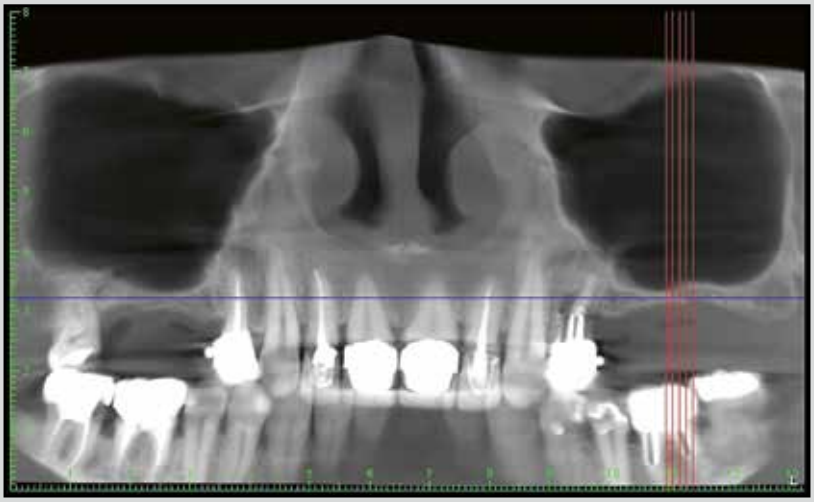

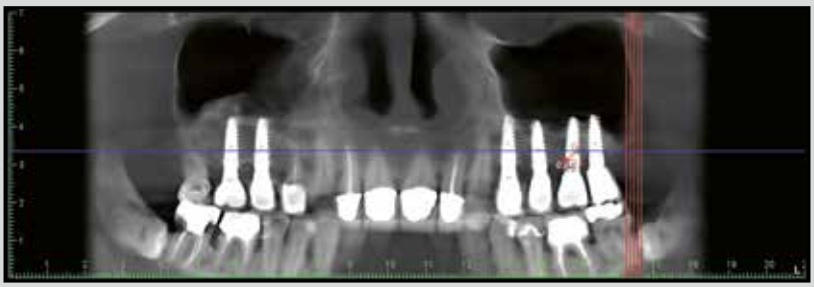

Supercritical CO_2 Viral-Inactivated Allogenic Bone Graft in Maxillary Sinus Augmentation Procedures: 10-Year Retrospective Clinical and Radiographic Results

Jean-Jacques Chalard, DDS[1]

The aim of this retrospective study was to evaluate the long-term performance of the supercritical CO_2 (Supercrit, BIOBank) viral-inactivated bone allografts in maxillary sinus augmentation. Thirty-four consecutive patients underwent 50 maxillary sinus augmentation procedures, and 103 implants were placed. At a mean of 8.8 years after graft surgery, 95 implants were well osseointegrated and functioning. Eight implants failed, and the overall implant survival rate at 10 years was 92.2%. The marginal bone loss averaged 1.2 ± 1.3 mm. Within the limitations of this study, the supercritical CO_2 viral-inactivated bone allograft is a valuable bone graft material, achieving long-term satisfying outcomes when used alone.
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Performing sinus floor augmentation to achieve sufficient bone for implant placement is a successful technique, and the use of autogenous bone is considered the gold-standard bone grafting material due to its potential osteoconduction, osteoinduction, and osteogenic properties and the limited risk of disease transmission.[1–3] Autogenous bone is harvested from extraoral sites (such as the iliac crest, cranial arch, and tibial plateau) and from intraoral sites (such as the mandibular symphysis, tuberosity of the maxilla, and ramus).[3] However, its use has several drawbacks, such as limited availability and donor site morbidity.[4] In addition, the use of autogenous bone grafts for sinus augmentation is associated with unpredictable graft resorption.[5,6] To overcome these disadvantages, different substitute materials, such as allografts, xenografts, and alloplastic biomaterials, have been tested and used to fill bone defects.[7] Whether fresh, frozen, or freeze-dried, allogenic bone grafts have several benefits, including reduced surgical morbidity, reduced operating time, and greater availability and quantity compared to autogenic bone.[8,9] Histologic and histomorphometric results demonstrate that allogenic bone has osteoconductive properties comparable to autogenic bone.[10]

