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Starch-Jensen, T.; Bruun, N. H.; Spin-Neto, R.

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Randomized Controlled Trial

Pre-Implant Surgery

Endo-sinus bone gain following sinus membrane elevation without graft compared with sinus floor augmentation and a composite graft: a one-year single-blind randomized controlled trial

T. Starch-Jensen[a], N.H Bruun[b], R. Spin-Neto[c]

[a]Department of Oral and Maxillofacial Surgery, Aalborg University Hospital, and Department of Clinical Medicine, The Faculty of Medicine, Aalborg University, Aalborg, Denmark; [b]Unit of Clinical Biostatistics, Aalborg University Hospital, Aalborg, Denmark; [c]Department of Dentistry and Oral Health, Section for Oral Radiology, Faculty of Health, Aarhus University, Aarhus, Denmark

T. Starch-Jensen, N. H. Bruun, R. Spin-Neto: Endo-sinus bone gain following sinus membrane elevation without graft compared with sinus floor augmentation and a composite graft: a one-year single-blind randomized controlled trial. Int. J. Oral Maxillofac. Surg. 2024; 53: 319–332.

Abstract. The objective of this study was to assess endo-sinus bone gain (ESBG) and bone density (BD) following maxillary sinus membrane elevation without graft (test) compared with maxillary sinus floor augmentation and 1:1 ratio of autogenous bone from the buccal antrostomy and deproteinized porcine bone mineral (control) using two- and three-dimensional radiographic methods. Forty healthy patients were randomly allocated to the test and control groups. Cone beam computed tomography scans were obtained at enrolment (T0), immediately after surgery (T1), at delivery of the prosthetic rehabilitation (T2), and 1 year after functional implant loading (T3). Mean differences were expressed with the 95% confidence interval. Significance was set at ≤ 0.05. ESBG and BD were significantly higher in the control group than test group at T1, T2, and T3 ($P < 0.001$). A significant decrease in ESBG and increase in BD was observed from T1 to T3 with both treatments ($P < 0.001$). There was a non-significant positive correlation of ESBG with implant protrusion length and non-significant negative correlation with residual bone height. In conclusion, test was associated with significantly lower ESBG and BD compared with control. However, the lower ESBG and BD did not appear to negatively affect the implant stability quotient or implant treatment outcome after 1 year of functional implant loading.

Keywords: Alveolar ridge augmentation; Dental implants; Maxilla; Randomized controlled trial; Sinus floor augmentation.

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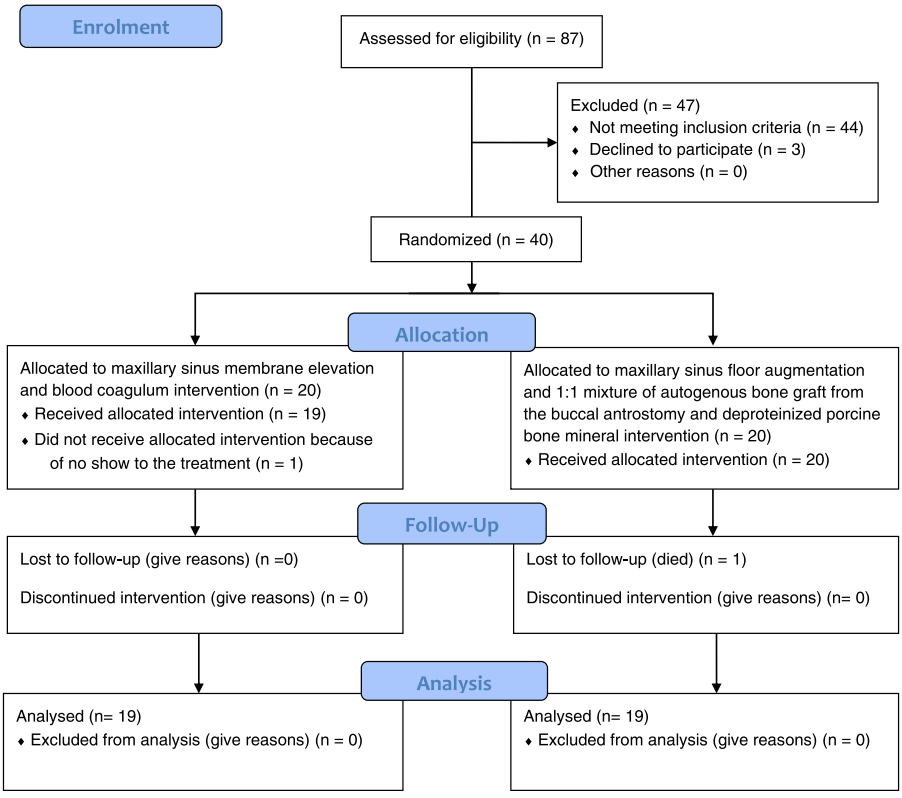

Fig. 1. CONSORT 2010 flow diagram of the study process.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria:
- Age > 20 years
- Missing one posterior maxillary tooth for more than 4 months
- Residual alveolar ridge height at implant site ≥4 mm and ≤7 mm, as measured on cone beam computed tomography
- Width of the alveolar ridge ≥6.5 mm
- Mandibular occluding tooth/teeth
- Able to understand and sign informed consent

Exclusion criteria:
- Contraindications to implant therapy
- Full mouth plaque score > 25%
- Progressive marginal periodontitis
- Acute infection in the area intended for implant placement
- Parafunction, bruxism, or clenching
- Psychiatric problems or unrealistic expectations
- Heavy tobacco use, defined as > 10 cigarettes per day
- Current pregnancy at the time of recruitment
- Physical handicaps that would interfere with the ability to perform adequate oral hygiene
- Inability or unwillingness to regularly attend the scheduled follow-up visits

The application of a graft underneath the Schneiderian membrane in conjunction with maxillary sinus floor augmentation (MSFA) aims to facilitate endo-sinus bone gain (ESBG) and bone-to-implant contact (BIC), and to ensure adequate bone quantity to support implants. Autogenous bone is the most used graft for MSFA due to its osteogenic, osteoinductive, and osteoconductive characteristics[1,2]. However, autogenous bone graft (ABG) is associated with unpredictable resorption[3–5], and long-term studies have reported significant graft reduction during the first year following MSFA, after which the resorption diminishes and the grafted volume stabilizes[6,7]. Volumetric graft stability represents an important parameter for a successful implant treatment outcome[5,8]. The ABG is therefore often combined or replaced with non-resorbable bone substitutes to enhance the volumetric stability of the graft. However, comparable implant treatment outcomes following MSFA irrespective of the graft applied have been reported in systematic reviews[9–11], and the reduction in graft volume seems not to compromise any of the clinical parameters[5]. Moreover, the graft volume necessary to ensure adequate implant support, ESBG, and the best BIC in conjunction with MSFA has not been elucidated.

Maxillary sinus membrane elevation (MSME) without a graft combined with simultaneous implant placement to support the elevated Schneiderian membrane was introduced in 2004[12]. Systematic reviews have demonstrated comparable implant treatment outcomes following MSME without a graft compared with MSFA and a graft, in short-term studies[13,14]. However, randomized controlled trials (RCTs) assessing ESBG, bone density (BD), and volumetric graft stability have revealed conflicting conclusions[15–18], indicating that ESBG may be influenced by other parameters such as the implant protrusion length (IPL), residual bone height (RBH), radiographic assessment method, or length of the observation period[16,19,20].

The clinical implant treatment outcomes and patient-reported outcome measures determined as part of the present RCT have been published

Table 2. Pre- and postoperative medications and instructions.

Preoperative medications:
One hour prior to surgery: • 400 mg ibuprofen (Burana; Teva, Denmark) • 1000 mg paracetamol (Pamol; Takeda Pharma A/S, Denmark) • 2 g amoxicillin (Imadrax; Sandoz, Denmark), or 600 mg clindamycin (Dalacin; Alternova, Denmark) if allergic to penicillin
All patients rinsed with 0.12% chlorhexidine solution for 1 minute immediately before surgery
Postoperative medications:
• 400 mg ibuprofen (Burana; Teva, Denmark), 1 tablet 3 times per day, if required • 500 mg paracetamol (Pamol; Takeda Pharma A/S, Denmark), 2 tablets 4 times per day, if required • 800 mg phenoxymethylpenicillin (Primcillin; Meda, Denmark), 2 tablets 3 times per day for 7 days; in the case of penicillin allergy, 300 mg clindamycin (Dalacin; Alternova, Denmark), 1 tablet 3 times per day for 7 days
Postoperative instructions:
Rinse with 0.12% chlorhexidine solution twice a day until suture removal has taken place after 7–10 days
Avoid any physical activity that will abruptly raise or lower pressure in the sinus cavity and avoid vigorous mouth rinsing, smoking, or touching the gums for at least 10 days following surgery

previously, without the radiographic assessment of ESBG[21,22]. The objective of this part of the RCT was therefore to assess ESBG using two-dimensional (2D) and three-dimensional (3D) radiographic measurements following MSME without a graft compared with MSFA and a 1:1 ratio of ABG and deproteinized porcine bone mineral (DPBM) after 1 year of functional implant loading, including an analysis of the potential parameters influencing the amount of ESBG.

