A Novel Xenograft Bone Substitute Supports Stable Bone Formation in Circumferential Defects Around Dental Implants in Minipigs

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Purpose: The aim of this study was to evaluate and compare bone growth and implant integration in circumferential defects with two commercially available bone substitutes (demineralized bovine bone mineral [DBBM]). ***Materials and Methods:*** Circumferential defects were created in the mandibles of minipigs (n = 10), and Bone Level Tapered implants (Straumann Roxolid with SLActive surface) were placed. The defects (4-mm-deep circumferential defect, 2 mm around each implant) were augmented with either sintered bovine bone mineral (test, cerabone) or natural bovine bone mineral (control, Bio-Oss). Bone formation and tissue composition in augmented sites were histomorphometrically assessed after 8 and 12 weeks of healing time (n = 5 each), respectively, in terms of the percentage of area of newly formed bone to total area, bone-to-implant contact (BIC), and crestal bone height relative to the implant shoulder (first bone-to-implant contact [fBIC]). ***Results:*** Bone formation in all defect sites was adequate and equivalent for both groups at individual healing time points. The amount of residual graft material was comparable in both groups after 8 and 12 weeks, with no significant resorption in either group. The mean newly formed bone area in the test group amounted to 46.7% ± 5.1% and 48.7% ± 4.0% after 8 and 12 weeks vs 47.0% ± 4.8% and 47.8% ± 7.3% in the control group, respectively. BIC and fBIC as individually assessed for the lingual and buccal aspects were comparable at both healing time points without any statistically significant differences between the groups. A slightly greater variability of fBIC was observed within the test group. ***Conclusion:*** The results of this study indicate that test and control materials both represent viable bovine bone graft material that equivalently support the formation of new and stable bone volume specifically when used for simultaneous augmentation around implants. *Int J Oral Maxillofac Implants 2020;35:1122–1131. doi: 10.11607/jomi.8265*

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Bone substitutes are frequently used to augment missing bone tissue as part of restorative and regenerative dental procedures. From a biologic point of view, autologous bone is considered the gold standard for these procedures,[1–3] since it displays osteogenic, osteoinductive, and osteoconductive properties. However, its practical use is inherently limited by its limited availability and invasive harvesting procedure, with increased associated patient morbidity.[4] As a result, many commercial bone graft materials such as allografts (grafts from a member of the same species), xenografts (grafts from a different species), and alloplastic (synthetic) materials have been developed. These materials are now well established for the augmentation of small peri-implant and periodontal defects and also larger bone augmentation procedures in the mandible or maxilla.

Deproteinized natural bovine bone mineral (DBBM) represents one of the best established and researched types of commercially available xenogeneic bone substitutes.[5–7] DBBM granulate materials possess an open porous structure comparable to cancellous bone and display a high surface area that is biologically readily

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available for bone apposition.[8] The efficacy of DBBM in immediate or staged implant procedures has been shown in both preclinical and clinical histologic studies, where a high degree of biocompatibility has been reported.[6,8–11] Moreover, a systematic literature review addressing the clinical efficacy of bone graft materials in horizontal and vertical augmentation procedures suggested that DBBM has a comparable clinical performance to autologous bone or allografts.[12]

Bio-Oss (Geistlich Pharma) is a DBBM with an open porous structure comparable to natural bone.[13,14] The mineral phase of Bio-Oss is comparable to the hydroxyapatite phase of bone.[15] The material is deproteinized to completely remove potential immunogenic or pathogenic components by extraction with organic solvents followed by thermal (< 300°C) and alkaline treatment.[16,17] Histologic studies have confirmed the osteoconductive properties of Bio-Oss upon implantation into bone as part of dental implant placement procedures.[18,19] Furthermore, osseointegration combined with no or minimal resorption has been reported.[8,15,20,21] The use of Bio-Oss has been well established in ridge augmentation and sinus grafting as part of dental implant placement procedures.[20,21]

Cerabone (botiss biomaterials) is a sintered DBBM with a bone-like trabecular structure and was recently introduced into dental procedures.[5] Cerabone is sintered at a high temperature (> 1,200°C), resulting in a highly crystalline hydroxyapatite mineral phase of low bioresorbability.[15] Preclinical histologic studies have reported osteoconductive properties for cerabone, coupled with low immunogenic potential and the ability to support angiogenesis.[22–24] Its efficacy has been clinically evaluated in socket preservation and sinus floor augmentation, with histologic documentation of osseointegration.[24–26] Cerabone has also been compared with Bio-Oss in bilateral sinus augmentation as part of a staged implantation procedure.[25]

To the authors' knowledge, there are no reported preclinical or clinical studies that have histologically evaluated cerabone as part of a simultaneous dental implant placement and bone augmentation procedure. The objective of this study was to experimentally evaluate the performance of test DBBM (cerabone) in comparison to the well-established control DBBM (Bio-Oss) when used as part of simultaneous bone augmentation procedures around implants. Specifically, implant integration, bone formation, and coronal bone height were histologically evaluated and histomorphometrically quantified in a temporally dependent manner after 8 and 12 weeks of membrane-covered, submerged healing using a well-defined contained circumferential defect model in the mandibles of minipigs.

