correlated with aging. These results suggested that DWI is useful for differential diagnosis in the tongue and jawbone marrow.

Key Words: Apparent diffusion coefficient (ADC), Tongue, Diffusion-weighted imaging (DWI), Age-related changes, Jawbone marrow

2. Introduction

Oral cancer accounts for 1 % of all cancers[1], with more than 90 % of these being oral squamous cell carcinoma (OSCC)[2]. Most commonly, OSCC occurs on the tongue and accounts for approximately 40 % of all cases of OSCC[3]. Previous studies of oral cancer have shown that OSCC occurs more often in men over 40 years of age, and tongue cancer is particularly prevalent in men over 60 years of age[4]. There are various diagnostic imaging modalities for oral cancer imaging, but magnetic resonance imaging (MRI), which has better contrast resolution of soft tissues compared to computed tomography (CT), is often used to assess tongue cancer[5,6]. The sequences of MRI for detecting tongue cancer include T1-weighted image (T1WI), T2-weighted image (T2WI), contrast-enhanced (CE)-T1WI, and diffusion-weighted imaging (DWI)[7,8].

The bone marrow, which lies within the confines of the skeleton, is one of the largest organs of the human body. The weight of the bone marrow is approximately 3,000 g in adult men and 2,600 g in adult women[9]. It plays an important role in many physiological processes, such as hematopoiesis, immunological response, and metabolism[10]. Various diseases manifest initially within the bone marrow. The bone marrow in the jaw of a normal adult consists of yellow (fatty) marrow, which replaces red (hematopoietic) marrow as a result of aging[10]. MRI is known to be highly sensitive for the detection of

bone marrow abnormalities, and short tau inversion recovery (STIR) imaging is particularly useful for this purpose. The importance of MRI in diagnosing patients with disorders of the jaw has been emphasized in the literature[11-16].

DWI provides signal contrast utilizing differences in diffusion and movement of water molecules within various tissues, making it possible to detect subtle anomalies. This means changes in tissue structure can be detected at the molecular level. Quantitative evaluation is possible by acquiring the apparent diffusion coefficient (ADC) calculated from diffusion-weighted images with multiple b values. Several studies have evaluated the ADC values calculated from DWI[17-20]. However, few studies have used DWI to quantitatively assess age-related changes in the tongue and normal jawbone marrow.

The purposes of this study were to 1) quantitatively assess the age-related changes in the ADC value of the tongue using DWI and, 2) to quantitatively assess the age-related changes in ADC values of the normal jawbone marrow using DWI.

3. Materials and Methods

This study was approved by the ethics committee, Nihon University School of Dentistry at Matsudo (EC19-18-002-1, EC19-011).

3-1. Quantitative analysis of tongue changes with aging using diffusion-weighted magnetic resonance imaging

Patients

The study population included 480 patients (230 men and 250 women, aged 20 to 89 years, mean age 53.66 years) who underwent MRI at the Nihon University Hospital at Matsudo between January 2018 and February 2020 for screening for cysts and tumors of the jaw and temporomandibular disorders. Patients with severe susceptibility artifacts (n=25) and tumors or cysts of the tongue (n=10) were excluded based on clinical and MRI findings.

Image acquisition

The MRI system was executed using a 1.5 T superconductive MRI unit (Intera Achieva® 1.5 T Nova; Philips Medical Systems, Best, The Netherlands) with a 5-channel phased array coil. The parameters of the single shot echo planner imaging (EPI)-DWI were as follows: repetition time/echo time = 5,100/70; 6.0-mm section thickness;

256×256 matrix; 250×250 mm field of view; intersection gap 1.4 mm; imaging time 3 min 29 s and b = 0, 1,000 s/mm^2. An ADC map was created using an MRI console. On the ADC map, the region of interest (ROI) was the largest one showing features of the tongue that excluded the cortical bone and around the tissue such as the adipose tissue and tonsils (avoiding 2 mm inside the perimeter) (Figure 1). The ADC values of the tongue were acquired on the ADC map by two oral radiologists (T. K., 3 years of experience; K. I., 10 years of experience).

Statistical analysis

The values of the intraclass correlation coefficient (ICC) (model; 2, 1) were construed as follows: values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90, indicative of poor, moderate, good, and excellent reliability, respectively[21]. The Mann-Whitney *U* test was performed with the ADC value of the tongue as the outcome variable and sex as the predictor variable. Moreover, the author calculated the Spearman's correlation coefficient with age as the criterion variable, and ADC value as the explanatory variable. These statistical analyses were implemented using a statistical package (SPSS version 21.0®, IBM Japan Inc., Tokyo, Japan). $P<0.05$ was considered to indicate statistical significance.

3-2. Quantitative assessment of age-related changes in the mandibular bone marrow using apparent coefficient value

Subjects

The study population consisted of 351 patients (140 men and 211 women, aged 15 to 89 years; mean age, 46.01 years) who had undergone panoramic radiography and MRI scan between April 2018 and November 2020, and those with severe metal artifact, severe periodontitis, apical periodontitis, tumors or cysts of the mandible, hematological disorders, smoking, and osteomyelitis were excluded based on the clinical findings, panoramic radiography, and MRI.

