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Correlation of postoperative thickening of the sinus mucosa in cone beam computed tomography with decreased voxel brightness of the regenerated bone after sinus floor augmentation: a prospective study

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T. Uematsu, K. Ito, T. Tsukioka, K. Isobe, H. Okudera, T. Kaneda: Correlation of postoperative thickening of the sinus mucosa in cone beam computed tomography with decreased voxel brightness of the regenerated bone after sinus floor augmentation: a prospective study. Int. J. Oral Maxillofac. Surg. 2025; xx: 1–9.

Abstract. Although postoperative thickening of the sinus membrane is a risk in maxillary sinus floor augmentation (MSFA), the relationship between postoperative mucosal thickening (MT) and the quality of the augmented bone has not been clarified. The aim of this study was to evaluate the characteristics of the augmented bone after MSFA using cone beam computed tomography (CBCT) histograms, comparing patients with and without postoperative maxillary sinus MT. Patients who underwent MSFA with beta-tricalcium phosphate and simultaneous implantation between 2021 and 2023 were included (14 regions in 12 patients). CBCT images obtained pre-surgery (C1) and at 6 months post-surgery (C2) were used for comparisons between a No-MT group (≤2 mm) and an MT group (> 2 mm). Three-dimensional bone subtraction (C2 − C1) was performed for the analysis of voxel brightness and quantification of the augmented bone volume. Histogram analysis showed that the MT group had a significantly lower mean brightness value (P = 0.004) and higher skewness (P = 0.003) and kurtosis (P = 0.006) values than the No-MT group. Thus, histogram-based assessment of bone quality in MSFA may be used as a prognostic marker for implant success by monitoring changes in brightness, skewness, and kurtosis during the augmented bone healing process.

Keywords: Cone-beam computed tomography; Bone substitutes; Dental implants; Sinus floor augmentation; Maxillary sinus.

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Maxillary sinus floor augmentation (MSFA) with simultaneous implant placement is widely used to increase the bone volume and shorten the waiting period for implant prostheses[1,2]. However, postoperative complications such as sinus membrane perforation and nasal haemorrhage may occur[3–5], eventually leading to postoperative maxillary sinus mucosal thickening (MT) and the development of maxillary sinusitis[6]. Even in patients with a good clinical course, clinicians have observed transient postoperative thickening of the sinus membrane during bone regeneration[7–9]. The causes of mucosal thickening include osteitis, and pathological studies have revealed that postoperative mucosal thickening is caused by bone remodelling processes such as inflammation of the submucosal bone and bone formation[8]. Therefore, mucosal thickening after MSFA reflects the bone quality based on the degree of remodelling of the augmented bone[10] and bone maturation[11,12]. However, the precise relationship between postoperative mucosal thickening and bone quality is yet to be clarified[13].

A sinus mucosa thicker than 2 mm affects the anatomy of the sinus, and a thickness of 2 mm is considered a reliable clinical threshold for pathological mucosal thickening[9,14,15]. When MSFA is performed, if the postoperative thickness of the maxillary sinus mucosa is <2 mm, it is considered healthy[9]. Although these observational considerations of the maxillary sinus mucosa have been reported, an objective method for assessing the area of bone augmentation that affects postoperative mucosal thickness remains to be elucidated.

Three-dimensional (3D) cone beam computed tomography (CBCT) analysis is an effective tool for preoperative implant placement planning, as well as postoperative assessment of the bone structure[16]. Furthermore, although image brightness (grey values) cannot be used to assess actual bone density, attempts have been made to evaluate the bone structure based on the CBCT brightness values[17]. Using 3D CBCT images, grey-level histograms and their characteristics (skewness and kurtosis) have also been used to evaluate the distribution of oral bone mineral within individual images[18]. Thus, in addition to the traditional assessment of augmented bone volume, a comparison of the bone quality by measuring the brightness of the augmented bone, as well as the skewness and kurtosis, between patients with and without postoperative mucosal thickening, using

