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Randomised Controlled Trial

Dental implants

Endo-sinus bone gain following osteotome-mediated sinus floor elevation with Bio-Oss Collagen compared with no grafting material: a one-year single-blind randomized controlled trial

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Abstract. The objective of this study was to assess endo-sinus bone gain (ESBG) following osteotome-mediated sinus floor elevation with Bio-Oss Collagen (test) compared with no grafting material (control) using two- and three-dimensional radiographic methods, as part of a randomized controlled trial (ClinicalTrials.gov, NCT04618900). Forty healthy patients who met the necessary eligibility criteria were allocated by block randomization to either the test group (20 patients) or control group (20 patients). 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 $P < 0.05$. ESBG was significantly increased with Bio-Oss Collagen compared with no grafting material at T1, T2, and T3 ($P < 0.001$). A gradual decrease in ESBG was observed over time with both treatment modalities ($P < 0.001$), which diminished the difference between the test and control groups at T2 and T3. ESBG was observed to be positively correlated with implant protrusion length and negatively correlated with the residual bone height. In osteotome-mediated sinus floor elevation, the application of Bio-Oss Collagen underneath the elevated Schneiderian membrane improved ESBG significantly when compared with no grafting material. However, the

Keywords: Alveolar ridge augmentation; Cone-beam computed tomography; Dental implants; Maxilla; Radiography; Randomized controlled trial; Sinus floor augmentation.

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increased ESBG seems not to have positively improved the treatment outcomes in terms of the implant stability quotient or the survival of the implants or suprastructures.

Osteotome-mediated sinus floor elevation (OMSFE) with or without a grafting material is characterized by comparable long-term survival of implants, peri-implant marginal bone loss, and frequency of complications, as documented in systematic reviews and meta-analyses.[1–5] The necessity of a grafting material underneath the elevated Schneiderian membrane in conjunction with OMSFE is therefore controversial from a clinical and patient perspective, since implant treatment outcomes appear not to be beneficially improved, while the risk of infection and costs are increased. Simultaneous implant placement in conjunction with OMSFE is needed to support the elevated membrane. The application of a grafting material underneath the membrane is intended to maintain the space for bone regeneration and increase the volume supporting the implant.[6] Randomized controlled trials (RCTs) have revealed significantly increased radiographic endo-sinus bone gain (ESBG) with a grafting material compared with no grafting material,[7,8] which is in accordance with the conclusions of systematic reviews and meta-analyses.[9,10] However, a recent RCT disclosed no significant difference in ESBG following OMSFE with autogenous bone mixed with deproteinized bovine bone mineral compared with no grafting material, after 10 years.[11] Hence, opposing conclusions have been reported regarding the amount of ESBG following OMSFE with or without a grafting material, indicating that bone regeneration could be influenced by other aspects such as the grafting material used, implant protrusion length within the maxillary sinus, residual bone height, radiographic assessment method, or length of the observation period.[12,13]

ESBG following OMSFE with or without a grafting material is frequently assessed using two-dimensional (2D) linear measurements on radiographs or cone beam computed tomography (CBCT) scans.[7,14–16] However, the grafting material applied within the maxillary sinus is an inhomogeneous and three-dimensional (3D) anisotropic structure, which necessitates the use of 3D radiographic modalities for accurate assessment of ESBG and volumetric changes of the grafting material over time.[14,15,17] 3D volumetric assessments of ESBG following OMSFE with or without a grafting material have previously been compared within an RCT.[14] Deproteinized bovine bone mineral, β-tricalcium phosphate, or a combination of the two were compared with no grafting material, revealing comparable ESBG after 2 years.[14] However, a significant shrinkage of the ESBG was shown for all treatment modalities.[14] The objective of the present study was therefore to assess ESBG using a novel 3D radiographic method, following OMSFE with Bio-Oss Collagen compared with no grafting material after 1 year of implant loading, including an analysis of potential parameters influencing the amount of ESBG.

Materials and methods

This study forms part of an RCT that has been registered at ClinicalTrials.gov (NCT04618900) and is reported according to the CONSORT statement. Full details of the study design and patient characteristics have been reported previously.[18,19]

In brief, the trial patients were recruited starting in October 2018. All patients completed a 1-year observation period after functional implant loading (finalized in March 2022). The patients had to be > 20 years of age, missing one posterior maxillary tooth for > 4 months (single tooth gap, including free end), have a ridge width ≥ 6.5 mm, and have the mandibular occluding tooth. Those with any contraindication to implant treatment, a full mouth plaque score > 25%, progressive marginal periodontitis, acute infection in the region for implant placement, parafunctional habits, psychiatric problems, a heavy smoking habit, pregnancy, physical handicap preventing adequate oral hygiene, or inability or unwillingness to attend the scheduled follow-ups were excluded. The patients were assigned to the two study groups by block randomization and were blinded to the group allocation. All patients provided signed informed consent before participation. The test group patients underwent OMSFE with Bio-Oss Collagen 250 mg (0.4–0.5 cm^3; Geistlich Pharma AG, Wolhusen, Switzerland), while the control group patients underwent the same OMSFE procedure with no grafting material.

The maxillary sinus floor was elevated using osteotomes, piezo-electric surgery, and a hydraulic pressure technique (Sinus Physiolift II; Mectron, Carasco, Italy), before patient allocation to the test or control group. In the test group, a Bio-Oss Collagen sponge was applied through the implant site underneath the Schneiderian membrane. An implant (straight 13 mm, diameter 3.6, 4.2, or 4.8 mm, Astra Tech Implant System EV; Dentsply Sirona, Mölndal, Sweden) was inserted with a cover screw. Healing abutment connection was performed after 6 months. The implant stability quotient (ISQ) was measured at implant placement and at healing abutment connection (Penguin; Integration Diagnostics Sweden AB, Gothenburg, Sweden). The prosthetic solution was finalized 3 weeks later.

Radiographic assessment

Three-dimensional measurement

The 3D assessment of ESBG was conducted using CBCT volumes (i-CAT; Imaging Sciences International, Hatfield, PA, USA) acquired at enrolment (T0), immediately after OMSFE (T1), at delivery of the prosthetic rehabilitation (T2), and 1 year after 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-second images. All volumes were generated as DICOM datasets (Digital Imaging and Communications in Medicine) using dedicated software (OnDemand3D Application version 10; Cybermed, Seoul, South Korea). The ESBG at T1 was used as the reference and matched with the ESBG at T2 and T3. Pair-wise