Materials and methods

A detailed description of the study design and methods applied has been published previously[21,22]. Thus, only a summary is presented here.

The study was performed in accordance with the Declaration of Helsinki and International Conference on Harmonization (ICH) for Good Clinical Practice (GCP). The protocol was approved by The North Denmark Region Committee on Health Research Ethics (approval No. N-20180080) and registered at Clinicaltrials.gov (NCT04667260), and RCT standards were followed (Fig. 1) (CONSORT; http://www.consort-statement.org/).
The enrolment of patients was initiated in January 2019. The 1-year follow-up was finalized in December 2022.

Forty patients with a missing posterior maxillary tooth and RBH at the implant site of between 4 mm and 7 mm were included (Table 1). These patients were randomly allocated by concealed method to either MSME without a graft (test group; $n = 20$) or MSFA with 1:1 ratio of ABG and DPBM (control group; $n = 20$).

The surgical procedures and radiographic assessment were conducted by the first author (T.S.J.).

Surgical procedures

The surgical procedures were performed under local anaesthesia. A crestal incision combined with anterior vertical releasing incision was made. A full-thickness mucoperiosteal flap was raised exposing the lateral sinus wall. A bony window to the sinus was made with burrs before elevating the Schneiderian membrane. If a minor membrane perforation arose, it was shielded with a resorbable collagen membrane (Symbios pre-hydrated; Dentsply Sirona Implants, Mölndal, Sweden). If a larger perforation arose, then the patient was excluded from the study. The implant bed preparation was performed step-by-step according to the manufacturer's protocol. A straight 13-mm implant (OsseoSpeed EV, Astra Tech Implant System, diameter 4.2 mm or 4.8 mm; Dentsply Sirona Implants) was placed. The implant stability quotient (ISQ) was measured by resonance frequency analysis (Penguin; Integration Diagnostics Sweden AB, Gothenburg, Sweden). The Schneiderian membrane was maintained in its raised position by the tip of the protruding implant within the sinus, creating a compartment between the elevated membrane and original sinus floor. In the test group, 2 ml of autologous blood was aspirated from the surgical site and injected underneath the membrane around the exposed implant surface. In the control group, ABG was harvested from the buccal antrostomy (Curved SafeScraper; Fischer Medical ApS, Glostrup, Denmark): a total of 1.0 cm^3 ABG was collected, as estimated using a measuring cup (1.0 cm^3), and mixed with 1.0 ml DPBM (Symbios Xenograft Granules, grain size 1.0–2.0 mm; Dentsply Sirona Implants). The graft was soaked in autologous blood from the surgical field before the entire graft was applied underneath the elevated membrane. In both groups, a cover screw was mounted. The window created to the sinus was covered with a resorbable collagen membrane (Symbios pre-hydrated, 20 mm × 30 mm; Dentsply Sirona Implants). The periosteum and mucosa were then sutured (Vicryl 4–0, Ethicon FS-2; Ethicon, St-Stevens-Woluwe, Belgium). No provisional restoration was inserted. The pre- and postoperative medications and instructions are listed in Table 2.

The implant was mounted with a prefabricated healing abutment after 6 months. The ISQ was measured before the healing abutment was mounted.

Prosthetic rehabilitation was finalized by the patient's dentist, 3 weeks after healing abutment connection, and included an Atlantis abutment (Dentsply Sirona Implants) and a cemented or screw-retained single-crown restoration.

Radiographic assessment

Three-dimensional measurement

The 3D assessment of ESBG was performed using cone beam computed tomography (CBCT) volumes (i-CAT; Imaging Sciences International, Hatfield, PA, USA) obtained at enrolment (T0), immediately after MSME/MSFA (T1), at completion of the prosthetic rehabilitation (T2), and at 1 year of functional implant loading (T3). CBCT volumes were acquired using fixed exposure parameters of 120 kV, 18.5 mA, 160 × 60 mm field of view, 0.20 mm voxel size, and 8.9 seconds images. Volumes were generated as DICOM-based datasets using OnDemand3D Application 10

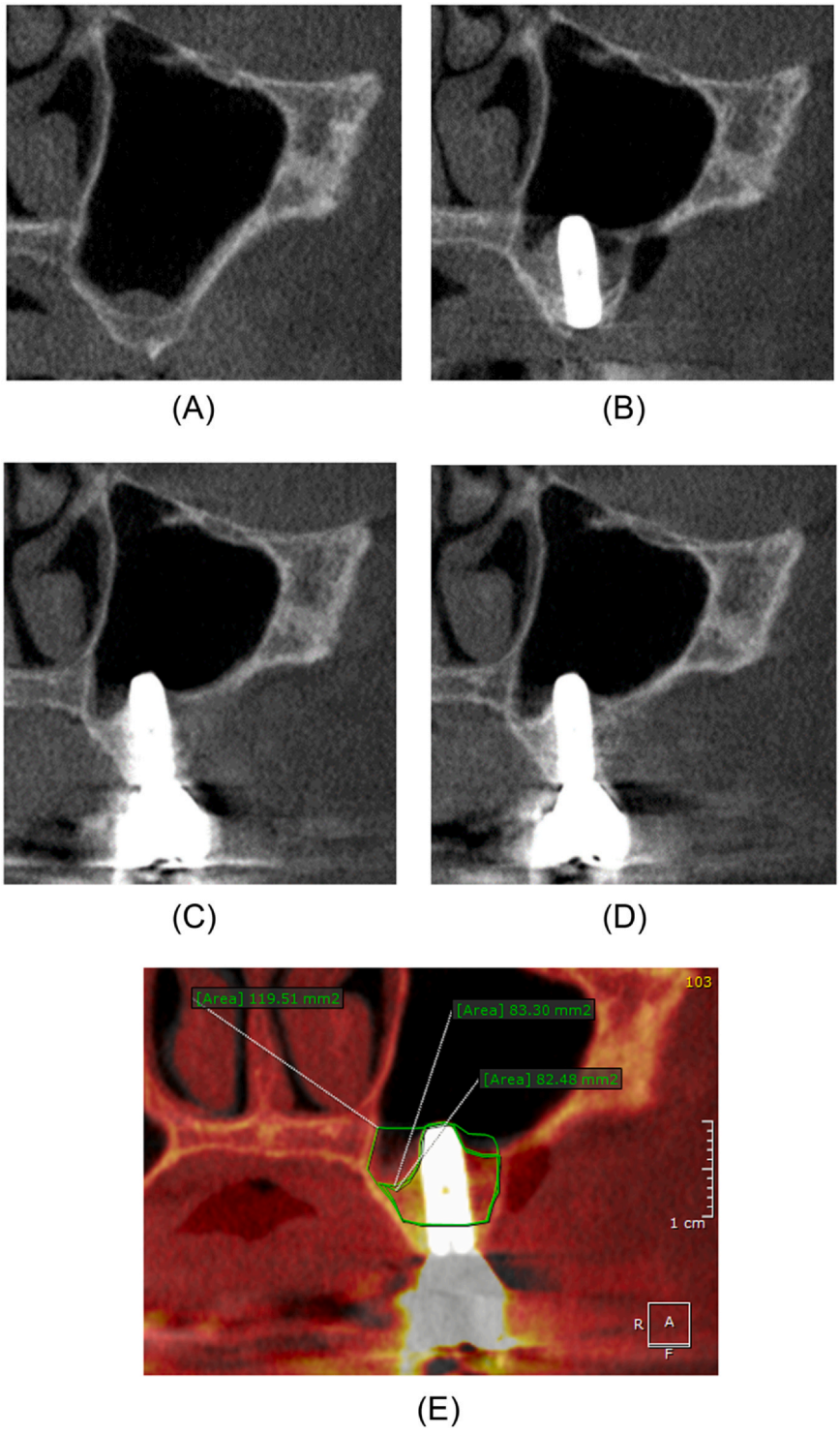

Fig. 2. Three-dimensional radiographic assessment following maxillary sinus membrane elevation without a graft. Coronal CBCT scan obtained (A) at enrolment, (B) immediately after maxillary sinus membrane elevation, (C) at completion of the prosthetic rehabilitation, and (D) at 1 year of functional implant loading. (E) The CBCT scans obtained at the different time-points were superimposed. The original border of the maxillary sinus and circumference of the augmented area were manually traced (mm^2) before the volume of the graft was calculated, at the different time periods.