Supercritical CO_2 (Supercrit, BIOBank) viral-inactivated allogenic

Fig 1 *Supercritical CO_2 procedure showing the trabecular bone tissue* (a) *before,* (b) *during, and* (c) *after cleaning, with the initial architecture and volume retained at the end of the process.*

bone grafts are exclusively derived from human femoral heads collected from living donors operated on for hip replacement in accordance with European regulations. For cleaning and viral inactivation, the femoral heads are processed using supercritical CO_2 extraction technology based on the delipidation of the bone tissue by a nontoxic fluid and CO_2 in supercritical state combined with a chemical oxidation of the residual proteins located in the pores of the cancellous tissue.[11] The supercritical CO_2 process is totally neutral on the mineral and collagen composition of the bone matrix, preserving the integrity of the trabecular bone tissue and a mechanical strength comparable to fresh bone. Thus, the osteoconductive properties of the supercritical CO_2 processed bone is comparable to autogenic bone.[11–14] Long-term clinical efficacy of bone grafts in maxillary sinus elevation has been largely reported, but there is a lack of such data regarding the use of allogeneic bone grafts.[15,16] The present study aimed to evaluate, for the first time, the 10-year results of maxillary sinus augmentation using the BIOBank supercritical CO_2 viral-inactivated allogenic bone graft with immediate or delayed implant placement. Osseointegration, implant survival, and radiographic changes in the graft area were compared to previous reports of other graft materials.

Materials and Methods

Inclusion and Exclusion Criteria

Patients who received maxillary sinus bone graft in the Oral Surgery Department, Clinique du Parc in Lyon from March 2009 to January 2011 were recruited in this study. The inclusion criteria were as follows: *(1)* at least 18 years of age; *(2)* absence of any local or systemic diseases that may contraindicate the sinus elevation surgical treatment; *(3)* need for bone graft operation for lateral sinus floor augmentation with the supercritical CO_2 processed cancellous bone powder, possibly associated with dental extraction, and immediate or delayed placement of one or several implants; *(4)* having been evaluated preoperatively, immediately postoperative, and at long-term follow-ups by means of CBCT and/or panoramic radiographs; and *(5)* able to read and understand the patient information form.

This study was conducted in accordance with all applicable regulations including the French Data Protection Authority (the CNIL) Reference Methodology MR003 and with the principles of the Declaration of Helsinki. All eligible patients were informed and consented before participating in any study-related activities.

Graft Material Preparation

The graft material used was the BIOBank viral-inactivated cancellous bone allograft powder processed by the supercritical CO_2 technology (Supercrit). The allografts were prepared from living donor femoral heads treated by the supercritical CO_2 process through degreasing steps and a gentle chemical oxidation of the residual proteins (Fig 1) with preserved bone architecture (Fig 2). Before sinus filling, the bone allograft powder drawn from the cleaned femoral head and packed in a syringe or vial

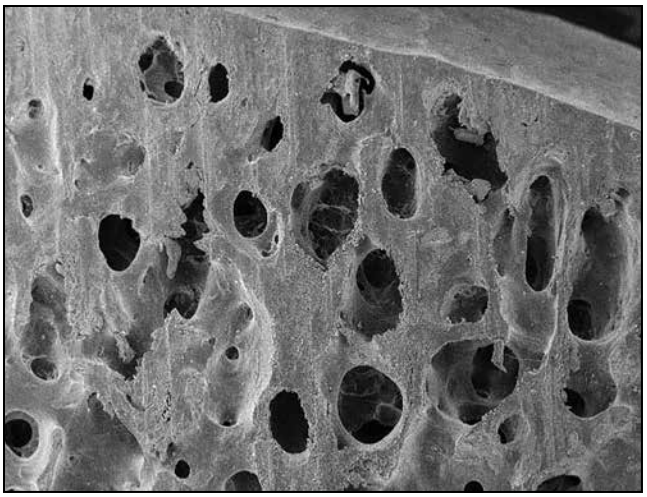

Fig 2 *Cross-section of a processed supercritical CO_2 corticocancellous bone block showing preserved bone architecture, taken with a scanning electron microscope at ×60 magnification.*