MATERIALS AND METHODS

This study was approved by the Ethical Committee of Lund University in Sweden (M-192-14), performed in accordance with ISO 10993-6 (Biological evaluation of medical devices—Part 6: Tests for local effects after implantation), and reported according to the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines regarding all relevant items.[27] The study was performed on 10 female Göttingen Minipigs (Ellegaard), with a mean age of 20 months (range: 19.5 to 21 months) and a mean body weight of 34 kg. Prior to the surgical procedures, the animals were kept for 1 week in standard boxes, in groups of three or four, to adapt to the animal experimental facilities. Animals were fed on a restricted soft diet to control their weight gain (Special Diet Services [SDS], Witham, UK #801586).

Surgical Procedure

All surgical procedures were performed as previously described.[28] Briefly, anesthetic induction was performed using ketamine (Ketalar Vet, Pfizer, 50 mg/mL) and 3 mL midazolam (Dormicum 5 mg/mL, Roche) via intramuscular injection. Anesthetic maintenance was accomplished with an intravenous ketamine/midazolam mix. Local anesthesia (Xylocain Dental adrenalin 20 mg/mL + 12.5 mg/mL, 3.6 mL each side, Astra) was given. Animals were monitored routinely, and analgesics were given over a 3-day postoperative period (3 to 5 mL/pig intramuscularly twice a day; Temgesic, Essex Pharma).

Two surgical interventions were performed on each animal. In the first surgery, the mandibular premolars (P2 to P4) and the first molar (M1) were removed after carefully elevating a full-thickness flap.

After 3 months of healing, full-thickness buccal and lingual flaps were raised after midcrestal incision. After raising the flaps, the alveolar ridge was flattened by means of a rotating Ø 2.3-mm round bur under irrigation.

Three circumferential defects were created in each hemimandible. The defects were created in a single drill step by means of an adapted Ø 2.8 mm Pilot Drill with a "step" collar 4 mm from the drill apex. This simultaneously created an 8-mm-deep implant site (4 mm for the apical part of the implant and a 4-mm-deep circumferential defect to allow a gap of 2 mm around the placed implant). Bone Level Tapered Roxolid implants (Institut Straumann) were placed (SLActive in one hemimandible and SLA in the other hemimandible) so that the implant platform was located at the defect margin (Fig 1). The implants were Ø 3.3 mm with a length of 8 mm and were placed using a Loxim transfer piece, ratchet, and hexagonal screwdriver, and a cover screw was placed on each one.