computer software (Cybermed, Seoul, South Korea). The ESBG at T1 was used as reference and matched with ESBG at T2 and T3. Registration was done pair-wise (i.e., T1 and T2, T1 and T3), based on the automated detection of hundreds of virtual volume landmarks, and manually adjusted by the assessor based on anatomical landmarks. The axial, coronal, and sagittal planes were adjusted based on the centre of the longitudinal implant axis, as seen in T1, and to fit to the augmented area, as seen in the 'matched' image. In the sequence, cross-sections (i.e., coronal sections) with a thickness of 1 mm and representative of the augmented area, were generated from T1, T2, and T3. This registration process ensured that the images represented the same region, based on the same orientation and reconstruction planes. The number of cross-sections varied among sites depending on individual size, but the same number of sections was generated and evaluated for each area at T1, T2, and T3. The images were stored in BMP (bitmap) format. Using the same software, each selected cross-sectional image of the augmented area at T1, T2, and T3 was assessed by manually tracing the augmented area (mm^2) (Figs. 2 and 3). The grafted volume at the implant sites, in cubic millimetres (mm^3), was calculated by adding the measured areas of each selected cross-section image, for each period of evaluation. Volumetric changes at the augmented sites (mm^3) were calculated by subtraction of the measured volumes at T2 and T3 from the volume at T1.

The 3D ESBG at each time point (T1, T2, and T3) was correlated with IPL at T1 and with RBH at T0.

Two-dimensional measurement

2D coronal CBCT sections were used for linear measurements of RBH, IPL, and ESBG (Figs. 4 and 5).

RBH at the implant site was measured at T0. A perpendicular line from the centre of the alveolar crest to the cortical border line of the sinus was used to define RBH. Moreover, RBH was measured separately for the facial and oral implant surfaces at T1.

The IPL was measured separately for the facial and oral implant surfaces

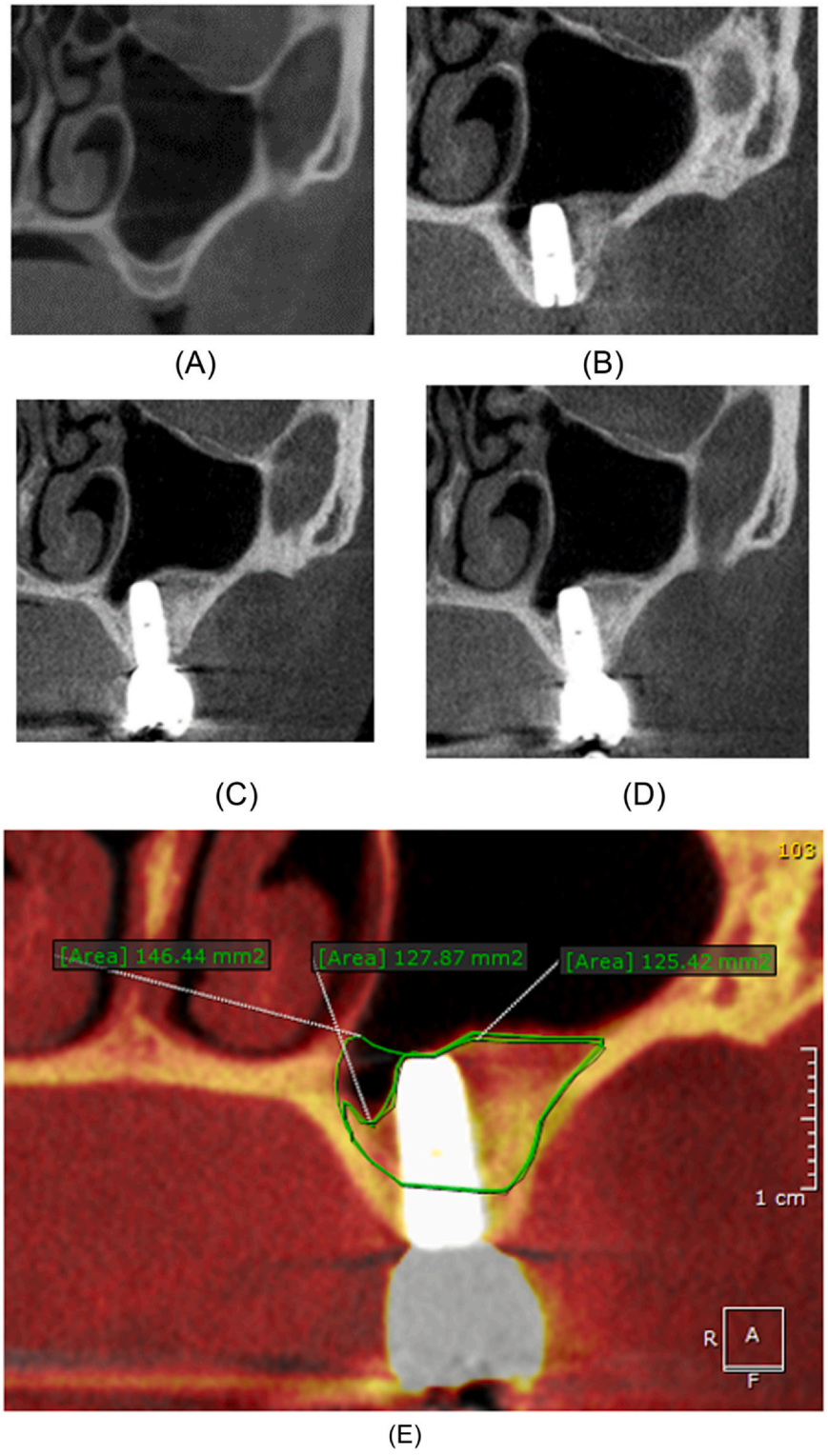

Fig. 3. Three-dimensional radiographic assessment following maxillary sinus floor augmentation with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral. Coronal CBCT scan obtained (A) at enrolment, (B) immediately after maxillary sinus floor augmentation, (C) at completion of the prosthetic rehabilitation, and (D) at 1 year of functional implant loading. (E) The CBCT scans obtained at the different time-points were superimposed. The original border of the maxillary sinus and circumference of the augmented area were manually traced (mm^2) before the volume of the graft was calculated, at the different time periods.

within the sinus at T1, based on the known implant length (13 mm). 2D linear measurements at the longitudinal facial and oral axis of the implants from the border of the original sinus floor to the apex of the implant were performed and defined as IPL within the sinus at T1.

ESBG at the facial and oral implant surfaces was measured at T1, T2, and T3. 2D linear measurements at the longitudinal facial and oral surfaces of the implants from the border of the original sinus floor to the highest point of the endo-sinus bone were performed and defined as ESBG at T1, T2, and T3.

The association between IPL at T1 and ESBG at T1, T2, and T3 was assessed using 2D coronal CBCT sections. The amount of bone covering the facial or oral implant surface within the sinus was estimated using linear measurements from the original border of the sinus to the most apical part of bone covering the implant surface at T1, T2, and T3 and correlated with IPL at T1. The association between RBH at T0 and ESBG at T1, T2, and T3 was also assessed using 2D coronal CBCT sections.

Bone density

BD within the graft was estimated at T1, T2, and T3 using Hounsfield units (HU) on 2D coronal CBCT sections (Figs. 6 and 7). BD at T1 was used as reference and matched with BD at T2 and T3. BD was measured on 10 sections, five on each side of the longitudinal implant axis. A standardized 10×10 square was created and randomly positioned within the graft using OnDemand3D software. HU values within the square were automatically displayed.