Methods

Panoramic radiography was performed using a digital panoramic radiography (Veraviewepocs; J. Morita Ltd., Kyoto, Japan) at 1- 10 mA and a peak kV of 60- 80. MRI was performed using a 1.5-T superconductive MR unit (Intera Achieva® 1.5 T Nova, Philips Medical Systems, Best, The Netherlands) and a 5-channel phased array coil. EPI-DWI scans were performed using the following parameters: TR/TE = 5,100/70; section thickness, 6.0 mm; matrix, 192; FOV, 350 mm; intersection gap, 1.4 mm; imaging time, 3 min 29 s; and b = 0, 1,000 s/mm^2. Segmentation and ADC calculation were performed

at a dedicated off-line workstation (Philips Medical Systems, Best, The Netherlands). ROIs, with 5 mm diameter, were manually assigned on the ADC map over the mandibular bone marrow on both sides, or just below the first molar to reduce the influence of the anatomical structure. The mandibular tooth germ, canal, root, and cortical bone were excluded (Figure 2). The ADC values of each participant were independently measured one time and recorded by two oral radiologists on the same slice (K. I., 10 years of experience; H. M., 9 years of experience).

Statistical analysis

The values of the ICC (model; 2, 1) were construed as follows: values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90, indicative of poor, moderate, good, and excellent reliability, respectively[21]. Spearman's correlation coefficients were calculated using the ADC values of the mean of the bilateral sides as the criterion variable and age as the explanatory variable. These analyses were performed using a statistical package (SPSS version 21.0®, IBM Japan Inc., Tokyo, Japan); $P<0.05$ was considered significant.

4. Results

4-1. Quantitative analysis of tongue changes with aging using diffusion-weighted magnetic resonance imaging

The ICC values were in good agreement with those of the ADC of the tongue (0.77). Figure 3 shows the correlation between sex and tongue ADC values. The mean ADC values of the tongue were $1.32 \pm 0.15 \times 10^{-3}$ mm^2/s and $1.35 \pm 0.15 \times 10^{-3}$ mm^2/s in men and women, respectively. No significant differences were found between the sex and ADC values of the tongue (P=0.19). Figure 4 shows the relationship between the age groups of men and the ADC values of the tongue, according to the age groups (P<0.001, r=0.40). Moreover, Figure 5 shows the relationship between the age groups of women and the ADC values of the tongue, according to the age groups (P<0.001, r=0.27). The ADC values of the tongue increased with aging in the men and women groups.

4-2. Quantitative assessment of age-related changes in the mandibular bone marrow using apparent coefficient value

The ICC values were in moderate agreement with those of the ADC of the bone marrow (0.72). The mean ADC value for all the age groups was $0.91 \pm 0.18 \times 10^{-3}$ mm^2/s in men and $0.86 \pm 0.16 \times 10^{-3}$ mm^2/s in women (P=0.016) (Table 1). The mean ADC

values of the men were as follows: 1.2 ± 0.12 $\times 10^{-3}$ mm^2/s (15- 19 years; n=9), 1.13 ± 0.14 $\times 10^{-3}$ mm^2/s (20- 29 years; n=19), 0.96 ± 0.11 $\times 10^{-3}$ mm^2/s (30- 39 years; n=30), 0.85 ± 0.09 $\times 10^{-3}$ mm^2/s (40- 49 years; n=25), 0.84 ± 0.07 $\times 10^{-3}$ mm^2/s (50- 59 years; n=21), 0.79 ± 0.1 $\times 10^{-3}$ mm^2/s (60- 69 years; n=22), 0.72 ± 0.11 $\times 10^{-3}$ mm^2/s (70- 79 years; n=11), and 0.7 ± 0.08 $\times 10^{-3}$ mm^2/s (80- 89 years; n=3), according to age (r= -0.781, P<0.001) (Table 2). The mean ADC values of the women were as follows: 1.08 ± 0.16 $\times 10^{-3}$ mm^2/s (15- 19 years; n=19), 0.98 ± 0.1 $\times 10^{-3}$ mm^2/s (20- 29 years; n=31), 0.97 ± 0.11 $\times 10^{-3}$ mm^2/s (30- 39 years; n=25), 0.83 ± 0.09 $\times 10^{-3}$ mm^2/s (40- 49 years; n=37), 0.81 ± 0.09 $\times 10^{-3}$ mm^2/s (50- 59 years; n=45), 0.72 ± 0.09 $\times 10^{-3}$ mm^2/s (60- 69 years; n=28), 0.71 ± 0.1 $\times 10^{-3}$ mm^2/s (70- 79 years; n=23), and 0.69 ± 0.08 $\times 10^{-3}$ mm^2/s (80- 89 years; n=3), according to age (r= -0.725, P<0.001) (Table 2). Thus, the ADC values showed a significant negative correlation with aging (Figure 6 and 7).

5. Discussion

In this study, ADC values of the tongue increased with aging. On the other hand, ADC values of the jawbone marrow decreased with aging.