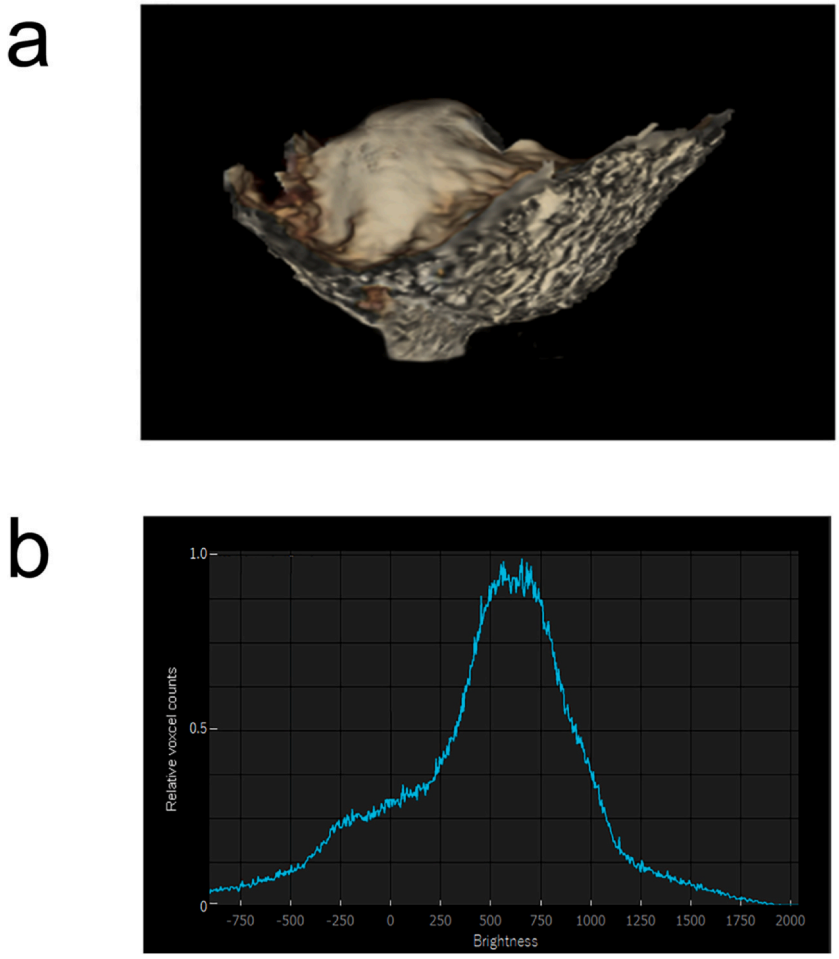

Fig. 2. (a) Bone subtraction for extracting the precise region of regenerated bone, using Synapse Vincent. The 3D CBCT image obtained before MSFA was subtracted from the 3D CBCT image obtained 6 months after MSFA. (b) Brightness histogram analysis of the generated bone extracted by bone subtraction using Synapse Vincent.

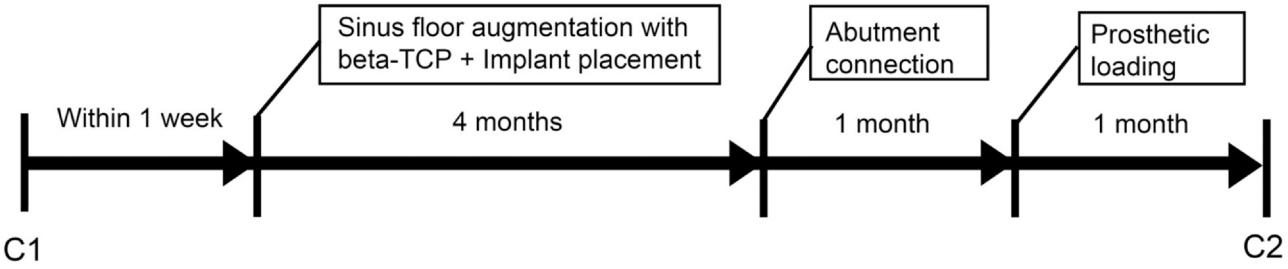

Fig. 1. Timeline of the evaluation using CBCT. CBCT images were obtained before (C1) and 6 months after (C2) maxillary sinus floor augmentation.