Statistical analyses

The data management and analysis was conducted using Stata Statistical Software release 17 (StataCorp LLC, College Station, TX, USA). The characteristics of the patients at enrolment were compared by *t*-test for continuous data and Pearson χ^2 test for categorical data. The mean, standard deviation, and 95% confidence interval of the mean were used to describe the 2D and 3D radiographic assessments of ESBG, using ordinary least squares (OLS)

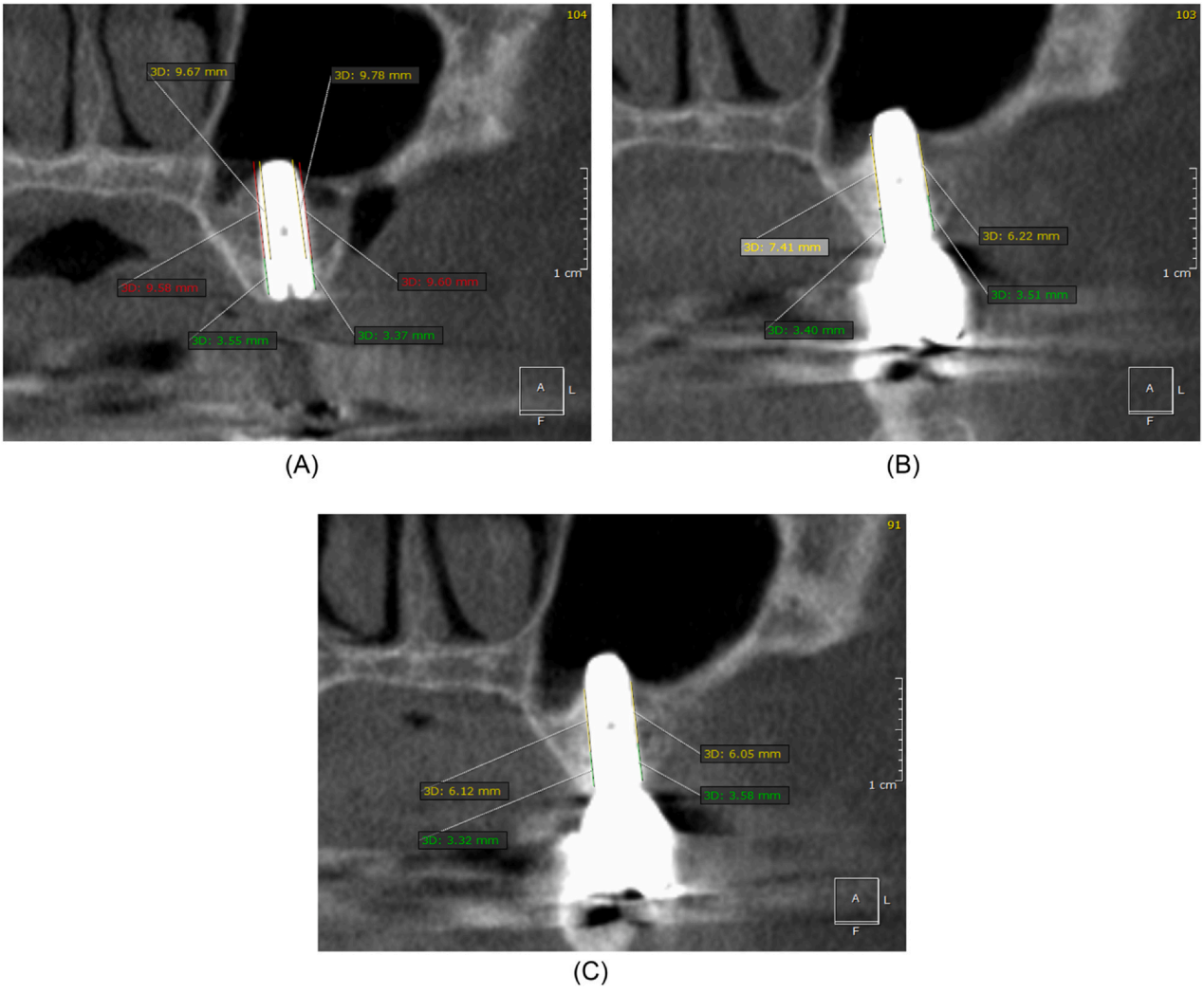

Fig. 4. Two-dimensional radiographic assessment following maxillary sinus membrane elevation without a graft. Two-dimensional linear measurements on the facial and oral implant surfaces of endo-sinus bone gain (yellow lines), residual bone height (green lines), and implant protruding length (red lines) using coronal CBCT scans: (A) immediately after maxillary sinus membrane elevation; (B) at completion of prosthetic rehabilitation; (C) at 1 year of functional implant loading.

regression with robust variance estimation and clusters by participant ID. The correlations between ESBG and IPL or RBH were estimated by Spearman's rank correlation coefficient. The level of significance was set at ≤ 0.05.

Results

Forty patients were enrolled and allocated to the test or control group. Patient demographics are outlined in Supplementary Material Table S1. There was no significant difference in sex distribution ($P = 0.716$), age ($P = 0.198$), smoking habit, RBH ($P = 0.076$), width of the alveolar process at the implant site ($P = 0.401$), implant location, or implant diameter at T0. One patient allocated to the test group never showed up for treatment and did not respond to several phone calls, emails, and text messages. Hence, this patient was excluded. One patient allocated to the control group died before attending the 1 year examination. Thus, 19 patients attended the 1 year examination in each group. Survival of the suprastructures and the implants at T3 was 100% with both treatments. In the test group, ISQ was 64.5 ± 14.2 at T1 and 79.3 ± 11.0 at healing abutment connection, while in the control group, ISQ was 66.3 ± 8.8 and 78.8 ± 13.4, respectively. There was no significant difference in ISQ between the test and control groups at T1 ($P = 0.638$) or at healing abutment connection ($P = 0.366$). ISQ increased significantly from T1 to healing abutment connection in both the test ($P < 0.001$) and control group ($P < 0.001$). The implants were restored with a cemented or screw-retained single-crown restoration, all of which were well-functioning at T2 and T3.

Radiographic analyses

Three-dimensional assessment

The results of the 3D volumetric assessment of ESBG at T1, T2, and T3 are summarized in Table 3. In the test group, ESBG was 76.1 ± 17.0 mm^3 at T1, 45.8 ± 9.4 mm^3 at T2, and 38.8 ± 8.4 mm^3 at T3. In the control

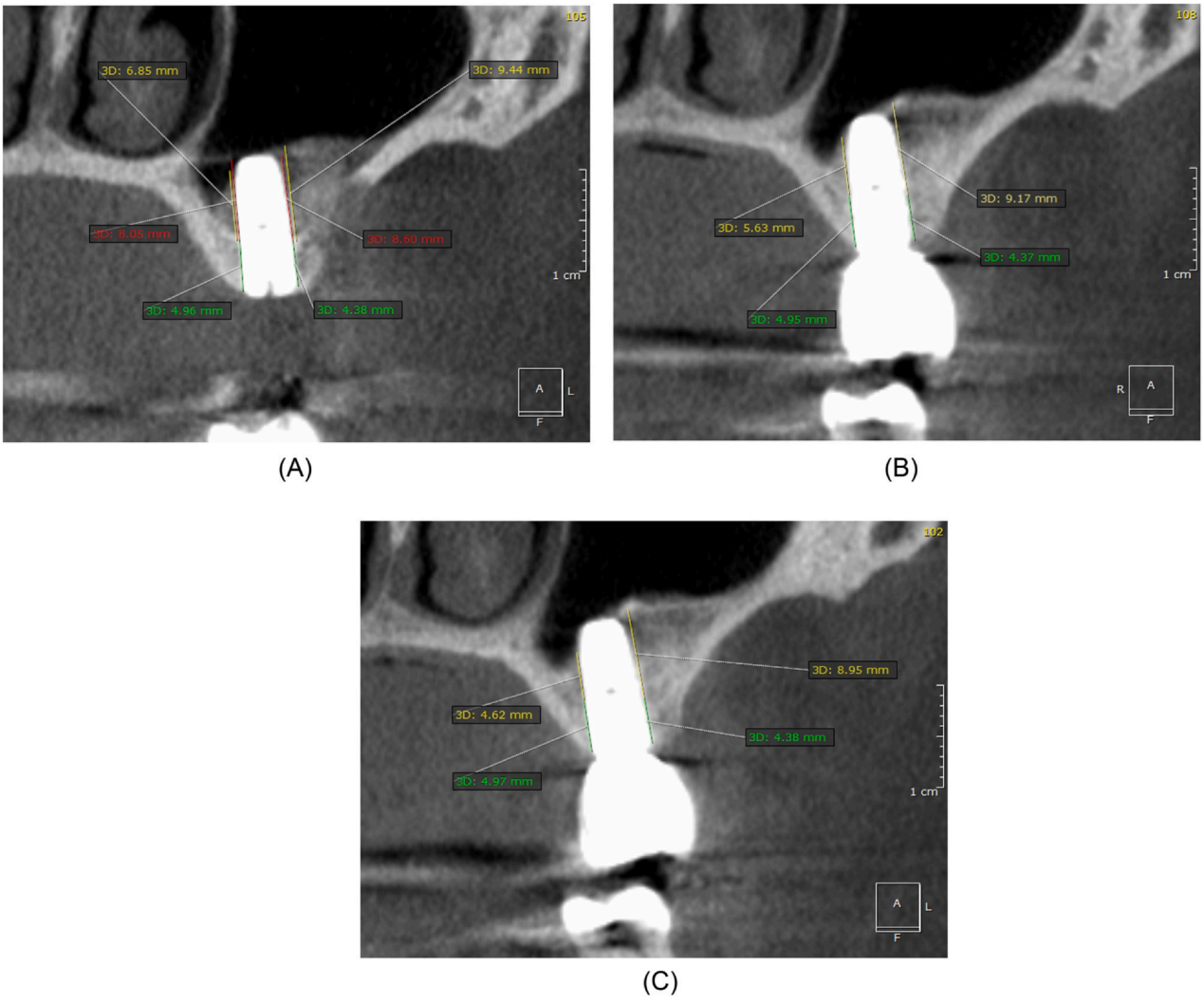

Fig. 5. Two-dimensional radiographic assessment following maxillary sinus floor augmentation with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral. Two-dimensional linear measurements on the facial and oral implant surfaces of endo-sinus bone gain (yellow lines), residual bone height (green lines), and implant protruding length (red lines) using coronal CBCT scans: (A) immediately after maxillary sinus floor augmentation; (B) at completion of prosthetic rehabilitation; (C) at 1 year of functional implant loading.