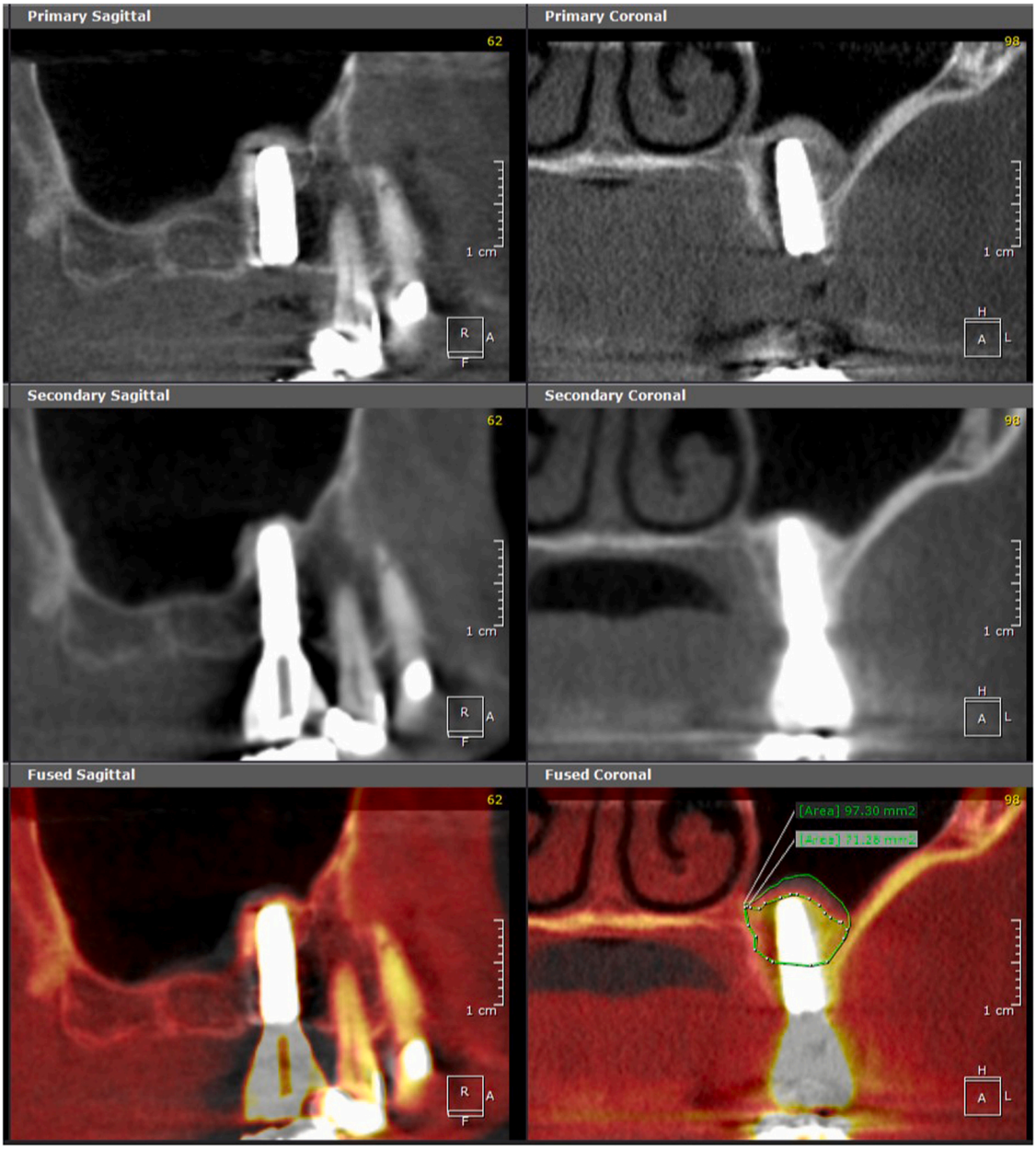

Fig. 1. Cone beam computed tomography scans obtained immediately after osteotome-mediated sinus floor augmentation and simultaneous implant placement were superimposed with the scans taken after delivery of the prosthetic rehabilitation. The original border of the maxillary sinus and circumference of the augmented area were outlined before the volume of the grafting material was calculated, at each of the different time periods.

registration was done (i.e., T1 and T2, T1 and T3), based on the automated detection of hundreds of virtual landmarks in the volumes; these can later be manually adjusted by the operator, based on visible (i.e., anatomical) landmarks. The axial, coronal, and sagittal planes were adjusted based on the centre of the longitudinal implant axis, as seen at T1, and to fit to the augmented site, as seen in the 'matched' image. In the sequence, cross-sections (i.e., coronal sections) with a thickness of 1 mm that were representative of the augmented area were generated for 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 exported and saved in BMP (bitmap) format. Using the same software, each selected cross-sectional image of the augmented sites at T1, T2, and T3 were assessed by one trained observer (T.S.J.) who manually traced the augmented area, in square millimetres (mm^2), with the aid of the computer mouse (Fig. 1). The augmented volume of the 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 in the augmented sites (mm^3) were finally calculated by subtraction of the measured volumes at T2 and T3 from the T1 volume.

The correlations between the implant protrusion length at T1 and 3D ESBG at T1, T2, and T3, and the correlations between the residual bone height at T0 and 3D ESBG at T1, T2, and T3 were assessed.

Two-dimensional measurement

2D coronal CBCT sections were used for linear measurements of the residual bone height, implant protrusion length, and ESBG. All sections were evaluated by one examiner (T.S.J.).

The residual bone height at the planned implant site was measured initially at T0. A perpendicular line from the centre of the alveolar crest to the cortical border line of the maxillary sinus was used to define the residual bone height. The residual bone heights corresponding to the mesial and distal implant surfaces were measured at T1.

The implant protrusion length corresponding to the facial and oral implant surfaces within the maxillary sinus were measured 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 maxillary sinus floor to the apex of the implant were performed and defined as the implant protrusion length within the maxillary sinus at T1.

The ESBG corresponding to the facial and oral implant surfaces was measured at T1, T2, and T3 (Figs. 2 and 3). 2D linear measurements at the longitudinal facial and oral surface of the implants from the border of the original maxillary sinus floor to the highest point of the endo-sinus bone were performed and defined as the ESBG at T1, T2, and T3.

The association between the implant protrusion length at T1 and ESBG at T1, T2, and T3 was estimated using 2D coronal CBCT sections. The amounts of bone covering the facial and oral implant surfaces within the maxillary sinus were measured using linear measurements from the original border of the maxillary sinus to the most apical part of the bone covering the implant surface at T1, T2, and T3 and correlated with the implant protrusion length at T1.

Statistical analyses

The data management and analysis was conducted using Stata Statistical Software release 17 (StataCorp, College Station, TX, USA). The mean, standard deviation, and 95% confidence interval (CI) of the mean were used to describe the 2D and 3D radiographic assessment of ESBG, using ordinary least squares (OLS) regression with robust variance estimation and clusters by participant ID. The correlations between ESBG and implant protrusion length/residual bone height were estimated by Spearman's rank correlation coefficient. The level of significance was set at $P < 0.05$. All procedures were repeated on three randomly selected patients from each of the test and control groups. Repeated measures were used to estimate the intra-observer reliability with 95% CI using the intraclass correlation coefficient from a two-way random-effects model.