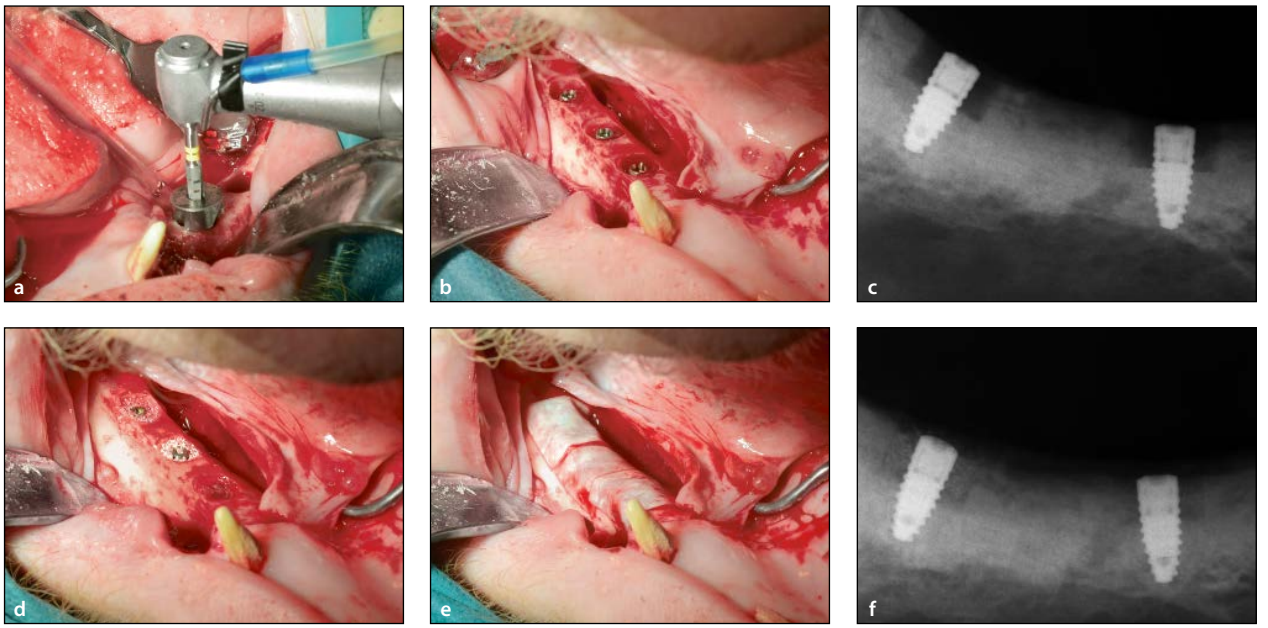

Fig 1 Surgical procedure consisting of *(a)* creation of a circumferential defect in a one-step drilling procedure by use of a combined drill and trephine, *(b)* placement of implants, *(d)* augmentation of the circumferential defects with bone substitute, and *(e)* placement of a membrane. *(c, f)* Radiographs of the circumferential defect *(c)* before and *(f)* after placement of DBBM.

After placement of the implants, the peri-implant circumferential defects were filled with either cerabone (0.5- to 1.0-mm granules, botiss biomaterials; test DBBM), Bio-Oss (0.25- to 1-mm, Geistlich Pharma; control DBBM), or maxgraft (data reported elsewhere; see below) up to the level of the bone crest. Bone substitutes were mixed with blood prior to placement and gently compacted into the defect. The defects were covered with collagen membranes (Jason, botiss biomaterials), and the flaps were repositioned and sutured with Vicryl 4-0 (Ethicon).

Figure 1 shows the creation of the defects, implant placement, addition of bone substitute and membrane placement, as well as radiographs of the defects before and after addition of the bone substitute material.

This study details the comparison of the two bovine bone graft materials, test and control DBBM, placed in conjunction with implants containing an SLActive surface. In accordance with the principle of 3 Rs (reduce, refine, replace), the results comparing the effect of SLA and SLActive implants in bovine graft material (cerabone) compared with allograft (maxgraft) is the subject of a separate paper.[28] The study adopted a split-mouth design with a contralateral arrangement of implant types (SLActive and SLA) and three defect/implantation sites per hemimandible. For this study, only hemimandibles with SLActive implants were considered. Different bone graft materials were allocated to mesial, middle, and distal defects in a rotating fashion; ie, sample numbers for the corresponding positions were n = 4, n = 3, and n = 3 for Bio-Oss and n = 3, n = 4, and n = 3 for cerabone, respectively. Samples were randomized and blinded for histomorphometric analysis.

After 8 weeks and 12 weeks, the minipigs were sacrificed (five at each time point) by an intracardiac injection of a 20% solution of pentobarbital (Pentobarbital-natrium, Apoteket, 60 mg/mL).

Sample Preparation and Processing

Block sections of the implant sites with surrounding intact soft tissues were prepared using an oscillating autopsy saw. The mandibles were fixed in formalin (formaldehyde 4% solution) for 2 weeks with repeated change of formalin every second day, prior to nondecalcifying histologic processing.

Histology and Histomorphometry

Histologic and histomorphometric assessment was performed as previously described.[29]

The buccolingual sections with the augmented areas of the circumferential defects were analyzed for distance from the implant platform (platform between cover screw and implant) to the first bone-to-implant contact (fBIC; buccal and lingual, µm), total bone-to-implant contact (BIC; buccal and lingual, µm), and composition of tissues in the augmented defect area (4 mm deep and 2 mm around the implants).

Statistical Analysis

Descriptive statistics were performed by biomaterial, and a paired *t* test and Wilcoxon signed-rank test were used to evaluate differences between the biomaterials.