group, ESBG was 117.8 ± 23.5 mm^3, 91.1 ± 19.3 mm^3, and 84.6 ± 15.7 mm^3 at these respective time-points. ESBG was significantly greater in the control group when compared with the test group at T1, T2, and T3 (all $P < 0.001$).

ESBG decreased significantly from T1 to T2, T1 to T3, and T2 to T3 in both the test ($P < 0.001$) and control group ($P < 0.001$) (Fig. 8).

Two-dimensional assessment

The results of the 2D assessment of ESBG at T1, T2, and T3 are summarized in Table 4. In the test group, ESBG at the respective facial and oral implant surfaces was 9.1 ± 1.5 mm and 8.5 ± 1.2 mm at T1, 6.8 ± 1.2 mm and 4.6 ± 1.4 mm at T2, and 6.2 ± 1.1 mm and 4.1 ± 1.0 mm at T3. In the control group, ESBG was 11.2 ± 1.8 mm and 10.1 ± 2.2 mm, 10.0 ± 2.0 mm and 7.9 ± 1.8 mm, and 9.4 ± 1.8 mm and 7.2 ± 1.9 mm at the respective time-points. ESBG at the facial and oral implant surfaces was significantly higher in the control group when compared with the test group at T1 ($P < 0.001$, $P = 0.009$), T2 ($P < 0.001$, $P = 0.002$), and T3 ($P < 0.001$, $P = 0.004$).

In the test group, ESBG at the facial and oral implant surfaces decreased significantly from T1 to T2 (both $P < 0.001$), T1 to T3 (both $P < 0.001$), and T2 to T3 ($P < 0.001$, $P = 0.002$). Correspondingly, a significant decrease was observed in the control group from T1 to T2 ($P = 0.004$, $P < 0.001$), T1 to T3 (both $P < 0.001$), and T2 to T3 ($P = 0.014$, $P = 0.001$) (Fig. 9).

Implant protrusion length

The IPL within the sinus at T1 is reported in Supplementary Material Table S2 and Table 5. There was no significant difference in IPL between the test and control groups as evaluated by 3D measurements ($P = 0.083$) or 2D measurements on the facial ($P = 0.203$) and oral implant surfaces ($P = 0.052$).

A non-significant positive correlation between IPL and ESBG at all time-

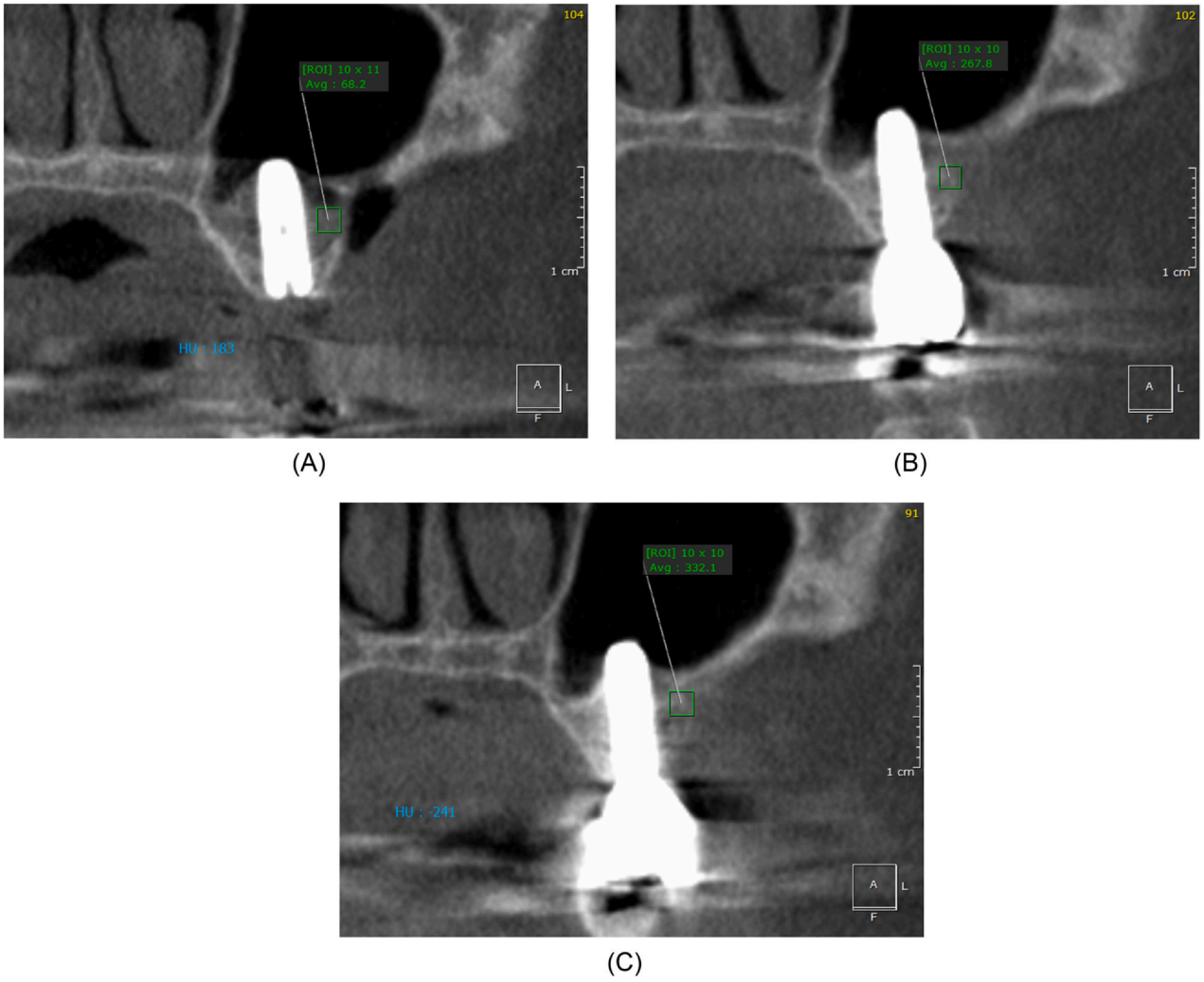

Fig. 6. Bone density measurements using Hounsfield units following maxillary sinus membrane elevation without a graft. Coronal CBCT scans. A standardized 10 × 10 square was created and randomly positioned within the graft: (A) immediately after maxillary sinus membrane elevation; (B) at completion of prosthetic rehabilitation; (C) at 1 year of functional implant loading.

points was revealed for both treatments, as evaluated by 2D and 3D radiographic measurements, although a significant correlation was observed between IPL at the oral implant surface and ESBG at T2 in the test group ($P = 0.045$) (Supplementary Material Table S2 and Table 5).

Residual bone height

The RBH is reported in Supplementary Material Table S3 and Table 6. There was no significant difference in RBH between the test and control groups as evaluated by 3D measurements ($P = 0.058$). However, 2D measurements revealed a significant difference at the oral implant surface ($P = 0.042$), while no significant difference was observed at the facial surface ($P = 0.104$).

A non-significant negative correlation between RBH and ESBG at all timepoints was revealed for both treatments, as evaluated by 2D and 3D radiographic measurements (Supplementary Material Table S3 and Table 6).

Bone density

The HU values are reported in Table 7. In the test group, HU values were 203.5 ± 77.6 at T1, 465.2 ± 139.4 at T2, and 530.8 ± 159.6 at T3. In the control group, the respective HU values were 481.3 ± 159.2, 835.5 ± 172.2, and 847.0 ± 154.5. HU values were significantly higher in the control group when compared with the test group at T1, T2, and T3 (all $P < 0.001$).