Results

All patients attended the 1-year follow-up examination. Patient demographic characteristics are reported in Table 1 and the frequency of complications in Table 2. Implant survival and suprastructure survival were both 100% after 1 year of implant loading, for both treatment modalities. No significant difference in ISQ was registered between the test and control groups at T1 ($P = 0.351$) or at healing abutment connection ($P = 0.406$). The ISQ increased significantly from T1 to healing abutment connection in the test group ($P = 0.006$) and control group ($P = 0.012$). All implants were restored with a cemented or screw-retained

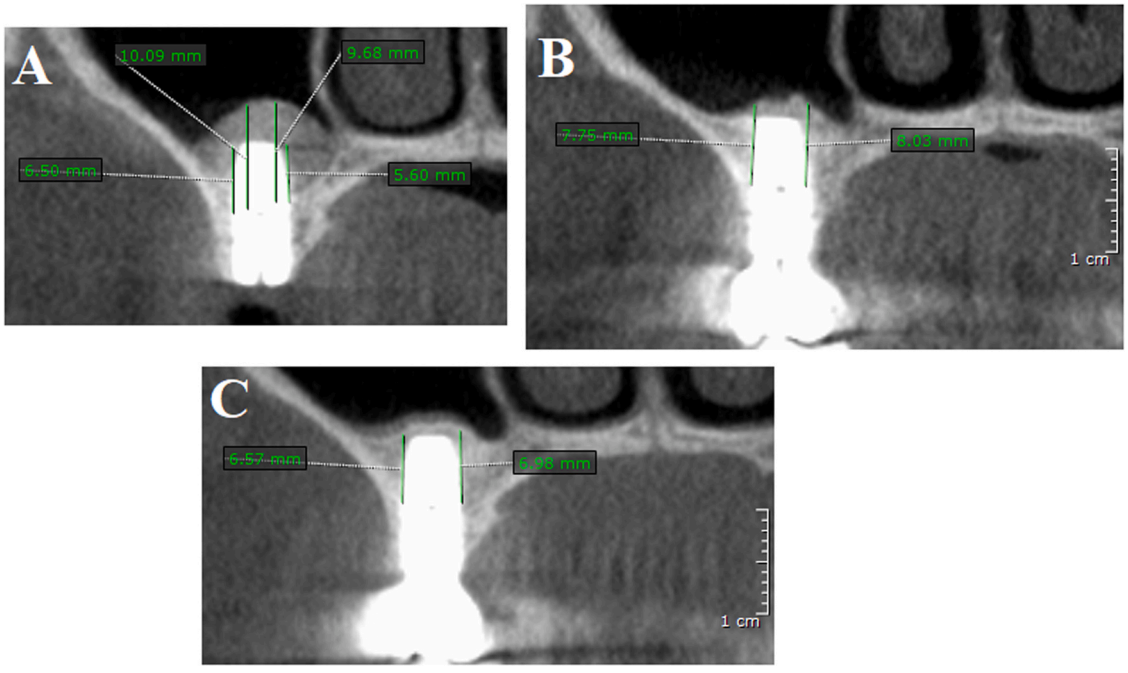

Fig. 2. (A) A two-dimensional coronal scan image was used for linear measurements of the residual alveolar bone height, endo-sinus bone gain, and implant protrusion length along the facial and oral implant surfaces immediately after osteotome-mediated sinus floor elevation with Bio-Oss Collagen. (B) (C) Identical measurements were conducted at the delivery of the prosthetic rehabilitation and 1 year after functional implant loading.

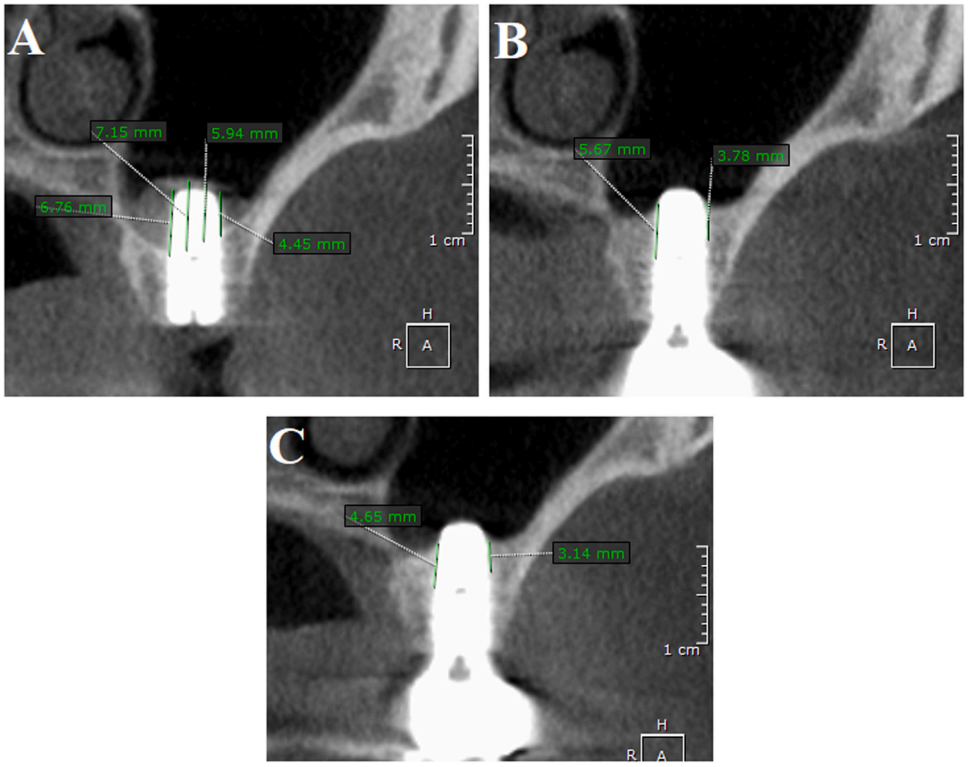

Fig. 3. (A) A two-dimensional coronal scan image was used for linear measurements of the residual alveolar bone height, endo-sinus bone gain, and implant protrusion length along the facial and oral implant surfaces immediately after osteotome-mediated sinus floor elevation with no grafting material. (B) (C) Identical measurements were conducted at the delivery of the prosthetic rehabilitation and 1 year after functional implant loading.

Table 1. Demographic characteristics of the included patients; mean ± standard deviation values.

	OMSFE with Bio-Oss Collagen $n = 20$	OMSFE with no grafting material $n = 20$	*P*-value
Sex, female/male, *n*	17/3	10/10	0.041 *
Age at the time of OMSFE (years)	50.2 ± 14.2	48.1 ± 9.1	0.590
Smoking habit, *n*	0	1	1.000
Residual alveolar bone height (mm) at implant site	6.8 ± 0.9	7.2 ± 1.1	0.356
Width of the alveolar ridge (mm) at implant site	9.1 ± 0.6	9.1 ± 0.8	0.823
Implant location, *n*			0.185
Second premolar	9	5	
First molar	11	12	
Second molar	0	3	
Implant diameter, *n*			0.501
3.6 mm	1	0	
4.2 mm	7	5	
4.8 mm	12	15	
Implant surface protrusion into the sinus (mm)	6.3 ± 1.2	5.4 ± 1.4	0.026 *
ISQ			
At implant placement	73.3 ± 9.7	76.0 ± 8.8	0.351
At healing abutment connection	80.0 ± 10.0	82.1 ± 5.6	0.406

ISQ, implant stability quotient; OMSFE, osteotome-mediated sinus floor elevation. *Statistically significant (t-test), $P < 0.05$.