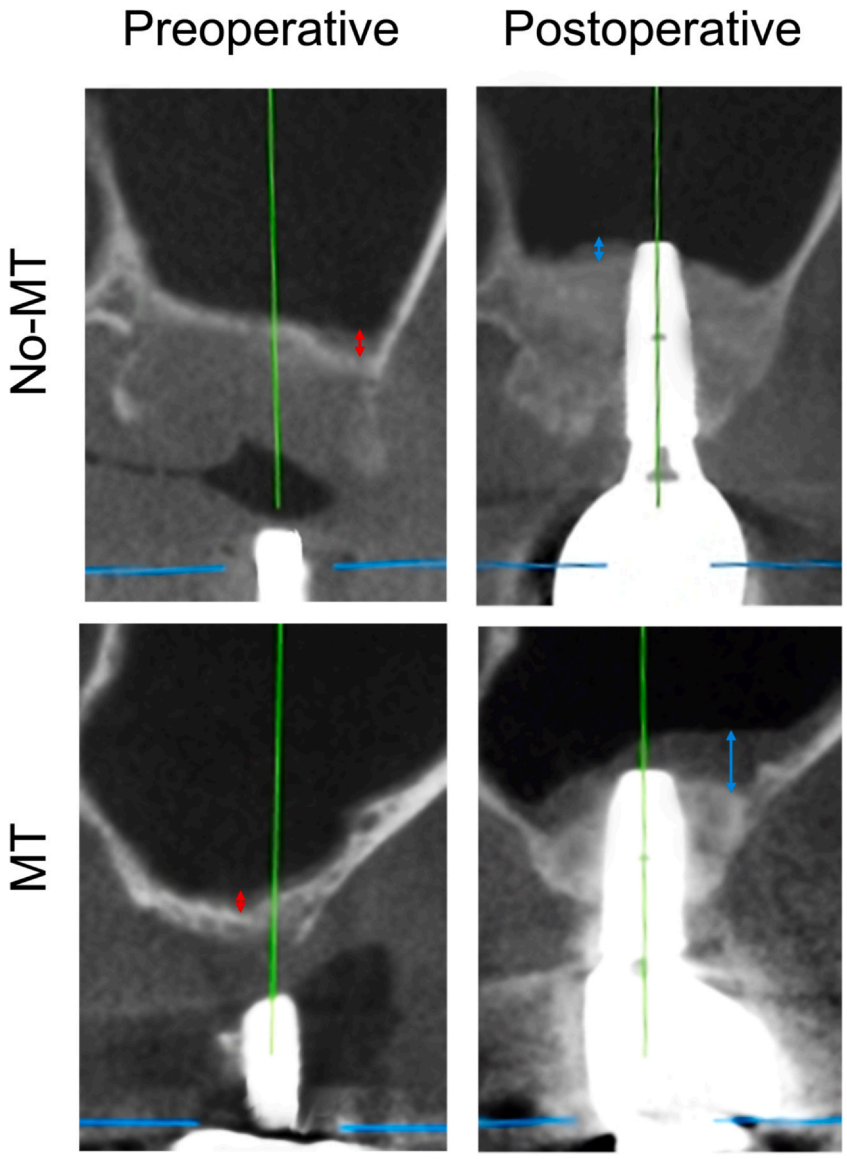

Fig. 3. Measurement of membrane thickness on a CBCT coronal slice. To assess the presence or absence of mucosal thickening (MT) before MSFA, the maximum thickness of the maxillary sinus mucosa (red arrows) was measured on a CBCT coronal slice displaying the surgical template. Cases with mucosal thickening of > 2 mm before MSFA were excluded from the study. To evaluate mucosal thickening after MSFA, the maximum thickness of the maxillary sinus mucosa (blue arrows) was measured on a CBCT coronal slice showing the implant fixture. The preoperative and postoperative membrane thicknesses were measured using NEOPREMIUM2.

CBCT grey-level histograms, may elucidate the postoperative changes following MSFA.

Beta-tricalcium phosphate (β-TCP) is a widely used bone-grafting scaffold that induces a similar degree of oedema and inflammation as autogenous bone or natural bone substitutes[19,20]. Histological and radiological analyses have indicated that β-TCP is slowly resorbed, which results in the presence of unresorbed β-TCP even at 6 months post-surgery. Moreover, its replacement with new bone occurs gradually over approximately 1 year[20]. Thus, the augmented bone at 6 months to 1 year post-surgery reflects the progress of postoperative bone remodelling.

The aim of this prospective study was to evaluate the characteristics of the augmented bone after MSFA using CBCT histograms and compare them between patients with and without postoperative mucosal thickening.

Materials and methods

Study design and participants

This prospective study included patients who underwent MSFA and simultaneous implant placement in the edentulous maxillary molar region between 2021 and 2023 3–6 mm; and age 20–79 years. The exclusion criteria were a history of diabetes, malignant disease or radiation therapy, steroid or bisphosphonate use; any immune deficiency, connective tissue disease, or infection; disorders of the blood, digestive system, urinary system, respiratory system, circulatory system, or bone metabolism; pregnancy or lactation; alcohol or substance abuse; otorhinolaryngological disorders, including any maxillary sinus pathology or thickened maxillary sinus membranes (> 2 mm) in the preoperative imaging evaluation; and uncontrolled periodontal disease or oral infections. No previous reports of similar studies could be identified; therefore, no sample size calculation was performed prior to conducting this study.

MSFA

An expert oral surgeon with more than 20 years of clinical experience performed all of the MSFA surgical procedures. No intraoperative perforation of the sinus membrane occurred in any patient.

