Quantitative assessment of the bone marrow in the mandible using diffusion-weighted magnetic resonance imaging

(MRI 拡散強調像を用いた下顎骨骨髄の定量評価)

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本論文は、

1) Quantitative assessment of the mandibular bone marrow of diabetes mellitus patients using diffusion-weighted magnetic resonance imaging

Oral Radiology (In press)

2) Quantitative assessment of mandibular bone marrow in patients with periodontitis by using diffusion-weighted imaging

International Journal of Oral-Medical Sciences (In press)

をまとめたものである。

1. Abstract

Purposes:

The purposes of these studies were to 1) quantitatively assess the mandibular bone marrow of patients with diabetes mellitus (DM) using the apparent diffusion coefficient (ADC) values on diffusion-weighted images (DWI) and 2) to quantitatively assess the mandibular bone marrow in the patients with periodontitis using the ADC values on DWI.

Materials and Methods:

This study was approved by the Institutional Review Board (EC19 - 011).

1. All participants underwent magnetic resonance imaging (MRI) examinations of the temporomandibular joints in the Nihon University Hospital at Matsudo. For the examinations, 65 patients with DM (28 male, 37 female, 29- 84 years of age, mean age 55.7 ± 15.7 years) and mean age, and sex and stage of radiographic bone loss (RBL) matched 65 patients without DM who had underwent MRI examinations between April 2006 and March 2018 were included in this study. The diagnosis of DM was based on the diagnostic criteria of the American Diabetes Association (ADA).

2. 306 patients with periodontitis (141 male, 165 female; age, 41- 85 years; mean age, 65.2 ± 11.4 years) who underwent MRI examinations for suspected trigeminal neuropathy from April 2006 to March 2020 were contained in this study.

Results:

1. The mean ADC values of the mandibular bone marrow of patients with and without DM were $1.18 \pm 0.21 \times 10^{-3}$ mm²/s and $0.83 \pm 0.14 \times 10^{-3}$ mm²/s, respectively. The ADC values of the patients with DM were significantly higher than those of the patients without DM.

2. The mean ADC values of the bone marrow with RBL stages I, II, and III patients with periodontitis were $0.90 \pm 0.16 \times 10^{-3}$ mm²/s, $1.10 \pm 0.11 \times 10^{-3}$ mm²/s, and $1.27 \pm 0.15 \times 10^{-3}$ mm²/s, respectively.

Conclusion:

This study presented the ADC values of the mandibular bone marrow of the patients with DM and the patients with periodontitis. DWI could quantitatively assess the mandibular bone marrow of the patients with DM and the patients with periodontitis.

Key Words: Diabetes mellitus (DM), Apparent diffusion coefficient (ADC), Diffusion-weighted images (DWI), Radiographic bone loss (RBL)

2. Introduction

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, action, or both. Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels (1- 3). There are two main types of DM. In type I DM, there is a selective loss of β cells in the endocrine pancreas, which most likely results from a slowly acting autoimmune process depending on both genetic and environmental factors. In type II DM, β cells are always present, regardless of the duration and severity of the disease, but lack any signs of functional activity. This reflects the secretory defect in β cells which becomes evident in the presence of obesity, hyperinsulinism, and insulin resistance (4). Imaging of DM is among the most challenging areas in radiology. In the previous studies, the mandibular bone in DM was reported to show signal abnormalities on magnetic resonance imaging (MRI) (5). However, few studies have performed imaging assessment of the mandibular bone marrow in patients with DM using diffusion-weighted images (DWI).

Periodontitis is a multifactorial disease involving, microorganisms, host, and environmental factors (6, 7). Periodontitis has been reported to cause gingival inflammation, alveolar bone resorption, and loss of teeth (6, 8). Alveolar bone

resorption is one of the critical features of periodontitis. There are various risk factors associated with periodontitis such as smoking and alcohol consumption, and periodontitis has been reported as a risk factor for systemic diseases such as cerebrovascular accidents and cardiovascular diseases (9, 10). Mandibular bone mainly consists of cancellous bone, bone marrow, and cortical bone. The radiography is useful in the measurement of periodontal bone loss (11).

In the previous study, the mandibular bone marrow in periodontitis was reported to cause signal abnormalities on MRI (12). However, there are few studies using DWI for the evaluation of the mandibular bone marrow in patients with periodontitis. The purpose of this study was to quantitatively assess the mandibular bone marrow in the patients with periodontitis by using apparent diffusion coefficient (ADC) values on DWI.