Currently, DWI is used in head and neck tumor imaging. Generally, the ADC values for solid benign tumors and cystic lesions are higher than those for malignant tumors[22,23]. A report investigating tongue lesions using DWI reported that the mean ADC value for malignant tongue disease was significantly lower than benign solid and cystic lesions (malignant; $1.08 \pm 0.16 \times 10^{-3}$ mm^2/s; benign solid lesions; $2.21 \pm 0.35 \times 10^{-3}$ mm^2/s, cystic lesions; $1.68 \pm 0.33 \times 10^{-3}$ mm^2/s)[8]. The authors suggested that the ADC value of malignant diseases is low because excess cells reduce the diffusion area of water protons in the extracellular matrix and the extracellular compartment. When the nucleus expands, the intracellular size decreases, and the ADC value decreases.

On the other hand, studies investigating the skeletal muscles have cleared ADC values for normal sternocleidomastoid muscles (0.99×10^{-3} mm^2/s)[24]. Histologically, skeletal muscle causes muscle fiber loss with age; however, there are contradictory reports that muscle fibers increase or decrease with age in the tongue[25,26]. This study found that ADC values in the normal tongue tended to increase with age and that this tendency was greater in men. Furthermore, there was no difference in ADC values between men and women.

However, regarding these ADC values, there was a difference in the correlation between men and women that was more commonly higher in men. Previous reports have indicated that men may be more susceptible to muscle deterioration due to aging than may do women, and the correlation was higher in men than in women in this study[27]. Generally, fat ADCs are lower than muscle ADCs, and tissues degenerated from adipose tissue are expected to have lower ADCs; however, this study indicated elevated ADCs with aging[28]. Therefore, the ADC values of the aged tongue were believed to be caused by loss of muscle fibers or interstitial changes by frequent external stimuli, rather than replacement with adipose tissue[26,28]. On the other hand, it has also been reported that muscle fibers of the tongue tended to increase with age, which are thought to cause increases in ADC values[25]. This result can help improve the accuracy of the differential diagnosis of tongue lesions using ADC values.

Previous studies on bone marrow diffusion using ADC values have been reported[29]. The jaw is rich in bone marrow and usually shows low signal intensity in MRIs performed on adults. By the age of 25- 30 years, most of the marrow in the mandible changes to yellow marrow[10]. Nonomura, et al.[30] reported that the mean ADC values of the normocellular marrow of the posterior ileum in adults and the hypercellular marrow in children were $0.83 \pm 0.71 \times 10^{-3}$ mm^2/s and $1.29 \pm 0.59 \times 10^{-3}$ mm^2/s, respectively.

Herrmann et al.[31] reported that the mean ADC values of the vertebral marrow in the age groups 0- 29 years and 30- 88 years were $0.54 \pm 0.07 \times 10^{-3}$ mm^2/s and $0.47 \pm 0.08 \times 10^{-3}$ mm^2/s, respectively. Li, et al.[29] reported that there was a significant negative correlation between the ADC values and age, in both the parietal and occipital bones. Similar to this report, we found a statistically significant negative correlation between the mean ADC values of the mandibular bone marrow and age. A possible explanation for these results is that an increase in the proportion of fat in the bone marrow attributed to aging causes a decrease in the overall water content. Li, et al.[29] explained the relevance of DWI to detect age-related changes in the bone marrow, stating that the diffusion of fat bound water molecules is low in the yellow marrow, which contains more fat content, than that in tissues with more water content. Furthermore, trabecular loss can also increase the amount of adipose tissue. Deterioration of the microarchitecture of the trabecular bone network increases with advancing aging and this process is further accelerated in osteoporosis related conditions[32]. This effect is compounded with a loss in mechanical competence (occlusal force). Yeung, et al.[33] investigated the ADC values of the vertebral body marrow with quantitative MR diffusion imaging in participants with postmenopausal osteoporosis and premenopausal control participants, and reported a significantly lower mean ADC for postmenopausal participants with reduced bone

mineral density (0.41×10^{-3} mm^2/s). This could be the reason for the low ADC value of women in all age groups.

6. Conclusion

ADC values of the tongue and jawbone marrow were significantly correlated with aging. These results suggested that DWI is useful for differential diagnosis in the tongue and jawbone marrow.

7. References

1. Oikawa Y, Kugimoto T, Kashima Y, Okuyama K, Ohsako T, Kuroshima T, Hirai H, Tomioka H, Shimamoto H, Michi Y, Harada H. Surgical treatment for oral tongue squamous cell carcinoma: A retrospective study of 432 patients. Glob Health Med. 2021; 3: 157-162.
2. Bagan J, Sarrion G, Jimenez Y. Oral cancer: Clinical features. Oral Oncol. 2010; 46: 414-417.
3. Troiano G, Rubini C, Togni L, Caponio VCA, Zhurakivska K, Santarelli A, Cirillo N, Lo Muzio L, Mascitti M. The immune phenotype of tongue squamous cell carcinoma predicts early relapse and poor prognosis. Cancer Med. 2020; 9: 8333-8344.
4. Bachar G, Hod R, Goldstein DP, Irish JC, Gullane PJ, Brown D, Gilbert RW, Hadar T, Feinmesser R, Shpitzer T. Outcome of oral tongue squamous cell carcinoma in patients with and without known risk factors. Oral Oncol. 2011; 47: 45-50.
5. Lam P, Au-Yeung KM, Cheng PW, Wei WI, Yuen AP, Trendell-Smith N, Li JH, Li R. Correlating MRI and histologic tumor thickness in the assessment of oral tongue cancer. AJR am J Roentgenol. 2004; 182: 803-808.
6. Arya S, Rane P, Deshmukh A. Oral cavity squamous cell carcinoma: Role of pretreatment imaging and its influence on management. Clin Radiol. 2014; 69: 916-

930.