Table 2. Frequency of biological complications.

Type of complication	OMSFE with Bio-Oss Collagen	OMSFE with no grafting material
Perforation of the Schneiderian membrane	-	1
Minor postoperative epistaxis	4	1
Late postoperative infection	1	-
Exposed cover screw with infection and peri-implant bone loss	1	-

OMSFE, osteotome-mediated sinus floor elevation.

single-crown restoration, which were all well-functioning at T2 and T3.

Radiographic analyses

Three-dimensional assessment

The results of the 3D volumetric assessment of ESBG following OMSFE with Bio-Oss Collagen or no grafting material at T1, T2, and T3 are outlined in Table 3. The ESBG was 617.4 ± 228.2 mm^3 at T1, 388.3 ± 157.6 mm^3 at T2, and 341.6 ± 153.0 mm^3 at T3 following OMSFE with Bio-Oss Collagen. The corresponding measurements were 317.3 ± 120.5 mm^3 at T1, 217.7 ± 93.0 mm^3 at T2, and 193.3 ± 86.3 mm^3 at T3 following OMSFE with no grafting material. The ESBG was significantly higher following OMSFE with Bio-Oss Collagen compared with no grafting material at T1, T2, and T3 (all $P < 0.001$).

The ESBG decreased significantly from T1 to T2, T1 to T3, and T2 to T3 (all $P < 0.001$) following OMSFE with Bio-Oss Collagen. Correspondingly, a significant decrease in ESBG was observed following OMSFE with no grafting material (all $P < 0.001$) (Fig. 4).

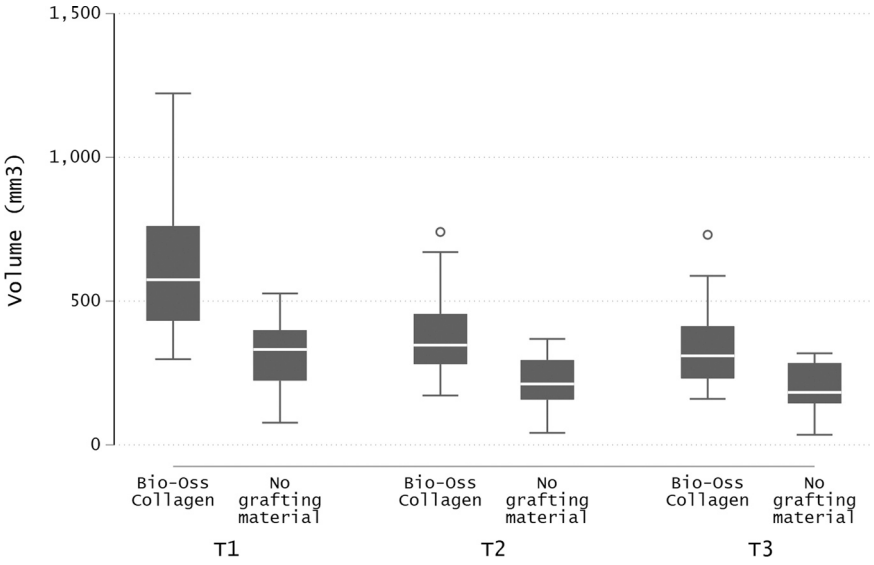

Fig. 4. Three-dimensional volumetric assessment of endo-sinus bone gain following osteotome-mediated sinus floor elevation with Bio-Oss Collagen or no grafting material, immediately after surgery (T1), at delivery of the prosthetic rehabilitation (T2), and at 1 year after functional implant loading (T3).

Two-dimensional assessment

The results of the 2D assessment of ESBG following OMSFE with Bio-Oss Collagen or no grafting material at T1, T2, and T3 are outlined in Table 4. The ESBG at the facial and oral implant surfaces were respectively 9.1 ± 2.0 mm and 8.7 ± 2.4 mm at T1, 6.0 ± 1.1 mm and 6.4 ± 1.9 mm at T2, and 5.5 ± 1.2 mm and 5.7 ± 1.6 mm at T3 following OMSFE with Bio-Oss Collagen. The corresponding measurements were respectively 6.6 ± 1.2 mm and

Table 3. 3D volumetric assessment of endo-sinus bone gain.

ESBG (mm^3)	OMSFE with Bio-Oss Collagen Mean ± SD (95% CI)		OMSFE with no grafting material Mean ± SD (95% CI)	
				P-value[a]
T1	617.4 ± 228.2 (508.2–726.5)		317.3 ± 120.5 (259.7–374.9)	< 0.001 *
T2	388.3 ± 157.6 (312.9–463.6)		217.7 ± 93.0 (173.2–262.1)	< 0.001 *
T3	341.6 ± 153.0 (268.4–414.8)		193.3 ± 86.3 (152.0–234.5)	< 0.001 *
Change in ESBG (mm^3)		*P*-value[b]		*P*-value[b]
T1–T2	229.1 (173.6–284.6)	< 0.001 *	99.6 (78.1–121.1)	< 0.001 *
T2–T3	46.7 (33.2–60.1)	< 0.001 *	24.4 (18.3–30.6)	< 0.001 *
T1–T3	275.8 (218.3–333.2)	< 0.001 *	124.0 (100.3–147.8)	< 0.001 *

3D, three-dimensional; CI, confidence interval; ESBG, endo-sinus bone gain; OMSFE, osteotome-mediated sinus floor elevation; SD, standard deviation; T1, immediately after surgery; T2, at delivery of the prosthetic rehabilitation; T3, 1 year after functional implant loading.

[a]*P*-value for the comparison of ESBG between the groups at each time point (inter-group comparison). *Statistically significant, $P < 0.05$.

[b]*P*-value for the change in ESBG between time points, within each group (intra-group comparison). *Statistically significant, $P < 0.05$.

Table 4. 2D assessment of endo-sinus bone gain.