Several imaging modalities, including MRI, have been used for assessments related to the bone marrow. MRI is often used to examine the bone marrow in the jaw and has been reported to aid in diagnosing mandibular osteomyelitis (13, 14).

DWI is a recent addition to conventional MRI sequences. DWI provides information about the Brownian movement of water, and it has been applied to a variety of lesions, including tumors and cysts, in recent years. Many studies have evaluated the ADC

values (normal bone marrow, osteoporosis, osteomyelitis malignancy, and trauma) using DWI. DWI evaluates the biologic characteristics of bone marrow (15).

The purposes of these studies were to quantitatively assess the mandibular bone marrow of patients with DM and periodontitis using the ADC values of DWI.

3. Materials and Methods

This study was approved by the ethics committee, Nihon University School of Dentistry at Matsudo (EC19 - 011), and the need for informed consent was waived.

1. Quantitative assessment of the mandibular bone marrow of diabetes mellitus patients using diffusion-weighted magnetic resonance imaging

Subjects

All participants underwent MRI examination of the temporomandibular joints in the Nihon University Hospital at Matsudo. For the examinations, 65 patients with DM (28 male, 37 female, 29- 84 years of age, mean age 55.7 ± 15.7 years) and mean age, and sex and stage of radiographic bone loss (RBL) matched 65 patients without DM who had undergo MRI examinations between April 2006 and March 2018 were included in this study (Table 1). The exclusion criteria included history of radiotherapy, severe metal artifacts in the bone marrow, prior history of using bisphosphonates, and diseases affecting the mandibular bone marrow (e.g. osteomyelitis, tumors or cysts in the mandible, and inflammatory diseases). Fig. 1 presents the flow diagram of eligible study participants. The diagnosis of DM was based on the diagnostic criteria of the American Diabetes Association (ADA) (Table 2) (16). Patients were diagnosed with DM according to the ADA criteria. None of the patients in the control group met the ADA criteria for DM. The

participants in the control group had no other systemic illnesses.

Periodontitis may affect edema in the mandibular bone marrow (12). Therefore, the stage of RBL was matched with and without DM. The stage of RBL was assessed by the degree of alveolar bone resorption in the right lower first molar to the lower second molar. A, stage I: RBL indicating alveolar bone resorption of less than 15%. B, stage II: RBL indicating alveolar bone resorption greater than 15% and less than 33%. C, stage III: RBL indicating alveolar bone resorption of 33% or greater (Fig. 2). The degree of alveolar bone resorption was classified by the American Academy of Periodontology (AAP) staging system (8). The stage IV is characterized by the presence of deep periodontal lesions that extend to the apical portion of the root and/or history of 5 or more teeth loss due to periodontitis. Therefore, the stage IV was excluded.

MRI evaluation

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 five-channel phased-array coil. Single shot echo-planar DWI scans were performed using the following parameters: TR/TE = 5100/70; 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. The ADC map was created on the MRI console.

The ADC was calculated using the ADC visualization tool implemented in a dedicated off-line workstation (Philips Medical Systems, Best, The Netherlands). The regions of interest (ROI) were manually placed on the ADC map, on which, the right mandibular bone marrow from the lower first molar to the lower second molar was observed in patients with and without DM. Regarding the ROI setting, it is the area superior to the mandibular canal. The mandibular tooth germ, canal, root, and cortical bone were excluded (Fig. 3). This study used the averages of the ADC values of the mandibular bone marrow by the two oral radiologists for each patient (K. I. 10 years of experience; S. O. 4 years of experience). The intraclass correlation coefficient (ICC) was interpreted as follows: Based on the 95% confident interval of the ICC estimate, values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 are indicative of poor, moderate, good, and excellent reliability, respectively (17).

Statistical analysis

The Mann-Whitney *U* test was used to compare the ADC values of the mandibular bone marrow between the patients with patients with DM and the patients without. The Mann-Whitney U test was performed with a statistical package (SPSS version 21.0®, IBM Japan Inc. Tokyo, Japan). $P < 0.05$ was considered significant. The receiver operating characteristic (ROC) curve analysis was performed to assess the ability of ADC value to

predict DM, and the area under the curve (AUC) was calculated. The ROC curve was created using the ROCR package of statistical analysis software R (R 4.0.3, R Foundation for Statistical Computing, Vienna, Austria) with DM as the objective variable and ADC value as the explanatory variable. The cutoff value was calculated to distinguish DM from non-DM. This involved using the Youden statistic to find the cutoff ADC value that would maximize sensitivity and specificity in distinguishing DM from non-DM.