Following elevation of the sinus membrane, β-TCP granules (OSferion; Olympus Terumo Biomaterials Corp.,

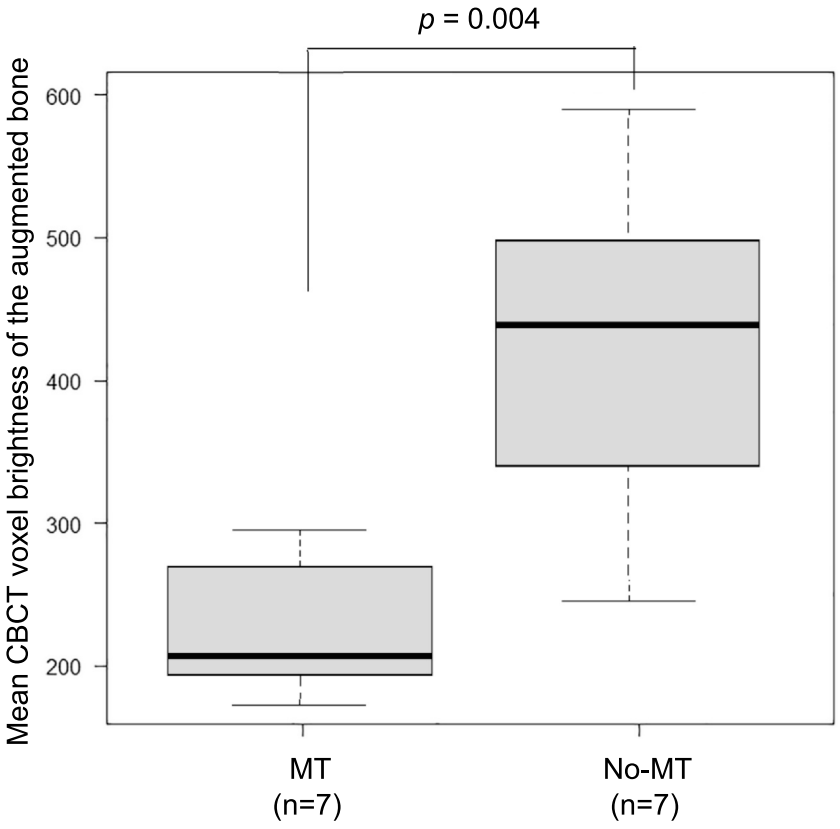

Fig. 4. Boxplot of the mean CBCT voxel brightness of the augmented bone in the mucosal thickening group (MT; membrane thickness > 2 mm) and no mucosal thickening group (No-MT; membrane thickness ≤2 mm) at 6 months after maxillary sinus floor augmentation.

Tokyo, Japan) soaked in saline were used to fill the space. Immediately afterwards, implant placement was performed according to the standard protocol of the implant manufacturer (NobelParallel Conical Connection; Nobel Biocare, Gothenburg, Sweden). After implant placement, the mucoperiosteal flap was repositioned and sutured. Antibiotic drugs were administered to prevent infection, and the patients were recalled after 7–10 days for clinical examination and suture removal.

Radiographic examination

A hybrid digital panoramic/CBCT system, AUGE (Asahi Roentgen Industry, Kyoto, Japan) (panoramic: 62 kV, 8 mA, 12 s, 14.2 μSv; CBCT: 85 kV, 8 mA, 17 s, field of view (FOV) 51 × 55 mm, 35.4 μSv), was used in this study. Fig. 1 shows the timeline of the imaging examinations. The following radiographic examinations were performed: (1) panoramic radiography and CBCT (C1) before MSFA with simultaneous implant placement, for preoperative imaging evaluation of the implant surgery; (2) panoramic radiography alone immediately postoperative (to minimize radiation exposure), for the evaluation of implant placement; and (3) panoramic radiography and CBCT (C2) at the 6-month follow-up. The CBCT images were stored as DICOM files (Digital Imaging and Communications in Medicine). The digital radiographs were analysed using NEOPREMIUM2 software (Asahi Roentgen Industry).

The augmented bone area was extracted by applying the bone subtraction method described by Nagata et al.[20], using the bone subtraction function of a 3D image analysis system volume analyser (Synapse Vincent; Fujifilm, Tokyo, Japan). Briefly, the C1 3D image was subtracted from the C2 3D image, from which the implant was removed using the trimming function, as per the manufacturer's instructions (Fig. 2a); this was used as the region of interest (ROI) for the histogram analysis and quantification of the augmented bone volume as the generated bone at 6 months after MSFA (Fig. 2b)[21].

The image voxel brightness in the ROI was subjected to histogram analysis and compared between the group with sinus mucosa thickness > 2 mm (MT group) and the group with sinus mucosa thickness ≤2 mm (No-MT group) measured 6 months after MSFA.