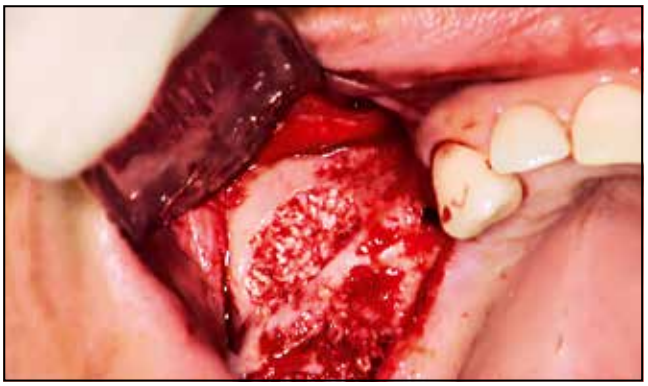

Fig 3 *Supercrit bone allograft (BIOBank) packed into the sinus cavity.*

was hydrated using Metronidazole 0.5% solution (B. Braun).

Surgical Protocol

Partial augmentation of the maxillary sinus underlying the sinus membrane was performed to introduce the allograft material prior to immediate or delayed implant placement. A crestal incision was made with mesial-side discharge of the filling area. A full-thickness flap was elevated to expose the lateral wall of the maxillary sinus. A bony window was created with a diamond-mounted reamer (Komet) on a handpiece (W&H Dentalwerk). Partial augmentation was performed with a piezoelectric insert (Mectron) on an area of about 1 to 2 cm^2 to reduce the risk of membrane perforation, which was pushed back like an eggshell, making a concave shape. The sinus mucosa was elevated inside and up while exposed and still adhering to the bony flap. The membrane was detached using curettes (Laboratoires PRED). If possible, crestal drilling was performed before implant placement. In the event of accidental perforation, Vicryl membrane was used to seal the perforation before introducing the bone graft material through the lateral window with a curette and a rammer (Fig 3). If possible, the implant was inserted immediately, and platelet-rich fibrin membranes were used to cover the vestibular access window to ensure graft stabilization before the hermetic closure with resorbable sutures (4-0 Biosyn, Medtronic). Patients then received prophylactic antibiotic therapy consisting of 2 g of amoxicillin-clavulanic acid per day for 7 days postsurgery.

All patients were assessed preoperatively to determine their dental and general health status, and assessments were performed at the postgrafting follow-up visits. Outcome measures included implant failure (defined as mobility of the implant or the implant requiring removal due to infection or bone loss) and any complication such as chronic pain, sinusitis, or infection.

Radiographic Analysis

Radiographic analysis was performed using CBCT and/or panoramic radiographs taken before and after sinus augmentation and at long-term follow-ups (Fig 4). Software programs were used to calculate bone height in millimeters (Romexis 2D and 3D, Planmeca). The following linear measurements were taken from the radiographs:

- Original sinus height (OSH) prior to surgery, measured from the alveolar crest to the base of the sinus (Figs 4a and 4b).
- Augmented sinus height (ASH), measured from the first bone-to-implant contact point to the base of the maxillary sinus (Fig 4c)
- Marginal peri-implant bone loss (bone loss around the implant