2. Quantitative assessment of mandibular bone marrow in patients with periodontitis by using diffusion-weighted imaging

Subjects

It included 306 patients with periodontitis (141 male, 165 female; 41- 85 years of age, mean age, 65.2 ± 11.4 years) with who underwent MRI examination for suspected trigeminal neuropathy at the Nihon University Hospital at Matsudo from April 2006 to March 2020.

Panoramic radiographs have been reported to be used to assess bone loss in periodontitis (18). The degree of alveolar bone resorption was classified by AAP staging system (8). The stage of RBL was assessed by the degree of alveolar bone resorption in the right lower first molar to the lower second molar. A, stage I: RBL indicating bone

resorption of less than 15%. B, stage II: RBL indicating bone resorption greater than 15 % and less than33%. C, stage III: RBL indicating bone resorption of 33% or greater (Fig. 2). In this study, age and sex were matched for each stage of RBL. The stage IV is characterized by the presence of deep periodontal lesions that extend to the apical portion of the root and/or history of 5 or more teeth loss due to periodontitis. Therefore, the stage IV was excluded. The exclusion criteria were as follows: history of radiotherapy, severe metal artifacts in the bone marrow, prior history of bisphosphonate use, and disease affecting the mandibular bone marrow (e.g. osteomyelitis, tumor or cyst of the mandible, and inflammatory disease). None of the participants had any other systemic illness.

MRI evaluation

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 five-channel phased-array coil. Single shot echo-planar DWI scans were performed using the following parameters: TR/TE = 5100/70; 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. The ADC map was created on the MRI console.

The ADC values were calculated using the ADC visualization tool implemented in a dedicated offline workstation (Philips Medical Systems, Best, The Netherlands). The ROI

were manually placed on the ADC map on which the right mandibular bone marrow from the lower first molar to the lower second molar was observed in the patients with periodontitis. The ROI was determined in an area superior to the mandibular canal, and the mandibular tooth germ, canal, root, and cortical bone were excluded (Fig. 4). This study used the averages of the ADC values of the right mandibular bone marrow obtained by two oral radiologists for each patient (H. M. 9 years of experience; S. O. 4 years of experience). The ICC values were interpreted as follows: Based on the 95% confident interval of the ICC estimate, values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 are indicative of poor, moderate, good, and excellent reliability, respectively (17).

Statistical analysis

Kruskal–Wallis and Steel–Dwass tests were used to compare the ADC values of the mandibular bone marrow between the stage of RBL. ROC curve analysis was performed to assess the ability of the ADC values to predict stage III, and the AUC was calculated. This involved using the Youden statistic to find the cut-off ADC value that would maximize sensitivity and specificity in distinguishing stage III from stage I and II. The ROC curve was created using the ROCR package of the statistical analysis software R (R 4.0.3, R Foundation for Statistical Computing, Vienna, Austria). Statistical significance

was set at $P < 0.05$.

4. Results

1. Quantitative assessment of the mandibular bone marrow of diabetes mellitus patients using diffusion-weighted magnetic resonance imaging

Table 3 shows the ADC values of the bone marrow in the mandible of patients with and without DM. The mean ADC value of the mandibular bone marrow of patients was $1.18 \pm 0.21 \times 10^{-3}$ mm²/s, while it was $0.83 \pm 0.14 \times 10^{-3}$ mm²/s in patients without DM, which was higher than in those without DM. The mean ADC values in the patients with DM were $1.16 \pm 0.19 \times 10^{-3}$ mm²/s in stage I, $1.22 \pm 0.25 \times 10^{-3}$ mm²/s in stage II, and $1.38 \pm 0.44 \times 10^{-3}$ mm²/s in stage III. In the patients without DM, the mean ADC values were $0.82 \pm 0.14 \times 10^{-3}$ mm²/s in stage I, $0.89 \pm 0.13 \times 10^{-3}$ mm²/s in stage II, and $0.93 \pm 0.16 \times 10^{-3}$ mm²/s in stage III.

Table 4 reveals the diagnostic performances of ADC values to predict DM in patients. The cutoff values were determined with the best accuracy.

Based on the ROC curve, the ADC values in the patients with DM were significantly higher than those in patients without DM (Fig. 5). ROC analysis revealed a cutoff of 0.92 to the ADC values of the mandibular bone marrow of the patients with DM.

The interobserver agreement for the ADC values of the mandibular bone marrow of patients with DM and patients without DM was moderate agreement (ICC = 0.73).