The preoperative maximum mucosal thickness was measured in CBCT coronal slice images, perpendicular to the occlusal plane passing through the axis of the temporary seal of the surgical template, and postoperatively through the axis of the implant fixture, using NEOPREMIUM2 (Fig. 3)[16,22]. Both the preoperative and postoperative mucosal thickness were measured at the point of maximum thickness perpendicular to the underlying bone, and the

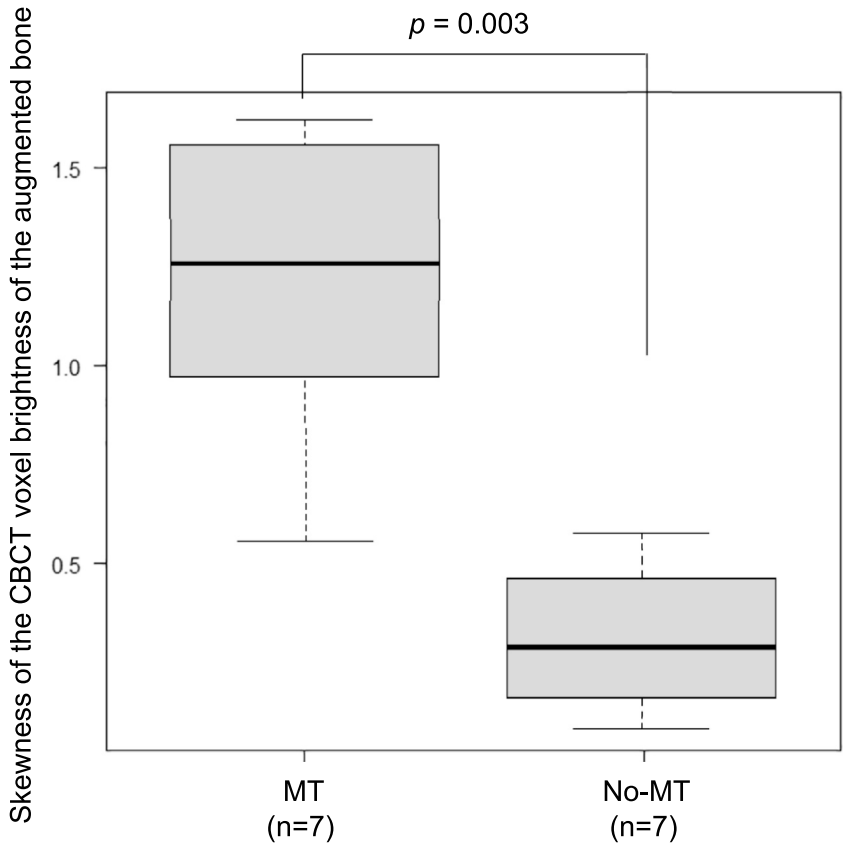

Fig. 5. Boxplot of the skewness of the CBCT voxel brightness of the augmented bone in the mucosal thickening group (MT; membrane thickness > 2 mm) and no mucosal thickening group (No-MT; membrane thickness ≤2 mm) at 6 months after maxillary sinus floor augmentation.

maximum thickness in each sinus was recorded.

Statistical analysis

The histograms showed that the data did not follow a normal distribution. The data were therefore reported as the median and interquartile range (IQR), and between-group comparisons were performed using the Mann–Whitney *U*-test. Spearman's rank correlation coefficient was calculated to examine correlations between variables. All statistical analyses were performed with IBM SPSS Statistics for Windows version 22.0 (IBM Japan, Tokyo, Japan). A *P*-value of ≤0.05 was considered statistically significant.

Results

Clinical evaluation

Fourteen maxillary sinus regions in 12 patients (eight female, four male) aged 45–79 years (mean ± standard deviation 60.9 ± 10.3 years) were included in the study. No patient dropped out during the observation period. A summary of the patient characteristics is given in Supplementary material Table S1. This prospective study involved seven regions in six patients, in each of the groups (MT group and No-MT group).

Radiographic evaluation

The mean CBCT voxel brightness was significantly lower in the MT group (median 204.1, IQR 191.3–279.1) than in the No-MT group (median 437.5, IQR 329.0–490.2) (P = 0.004; Fig. 4). Regarding the skewness of the histogram brightness, significantly higher values were observed in the MT group (median 1.23, IQR 0.98–1.58) than in the No-MT group (median 0.28, IQR 0.11–0.45) (P = 0.003; Fig. 5). Furthermore, upon comparing the kurtosis of the histogram, significantly higher kurtosis was noted in the MT group (median 5.18, IQR 4.76–5.81) than in the No-MT group (median 3.53, IQR 3.21–4.31) (P = 0.006; Fig. 6).

A significant negative correlation between the mean brightness and augmented bone volume was observed, with higher mean brightness associated with a lower augmented bone volume (R = −0.552, P = 0.041) (Fig. 7). A significant negative correlation was also observed between the mean brightness and postoperative maxillary sinus mucosal thickness, indicating that higher mean brightness was associated with lower maxillary sinus mucosal thickness (R = −0.851, P < 0.001) (Fig. 8). In contrast, no significant correlation was observed between the augmented bone volume and maxillary sinus mucosal thickness (R = 0.483, P = 0.080) (Fig. 9).