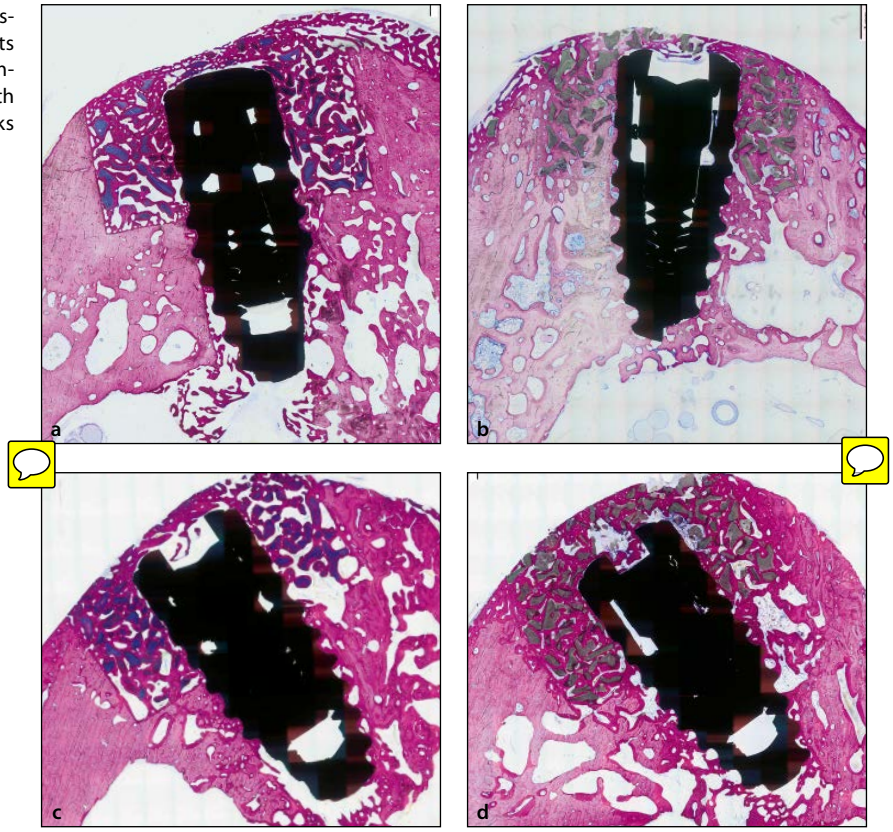

Fig 2 Representative buccolingual histologic sections of circumferential defects after placement of Bone Level Tapered implants and simultaneous augmentation with *(a, c)* control or *(b, d)* test DBBM *(a, b)* 8 weeks or *(c, d)* 12 weeks after implantation.

RESULTS

Recovery from surgery and subsequent healing were predictable and unremarkable in all animals. One implant in the control group was lost in the 8-week assessment group during the healing period. No other surgical or postsurgical complications or indications for peri-implant inflammation were noted at termination.

Descriptive Histology

As indicated by the histologic cross sections after 8 and 12 weeks of healing in Fig 2, the native bone of the implant bed could be well differentiated from the newly formed bone in the augmented area; bone substitute particles could be equally well differentiated. Good bone apposition and integration of the DBBM particles into newly formed bone, as well as good bone apposition to the surfaces of the Bone Level Tapered implant, were observed in both groups. Coronal aspects of the implants and healing caps were partly overgrown with newly formed bone. Within the defect, newly formed bone furthermore appeared to be more porous at the apical region of the defect compared with the coronal aspect. This qualitative observation seemed to be more pronounced in the control group compared with the test group. Furthermore, qualitative differences with regard to the size and shape of the tested bone graft particles became apparent. Specifically, control bone graft particles appeared to be more elongated and smaller in diameter compared with the more homogenous and relatively larger-sized particles in the test group.

Histomorphometric Analysis

No qualitative differences could be observed between the test and control groups after 8 or 12 weeks of healing (Table 1). As evidenced by the corresponding box plots in Figs 3a and 3b, fBIC values in both groups were highly comparable after 8 weeks of healing (mean buccal fBIC of –343.0 ± 609.0 µm in the test group and –380.3 ± 554.2 µm for the control group), with slight differences observed on the lingual side (mean lingual fBIC of –404.5 ± 579.2 µm for the test and –493.8 ± 576.5 µm for the control material). The percentile and minimum and maximum values of fBIC for both groups were again widely comparable.

Similarly, there were no significant differences in mean fBIC values between the groups at 12 weeks (mean buccal fBIC of –681.4 ± 984.3 µm for test and –281.5 ± 634.1 µm for the control group and mean lingual fBIC of –568.1 ± 970.8 µm for test and –217.0 ± 541.3 µm for the control group). Slight differences between the

Table 1 First Coronal Bone-to-Implant Contact (fBIC), Percentage Buccal and Lingual Bone-to-Implant Contact (%BIC), and Percentage of Bone and Bone Substitute for Test and Control Groups at 8 and 12 Weeks