In the test group, HU values increased significantly from T1 to T2 ($P < 0.001$), T1 to T3 ($P < 0.001$), and T2 to T3 ($P = 0.022$). Correspondingly, a significant increase was also observed in the control group from T1 to T2 ($P < 0.001$) and from T1 to T3 ($P < 0.001$); however, a non-significant increase was observed from T2 to T3 ($P = 0.701$) (Fig. 10).

Discussion

This RCT demonstrated that MSFA with a 1:1 ratio of ABG and DPBM facilitated significantly higher ESBG and BD compared with MSME without a graft. A significant, gradual

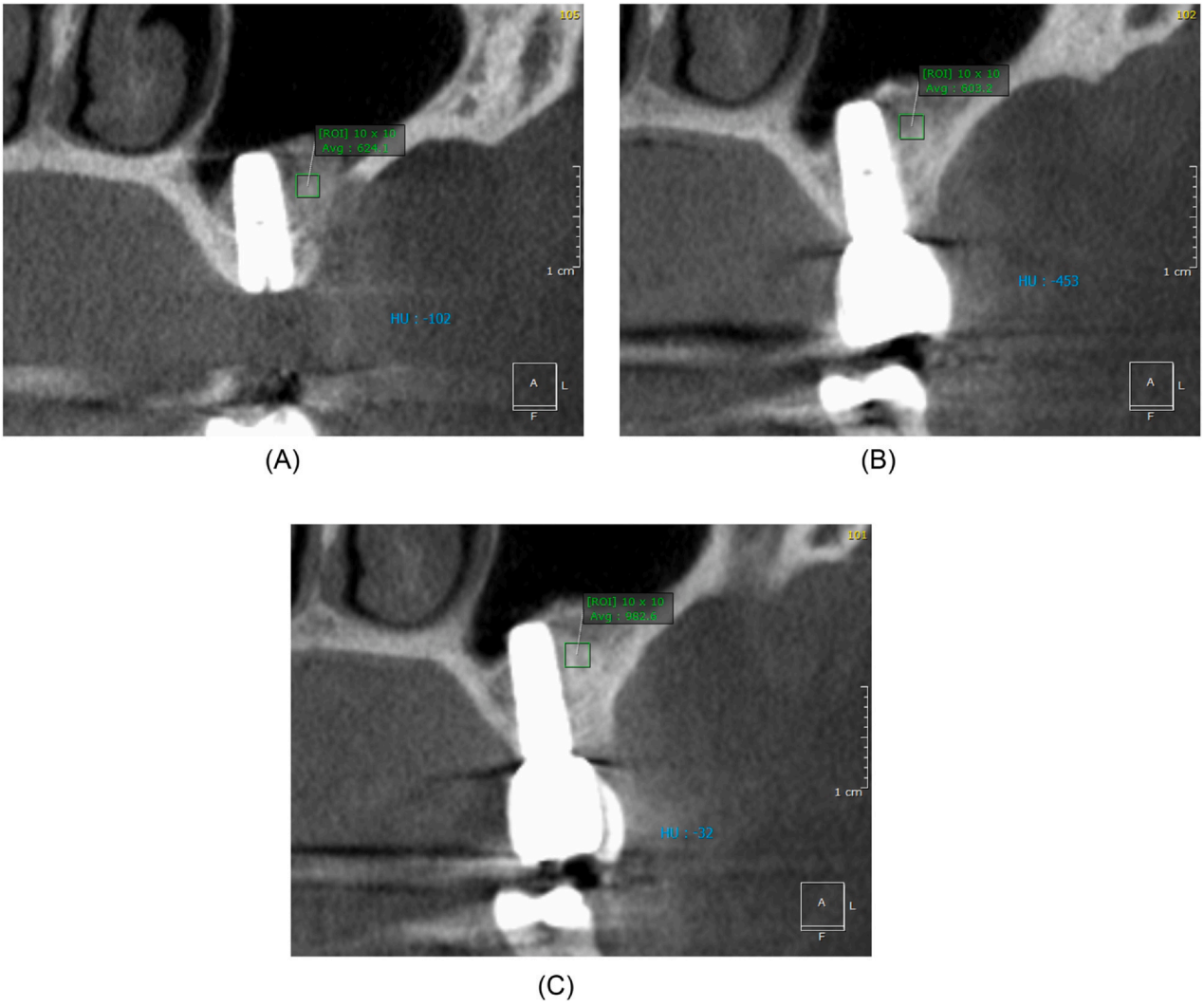

Fig. 7. Bone density measurements using Hounsfield units following maxillary sinus floor augmentation with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral. Coronal CBCT scans. A standardized 10 × 10 square was created and randomly positioned within the graft: (A) immediately after maxillary sinus floor augmentation; (B) at completion of prosthetic rehabilitation; (C) at 1 year of functional implant loading.

Table 3. Three-dimensional volumetric assessment of endo-sinus bone gain (mm^3).

	MSFA with 1:1 ratio ABG:DPBM (Control)		MSME without graft (Test)	
ESBG Mean ± SD (95% CI)				***P*-value[a]**
T1	117.8 ± 23.5 (106.7–128.8)		76.1 ± 17.0 (68.1–84.1)	< 0.001*
T2	91.1 ± 19.3 (82.1–100.2)		45.8 ± 9.4 (41.4–50.2)	< 0.001*
T3	84.6 ± 15.7 (77.2–91.9)		38.8 ± 8.4 (34.9–42.8)	< 0.001*
Change in ESBGMean (95% CI)		***P*-value[b]**		***P*-value[b]**
T1–T2	26.6 (19.6–33.7)	< 0.001*	30.3 (24.9–35.7)	< 0.001*
T2–T3	6.5 (4.0–9.1)	< 0.001*	7.0 (4.5–9.4)	< 0.001*
T1–T3	33.2 (25.5–40.9)	< 0.001*	37.2 (30.6–43.9)	< 0.001*

ABG, autogenous bone graft; CI, confidence interval; DPBM, deproteinized porcine bone mineral; ESBG, endo-sinus bone gain; MSFA, maxillary sinus floor augmentation; MSME, maxillary sinus membrane elevation; SD, standard deviation; T1, immediately after surgery; T2, delivery of prosthetic rehabilitation; T3, 1 year after functional implant loading.
[a]Difference in ESBG between the MSFA and MSME groups; *statistically significant between-group difference.
[b]Significance of the change in ESBG between time-points in the MSFA and MSME groups; *statistically significant difference.

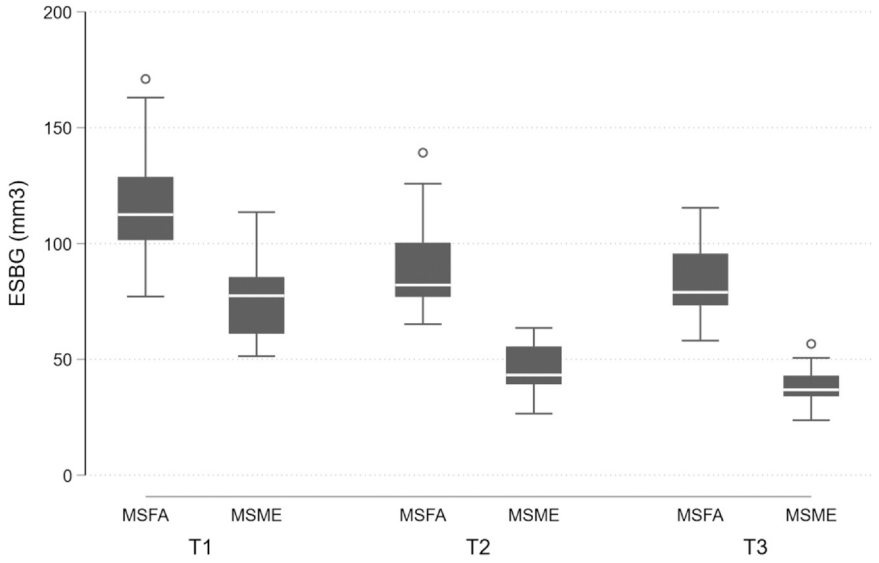

Fig. 8. Three-dimensional volumetric assessment of endo-sinus bone gain following maxillary sinus membrane elevation (MSME) without a graft or maxillary sinus floor augmentation (MSFA) with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral, immediately after surgery (T1), at completion of the prosthetic rehabilitation (T2), and at 1 year of functional implant loading (T3).

decrease in ESBG combined with an increase in BD was observed over time with both treatments. ESBG was non-significantly positively correlated with IPL and negatively correlated with RBH. MSME without a graft was associated with significantly lower ESBG and BD compared with MSFA and a 1:1 ratio of ABG and DPBM at all time-points. However, the lower ESBG and BD did not appear to negatively affect ISQ or the implant treatment outcome.