Discussion

In this study, a difference in the histogram of the bone augmentation area where regenerated bone existed was observed at 6 months post MSFA with simultaneous implant placement, at the boundary of 2.0 mm postoperative mucosal thickness. The results revealed a statistically significant difference in the CBCT brightness value of the bone augmentation area between the No-MT group (≤2 mm mucosal thickness) and MT group (> 2 mm mucosal thickness) after MSFA, suggesting a difference in postoperative submucosal bone quality. These results are consistent with those of previous reports suggesting that a mucosal thickness of ≤2 mm indicates a clinically healthy mucosa[9,14,15,22,23].

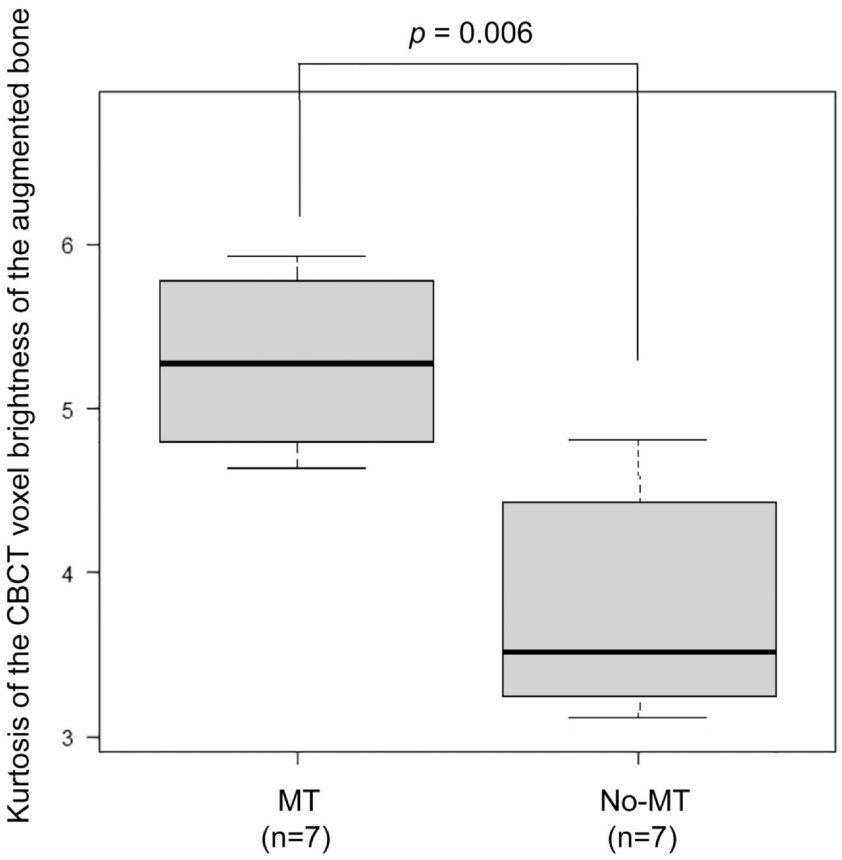

Fig. 6. Boxplot of the kurtosis of the CBCT voxel brightness of the augmented bone in the mucosal thickening group (MT; membrane thickness > 2 mm) and no mucosal thickening group (No-MT; membrane thickness ≤2 mm) at 6 months after maxillary sinus floor augmentation.

Due to the absence of similar past studies, an a priori sample size calculation could not be performed for this prospective study. However, despite the small sample size, statistically significant differences between the mucosal thickness groups were observed, suggesting that the sample size was sufficient.

While the brightness histogram gives a rough outline of the shape, two numerical measures of shape, i.e. skewness and kurtosis, allow a more precise assessment[24]. A positively skewed distribution (also called a right-skewed distribution) indicates that most of the values are concentrated in the left tail and there is a long right tail. A negatively skewed distribution is the exact opposite. Kurtosis is a statistical measure used to describe the probability distribution. Skewness distinguishes between the two tails, while kurtosis measures the extreme values in the left or right tail of the histogram.

This study revealed that the MT group, which included cases without postoperative infection but with postoperative mucosal thickening, was characterized by low mean brightness and high skewness and kurtosis, i.e. it showed the characteristics of a positively skewed distribution with a sharp peak in the low brightness region and a long right tail. In this state, the brightness value reflecting ossification is low, so it is speculated that the persistence of postoperative mucosal thickening indicates a delayed or prolonged callus formation phase and ongoing bone remodelling accompanied by inflammatory changes[18]. Considering mucosal thickening reflects inflammatory changes in bone remodeling[8,10–12], lower degrees of skewness and kurtosis and a higher mean brightness value in the histogram may indicate greater progression of ossification. Therefore, histogram analysis of the augmented bone may be used to evaluate bone quality following MSFA.