	8 weeks		12 weeks	
Outcome/Parameter	**Test**	**Control**	**Test**	**Control**
fBIC - buccal (µm)				
N	5	4	5	5
Mean ± SD	–342.99 ± 608.97	–380.28 ± 554.24	–681.43 ± 984.33	–281.48 ± 634.07
Median (Q1 to Q3)	0 (–734.74 to 113.89)	–220.86 (–799.24 to 38.69)	0 (–1,424.27 to 0)	0 (–57.59 to 19.13)
fBIC - lingual (µm)				
N	5	4	5	5
Mean ± SD	–404.49 ± 579.17	–493.75 ± 576.47	–568.12 ± 970.76	–217.84 ± 541.28
Median (Q1 to Q3)	0 (–891.34 to 0)	–494.43 (–992.25 to 4.75)	0 (–1,050.3 to 104.11)	0 (0 to 16.68)
Percent BIC of circumference - defect area, buccal (%)				
N	5	4	5	5
Mean ± SD	62.61 ± 9.49	67.33 ± 18.25	65.77 ± 27.55	71.26 ± 18.16
Median (Q1 to Q3)	60.51 (59.66 to 65.31)	70.78 (53.05 to 81.61)	78.09 (47.96 to 81.26)	74.61 (63.35 to 83.48)
Percent BIC of circumference - defect area, lingual (%)				
N	5	4	5	5
Mean ± SD	63.16 ± 10.19	69.64 ± 17.11	59.76 ± 13.97	69.06 ± 9.57
Median (Q1 to Q3)	58.01 (56.47 to 67.49)	71.950 (57.86 to 81.4)	59.97 (55.29 to 70.75)	70.67 (62.23 to 77.50)
Percent BIC of circumference - osteotomy area, buccal (%)				
N	5	4	5	5
Mean ± SD	65.33 ± 13.83	71.49 ± 17.99	75.12 ± 12.12	64.86 ± 19.13
Median (Q1 to Q3)	60.69 (54.32 to 75.65)	67.89 (57.21 to 85.77)	74.41 (66.18 to 84.85)	71.71 (46.15 to 78.46)
Percent BIC of circumference - osteotomy area, lingual (%)				
N	5	4	5	5
Mean ± SD	77.27 ± 6.04	74.09 ± 8.80	73.06 ± 19.33	77.91 ± 20.53
Median (Q1 to Q3)	78.52 (74.03 to 79.25)	71.37 (68.26 to 79.92)	72.26 (59.35 to 83.07)	85.33 (77.61 to 90.68)
Percent BIC of circumference (%)				
N	5	4	5	5
Mean ± SD	68.59 ± 7.79	70.93 ± 11.08	69.96 ± 15.24	71.07± 14.49
Median (Q1 to Q3)	65.24 (63.62 to 71.50)	73.62 (62.50 to 79.35)	71.92 (59.97 to 83.08)	75.46 (75.41 to 77.13)
Percent bone of total defect area (%)				
N	5	4	5	5
Mean ± SD	46.70 ± 5.07	47.02 ± 4.78	48.69 ± 4.01	47.82 ± 7.27
Median (Q1 to Q3)	47.39 (46.45 to 48.12)	47.24 (43.00 to 51.04)	49.51 (46.85 to 50.30)	46.54 (43.27 to 53.26)
Percent bone and substitute of total defect area (%)				
N	5	4	5	5
Mean ± SD	77.84 ± 6.93	73.16 ± 9.15	75.04 ± 13.87	72.84 ± 8.80
Median (Q1 to Q3)	81.32 (73.08 to 82.28)	71.70 (66.21 to 80.11)	81.34 (69.59 to 84.15)	69.51 (65.69 to 79.58)

groups were only observed with respect to the variability of the fBIC values as expressed by the 25th percentile and minimum fBIC values on the buccal and lingual side, which were markedly lower for the test group. On the lingual side, the values for the 25th percentile and lowest fBIC were –1,555.0 µm and –2,059.6 µm, respectively, in the test group compared with –592.2 µm and –1,184.4 µm, respectively, in the control group. On the buccal side, the values for the 25th percentile and lowest fBIC were –1,733.0 µm and –2,041.0 µm, respectively, in the test group compared with –736.0 µm and –1,414.0 µm, respectively, for the control group. Differences between the groups were not statistically significant.

The box plots of BIC values indicate that implant integration for the control and test groups were comparable at both healing time points (Figs 3c and 3d). Specifically, after 8 weeks, mean BIC for the test group was 62.6% ± 9.5% and 63.2% ± 10.2% on the buccal and lingual sides, respectively, compared with 67.3% ± 18.3% and 69.6% ± 17.1%, respectively, for the control group. Mean values on the buccal side increased slightly in both groups at 12 weeks (65.8% ± 27.6% and 71.3% ± 18.2% for the test and control groups, respectively), while corresponding values on the lingual side remained static for the control group (69.1% ± 9.6%) and slightly regressive in the test group (59.8% ± 14.0%). The variability of the values was comparable for both