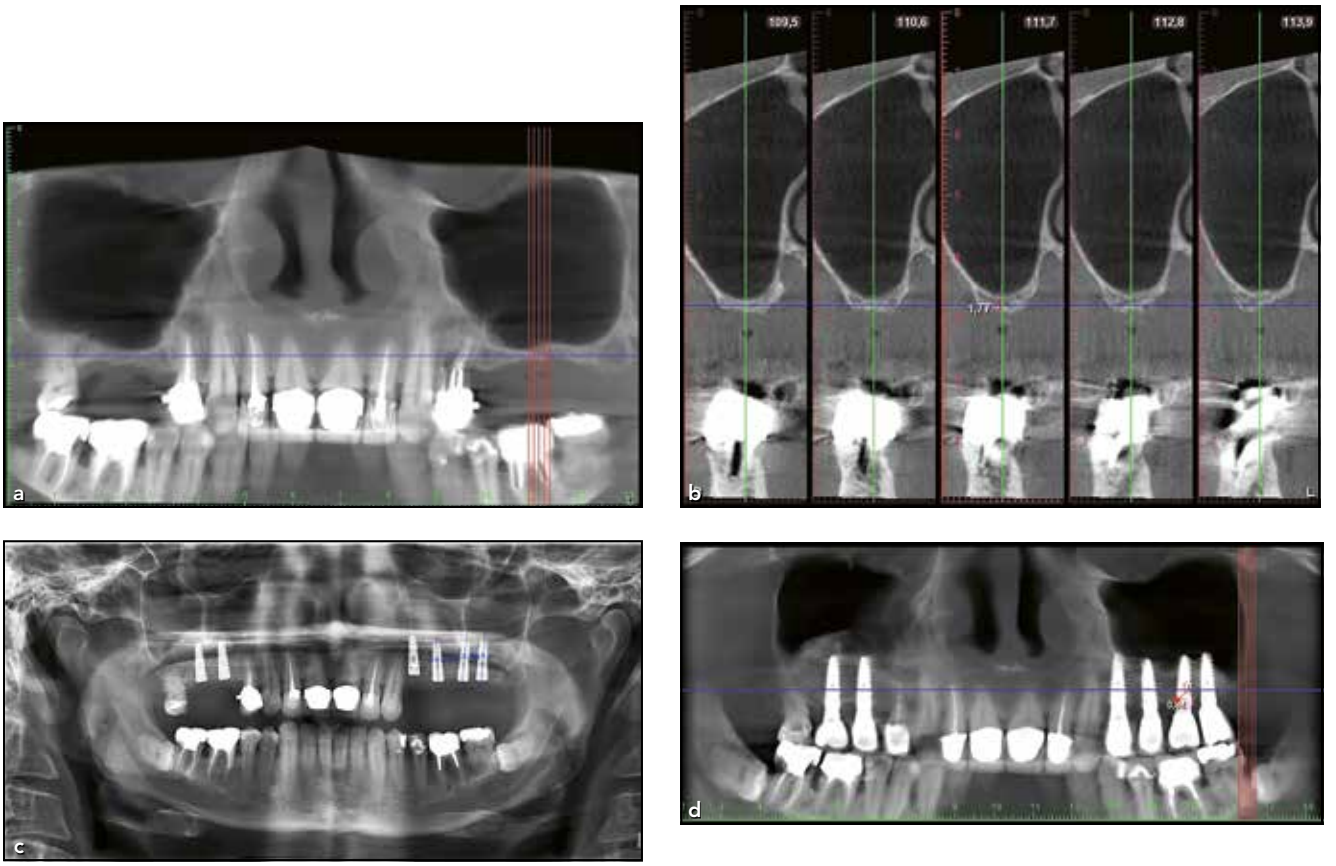

Fig 4 (a) *A preoperative panoramic radiograph shows the atrophic maxillary alveolar bone and the low sinus floor.* (b) *Preoperative CBCT measure of the original sinus height (OSH; 1.77 mm) at future implant position 26 (FDI tooth numbering system).* (c) *The immediately postoperative panoramic radiograph shows the augmented sinus height (ASH; 21.5 mm) after maxillary sinus elevation surgery, measured at implant position 26, and the placement of three implants (positions 25, 26, and 27).* (d) *The 9-year postoperative panoramic radiograph shows evidence of implant osseointegration at all three sites. The peri-implant marginal bone loss measured at the mesial and distal levels of implant 26 were 0 mm and 0.84 mm, respectively.*

shoulder), measured the mesial and distal levels and calculated to a mean value (Fig 4d)

Results

A total of 34 patients (20 women, 14 men) with a mean age of 57.7 years (range: 42 to 75 years) were included in the same center and underwent 50 sinus floor augmentations (16 bilateral cases). All patients received the supercritical CO_2 processed cancellous bone allograft. Only 2 patients were smokers (smoking 10 and 20 cigarettes/day). Demographic details are provided in Table 1.