Although the mean brightness values correlated with the augmented bone volume and mucosal thickening, no significant correlation was observed between the augmented bone volume and mucosal thickening, suggesting that the bone quality of the surgically augmented area affected the postoperative thickness of the mucous membrane. In recent years, researchers have quantitatively evaluated bone volume after MSFA using CBCT[20,25]. Generally, surgical results are discussed by measuring the bone volume; however, the evaluation of bone quality is also important. Considering the radiation exposure dose, obtaining frequent CBCT images is ethically problematic, and an experimental bone biopsy is difficult to perform. Therefore, a

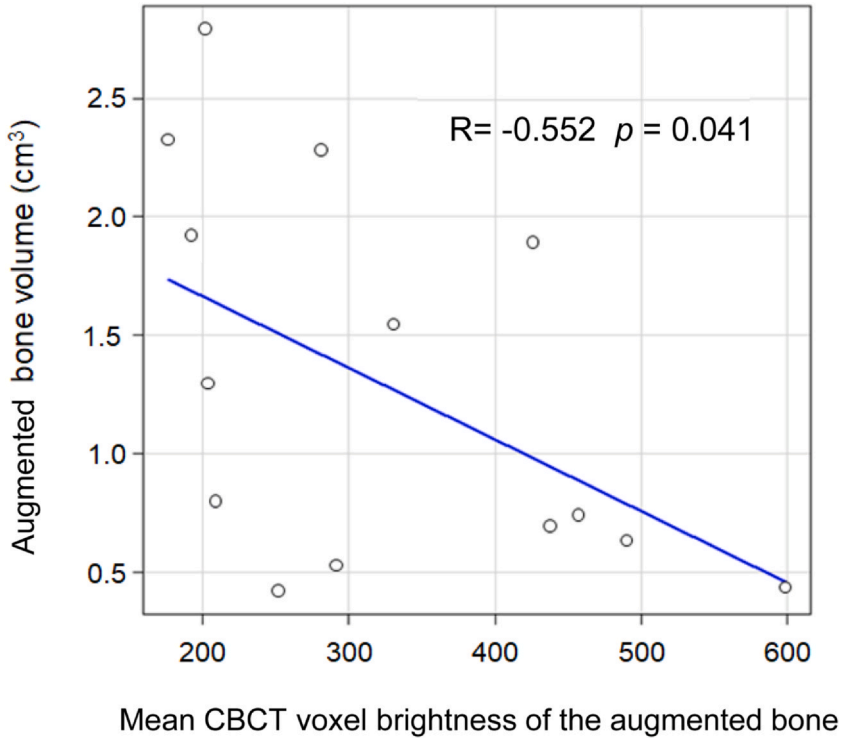

Fig. 7. Scatterplot of the mean CBCT voxel brightness and augmented bone volume at 6 months after maxillary sinus floor augmentation; Spearman's rank correlation coefficient (*R*) is shown.

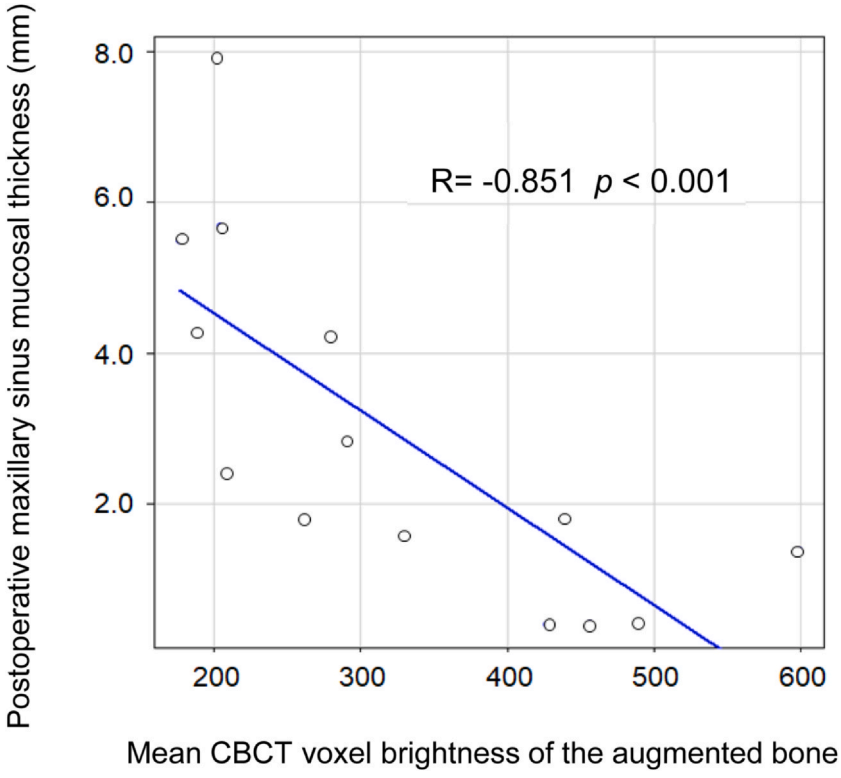

Fig. 8. Scatterplot of the mean CBCT voxel brightness and maxillary sinus mucosal thickness at 6 months after maxillary sinus floor augmentation; Spearman's rank correlation coefficient (*R*) is shown.

histogram analysis of brightness may be considered useful for solving this problem[26]. In addition, the mucosal thickening in patients who underwent MSFA can be explained by the brightness of the histogram corresponding to bone quality, its skewness and kurtosis. This tool could be used to explain the state of the mucosal thickening in patients with a good postoperative course, which is often observed in clinical practice.