7. Haraguchi K, Yoshiga D, Oda M, Tabe S, Mitsugi S, Takahashi O, Habu M, Sasaguri M, Morimoto Y, Yoshioka I, Tominaga K. Depth of invasion determined by magnetic resonance imaging in tongue cancer can be a predictor of cervical lymph node metastasis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2021; 131: 231-240.
8. Li S, Cheng J, Zhang Y, Zhang Z. Differentiation of benign and malignant lesions of the tongue by using diffusion-weighted MRI at 3.0 T. Dentomaxillofac Radiol. 2015; 44: 20140325.
9. Vogler JB, Murphy WA. Bone marrow imaging. Radiology. 1988; 168: 679-693.
10. Kaneda T, Minami M, Ozawa K, Akimoto Y, Okada H, Yamamoto H, Suzuki H, Sasaki Y. Magnetic resonance appearance of bone marrow in the mandible at different ages. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996; 82: 229-233.
11. Gold RH, Hawkins RA, Katz RD. Bacterial osteomyelitis: findings on plain radiography, CT, MR, and scintigraphy. AJR Am J Roentgenol. 1991; 157: 365-370.
12. Kaneda T, Minami M, Ozawa K, Akimoto Y, Utsunomiya T, Yamamoto H, Suzuki H, Sasaki Y. Magnetic resonance imaging of osteomyelitis in the mandible. Comparative study with other radiologic modalities. Oral Surg Oral Med Oral Pathol Oral Radiol

Endod. 1995; 79: 634-640.

13. Reinert S, Widlitzek H, Venderink DJ. The value of magnetic resonance imaging in the diagnosis of mandibular osteomyelitis. Br J Oral Maxillofac Surg. 1999; 37: 459-463.

14. Lee K, Kaneda T, Mori S, Minami M, Motohashi J, Yamashiro M. Magnetic resonance imaging of normal and osteomyelitis in the mandible: assessment of short inversion time inversion recovery sequence. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003; 96: 499-507.

15. Quinn SF, Murray W, Clark RA, Cochran C. MR imaging of chronic osteomyelitis. J Comput Assist Tomogr. 1988; 12: 113-117.

16. Unger E, Moldofsky P, Gatenby R, Hartz W, Broder G. Diagnosis of osteomyelitis by MR imaging. AJR Am J Roentgenol. 1988; 150: 605-610.

17. Muraoka H, Ito K, Hirahara N, Okada S, Kondo T, Kaneda T. Quantitative assessment of the apparent diffusion coefficient values of the inflammatory connective tissue around the mandibular condyle in rheumatoid arthritis. J Oral Maxillofac Surg. 2021; 79: 1230-1235.

18. Ozgen B, Oguz KK, Cila A. Diffusion MR imaging features of skull base osteomyelitis compared with skull base malignancy. AJNR am J Neuroradiol. 2011;

32: 179-184.

19. Muraoka H, Ito K, Hirahara N, Ichiki S, Okada S, Kondo T, Kaneda T. Efficacy of diffusion-weighted imaging in the diagnosis of osteoporosis suggested by the correlation between mandibular cortex width and apparent diffusion coefficient of the mandibular bone marrow. Oral Sci Int. 2022; 19: 88-94.
20. Huisman TA. Diffusion-weighted imaging: Basic concepts and application in cerebral stroke and head trauma. Eur Radiol. 2003; 13: 2283-2297.
21. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016; 15: 155-163.
22. Wang J, Takashima S, Takayama F, Kawakami S, Saito A, Matsushita T, Momose M, Ishiyama T. Head and neck lesions: Characterization with diffusion-weighted echo-planar MR imaging. Radiology. 2001; 220: 621-630.
23. Abdel Razek AA, Gaballa G, Elhawarey G, Megahed AS, Hafez M, Nada N. Characterization of pediatric head and neck masses with diffusion-weighted MR imaging. Eur Radiol. 2009; 19: 201-208.
24. Kolff-Gart AS, Pouwels PJ, Noij DP, Ljumanovic R, Vandecaveye V, de Keyzer F, de Bree R, de Graaf P, Knol DL, Castelijns JA. Diffusion-weighted imaging of the head and neck in healthy subjects: Reproducibility of ADC values in different MRI

systems and repeat sessions. AJNR am J Neuroradiol. 2015; 36: 384-390.

25. Rother P, Wohlgemuth B, Wolff W, Rebentrost I. Morphometrically observable aging changes in the human tongue. Ann Anat. 2002; 184: 159-164.

26. Cullins MJ, Connor NP. Alterations of intrinsic tongue muscle properties with aging. Muscle Nerve. 2017; 56: E119-E125.

27. Kim KM, Lim S, Oh TJ, Moon JH, Choi SH, Lim JY, Kim KW, Park KS, Jang HC. Longitudinal changes in muscle mass and strength, and bone mass in older adults: Gender-specific associations between muscle and bone losses. J Gerontol a Biol Sci Med Sci. 2018; 73: 1062-1069.