In total, 103 implants were inserted, 95 (92.2%) simultaneously with the grafting procedure and 8 (7.8%) delayed by 3 to 7 months, as the OSH was < 2 mm. Implants were placed mainly in positions 16, 26, and 27 (FDI tooth numbering system; Fig 5) and were most frequently 13 mm in length and 4.2 mm in diameter (Table 2).

No sinus membrane perforations were reported, and no complications were recorded during surgery. All implants displayed primary stability with an average torque of 50 Ncm, regardless of their design, diameter, and length. The mean follow-up time from graft surgery was 8.8 years (range: 8 to 10 years). During this period, one case of gingival inflammation was reported at 9 years postsurgery with no effect on implant stability. Radiographic results showed a mean OSH of 3.9 mm (range: 1.7 to 8.6 mm) and a mean ASH of 20.0 mm (range: 12.6 to

Table 1 Demographic Characteristics of the Study Patients	
Patients, n	
Total	34
Women	20
Men	14
Mean age, y	57.7
Smokers, n	2
Sinuses, n	50
Implants, n	
Total	103
Simultaneous	95/8
Delayed	8

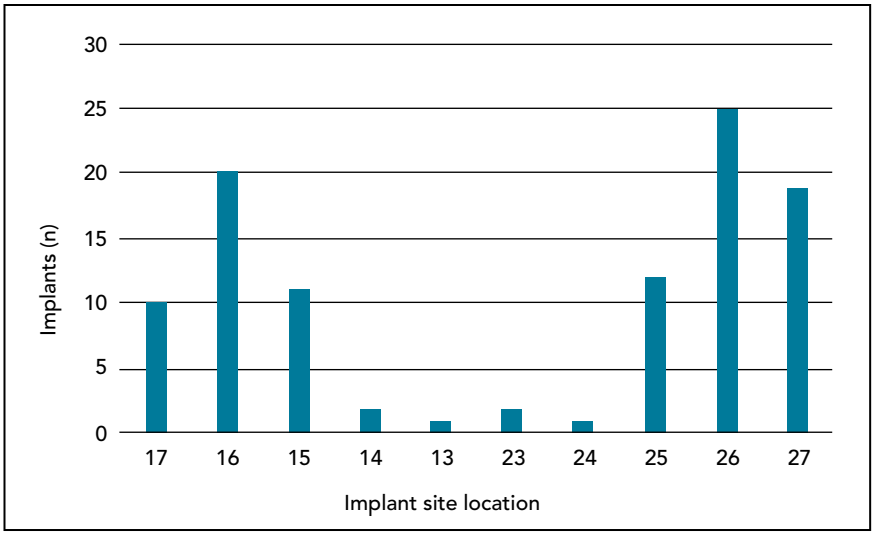

Fig 5 *Distribution of the 103 implant locations in the present study according to the FDI tooth numbering system.*

32.0 mm) postsurgery. The mean bone height gain was 16.5 mm (range: 4.9 to 29.4 mm). The mean peri-implant marginal bone loss was 1.2 ± 1.3 mm up to 10 years. At a mean of 8.8 years postsurgery (range: 8 to 10 years), 95 implants (92.2%) were well osseointegrated and functioning. Comparison between cases with < 4 mm OSH and cases with ≥ 4 mm OSH using chi-square test showed no statistically significant difference between groups (P = .52), with 91.5% and 93.7% osseointegration, respectively (Table 3).

A total of eight implants (7.8%) failed in six patients and were removed: Two implants were removed in one patient, one due to osseointegration failure 4 months after placement near the opening of the gum and the other due to contamination of the graft material without sinusitis. Two implants were removed in two patients at 4 and 5 months postsurgery, respectively, due to sinusitis causing partial rupture of the mucosa and graft material leakage. One implant was removed in one smoking patient 6 months after placement due to insufficient sinus augmentation. Two implants were removed in one patient at 2.5 years postsurgery and one implant in one patient at 6 years postsurgery due to osseointegration failure consecutive to implant malocclusion. All failed implants were placed simultaneously with grafting. The overall implant survival rate at 10 years was 92.2% (range: 87% to 97.4%; Fig 6).