	OMSFE with Bio-Oss Collagen Mean ± SD (95% CI)				OMSFE with no grafting material Mean ± SD (95% CI)			
							P-value[a]	
ESBG (mm)	FIS	OIS			FIS	OIS	FIS	OIS
T1	9.1 ± 2.0 (8.2–10.1)	8.7 ± 2.4 (7.5–9.8)			6.6 ± 1.2 (6.0–7.2)	6.3 ± 1.5 (5.6–7.0)	< 0.001 *	< 0.001 *
T2	6.0 ± 1.1 (5.5–6.6)	6.4 ± 1.9 (5.5–7.3)			5.0 ± 1.0 (4.5–5.5)	4.6 ± 1.4 (4.0–5.3)	< 0.001 *	< 0.001 *
T3	5.5 ± 1.2 (4.9–6.1)	5.7 ± 1.6 (4.9–6.4)			4.4 ± 0.7 (4.0–4.7)	4.1 ± 1.0 (3.6–4.6)	< 0.001 *	< 0.001 *
Change in			*P*-value[b]				*P*-value[b]	
ESBG (mm)	FIS	OIS	FIS	OIS	FIS	OIS	FIS	OIS
T1–T2	3.1 (2.2–4.0)	2.3 (1.4–3.2)	< 0.001 *	< 0.001 *	1.6 (1.2–2.0)	1.7 (1.3–2.1)	< 0.001 *	< 0.001 *
T2–T3	0.5 (0.3–0.7)	0.7 (0.2–1.3)	< 0.001 *	0.013 *	0.6 (0.3–0.9)	0.5 (0.1–0.8)	< 0.001 *	0.009 *
T1–T3	3.6 (2.7–4.5)	3.0 (2.0–4.0)	< 0.001 *	< 0.001 *	2.2 (1.8–2.7)	2.2 (1.7–2.7)	< 0.001 *	< 0.001 *

2D, two-dimensional; CI, confidence interval; ESBG, endo-sinus bone gain; FIS, facial implant surface; OIS, oral implant surface; OMSFE, osteotome-mediated sinus floor elevation; SD, standard deviation; T1, immediately after surgery; T2, at delivery of the prosthetic rehabilitation; T3, 1 year after functional implant loading.

[a]*P*-value for the comparison of ESBG between the groups at each time point (inter-group comparison). *Statistically significant, $P < 0.05$.

[b]*P*-value for the change in ESBG between time points, within each group (intra-group comparison). *Statistically significant, $P < 0.05$.

6.3 ± 1.5 mm at T1, 5.0 ± 1.0 mm and 4.6 ± 1.4 mm at T2, and 4.4 ± 0.7 mm and 4.1 ± 1.0 mm at T3 following OMSFE with no grafting material. The ESBG at the facial and oral implant surfaces was significantly higher following OMSFE with Bio-Oss Collagen compared with no grafting material at T1, T2, and T3 (all $P < 0.001$).

The 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 (facial surface $P < 0.001$, oral surface $P = 0.013$) following OMSFE with Bio-Oss Collagen. Correspondingly, a significant decrease in ESBG was observed from T1 to T2 (both $P < 0.001$), T1 to T3 (both $P < 0.001$), and T2 to T3 (facial surface $P < 0.001$, oral surface $P = 0.009$) following OMSFE with no grafting material (Fig. 5).

Implant protrusion length

The implant protrusion length within the maxillary sinus at T1 and its correlation with ESBG following OMSFE with Bio-Oss Collagen or no grafting material is reported in Tables 5 and 6. There was a significant difference in implant protrusion length between the two treatment modalities on 3D assessment at T1 ($P = 0.026$). A positive

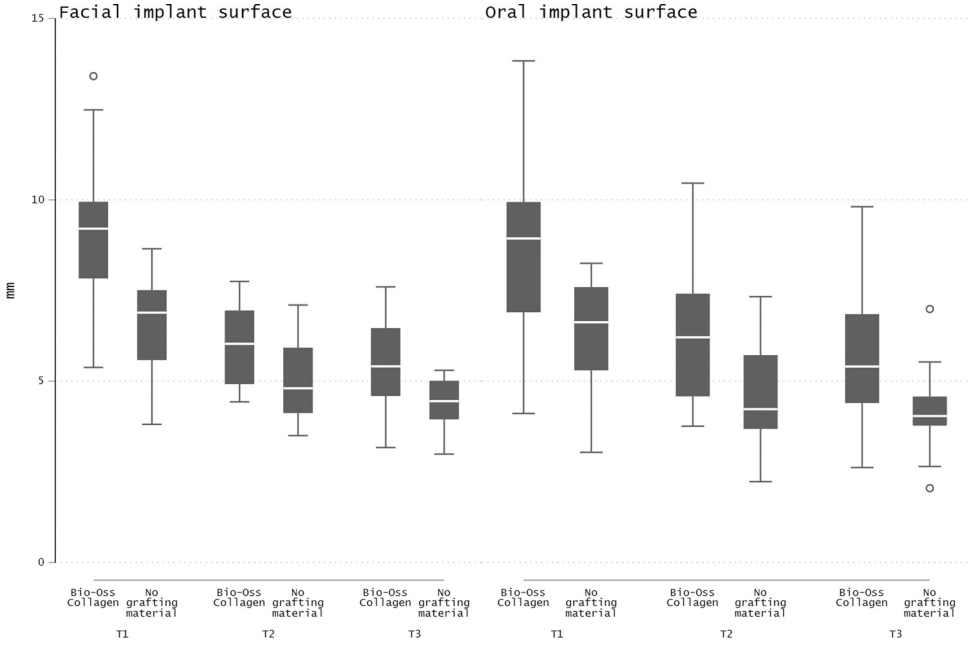

Fig. 5. Two-dimensional linear assessment of endo-sinus bone gain along the facial and oral implant surfaces following osteotome-mediated sinus floor elevation with Bio-Oss Collagen or no grafting material, immediately after surgery (T1), at delivery of the prosthetic rehabilitation (T2), and at 1 year after functional implant loading (T3).

Table 5. Correlation between implant protrusion length and 3D endo-sinus bone gain; the mean ± standard deviation and 95% confidence interval are presented.

	OMSFE with Bio-Oss Collagen Mean ± SD (95% CI)		OMSFE with no grafting material Mean ± SD (95% CI)	
				P-value[a]
IPL (mm)	6.3 ± 1.2 (5.8–6.9)		5.4 ± 1.4 (4.8–6.0)	0.026 *
Spearman's rho		*P*-value[b]		*P*-value[b]
T1	0.26	0.274	0.66	< 0.001 *
T2	0.47	0.038 *	0.74	< 0.001 *
T3	0.51	0.021 *	0.72	< 0.001 *

3D, three-dimensional; CI, confidence interval; IPL, implant protrusion length; OMSFE, osteotome-mediated sinus floor elevation; SD, standard deviation; T1, immediately after surgery; T2, at delivery of the prosthetic rehabilitation; T3, 1 year after functional implant loading.

[a]*P*-value for the comparison of implant protrusion length between the groups (inter-group comparison). *Statistically significant, $P < 0.05$.

[b]*P*-value for the correlation between implant protrusion length and 3D endo-sinus bone gain at each time point, within each group. *Statistically significant, $P < 0.05$.

correlation between implant protrusion length and both 3D and 2D radiographic measurements of ESBG was observed in both treatment groups (Tables 5 and 6). The association was most pronounced following OMSFE with no grafting material.

Residual alveolar bone height

The residual bone height at T0 and its correlation with ESBG following OMSFE with Bio-Oss Collagen or no grafting material is reported in Tables 7 and 8. There was no significant difference in residual bone height between the two treatment modalities on 3D assessment ($P = 0.356$). A negative correlation between residual bone height and both 3D and 2D radiographic measurements of ESBG was observed in both treatment groups (Tables 7 and 8). However, the correlation was only significant in the OMSFE with no grafting material group.