Limitations of this study include the small patient sample, inhomogeneous distribution of sexes with a higher ratio of female patients in both groups, and the single-blind study design. The term ESBG is misleading, since no histomorphometric assessment was conducted. Conclusions drawn from the results of this study should therefore be interpreted with caution. However, the study included the largest patient sample and longest observation period to date, as previous RCTs only included 6 months of follow-up[15–18].

Sufficient bone quantity, quality, and density are important predictors to obtain adequate primary stability and successful osseointegration of implants. However, the minimum amount of bone and BIC needed to retain implants are presently unknown. The ISQ indicates the level of stability and osseointegration of implants. In the present study, ISQ was comparable in the two groups and increased significantly with both treatments, indicating that placement of graft underneath the membrane seems not to improve ISQ compared with no graft. However, these results conflict with those of previous RCTs, which have revealed significantly higher ISQ following MSFA with a graft compared with MSME without a graft[16,17], while a non-significant difference has also been reported[18].

Volumetric graft stability is essential for a successful long-term implant treatment outcome[5,8]. The application of a graft is therefore intended to stabilize the space created and increase the

Table 4. Two-dimensional assessment of endo-sinus bone gain (mm).

	MSFA with 1:1 ratio ABG:DPBM (Control)				MSME without graft (Test)			
ESBG Mean ± SD (95% CI)	**FIS**	**OIS**			**FIS**	**OIS**	***P*-value[a]**	
							FIS	**OIS**
T1	11.2 ± 1.8 (10.4–12.1)	10.1 ± 2.2 (9.1–11.1)			9.1 ± 1.5 (8.4–9.8)	8.5 ± 1.2 (7.9–9.1)	< 0.001*	0.009*
T2	10.0 ± 2.0 (9.0–10.9)	7.9 ± 1.8 (7.0–8.7)			6.8 ± 1.2 (6.3–7.4)	4.6 ± 1.4 (4.0–5.3)	< 0.001*	0.002*
T3	9.4 ± 1.8 (8.5–10.2)	7.2 ± 1.9 (6.3–8.1)			6.2 ± 1.1 (5.6–6.7)	4.1 ± 1.0 (3.6–4.6)	< 0.001*	0.004*
Change in ESBGMean (95% CI)	**FIS**	**OIS**	***P*-value[b]**		**FIS**	**OIS**	***P*-value[b]**	
			FIS	**OIS**			**FIS**	**OIS**
T1–T2	1.3 (0.4–2.1)	2.2 (1.6–2.9)	0.004*	< 0.001*	2.3 (1.7–2.9)	2.3 (1.8–2.8)	< 0.001*	< 0.001*
T2–T3	0.6 (0.1–1.0)	0.7 (0.3–1.1)	0.014*	0.001*	0.7 (0.3–1.0)	0.6 (0.3–1.0)	< 0.001*	0.002*
T1–T3	1.9 (1.0–2.7)	2.9 (2.2–3.7)	< 0.001*	< 0.001*	2.9 (2.3–3.5)	2.9 (2.4–3.5)	< 0.001*	< 0.001*

ABG, autogenous bone graft; CI, confidence interval; DPBM, deproteinized porcine bone mineral; FIS, facial implant surface; MSFA, maxillary sinus floor augmentation; MSME, maxillary sinus membrane elevation; OIS, oral implant surface; SD, standard deviation; T1, immediately after surgery; T2, delivery of prosthetic rehabilitation; T3, 1 year after functional implant loading.
[a]Difference in ESBG between the MSFA and MSME groups; *statistically significant between-group difference.
[b]Significance of the change in ESBG between time-points in the MSFA and MSME groups; *statistically significant difference.

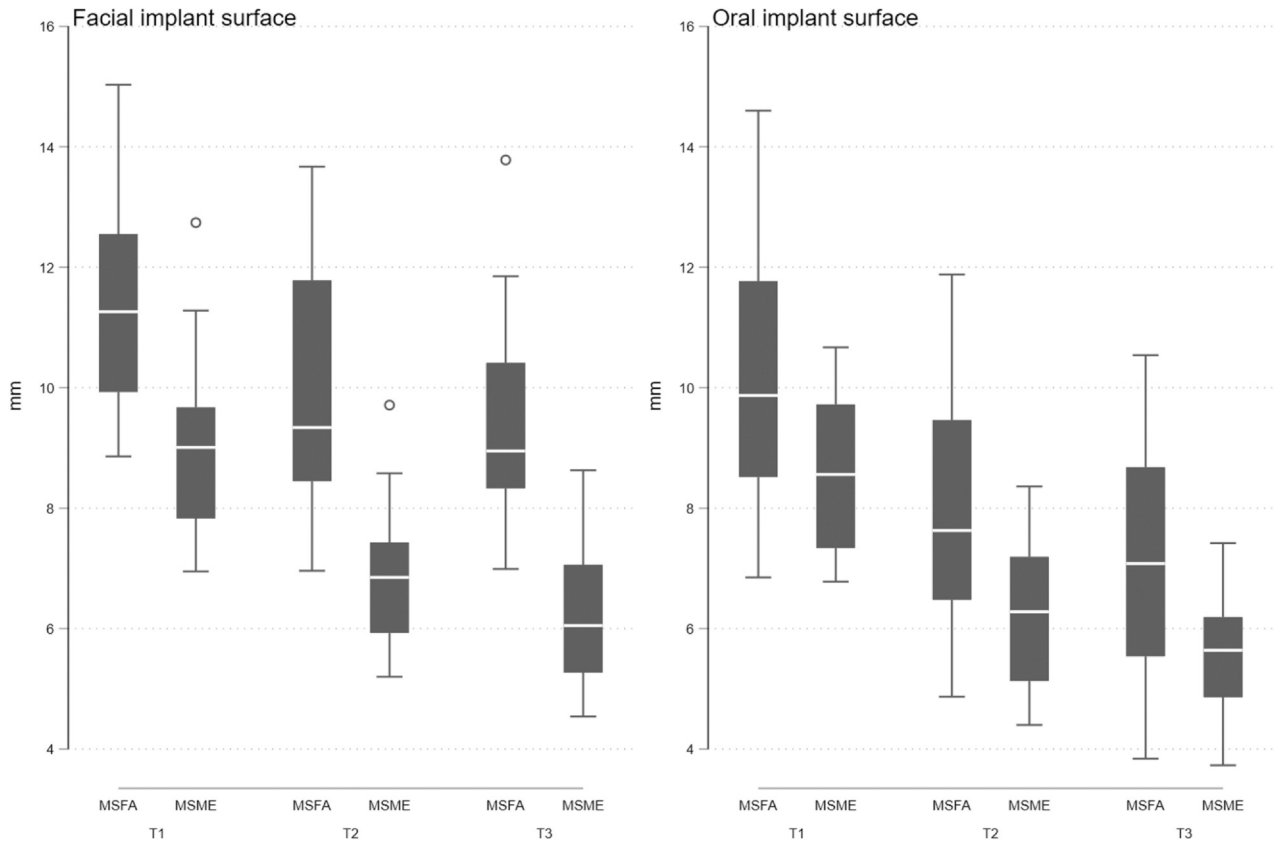

Fig. 9. Two-dimensional linear assessment of endo-sinus bone gain along the facial and oral implant surfaces following maxillary sinus membrane elevation (MSME) without a graft or maxillary sinus floor augmentation (MSFA) with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral, immediately after surgery (T1), at completion of the prosthetic rehabilitation (T2), and at 1 year of functional implant loading (T3).

Table 5. Correlation between implant protrusion length and two-dimensional endo-sinus bone gain.

	MSFA with 1:1 ratio ABG:DPBM (Control)				MSME without graft (Test)			
	FIS	**OIS**			**FIS**	**OIS**	***P*-value[a]**	
							FIS	**OIS**
IPL (mm) Mean ± SD (95% CI)	8.0 ± 1.3 (7.4–8.6)	8.5 ± 1.1 (8.0–9.0)			7.5 ± 1.3 (6.9–8.1)	7.7 ± 1.4 (7.0–8.3)	0.203	0.052
Correlation	**Spearman's rho**		***P*-value[b]**		**Spearman's rho**		***P*-value[b]**	
	FIS	**OIS**	**FIS**	**OIS**	**FIS**	**OIS**	**FIS**	**OIS**
T1	0.31	0.06	0.197	0.803	0.05	0.42	0.828	0.073
T2	0.13	0.28	0.601	0.239	0.14	0.46	0.561	0.045*
T3	0.12	0.15	0.634	0.535	0.04	0.32	0.856	0.177

ABG, autogenous bone graft; CI, confidence interval; DPBM, deproteinized porcine bone mineral; ESBG, endo-sinus bone gain; FIS, facial implant surface; IPL, implant protrusion length; MSFA, maxillary sinus floor augmentation; MSME, maxillary sinus membrane elevation; OIS, oral implant surface; SD, standard deviation; T1, immediately after surgery; T2, delivery of prosthetic rehabilitation; T3, 1 year after functional implant loading.
[a]Difference in IPL between the MSFA and MSME groups.
[b]Significance of the correlation between IPL and ESBG at each time-point in the MSFA and MSME groups; *statistically significant.