28. Baur A, Reiser MF. Diffusion-weighted imaging of the musculoskeletal system in humans. Skeletal Radiol. 2000; 29: 555-562.

29. Li Q, Pan SN, Yin YM, Li W, Chen ZA, Liu YH, Wu ZH, Guo QY. Normal cranial bone marrow MR imaging pattern with age-related ADC value distribution. Eur J Radiol. 2011; 80: 471-477.

30. Nonomura Y, Yasumoto M, Yoshimura R, Haraguchi K, Ito S, Akashi T. Relationship between bone marrow cellularity and apparent diffusion coefficient. J Magn Reson Imaging. 2001; 13: 757-760.

31. Herrmann J, Krstin N, Schoennagel BP, Sornsakrin M, Derlin T, Busch JD, Petersen

KU, Graessner J, Adam G, Habermann CR. Age-related distribution of vertebral bone-marrow diffusivity. Eur J Radiol. 2012; 81: 4046-4049.

32. Fathi Kazerooni A, Pozo JM, McCloskey EV, Saligheh Rad H, Frangi AF. Diffusion MRI for assessment of bone quality; a review of findings in healthy aging and osteoporosis. J Magn Reson Imaging. 2020; 51: 975-992.

33. Yeung DKW, Griffith JF, Antonio GE, Lee FKH, Woo J, Leung PC. Osteoporosis is associated with increased marrow fat content and decreased marrow fat unsaturation: a proton MR spectroscopy study. J Magn Reson Imaging. 2005; 22: 279-285.

8. Figures and legends

Figure 1 Apparent diffusion coefficient (ADC) map of the tongue

Region of interest (ROI) is the maximum area of the tongue on the apparent diffusion coefficient (ADC) map.

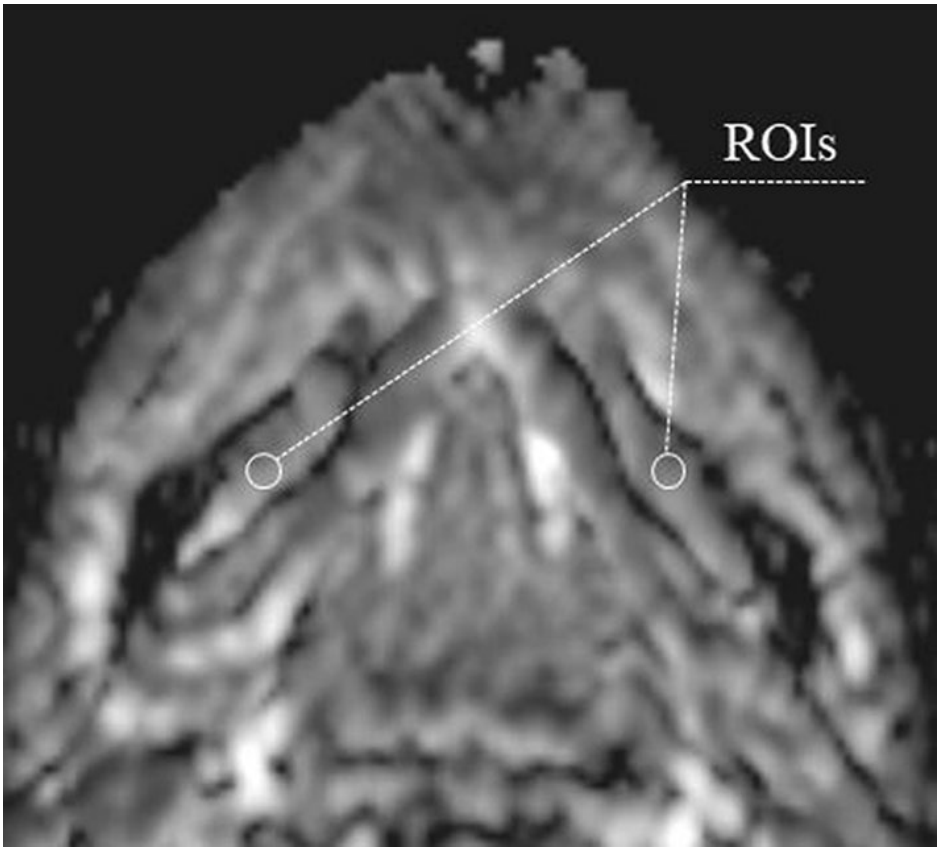

Figure 2 Apparent diffusion coefficient (ADC) map of the mandibular bone marrow

The regions of interest (ROIs), with 5 mm diameter, were manually assigned on the apparent diffusion coefficient (ADC) map over the mandibular bone marrow on both sides, or just below the first molar to reduce the influence of the anatomical structure.