Intra-observer reliability

The intra-class correlation was 0.92 (95% CI 0.89–0.94) indicating excellent reliability. The Bland–Altman plot revealed no relationship between the differences of the repeated estimates against the corresponding means (Fig. 6).

Discussion

This study demonstrated that the amount of ESBG was significantly increased with Bio-Oss Collagen when compared with no grafting material in conjunction with OMSFE. However, a gradual decrease in the ESBG was observed over time with both treatment modalities. ESBG was found to be positively correlated with implant protrusion length, while a negative correlation was found between ESBG and residual bone height. Consequently, the application of Bio-Oss Collagen underneath the elevated Schneiderian membrane in conjunction with OMSFE significantly improved ESBG compared with no

Table 6. Correlation between implant protrusion length and 2D endo-sinus bone gain; the mean ± standard deviation and 95% confidence interval are presented.

	OMSFE with Bio-Oss Collagen Mean ± SD (95% CI)				OMSFE with no grafting material Mean ± SD (95% CI)			
							P-value[a]	
	FIS	OIS			FIS	OIS	FIS	OIS
IPL (mm)	6.5 ± 1.3 (5.9–7.0)	6.2 ± 1.4 (5.6–6.8)			5.6 ± 1.2 (5.1–6.1)	5.2 ± 1.8 (4.4–6.0)	0.032 *	0.050 *
Spearman's rho			*P*-value[b]				*P*-value[b]	
	FIS	OIS	FIS	OIS	FIS	OIS	FIS	OIS
T1	0.36	0.63	0.117	0.003 *	0.84	0.85	< 0.001 *	< 0.001 *
T2	0.50	0.66	0.024 *	0.001 *	0.81	0.96	< 0.001 *	< 0.001 *
T3	0.60	0.64	0.005 *	0.002 *	0.66	0.77	0.002 *	< 0.001 *

2D, two-dimensional; CI, confidence interval; FIS, facial implant surface; IPL, implant protrusion length; OIS, oral implant surface; OMSFE, osteotome-mediated sinus floor elevation; SD, standard deviation; T1, immediately after surgery; T2, at delivery of the prosthetic rehabilitation; T3, 1 year after functional implant loading.

[a]*P*-value for the comparison of implant protrusion length between the groups (inter-group comparison). *Statistically significant, $P < 0.05$.

[b]*P*-value for the correlation between implant protrusion length and 2D endo-sinus bone gain at each time point, within each group. *Statistically significant, $P < 0.05$.

Table 7. Correlation between residual bone height and 3D endo-sinus bone gain; the mean ± standard deviation and 95% confidence interval are presented.

	OMSFE with Bio-Oss Collagen Mean ± SD (95% CI)		OMSFE with no grafting material Mean ± SD (95% CI)	
				P-value[a]
RBH (mm)	6.8 ± 0.9 (6.4–7.3)		7.2 ± 1.1 (6.7–7.6)	0.356
Spearman's rho		*P*-value[b]		*P*-value[b]
T1	0.08	0.724	− 0.55	0.011 *
T2	− 0.24	0.314	− 0.62	0.004 *
T3	− 0.33	0.162	− 0.60	0.005 *

3D, three-dimensional; CI, confidence interval; OMSFE, osteotome-mediated sinus floor elevation; RBH, residual bone height; SD, standard deviation; T1, immediately after surgery; T2, at delivery of the prosthetic rehabilitation; T3, 1 year after functional implant loading.

[a]*P*-value for the comparison of residual bone height between the groups (inter-group comparison). *Statistically significant, $P < 0.05$.

[b]*P*-value for the correlation between residual bone height and 3D endo-sinus bone gain at each time point, within each group. *Statistically significant, $P < 0.05$.

grafting. However, the increased ESBG seems not to have positively improved the ISQ or the survival of the implants or suprastructures after 1 year of implant loading.

In this study, ESBG was assessed using a novel 3D radiographic method. Repeated measurements revealed excellent intra-observer reliability, indicating that the method used is reliable. However, there are some limitations of the present study that should be mentioned, including the small patient sample, inhomogeneous sex distribution, CBCT artefacts around the dental implants complicating precise radiographic measurements, and the single-blind study design. Moreover, the term 'endo-sinus bone gain' is slightly misleading since a xenograft that solely possesses osteoconductive properties was used as the grafting material and no histomorphometric assessment was conducted. Conclusions drawn from the results of this study should therefore be interpreted with caution.

OMSFE without a grafting material has significant benefits for the patient and clinicians if comparable clinical and radiographic implant treatment outcomes are achieved. In the present study comparable survival of the implants and suprastructures were obtained in the two groups, which is in accordance with previous RCTs.[11,14,20–23] Consequently, the application of a grafting material underneath the elevated membrane in conjunction with OMSFE appears not to greatly improve the clinical implant treatment outcome.

Volumetric stabilization of the space created underneath the elevated membrane is considered an important factor for bone regeneration.[24] The application of a grafting material underneath the membrane in conjunction with OMSFE is therefore intended to stabilize the space created and increase the volume supporting the implant to improve bone regeneration and osseointegration.[25] Bio-Oss is assumed to be a slowly resorbed or non-resorbable bone substitute with small volumetric changes in the augmented area.[17] Bio-Oss Collagen contains 90% small Bio-Oss particles and 10% porcine collagen. The incorporation of Bio-Oss particles in collagen reduces the risk of particle migration in the case of membrane perforation during OMSFE. However, shrinkage of the collagen component during healing will decrease the volume of the augmented area, which could explain some of the gradual decrease in ESBG following OMSFE with Bio-Oss Collagen. The space created underneath the membrane following OMSFE

Table 8. Correlation between residual bone height and 2D endo-sinus bone gain; the mean ± standard deviation and 95% confidence interval are presented.

	OMSFE with Bio-Oss Collagen Mean ± SD (95% CI)				OMSFE with no grafting material Mean ± SD (95% CI)			
							P-value[a]	
RBH (mm)	6.8 ± 0.9 (6.4–7.3)				7.2 ± 1.1 (6.7–7.6)		0.356	
Spearman's rho			*P*-value[b]				*P*-value[b]	
	FIS	OIS	FIS	OIS	FIS	OIS	FIS	OIS
T1	− 0.05	− 0.04	0.827	0.880	− 0.62	− 0.74	0.004 *	< 0.001 *
T2	− 0.31	− 0.19	0.179	0.425	− 0.58	− 0.78	0.008 *	< 0.001 *
T3	− 0.34	− 0.22	0.138	0.340	− 0.37	− 0.71	0.108	< 0.001 *

2D, two-dimensional; CI, confidence interval; FIS, facial implant surface; OIS, oral implant surface; OMSFE, osteotome-mediated sinus floor elevation; RBH, residual bone height; SD, standard deviation; T1, immediately after surgery; T2, at delivery of the prosthetic rehabilitation; T3, 1 year after functional implant loading.