Table 6. Correlation between residual bone height and two-dimensional endo-sinus bone gain.

	MSFA with 1:1 ratio ABG:DPBM (Control)				MSME without graft (Test)			
	FIS	**OIS**			**FIS**	**OIS**	***P*-value[a]**	
							FIS	**OIS**
RBH (mm) Mean ± SD (95% CI)	4.8 ± 1.2 (4.3–5.4)	4.4 ± 1.0 (3.9–4.8)			5.5 ± 1.3 (4.9–6.0)	5.2 ± 1.3 (4.6–5.8)	0.140	0.042*
Correlation	**Spearman's rho**		***P*-value[b]**		**Spearman's rho**		***P*-value[b]**	
	FIS	**OIS**	**FIS**	**OIS**	**FIS**	**OIS**	**FIS**	**OIS**
T1	−0.19	−0.06	0.438	0.801	−0.09	−0.45	0.702	0.056
T2	−0.05	−0.29	0.852	0.219	−0.14	−0.41	0.566	0.084
T3	−0.09	−0.19	0.708	0.434	−0.04	−0.33	0.886	0.169

ABG, autogenous bone graft; CI, confidence interval; DPBM, deproteinized porcine bone mineral; ESBG, endo-sinus bone gain; FIS, facial implant surface; MSFA, maxillary sinus floor augmentation; MSME, maxillary sinus membrane elevation; OIS, oral implant surface; RBH, residual bone height; SD, standard deviation; T1, immediately after surgery; T2, delivery of prosthetic rehabilitation; T3, 1 year after functional implant loading.
[a]Difference in RBH between the MSFA and MSME groups; *statistically significant between-group difference
[b]Significance of the correlation between RBH and ESBG at each time-point in the MSFA and MSME groups.

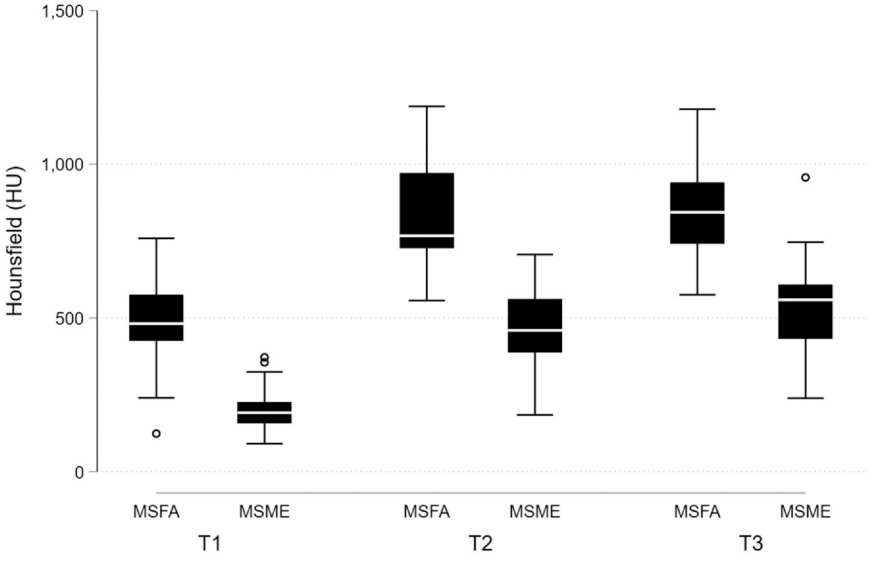

Fig. 10. Bone density measurements following maxillary sinus membrane elevation (MSME) without a graft or maxillary sinus floor augmentation (MSFA) with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral, immediately after surgery (T1), at completion of the prosthetic rehabilitation (T2), and at 1 year of functional implant loading (T3).

bone volume supporting the implant, to improve bone regeneration and BIC[17]. In the present study, ESBG decreased significantly over the observation period with both treatments. However, the graft volume changes were most pronounced in the initial phase of healing and appeared to stabilize over time. Further long-term studies assessing graft volume changes following MSME without a graft are therefore needed.

CBCT and HU are often used for the assessment of BD and bone quality at the implant site[23,24]. A systematic review has reported a positive correlation between BD and primary implant stability[25]. Previous RCTs have reported opposing results, with higher[15], comparable[16], or lower[17,18] BD following MSME without a graft compared with MSFA and a graft. In the present study, BD was significantly lower following MSME without a graft compared with MSFA and a 1:1 ratio of ABG and DPBM at all time-points. However, the BD is affected by the density of the bone substitute used, which is often radiographically denser than pristine bone, and is not completely replaced by 'native' bone within the current period of evaluation[26]. Moreover, increased BD alone does not have a direct clinical implication, either positive or negative, as this value is not necessarily associated with the amount of 'de novo' bone formation[27].

Previous studies have indicated that IPL and RBH influence ESBG following MSFA[16,28]. In the present study, ESBG showed a non-significant positive correlation with IPL and a non-significant negative correlation with RBH, which is in accordance with previous studies[16,25].

Within the limitations of this study, it can be concluded that endo-sinus bone gain and bone density were significantly higher following maxillary sinus floor augmentation with a 1:1 ratio of autogenous bone graft and deproteinized porcine bone mineral compared with maxillary sinus membrane elevation without a graft. However, the lower endo-sinus bone gain and bone density in conjunction with maxillary sinus membrane elevation without a graft appears not to

Table 7. Bone density—Hounsfield units (HU).

	MSFA with 1:1 ratio ABG:DPBM (Control)		MSME without graft (Test)	
HU Mean ± SD (95% CI)				***P*-value[a]**
T1	481.3 ± 159.2 (406.6–556.0)		203.5 ± 77.6 (167.1–239.8)	< 0.001*
T2	835.5 ± 172.2 (754.7–916.2)		465.2 ± 139.4 (399.8–530.5)	< 0.001*
T3	847.0 ± 154.5 (774.5–919.4)		530.8 ± 159.6 (455.9–605.6)	< 0.001*
Change in HUMean (95% CI)		***P*-value[b]**		***P*-value[b]**
T1–T2	354.2 (257.4–451.0)	< 0.001*	261.7 (180.9–342.5)	< 0.001*
T2–T3	11.5 (-48.6–71.6)	0.701	65.6 (10.0–121.2)	0.022*
T1–T3	365.7 (262.9–468.5)	< 0.001*	327.3 (248.2–406.4)	< 0.001*

ABG, autogenous bone graft; CI, confidence interval; DPBM, deproteinized porcine bone mineral; MSFA, maxillary sinus floor augmentation; MSME, maxillary sinus membrane elevation; SD, standard deviation; T1, immediately after surgery; T2, delivery of prosthetic rehabilitation; T3, 1 year after functional implant loading.
[a]Difference in HU between the MSFA and MSME groups; *statistically significant between-group difference.
[b]Significance of the change in HU between time-points in the MSFA and MSME groups; *statistically significant difference.

negatively affect the implant stability quotient or implant treatment outcome.

Trial registration

Registered at Clinicaltrials.gov (NCT04667260).

Ethical approval

The study protocol was approved by The North Denmark Region Committee on Health Research Ethics (approval No. N-20180080). Patients were recruited by public invitation through Facebook or when admitted to the Department of Oral and Maxillofacial surgery, Aalborg University Hospital, Denmark for implant placement in the posterior part of the maxilla.

Patient consent

Included patients received verbal and written information about the study and signed informed consent prior to enrolment.

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Competing interests

The authors declare no financial interest or conflict of interest, either directly or indirectly, in the products or information listed. However, Thomas Starch-Jensen gives lectures for Dentsply Sirona.

Data availability

The study protocol and all data are available from the corresponding author on reasonable request.

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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.2023.10.007.

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Correspondence to: Department of Oral and Maxillofacial Surgery
Aalborg University Hospital
18-22 Hobrovej
DK-9000 Aalborg
Denmark.
E-mail: thomas.jensen@rn.dk