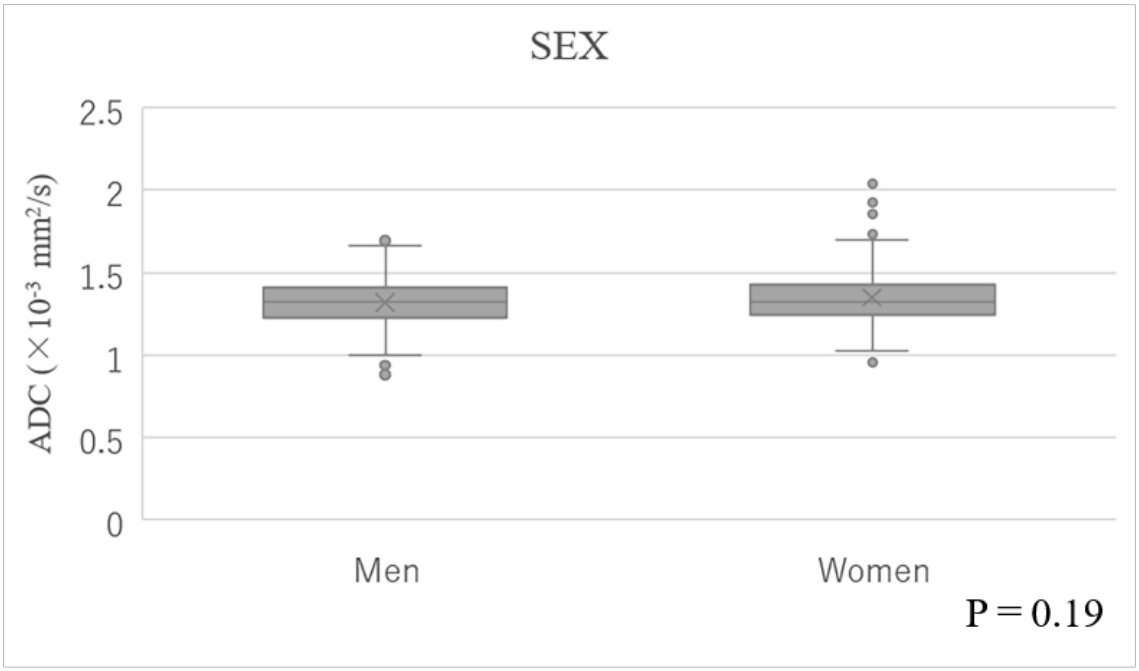

Figure 3 Box-and-whisker plot indicating the relationship between sex and apparent diffusion coefficient (ADC) value of the tongue

There was no significant differences between sex and ADC values of the tongue.

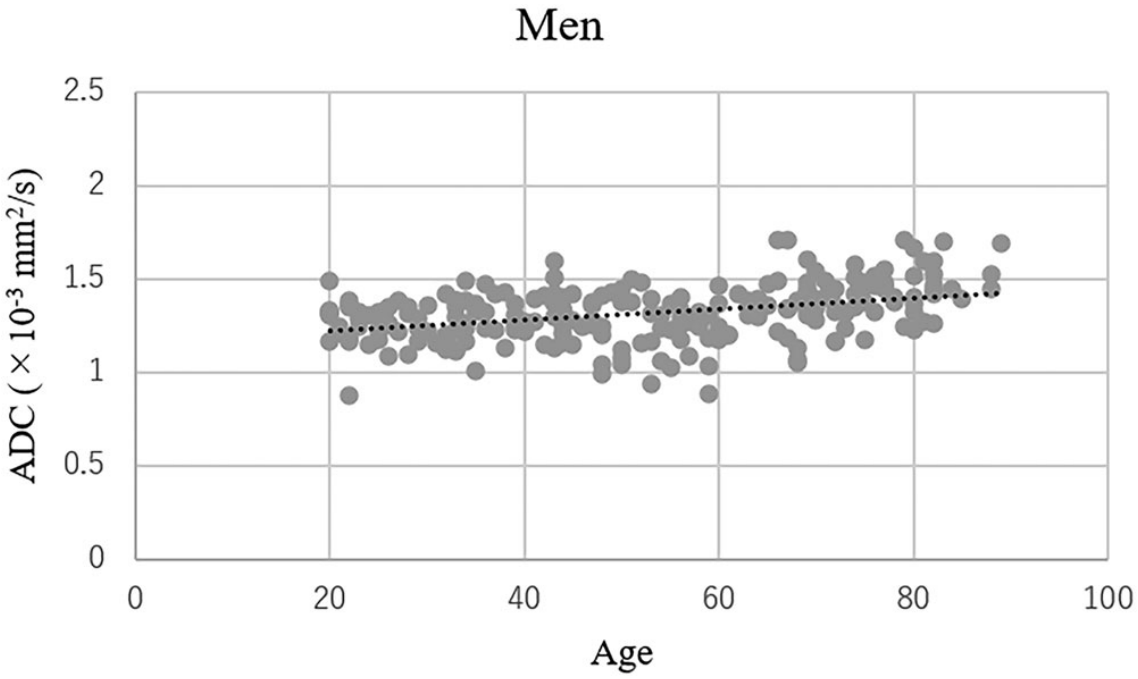

Figure 4 Scatter plot indicating the correlation between men's age and apparent diffusion coefficient (ADC) value of the tongue

Figure 4 shows the positive correlation between men's age and ADC values of the tongue.