[a]*P*-value for the comparison of residual bone height between the groups (inter-group comparison). *Statistically significant, $P < 0.05$.

[b]*P*-value for the correlation between residual bone height and 2D endo-sinus bone gain at each time point, within each group. *Statistically significant, $P < 0.05$.

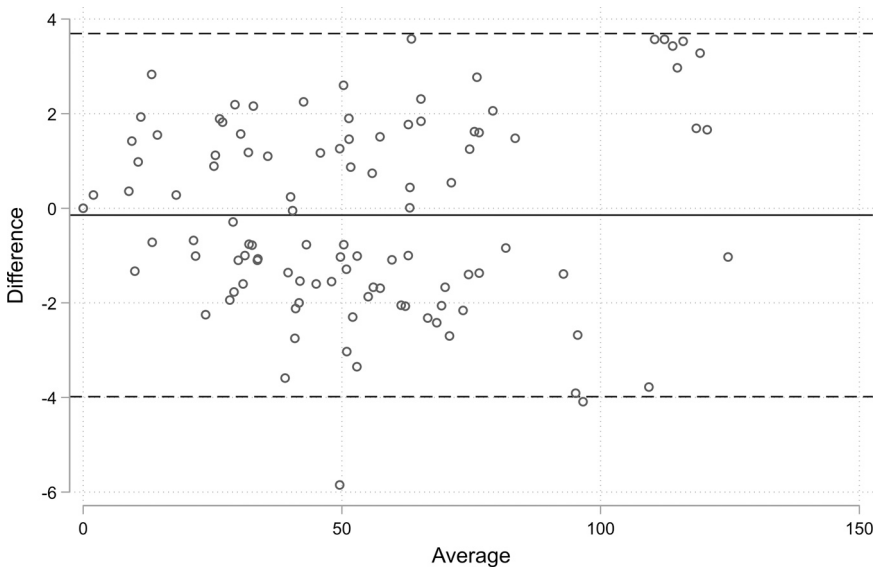

Fig. 6. Bland–Altman plot of repeated measurements.

without a grafting material is solely maintained by the implant and coagulum. The dissolving of the coagulum during the healing process causes collapse of the membrane, which diminishes the volume for bone regeneration. In the present study, the application of Bio-Oss Collagen underneath the elevated membrane facilitated a significantly higher ESBG. However, the exposed implant surface within the maxillary sinus following OMSFE without a grafting material was almost entirely covered by a thin layer of bone, which seems to be sufficient to achieved comparable ISQs.

The ISQ indicates the level of stability and osseointegration of the implant. In this study, the ISQ was significantly increased at healing abutment connection when compared with implant placement, for both treatment modalities, indicating that the placement of grafting material underneath the membrane does not positively improve the ISQ when compared with no grafting material; this is in accordance with the conclusions of the previous RCTs.[14,21,26]

A recently published literature review described a different dimensional behaviour of ESBG over time, with volumetric shrinkage observed following OMSFE with a grafting material, but a slight bone increase without a grafting material, after 3 years.[27] In the present study, a gradual decrease in ESBG over time was revealed for both treatment modalities. However, the difference diminished, indicating a different dimensional behaviour of ESBG following OMSFE with or without a grafting material, as reported previously in the literature review.[27]

Previous studies have indicated that the implant protrusion length within the maxillary sinus and residual bone height influence the ESBG following OMSFE with or without a grafting material.[19,28–30] The ESBG has been reported to be positively correlated with the implant protrusion length following OMSFE with or without a grafting material, which is in accordance with the present study findings.[19,28–30] However, the increased implant protrusion length seems not to be proportional to the amount of ESBG.[12,13] A previous study revealed a decrease in ESBG when the implant protrusion length exceeded 4 mm.[12] Moreover, an increased implant protrusion length in conjunction with OMSFE without a grafting material creates a larger cavity underneath the elevated membrane, which causes a greater pressure on the membrane during the early healing period, with the risk of the coagulum dissolving and compromised bone regeneration.[13] Consequently, it is recommended that the exposed implant surface within the maxillary sinus does not exceed 5 mm following OMSFE with or without a grafting material.

Previous studies have indicated that the residual bone height influences the amount of ESBG following OMSFE.[13,20] A short-term study reported a negative correlation between ESBG and residual bone height following OMSFE without a grafting material,[13] which is in accordance with the present study results. However, no association between ESBG and residual bone height was revealed in a long-term RCT.[20] A strong negative correlation between the width of the maxillary sinus and bone regeneration has been reported following maxillary sinus floor augmentation applying the lateral window technique.[31] The correlation between the width of the maxillary sinus and amount of ESBG following OMSFE has not been assessed previously. Consequently, the association between ESBG and residual bone height as well as the width of the maxillary sinus in conjunction with OMSFE needs further investigation.

Within the limitations of this study, it can be concluded that the application of Bio-Oss Collagen underneath the elevated Schneiderian membrane in conjunction with osteotome-mediated sinus floor elevation significantly improved the amount of endo-sinus bone gain compared with no grafting material. However, the increased endo-sinus bone gain did not positively improve the implant stability quotient or the survival of the implants or suprastructures. The differences in endo-sinus bone gain between the two treatment modalities diminished over time due to shrinkage of the augmented area. Thus, the application of a grafting material underneath the elevated membrane in conjunction with osteotome-mediated sinus floor elevation appears not to beneficially improve the outcome of clinical implant treatment.

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Data availability

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

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Competing interests

All authors declare no financial interest or conflict of interest, either direct or indirect, in relation to the products or information reported in the article. However, Thomas Starch-Jensen gives lectures for Dentsply Sirona and Plandent (Danish distributor of Geistlich products).

Patient consent

All included patients received verbal and written information about the study and signed an informed consent agreement prior to enrolment.

Trial registration

ClinicalTrials.gov registration number NCT04618900.

Ethical approval

The study protocol was approved by The North Denmark Region Committee on Health Research Ethics (approval No. N-20180027).