Discussion

Maxillary sinus floor augmentation using the lateral window technique was originally developed by Tatum in the mid-1970s and was later described by Boyne and James in 1980.[17,18] This surgical intervention is still the most frequently used method to increase the alveolar

Table 2 Implant Detail by Implant Type		
Diameter, mm	Length, mm	Quantity, n
MIS SEVEN[a]		
3.75	11.5	1
3.75	13	2
4.2	11.5	17
4.2	13	59
4.2	16	6
5	11.5	3
MIS BioCom External Hex[a]		
3.75	13	8
4.2	13	1
Universal+[b]		
3.75	11.5	2
4.45	13	2
Spiral[c]		
4.2	11.5	2

[a]MIS Implants.
[b]Euroteknika.
[c]Alpha Bio Tec.

Table 3 Implant Success According to the Original Sinus Height During Follow-up

	Implant outcome			
Original sinus height	Osteointegrated, n (%)	Failed, n (%)	Total, n (%)	*P*
< 4 mm	65 (91.5)	6 (8.5)	71 (100)	.52
≥ 4 mm	30 (93.7)	2 (6.3)	32 (100)	
Total	95 (92.2)	8 (7.8)	103 (100)	

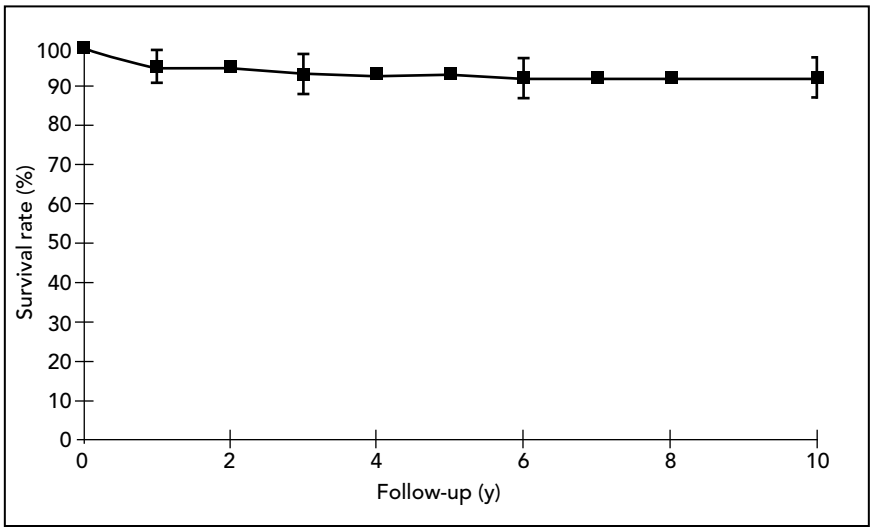

Fig 6 *Kaplan-Meier cumulative survival rate (with 95% confidence intervals) throughout the follow-up period.*

bone height of the posterior maxilla, with immediate or delayed implant placement (4 to 12 months after the transplant), and the results of the treatment have been reported in several systematic reviews.[1,2] Oral implants inserted into sinuses augmented with autogenous bone grafts have shown good long-term clinical results.[1,2] However, the scientific literature have reported unpredictable autograft resorption.[5,6] Additionally, their availability is limited, and morbidity related to the second surgical site is not negligible.[4] Among the alternative solutions to autografts, allogenic bone use has shown that bone allografts constitute a suitable alternative in terms of implant osteointegration, bone neoformation, and quality of the new bone tissue.[10]

Most of the available bone allografts (freeze-dried and demineralized freeze-dried) are derived from cadaver bone and processed through several methods, including physical debridement to remove soft tissue, ultrasonic washing to remove remnant cells and blood, and the use of strong organic solvents for delipidation and viral-inactivation.[19] The bone allografts in the present study are exclusively derived from living donors' femoral heads collected after hip replacement surgery and processed by supercritical CO_2 extraction technology. The supercritical CO_2 process—commonly used in the pharmaceutical and food industries for the splitting, extraction, and decontamination of organic materials—is the combination of a degreasing step by supercritical CO_2 and a gentle chemical oxidation of the residual proteins of the bone network. As shown by preclinical studies, this process applied to bone has neutral effects on the bone tissue composition and preserves its architecture and mechanical properties, particularly its high wettability, thus increasing its performance.[12–15]

The present study reported for the first time the long-term clinical performance and safety of the supercritical CO_2 viral-inactivated bone allograft used in sinus augmentation procedures.