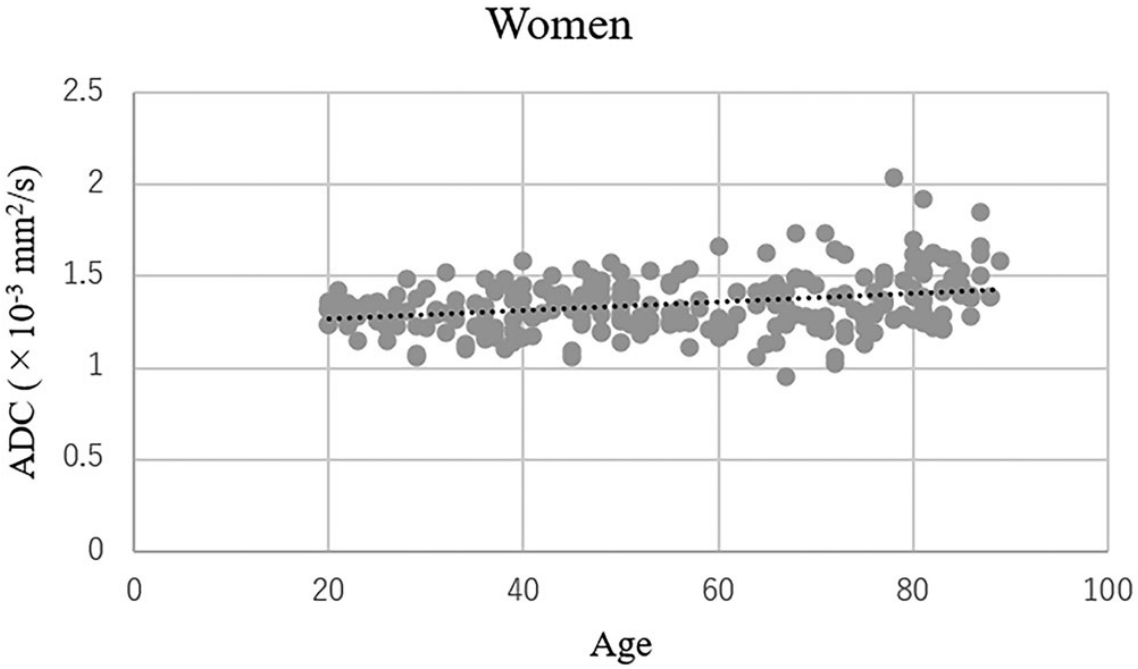

Figure 5 Scatter plot indicating the correlation between women's age and apparent diffusion coefficient (ADC) value of the tongue

Figure 5 shows the positive correlation between women's age and ADC values of the tongue.

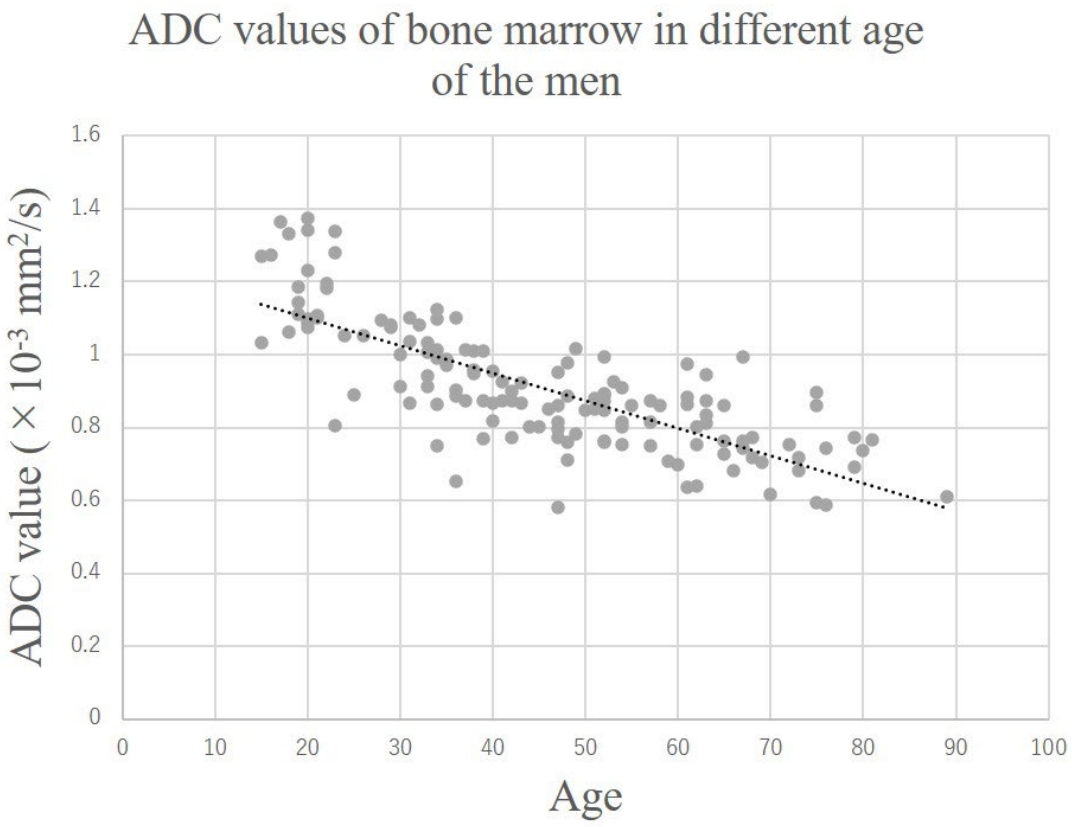

Figure 6 Scatter plot showing the relationship between the apparent diffusion coefficient (ADC) of the bone marrow and age in men

Figure 6 shows the negative correlation between men's age and ADC values of the bone marrow.