References

1. Del Fabbro M, Corbella S, Weinstein T, Ceresoli V, Taschieri S. Implant survival rates after osteotome-mediated maxillary sinus augmentation: a systematic review. *Clin Implant Dent Relat Res* 2012;**14**(Suppl 1):e159–68.
2. Shi JY, Gu YX, Zhuang LF, Lai HC. Survival of implants using the osteotome technique with or without grafting in the posterior maxilla: a systematic review. *Int J Oral Maxillofac Implants* 2016;**31**:1077–88.
3. Aludden H, Mordenfeld A, Hallman M, Christensen AE, Starch-Jensen T. Osteotome-mediated sinus floor elevation with or without a grafting material: a systematic review and meta-analysis of long-term studies (≥5-years). *Implant Dent* 2018;**27**:488–97.
4. Chen MH, Shi JY. Clinical and radiological outcomes of implants in osteotome sinus floor elevation with and without grafting: a systematic review and a meta-analysis. *J Prosthodont* 2018;**27**:394–401.
5. Călin C, Petre A, Drafta S. Osteotome-mediated sinus floor elevation: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants* 2014;**29**:558–76.
6. Pjetursson BE, Lang NP. Sinus floor elevation utilizing the transalveolar approach. *Periodontol 2000* 2014;**66**:59–71.
7. Nedir R, Nurdin N, Abi Najm S, El Hage M, Bischof M. Short implants placed with or without grafting into atrophic sinuses: the 5-year results of a prospective randomized controlled study. *Clin Oral Implants Res* 2017;**28**:877–86.
8. Trinh HA, Dam VV, Le B, Pittayapat P, Thunyakitpisal P. Indirect sinus augmentation with and without the addition of a biomaterial: a randomized controlled clinical trial. *Implant Dent* 2019;**28**:571–7.
9. Yang J, Xia T, Wang H, Cheng Z, Shi B. Outcomes of maxillary sinus floor augmentation without grafts in atrophic maxilla: a systematic review and meta-analysis based on randomised controlled trials. *J Oral Rehabil* 2019;**46**:282–90.
10. Yan M, Liu R, Bai S, Wang M, Xia H, Chen J. Transalveolar sinus floor lift without bone grafting in atrophic maxilla: a meta-analysis. *Sci Rep* 2018;**8**:1451.
11. Qian SJ, Mo JJ, Si MS, Qiao SC, Shi JY, Lai HC. Long-term outcomes of osteotome sinus floor elevation with or without bone grafting: the 10-year results of a randomized controlled trial. *J Clin Periodontol* 2020;**47**:1016–25.
12. Yu Y, Jiang Q, Zhang Z, Yu X, Deng F. Influence of implant protrusion length on non-grafting osteotome sinus floor elevation with simultaneous implant: a 3- to 9-year retrospective study. *Int J Implant Dent* 2021;**7**:22.
13. Suk-Arj P, Wongchuensoontorn C, Taebunpakul P. Evaluation of bone formation following the osteotome sinus floor elevation technique without grafting using cone beam computed tomography: a preliminary study. *Int J Implant Dent* 2019;**5**:27.
14. Marković A, Mišić T, Calvo-Guirado JL, Delgado-Ruíz RA, Janjić B, Abboud M. Two-center prospective, randomized, clinical, and radiographic study comparing osteotome sinus floor elevation with or without bone graft and simultaneous implant placement. *Clin Implant Dent Relat Res* 2016;**18**:873–82.
15. Gai L, Luo X, Guan Y, He F. Comparative evaluation of endo-sinus bone augmentation after osteotome sinus floor elevation without grafting using two radiographic methods. *Int J Oral Maxillofac Implants* 2021;**36**:154–64.
16. Verdugo F, Uribarri A, Laksmana T, D'addona A. Long-term stable vertical bone regeneration after sinus floor elevation and simultaneous implant placement with and without grafting. *Clin Implant Dent Relat Res* 2017;**19**:1054–60.
17. Jensen T, Schou S, Svendsen PA, Forman JL, Gundersen HJ, Terheyden H, Holmstrup P. Volumetric changes of the graft after maxillary sinus floor augmentation with Bio-Oss and autogenous bone in different ratios: a radiographic study in minipigs. *Clin Oral Implants Res* 2012;**23**:902–10.
18. Starch-Jensen T, Bruun NH. Patient's perception of recovery after osteotome-mediated sinus floor elevation with Bio-Oss Collagen compared with no grafting material: a randomized single-blinded controlled trial. *Int J Implant Dent* 2021;**7**:20.
19. Starch-Jensen T, Bruun NH, Spin-Neto R. Osteotome-mediated sinus floor elevation with Bio-Oss Collagen or no grafting material: a one-year single-blind randomized controlled trial. *Int J Oral Maxillofac Surg* 2022.
20. Si MS, Zhuang LF, Gu YX, Mo JJ, Qiao SC, Lai HC. Osteotome sinus floor elevation with or without grafting: a 3-year randomized controlled clinical trial. *J Clin Periodontol* 2013;**40**:396–403.
21. Merheb J, Nurdin N, Bischof M, Gimeno-Rico M, Quirynen M, Nedir R. Stability evaluation of implants placed in the atrophic maxilla using osteotome sinus floor elevation with and without bone grafting: a 5-year prospective study. *Int J Oral Implantol* 2019;**12**:337–46.
22. Nedir R, Nurdin N, Khoury P, Perneger T, Hage ME, Bernard JP, Bischof M. Osteotome sinus floor elevation with and without grafting material in the severely atrophic maxilla. A 1-year prospective randomized controlled study. *Clin Oral Implants Res* 2013;**24**:1257–64.
23. Nedir R, Nurdin N, Huynh-Ba G, Bischof M. Change in crown-to-implant ratio of implants placed in grafted and nongrafted posterior maxillary sites: a 5-year prospective randomized study. *Int J Oral Maxillofac Implants* 2019;**34**:1231–6.
24. Fouad W, Osman A, Atef M, Hakam M. Guided maxillary sinus floor elevation using deproteinized bovine bone versus graftless Schneiderian membrane elevation with simultaneous implant placement: randomized clinical trial. *Clin Implant Dent Relat Res* 2018;**20**:424–33.
25. Pjetursson BE, Ignjatovic D, Matuliene G, Brägger U, Schmidlin K, Lang NP. Transalveolar maxillary sinus floor elevation using osteotomes with or without grafting material. Part II: radiographic tissue remodeling. *Clin Oral Implants Res* 2009;**20**:677–83.
26. Si MS, Mo JJ, Zhuang LF, Gu YX, Qiao SC, Lai HC. Osteotome sinus floor elevation with and without grafting: an animal study in Labrador dogs. *Clin Oral Implants Res* 2015;**26**:197–203.
27. Santoro M, Pippi R. Intrasinus bone gain with the osteotome sinus floor elevation technique: a review of the literature. *Int J Oral Maxillofac Implants* 2018;**33**:995–1002.
28. Lai HC, Zhuang LF, Lv XF, Zhang ZY, Zhang YX, Zhang ZY. Osteotome sinus floor elevation with or without grafting: a preliminary clinical trial. *Clin Oral Implants Res* 2010;**21**:520–6.
29. Nedir R, Nurdin N, Vazquez L, Szmukler-Moncler S, Bischof M, Bernard JP. Osteotome sinus floor elevation technique without grafting: a 5-year prospective study. *J Clin Periodontol* 2010;**37**:1023–8.
30. Nedir R, Bischof M, Vazquez L, Szmukler-Moncler S, Bernard JP. Osteotome sinus floor elevation without grafting material: a 1-year prospective pilot study with ITI implants. *Clin Oral Implants Res* 2006;**17**:679–86.
31. Avila G, Wang HL, Galindo-Moreno P, Misch CE, Bagramian RA, Rudek I, Benavides E, Moreno-Riestra I, Braun T, Neiva R. The influence of the bucco-palatal distance on sinus augmentation outcomes. *J Periodontol* 2010;**81**:1041–50.

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