2. Quantitative assessment of mandibular bone marrow in patients with periodontitis by using diffusion-weighted imaging

Table 5 show a summary of the patient characteristics.

Table 6 shows the ADC values of the mandibular bone marrow of patients with stage I, II, and III. Table 6 shows that the ADC values were $0.90 \pm 0.16 \times 10^{-3}$ mm²/s in stage I, $1.10 \pm 0.11 \times 10^{-3}$ mm²/s in stage II, and $1.27 \pm 0.15 \times 10^{-3}$ mm²/s in stage III. The mean ADC values of patients with stage III were higher than those of patients with stage I and II, while the mean ADC values in stage II were higher than those in stage I.

Table 7 reveals the diagnostic performance of ADC values for predicting the stage of RBL in patients. The cutoff values were determined to have the best accuracy. The cutoff ADC value (>1.2) showed a high diagnostic performance (0.84) for predicting stage III (Fig. 6). The interobserver agreement for the ADC values of the mandibular bone marrow at the stage of RBL was good (ICC = 0.76).

5. Discussions

1. Quantitative assessment of the mandibular bone marrow of the patients with DM using diffusion-weighted magnetic resonance imaging

The mean ADC values of the mandibular bone marrow of the patients with DM were higher than those of the patients without DM. MRI is a diagnostic imaging technique based on nuclear resonance that has been mainly used for soft tissue imaging. MRI has major advantages over other imaging techniques, such as conventional radiography with tomograms and CT, in establishing the diagnosis of mandibular bone marrow diseases. MRI can demonstrate the bone marrow changes caused by edema or inflammatory tissue due to increase of water content (19). The ADC value is an objective parameter which can be used for tissue characterization (20- 24). However, there were few reports on ADC value in the evaluation of mandibular bone marrow of the patients with DM. In the study, the mean ADC value of the mandibular bone marrow of the patients with DM was higher than those of the patients without DM. DWI, quantified as the ADC, measures the degree of mobility of water protons in tissues. The mechanism by which ADC changes occur is not fully understood. However, it is generally accepted that conditions that dilate the extracellular space (e.g. vasogenic edema) result in increased ADC values, whereas conditions that result in causes cell swelling (e.g. hypoxic/ischemic injury or osmotic

swelling) result in decreased ADC values (25- 28). The mean ADC values of the mandibular bone marrow of the patients with DM were higher than those of patients without DM. In the previous studies, the mandibular bone in DM was reported to cause signal abnormalities on MRI (5). This result suggested that inflammatory reaction of patients with DM cause an increase in the overall water content. Therefore, increased ADC values in the mandibular bone marrow of patients with DM may indicate bone marrow edema. The cutoff of ADC values predict DM was 0.92×10^{-3} mm²/s, and has high sensitivity and specificity. Therefore, the cutoff value would be useful for the screening of DM. The mean ADC values of stage III in patients with and without DM were higher than those of stage I and II, while the mean ADC values in stage II were higher than those of stage I. In the previous study, the mandibular bone marrow in the patients with periodontitis was reported to cause signal abnormalities on MRI (12). The stage of RBL and ADC values are expected to be correlated.

There are limitations in this study. The severity of DM was not determined, and this would be required to corroborate findings. In the previous study, patients with severe DM were reported to have marked changes in the mandibular bone marrow (29). Therefore, the severity of DM and the ADC values are expected to be correlated. Second, the types of DM were not distinguished. Therefore, this study could not assess

whether the ADC values differed between type 1 DM and type 2 DM. The cause of tooth loss was not investigated in this study. If the differences between stages III and stages IV could be clarified, an index with higher diagnostic performance could be presented.

2. Quantitative assessment of mandibular bone marrow in patients with periodontitis by using diffusion-weighted imaging

Periodontitis is a multifactorial disease involving, microorganisms, host, and environmental factors. Periodontitis has been reported to cause gingival inflammation, destruction of periodontal tissues, and loss of teeth (6, 8). Therefore, the periodontitis is expected to reduce patient quality of life. In the previous study, MRI was used to evaluate bone marrow as a noninvasive imaging technique. Since MRI can detect marrow involvement, it is an important modality for detection of osteomyelitis (13, 14). MRI shows major advantages over other imaging techniques, such as conventional radiography with panoramic radiographs and computed tomography, in establishing the diagnosis of mandibular bone marrow diseases (19). MRI allows early detection of the stage when edema causes changes in the bone marrow.