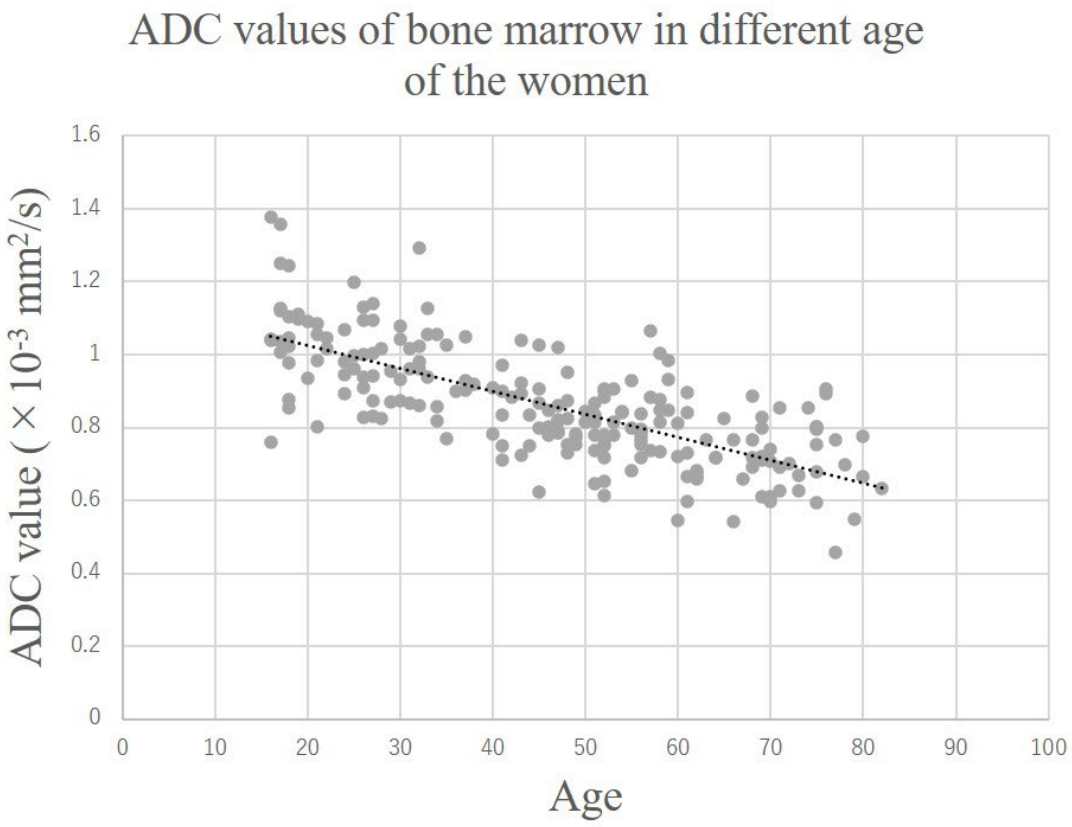

Figure 7 Scatter plot showing the relationship between the apparent diffusion coefficient (ADC) of the bone marrow and age in women

Figure 7 shows the negative correlation between women's age and ADC values of the bone marrow.

9. Table

Table 1 Mean ADC values of the bone marrow in the mandible

	Number of patients (n=Number of patients)		
	Men (n=140)	Women (n=211)	***P*-value**
Mean ADC value of the bone marrow ($\times 10^{-3}$ mm^2/s ±SD)	0.91 ± 0.18	0.86 ± 0.16	*P*=0.016

ADC= Apparent Diffusion Coefficient, SD= Standard Deviation
n=351

Table 2 Mean ADC values of the bone marrow in different age and sex

Age groups (yrs.)	Mean ADC value of bone marrow of men (n=140) (± SD×10^{-3} mm^2/s)	Mean ADC value of bone marrow of women (n=211) (± SD×10^{-3} mm^2/s)
15-19	1.2 ± 0.12 (n=9)	1.08 ± 0.16 (n=19)
20-29	1.13 ± 0.14 (n=19)	0.98 ± 0.1 (n=31)
30-39	0.96 ± 0.11 (n=30)	0.97 ± 0.11 (n=25)
40-49	0.85 ± 0.09 (n=25)	0.83 ± 0.09 (n=37)
50-59	0.84 ± 0.07 (n=21)	0.81 ± 0.09 (n=45)
60-69	0.79 ± 0.1 (n=22)	0.72 ± 0.09 (n=28)
70-79	0.72 ± 0.11 (n=11)	0.71 ± 0.1 (n=23)
80-89	0.7 ± 0.08 (n=3)	0.69 ± 0.08 (n=3)
r	-0.781**	-0.725**

** : $P<0.001$

ADC= Apparent Diffusion Coefficient, SD= Standard Deviation
n=351