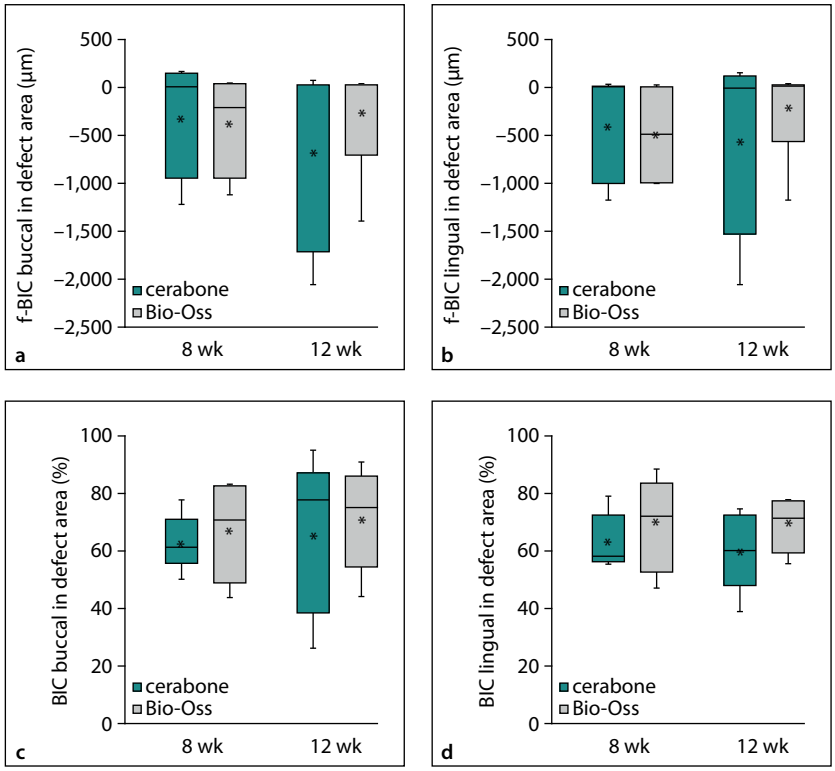

Fig 3 *(a)* Buccal and *(b)* lingual first bone-to-implant contact as the distance from the implant platform to the first coronal bone-to-implant contact (fBIC). *(c)* Buccal and *(d)* lingual bone-to-implant-contact (BIC) as determined in the augmented area on the coronal 4 mm of the parallel parts of the implant. Horizontal bars show median values, + signs indicate mean values, boxes designate the 25th and 75th percentile values, and error bars designate minimum and maximum values.

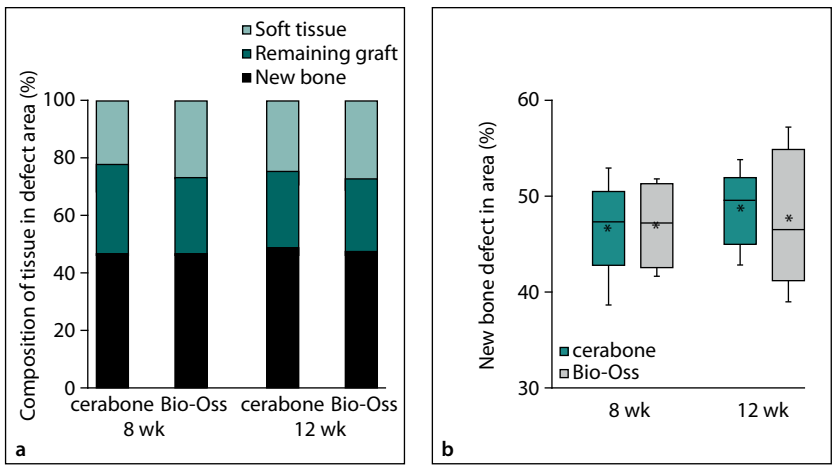

Fig 4 *(a)* Mean composition of tissues in the circumferential defect as determined in a region of interest (ROI) of 4-mm height in the augmented area of the circumferential defect 2 mm around the implants and *(b)* percentage of newly formed bone in the defect area. Median values are indicated by horizontal lines, + signs show mean values, boxes delineate the 25th and 75th percentile values, and error bars indicate the minimum and maximum values.

groups, except for slightly greater variability in buccal BIC at 12 weeks in the test group. The 25th percentile value was 37.5% for the test material at 12 weeks compared with 53.9% in the control group. Differences between groups were not statistically significant.

As illustrated by the plots of the relative tissue composition in the augmented area and the amount of newly formed bone in Figs 4a and 4b, no significant differences were observed between the groups at either 8 or 12 weeks. The amount of remaining bone graft and soft tissue were comparable between the groups and stayed constant at approximately 30% and 25%, respectively. Box plots of median, mean, 25th and 75th percentile, and the minimum and maximum values of the percentage of newly formed bone in the defect area (Fig 4b) revealed no statistically significant difference between the test and control groups. The mean relative amount of newly formed bone in both groups was approximately half of the total tissue in the defect (test: 46.7% ± 5.1% vs control: 47.0% ± 4.8% after 8 weeks) and slightly increased at 12 weeks (test: 48.7% ± 4.0% vs control: 47.8% ± 7.3%) for both groups.