Risks and complications of sinus augmentation include perforation of the sinus membrane, intraoperative or postoperative hemorrhage, infection, graft resorption, and loss of the graft or implants. In the sinus, some patients lose tightness of the sinus membrane. Sometimes, the perforation of this membrane is the origin of infection complications likely to occur within a fairly long period after the intervention. The negative

Table 4 Comparative Results of Maxillary Sinus Augmentation with Different Graft Materials

Study, y	Patients, n	Sinuses, n	Graft material	Implants, n	Residual bone height, mm	Follow-up, y	Implant survival rate	Marginal peri-implant bone loss, mm
Present study, 2021	34	50	Allogenic bone (Supercrit, BIOBank)	103	3.9	10	92.2%	1.2 ± 1.3
Scarano et al, 2010[21]	113	153	Porcine mixed bone particles (Apatos, OsteoBiol)	264	2–3	5	92%	2.6 ± 1.4
Caubet et al, 2011[22]	34	40	50% DBBM (Bio-Oss[a]) and 50% autogenous bone	63	< 4	5	96.9%	NR
Oliveira et al, 2012[23]	10	13	DBBM (Bio-Oss[a])	24	< 4	9	100%	NR
Cannizzaro et al, 2013[24]	20	20	50% DBBM (Bio-Oss[a]) and 50% autogenous bone	44	3–6	5	88.6%	0.7 ± 0.4
Mordenfeld et al, 2014[25]	20	30	80% Bio-Oss[a] and 20% autogenous bone	79	< 5	10	93.6%	1.5 ± 0.9
Lutz et al, 2015[26]	23 24	23 24	Autogenous bone Bio-Oss[a]	70 98	3.3 2.7	5	97.1% 94.9%	NR NR
Mordenfeld et al, 2016[27]	11	22	Bone Ceramic[b] (n = 11 patients) Bio-Oss[a] (n = 11 patients)	24 23	< 5	5	91.3% 91.6%	0.5 ± 0.7 0.7 ± 1.1
Khoury et al, 2017[28]	118	198	Phycogenic HA/autogenous bone	578	< 6	10	99.4%	NR

DBBM = deproteinized bovine bone mineral; HA = hydroxyapatite; NR = not reported.
[a]Geistlich.
[b]Straumann.

influence of membrane perforation on implant survival has also been reported, with a lower implant survival rate in sinus elevations with perforated membranes (69.5%) compared to those with intact membranes (100%).[20]

In the present study, implant failures occurred mainly due to maxillary sinusitis, implant malocclusion, and graft material contamination consecutive to the gum opening, without sinusitis. The mean implant survival rate with the supercritical CO_2 viral-inactivated bone allograft was 92.2% at 10 years, comparable with the mean survival rates reported in the scientific literature after 5 to 10 years (88% to 100%) for autogenous bone graft, a mixture of autogenous bone graft and bone substitutes, or bone substitutes alone (Table 4).[21–28]

Marginal peri-implant bone loss of 1.5 to 2 mm around the implant neck during the first year after functional loading has been consid-

ered a successful outcome.[29] However, tissue stability is expected at 1 year after placement, with a loss of < 0.2 mm per year.[30] Previous scientific literature has reported long-term marginal peri-implant bone loss between 0.5 and 2.6 mm with various bone graft materials.[21–28] With the supercritical CO_2 viral-inactivated allogenic bone graft in the present study, the mean marginal peri-implant bone loss at the 10-year follow-up was 1.2 mm, which is comparable with other graft materials (Table 4).

Conclusions

The clinical and radiographic results of the present retrospective study using the supercritical CO_2 viral-inactivated bone allograft for bone grafting are consistent with those reported in studies using other graft materials, thus confirming the long-term osseointegration of this material. Limitations include the uniformity of data collection and the heterogeneity of the follow-up.

Acknowledgments

The author declares no conflicts of interest.

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