A limitation is that determining the correlation dynamics of brightness, skewness, and kurtosis in CBCT histograms with histopathological findings is challenging[26]. Moreover, the fluctuations in the histogram may differ depending on the type and structure of the artificial bone material used for bone regeneration. Therefore, in the future, the correlation between CBCT histograms and histopathological images of different bone substitutes need to be studied in larger samples[27]. In this study, the lack of CBCT immediately post-surgery limited the ability to assess the changes in volume over time. Therefore, further studies clarifying the relationships between the anatomy of the maxillary sinus, bone volume on CBCT, and bone quality assessed using histograms are warranted. In cases where the postoperative mucosal thickening remains for a long period of time[7–9], it is necessary to consider the relationship between bone quality assessed using histograms and postoperative complications such as local inflammatory reactions and maxillary sinusitis.

In conclusion, the analysis of CBCT histograms of the augmented bone after MSFA revealed that the brightness value was significantly lower and the skewness and kurtosis were higher in cases with mucosal thickening. Thus, histogram-based assessments of bone quality in MSFA may be used as a prognostic marker for implant success by monitoring changes in brightness, skewness, and kurtosis during the healing process of the augmented bone. The study findings suggest that CBCT histograms can be used to assess the bone quality. However, further investigations are necessary to establish the relationship between the CBCT histogram features and histopathology for each transplant material. Future studies are required to determine the relationships between the parameters that affect healing in maxillary sinus augmentation surgery and postoperative mucosal thickening.

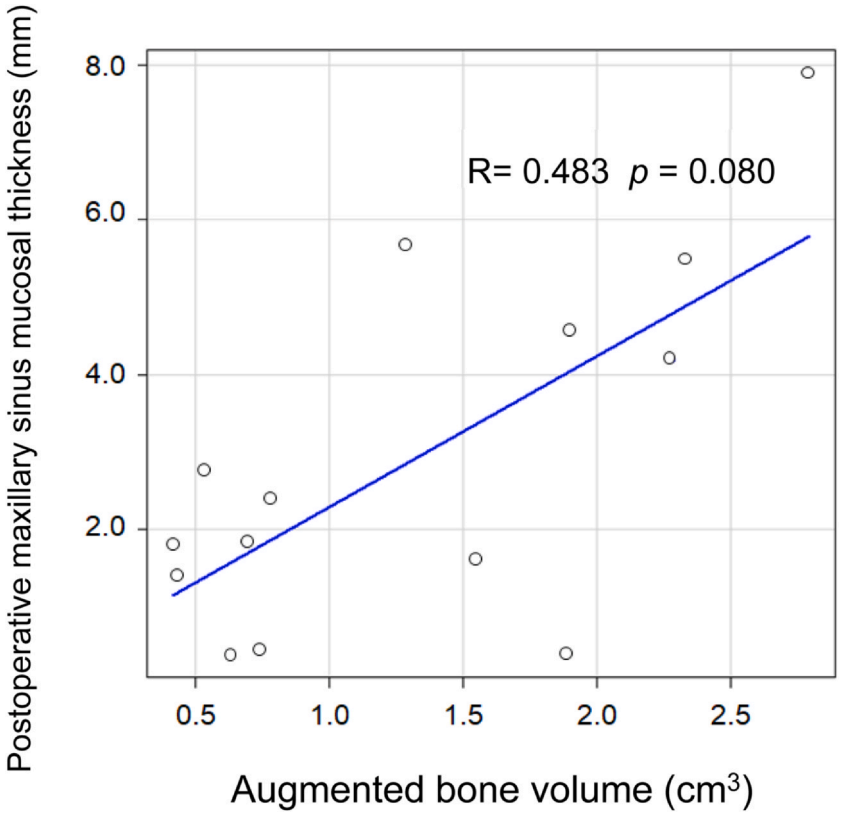

Fig. 9. Scatterplot of the augmented bone volume and maxillary sinus mucosal thickness at 6 months after maxillary sinus floor augmentation; Spearman's rank correlation coefficient (*R*) is shown.

Ethical approval

This study was approved by the Ethics Committee of the Tokyo Plastic Dental Society (Review Board No. 17000114), which is a designated training facility for the Japanese Society of Oral Implantology (Clinical Trial No. 21202).

Patient consent

Obtained.

Funding

None.

Competing interests

None.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijom.2025.06.013.

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