DISCUSSION

This comparative study examined the implant integration and bone formation around titanium/zirconium implants upon simultaneous augmentation of two different types of DBBM (test, cerabone vs control, Bio-Oss) in a circumferential defect model in minipigs. The study demonstrated that: *(1)* all defect sites were equally filled with newly formed bone, and the DBBM became equally incorporated into newly formed bone; *(2)* the amount of residual DBBM after 8 and 12 weeks was equivalent in both groups, with no significant resorption of DBBM; *(3)* the implant integration as indicated by the amount of newly formed bone around the implant (BIC) was comparable in both groups; *(4)* there was no difference between the groups in the coronal height of newly formed bone along the implant surface (fBIC); and *(5)* qualitative morphologic differences were noted with regard to the size and shape of bone particles and their integration into newly formed bone.

Difference Between Biomaterials

The control material represents one of the most extensively studied types of DBBM, while the test DBBM has been recently introduced into dental applications from the orthopedic field.[5,30] Both materials are produced from bovine bone and have similar chemical composition and structure.[5,8,15] The main difference between both materials is related to the manufacturing process. The control DBBM is manufactured via heat treatment at moderate temperatures of < 300°C followed by alkaline treatment, while the test material is sintered at high temperature (> 1,200°C) to remove any organic component. This high-temperature sintering has been reported to ensure complete removal of organic substances, while preserving the macroscopic trabecular structure of the bone mineral. Specifically, Tadic and Epple compared the physicochemical properties of both materials in detail and reported that the crystal structure of the control material is comparable to that of natural bone, while the test material is highly crystalline due to the heat treatment; it has therefore been classified as less bioresorbable compared with the control material.[15] Trajkovski et al have furthermore compared the herein-tested bone graft materials with regard to the hydrophilicity and their viscoelastic and physicochemical properties, which can be associated with their handling, regenerative potential, and clinical outcome.[31,32] As reported by the authors, control and test materials displayed significantly different hydrophilicities and associated abilities to adsorb blood, with the control material displaying the lowest and the test material showing the highest hydrophilicity of all materials tested within their study. The results of this study may contribute to the question of whether the difference in manufacturing process and physicochemical properties has any implications on new bone formation and implant integration.

Integration of Biomaterial and Resorption Characteristics

The results of this study indicated that both tested DBBMs comparably and adequately integrated into newly formed bone under negligible resorption, resulting in a matrix of living tissue within the defect area (bone aggregate). These results are in good agreement with other studies, which have reported new bone formation and integration of the control material into bone, with osteoconduction as the primary mechanism of bone formation but overall slow resorption.[8,11,19] Considering the test material, studies on comparable high-temperature sintered DBBM have reported good integration combined with slow resorption characteristics as well.[5,30,33] Specifically, the values of remaining bone substitute reported in this study were not significantly different between the groups (31.1% ± 3.2% and 26.4% ± 10.1% for the test material at 8 and 12 weeks, respectively, compared with 26.1% ± 13.2% and 25.0% ± 3.6% at 8 and 12 weeks, respectively, for the control material). These values compare well with other reports of similar investigations in various animal models. An analysis of the resorption characteristics of the control material in bone defects in dogs reported, eg, 17% remaining xenograft in the tissue of healed defects after 3 months.[8] In a circumferential defect model in monkeys 6 months after surgery, remaining DBBM accounted for approximately 21% of tissue.[19] A study of the control DBBM in cylindrical defects in dog mandibles reported that 26.4% of the defect area was occupied by DBBM after 3 months.[34]

The slow resorption of DBBM has been further confirmed by long-term studies of the control DBBM and comparative clinical studies of test and control DBBMs.[20,21,25,26] In a split-mouth, bilateral sinus augmentation study of test and control DBBMs, bone formation in both groups was comparable after 8 months, while the resorption of the DBBM in both groups was reported as very low.[25] An earlier investigation comparing both materials in the same indication at 8 months and 1 and 4 years after surgery showed a significantly higher volumetric loss for the control compared with the test material, which was most pronounced after 4 years.[35] The higher volumetric loss associated with the control material could be correlated with a higher rate of calcium release and smaller crystallinity compared to the higher crystallinity of the high-temperature sintered test material.[36,37] The time points chosen in this study revealed no differences between both materials in terms of bone integration and resorption kinetics. Since the differences in new bone formation and biomaterial

integration are small between the 8- and 12-week time points, it is suggested that most of the healing process occurred within the first 8 weeks. The results of this study show good osseointegration for both materials. Potential differences in early healing processes could not be assessed. Also, the differences in resorption kinetics between the materials were negligible. As shown in numerous studies, the resorption of DBBM is a long-term process, and therefore, this study was not designed to find differences between the groups. A recent study analyzed the bone-to-biomaterial interface and biomaterial mineral degradation in bone biopsy specimens following sinus augmentation with DBBM (Endobon).[38] Interestingly, elemental analysis showed a significantly higher Ca/P ratio in the residual biomaterial compared with the biomaterial interface and new bone suggesting a gradual diffusion of Ca ions from the biomaterial into the newly forming bone as part of the biomaterial resorption process. The possibility that the lower variability of fBIC values for the control material compared with the test material might be associated with possible differences in Ca release between both tested materials may warrant further investigation.[38]