The ADC value is an objective parameter that can be used for tissue characterization

(20- 24). However, there were few studies on DWI assessments of the mandibular bone marrow in the patients with periodontitis. The present study showed a statistically significant difference in the ADC values corresponding to stages I, II, and III.

ADC values measure the degree of mobility of water protons in the tissues. The precise mechanisms by which changes in ADC values occur in various disease states are not completely understood. However, it is generally accepted that conditions that expand the extracellular space (e.g. vasogenic edema) result in increased ADC values. In contrast, conditions that cause of cellular swelling (e.g. hypoxic/ischemic injury or osmotic swelling) result in decreased ADC values (25, 26). Therefore, as periodontitis progresses, water molecules and exudates in the cell stroma are expected to increase the diffusivity of bone marrow. In the previous study, the mandibular bone marrow in periodontitis was reported to cause signal abnormalities on MRI (12). The results of this study suggested that increased ADC values in the mandibular bone marrow of patients with periodontitis may indicate bone marrow edema. Additionally, ROC analysis revealed that the cut-off ADC values (1.2×10^{-3} mm^2/s) for distinguishing stage III from stages I and II. The sensitivity and specificity of ADC values were 0.81 and 0.84, respectively, indicating very high sensitivity and specificity. These findings suggest that ADC values can be beneficial in distinguishing the stages of RBL.

The cause of tooth loss was not investigated in this study. When the differences between stages III and stages IV could be clarified, an index with higher diagnostic performance could be presented. This study did not distinguish between acute and chronic inflammation. The ADC values may differ for acute or chronic inflammation. In the study, it will be necessary to distinguish between acute and chronic disease by assessing conditions bleeding and suppuration. This study did not investigate clinical attachment loss (CAL). When we can measure the CAL, it is possible that an index with higher diagnostic ability could be presented.

6. Conclusion

This study presented the ADC values of the mandibular bone marrow of the patients with DM and the patients with periodontitis. DWI could quantitatively assess the mandibular bone marrow of the patients with DM and the patients with periodontitis.