Qualitative differences with regard to the size and shape of bone graft materials as well as with regard to the morphology and overall structural porosity of the newly formed bone between both groups were identified. Although these differences did not translate into differences in the histomorphometrically derived parameters, they might be attributed to the differences in physicochemical characteristics as reported by Trajkovski et al.[32] As the authors have specifically reported differences in particle size and hydrophilicity between the materials, the apparent higher porosity of newly formed bone at the apical aspect of the defects might be, eg, attributed to a better ability of the test material to be compacted into the defect that might be associated with its higher hydrophilicity and stronger tendency to take up blood.

Implant Integration and Coronal Bone Height in Circumferential Defects

The outcomes of this study demonstrated good osseointegration and bone volume stability in a particularly challenging model mimicking implant placement in fresh extraction sockets with a simultaneous bone grafting procedure. The challenges of having circumferential coronal defects at implant placement were previously described in another study.[39] Circumferential defects with different diameters (0, 0.5, 0.975, and 1.35 mm) were created in the mandibles of mongrel dogs. After a healing period of 8 weeks, BIC in the defect area and fBIC were histologically evaluated. The results show that the BIC almost linearly decreased with increasing width of the gap, while the distance from the implant shoulder to the first bone contact (fBIC) increased. The same trend was observed in a clinical case study where the mean BIC decreased with increasing horizontal defect dimension of the extraction sockets.[40] Even though this case study only analyzed five implant sites, it suggests that this trend observed in preclinical studies is transferable to the clinical situation. The importance of using bone graft materials in marginal bone defects was shown in another study using a similar defect model.[41] In the study, 5-mm-deep defects, 1.35 mm around the implants, were created in the mandibles of dogs and were either filled with Bio-Oss or autogenous bone or left empty. A conventionally placed implant without a marginal bone defect served as a positive control. After a healing period of 3 months, BIC, fBIC, and bone area within the defect were histologically evaluated. Interestingly, the control and the nongrafted groups were widely comparable in all evaluated parameters. Both grafted groups showed significantly lower fBIC values and higher bone area within the defect compared with the control and nongrafted groups. Furthermore, the mean values for BIC were higher for the grafted groups compared with the control and nongrafted groups. These findings are in line with the results from Akimoto et al[39] and demonstrate the feasibility and importance of implant placement with simultaneous bone graft procedures in circumferential bone defects. The stabilization of the coronal bone height observed in this study is in line with the results of another study using a monkey model. Coronal bone heights of 100%, ie, up to the most coronal point of the implant, were reported for groups treated with a combination of membrane and DBBM after 6 months.[19] This is consistent with the fBIC values in the present study. A recent study analyzed bone formation and apposition at titanium implant surfaces in circumferential defects in a dog model for various types of bone graft materials.[42] The authors reported BIC values of 18% and 26% in the Bio-Oss group after 8 and 16 weeks, while the volume of newly formed bone decreased from 45% to 31% in the same time period. Although the values are lower than for this study due to the different animal model, the defect model is comparable to that used in the present study with respect to the use of contained membrane-covered defects. These kinds of defects are well characterized and provide ideal stabilization of the graft material to allow precise comparison of the effect of different bone substitutes and their properties on bone formation and implant integration.[19,42] With regard to fBIC values, it furthermore needs to be considered that implants healed fully submerged and covered by the membrane in the model herein. Bone formation was partly observed on the coronal aspect and over the implants and cover screws, which indicates that the model might result in higher fBIC values compared with transmembrane or transgingival healing.

CONCLUSIONS

The histomorphometric comparison of the two natural bovine bone minerals, Bio-Oss and cerabone, indicates that bone formation, implant integration, and crestal bone height relative to the coronal aspect of the implant were equivalent and temporally stable for both materials when used for simultaneous augmentations as part of implant placement. Greater variability of bone height and implant integration as observed in the cerabone group might possibly be related to the extent and geometry of the circumferential defect. Within the limitations of this study, the results support the use of cerabone as an alternative bovine bone mineral in procedures involving implant placement with simultaneous bone augmentation, especially in indications requiring extended volume stability and slow resorption of the graft material.

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