7. References

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8. Figures and legends

Fig. 1 Flowchart of this study

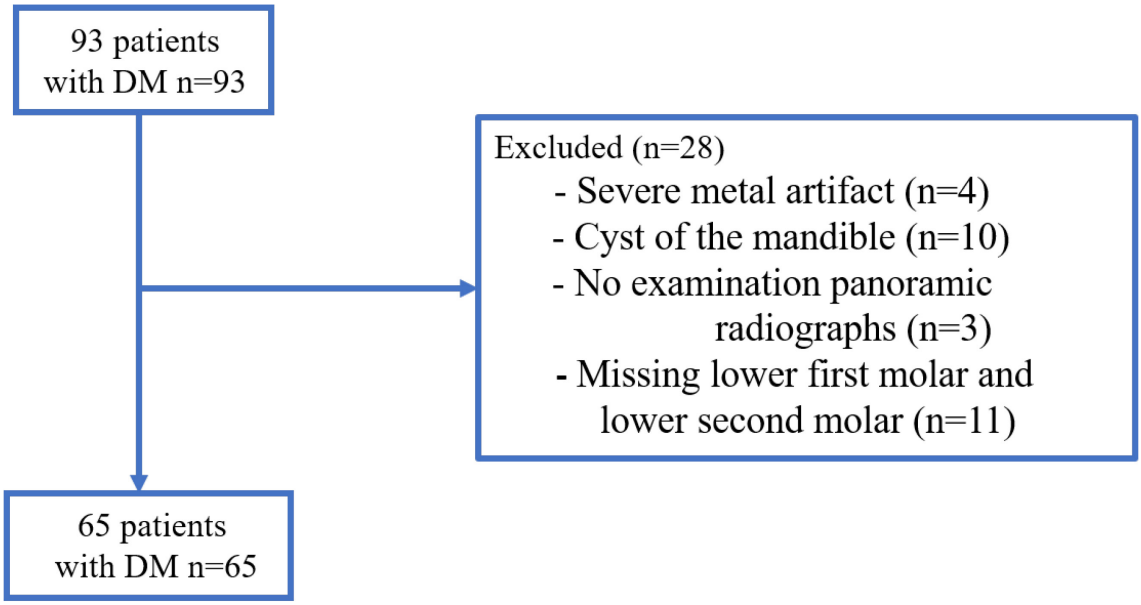
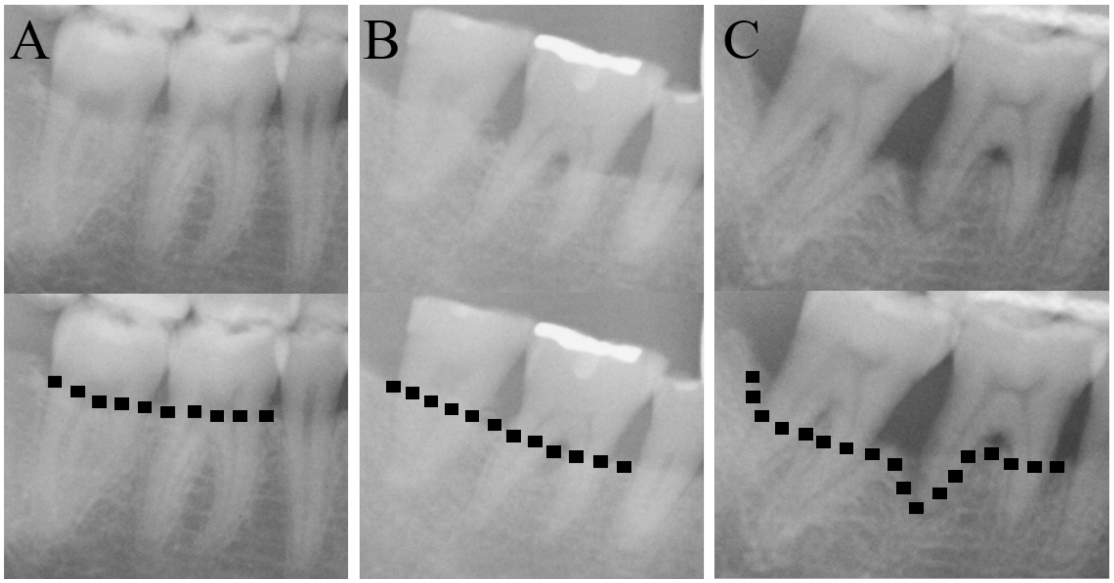
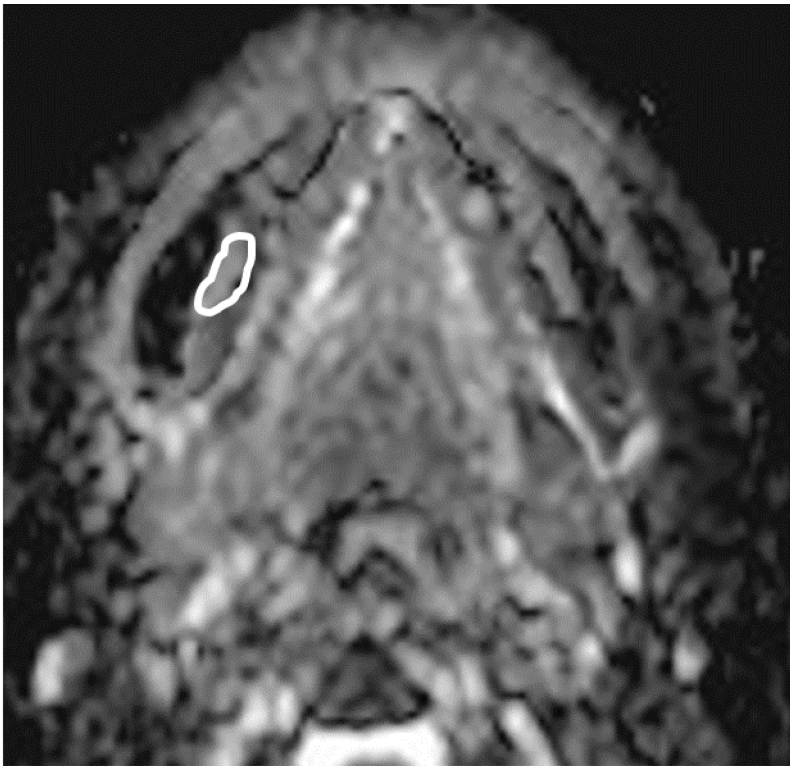


Fig. 2 Diagnostic criteria of the American Academy of Periodontology



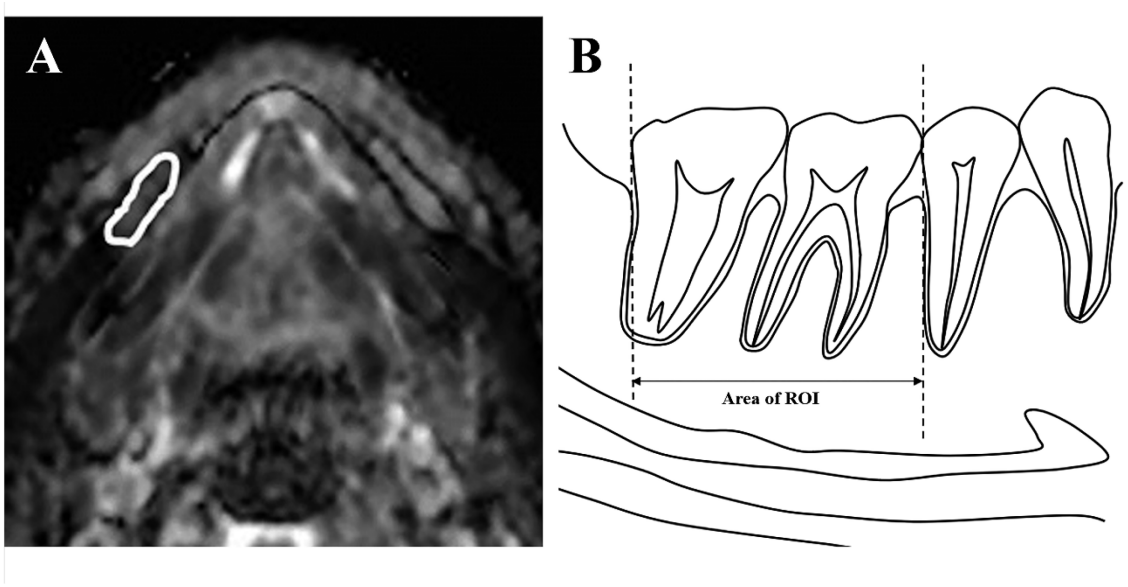
Panoramic radiographs show the periodontitis of mandibular right lower first molar to the lower second molar and the degree of alveolar bone loss (dotted lines).
A, Stage I: radiographic bone loss (RBL) indicates of alveolar bone loss of less than 15%.
B, Stage II: RBL indicates of alveolar bone loss greater than 15% and less than 33%.
C, Stage III: RBL indicates of alveolar bone loss of 33% or greater.

Fig. 3 Apparent diffusion coefficient (ADC) values of the mandibular bone marrow in the patients with DM



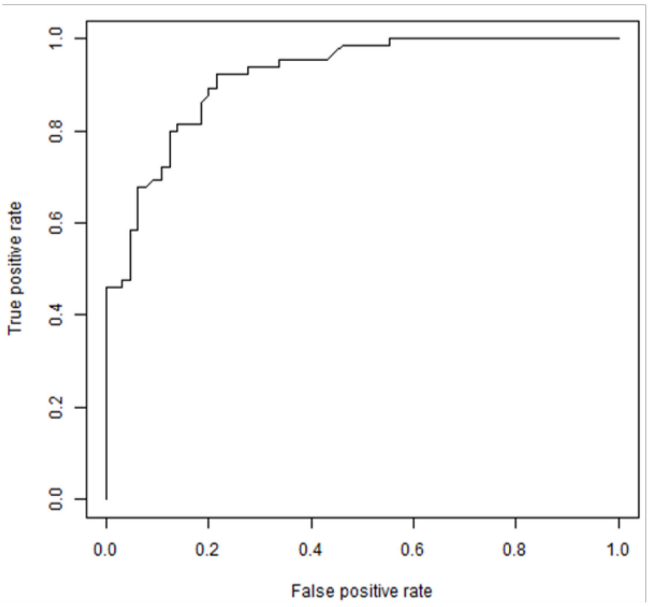
The regions of interest (ROI) place below the right lower first molar to the lower second molar. The ROI place in an area superior to the mandibular canal, and the canal, root, and cortical bone exclude.

Fig. 4 Region of interest (ROI) placement of mandibular bone marrow in the patients with periodontitis



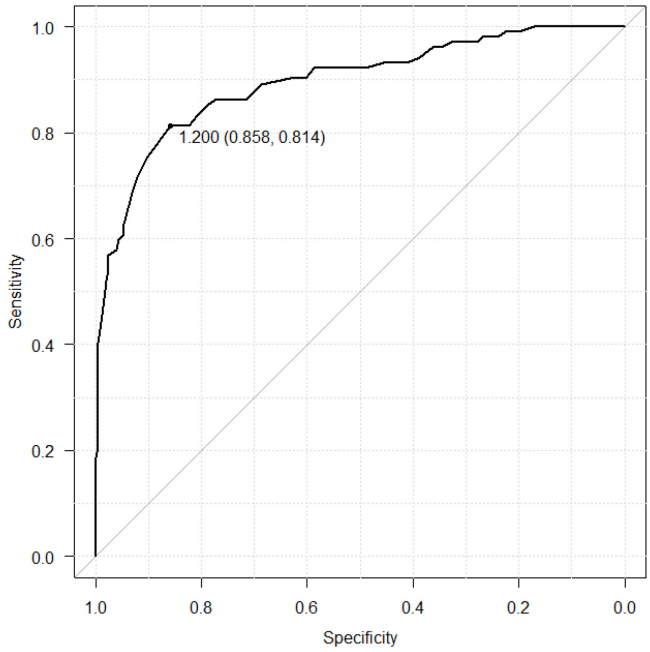
A, B: The regions of interest (ROI) place below the right lower first molar to the lower second molar. The ROI place in an area superior to the mandibular canal, and the canal, root, and cortical bone exclude.

Fig. 5 The receiver operating characteristic (ROC) curve for the assessment of diabetes mellitus (DM) associated apparent diffusion coefficient (ADC) value of the mandibular bone marrow using diffusion-weighted images (DWI)



The graph shows the ROC curve of the ADC values for predicting DM. ROC analysis reveals a cutoff of 0.92 to the ADC values of the mandibular bone marrow of the patients with DM.

Fig. 6 The receiver operating characteristic (ROC) curve for the assessment of periodontitis-associated apparent diffusion coefficient (ADC) values of the mandibular bone marrow using diffusion-weighted images (DWI)



The graph shows the ROC curve of the ADC values for predicting stage III. ROC analysis reveals a cutoff ADC value of 1.2 for the mandibular bone marrow of stage III.

9. Table

Table 1 Summary of patients with DM and patient without DM Characteristics

	Patients with DM	Patients without DM
Sex (No.)		
Male	28	28
Female	37	37
Age (yrs.)		
Mean ± SD	55.7 ± 15.7	55.7 ± 15.7
Range	29-84	29-84
Stage of RBL (No.)		
I	50	50
II	12	12
III	3	3

DM: Diabetes mellitus, RBL: Radiographic bone loss, SD: Standard deviation

Table 2　Diagnostic criteria of the American Diabetes Association

Criteria for the diagnosis of diabetes
FPG≧126mg/dL Fasting is defined as no caloric intake for at least 8 h.
OR
2-h PG ≧200 mg/dL during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.
OR
A1C ≧6.5% The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose≧200 mg/dL

DCCT: Diabetes Control and Complications Trial, FPG: fasting plasma glucose, OGTT: oral glucose tolerance test, WHO: World Health Organization, 2-h PG: 2h plasma glucose.

Table 3　Mean ADC values of the patients with DM and the patients without DM

	Patients with DM ($\times 10^{-3}$ mm²/s)	Patients without DM ($\times 10^{-3}$ mm²/s)
Total	1.18 ± 0.21	0.83 ± 0.14 *
Stage of RBL		
I	1.16 ± 0.19	0.82 ± 0.14 *
II	1.22 ± 0.25	0.89 ± 0.13 *
III	1.38 ± 0.44	0.93 ± 0.16 *

*P< 0.05

ADC: Apparent diffusion coefficient, DM: Diabetes mellitus, RBL: Radiographic bone loss

Table 4 Diagnostic performances of ADC values to predict patients with DM

Cut-off	TP	FP	FN	TN	Sensitivity	Specificity	Accuracy	AUC
0.93	60	14	5	51	0.92	0.78	0.85	0.91

Table 5　Summary of the patients with periodontitis characteristics

	Patients with periodontitis
Sex (No.)	
Male	141
Female	165
Age (yrs.)	
Mean ± SD	65.2 ± 11.4
Range	41-85
Stage of RBL (No.)	
I	102
II	102
III	102

RBL: Radiographic bone loss, SD: Standard deviation

Table 6 Mean ADC values of periodontitis

Stage of RBL	ADC values of patients with periodontitis ($\times 10^{-3}$ mm²/s)	
I	0.90 ± 0.16	*
II	1.10 ± 0.11	*
III	1.27 ± 0.15	

*P< 0.05

ADC: Apparent diffusion coefficient, RBL: Radiographic bone loss

Table 7 Diagnostic performances of ADC values to predict patients with periodontitis

Cut-off	TP	FP	FN	TN	Sensitivity	Specificity	Accuracy	AUC
1.2	83	29	19	175	0.81	0.84	0.84	0.85