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REVIEW ARTICLE

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Fresh-frozen allogeneic bone blocks grafts for alveolar ridge augmentation: Biological and clinical aspects

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Abstract
The possibilities for oral bone regeneration procedures vary depending on the type of bone defect to be treated, which in turn dictate the type of graft to be used. Atrophic alveolar ridges are non-contained defects and pose a challenging defect morphology for bone regeneration/augmentation. Successful results are regularly obtained with the use of particulate grafts in combination with barrier membranes. In cases of very narrow ridges with need of larger amount of bone augmentation, block grafts are often used. Fresh-frozen allogeneic bone block grafts have been proposed as an alternative to autogenous (AT) bone blocks. Based on a systematic appraisal of preclinical in vivo studies and clinical trials including a direct comparison of fresh-frozen bone (FFB) blocks versus AT bone blocks it can be concluded that a FFB block graft: (a) cannot be considered as a reliable replacement of a AT bone block, and (b) should only be considered in cases where the amount of necessary augmentation—in a lateral direction—is relatively limited, so that the main portion of the body of the implant lies within the inner (i.e., the vital) aspect of the block.

KEYWORDS
autogenous bone, block bone graft, fresh-frozen bone allograft

1 | WHY BONE BLOCK GRAFT FOR ALVEOLAR RIDGE AUGMENTATION?

Edentulism has a high negative impact on people's quality of life and despite the notable advances regarding treatment and prevention of oral diseases, it affects a considerable portion of the global population, that is, about 22% of the word population have some type of edentulism.[1,2] Dental implants are nowadays a standard treatment for the rehabilitation of partially or totally edentulous patients with very good long-term results, in terms of high survival rates of the implants and the prostheses (i.e., around 85%–95% after 10 years in function)[3] and improvement in quality of life.[4]

Proper implant therapy dictates that the implant is fully surrounded by bone; however, tooth loss often causes significant reduction in the alveolar ridge width which may prevent appropriate implant installation,[5,6] despite recent developments in dental implant technology, providing implants of reduced dimensions[7,8] and made of special alloys with increased strength.[9] It is thus common that with the available alveolar ridge dimensions proper implant installation is not possible[10] or a harmonic (aesthetic) result cannot be obtained.[11] Thus, bone regeneration procedures are often needed to generate bone, allowing proper implant installation.[10]

In this context, the possibilities for oral bone regeneration procedures vary depending on the type of bone defect to be treated.[12,13] Bone defects can be divided in confined/contained defects, for example the tooth post-extraction socket[13] or non-confined/non-contained, for example the atrophic (healed) alveolar showing limited bone volume in thickness or height.[12] Bone regeneration procedures in contained defects have better predictability, due the greater number of bone walls that serve as a source of tissue resources (e.g., undifferentiated mesenchymal cells, matrix residing growth factors etc.).[13,14] Further, a contained defect morphology facilitates use of bone grafts in particulate form; bone graft particles exhibit a large contact surface and thus increased potential for osteoconduction.[15]

In contrast, atrophic alveolar ridges are non-contained defects and pose a more challenging defect morphology for bone regeneration/augmentation. This is partly to the reduced tissue resources due to the reduced number/absence of bone walls, but also due to the reduced vascularization of the area associated with the corticalized recipient bed[5,16]; nevertheless, the latter issue is usually easily overcome in the clinic by perforating the recipient cortical bed, providing access to the bone marrow compartment and enhancing bleeding.[16] Another major issue challenging bone augmentation in atrophic ridges is the reduced mechanical stability of the wound complex and of the regenerate after closure and during the early healing period; mechanical stability is important for bone healing per se, but also in terms of space provision regarding the shape/volume of the regenerated bone. In the clinic, mechanical stability of the wound/regenerate in non-contained defects, when particulate grafts are used, is attempted with the use of a membrane and appropriate management (e.g., tightening and fixating the membrane with pins) and/or using reinforced membranes (e.g., with titanium), or using metal meshes.[17,18] Indeed, successful results are regularly obtained with the use of particulate grafts in combination with membranes (i.e., with guided bone regeneration; GBR), more-or-less irrespective of the type of graft.[19] Nevertheless, pre-clinical studies indicate that even with excellent space provision, there may be a limit in the extent of bone regeneration from a horizontal cortical bone wall or defects with limited-due to their shape-bone tissue resources, despite grafting.[20–24] This in turn would translate into that there is a certain limit in the amount of augmentation that can be achieved with GBR and particulate grafts in the clinic. Thus, in cases of very narrow ridges, where there is a need of larger amount of bone augmentation, block grafts can be an alternative. Indeed, larger amounts of alveolar ridge augmentation have been reported with the use of bone block grafts compared with what achieved with particulate grafts.[25,26]

2 | AUTOGENOUS- AND FRESH-FROZEN ALLOGENEIC BONE BLOCK GRAFTS

Autogenous (AT) bone is the most complete grafting material, as it provides not only the bone producing osteoblasts (i.e., osteogenesis), but also provides a scaffold for osteoblasts to proliferate and lay bone upon (i.e., osteoconduction) and osteogenic growth factors, for example, bone morphogenetic proteins, that enhance differentiation and proliferation of undifferentiated cells towards osteoblasts (i.e., osteoinduction).[27] Furthermore, AT bone is gradually largely remodeled (resorbed and replaced) and there are no problems with histocompatibility and immunologic reactions, and obviously there is no risk of disease transmission.[27] Therefore, AT bone grafts are often referred to as the gold standard. Nevertheless, harvesting an AT bone block, has drawbacks; surgery is relatively cumbersome, as it often necessitates the use of a second surgical site, thus adding to patient suffering due to donor site morbidity, extended surgical time, and increased post-surgical pain; there is also a risk for nerve and soft tissue injuries; and occasionally, the quality and quantity of available bone does not allow harvesting of a bone block, for example, in small size jaws after long-term edentulism.[28,29]

Allogeneic (AL) bone, in particular fresh-frozen bone (FFB) blocks (i.e., collected from another human, deceased or alive) have been proposed as an alternative to AT bone blocks[30,31]; AL bone is in general a widely used material, not only in dentistry, but also in orthopedics, with the obvious advantages of unlimited availability and reduced surgical time.[32] Concerns of the past about the use of AL bone, in terms of risk of disease transmission (e.g., hepatitis or HIV) and antigenicity[33,34] have been lessened during recent years due to the very strict guidelines for donor bone tissue sources and processing.[35] For example, in the protocol of the American Association of Tissue Banks, strict screening of the medical and social background of the donors is carried out; for example, no history of infection or infectious potential prior to harvesting, afebrile hospital stay, no respirator >72 h, no chronic or infectious disease, no chronic steroid drug use, no lifestyle associated with high risk of HIV, etc. For the FFB blocks, the harvested bone tissue is specifically processed, including removal of all soft tissues and periosteum, serial washing in sterile saline including antibiotics, and then packed and freezed at temperatures varying from −20°[36] to −40° or −80°.[37,38] In this context, it has been estimated that with the above processing, including the donor screening process, the risk that a FFB graft is contaminated with HIV, is 1 in 8 million.[39]

This processing has the additional advantage that although it devitalizes the very large majority of cells in the bone block, it does not compromise the mechanical properties of the bone block, in contrast with other methods of AL bone processing, for example, freeze-drying under vacuum (lyophilization) and/or demineralization, which weaken the bone block.[40,41] Thus, FFB blocks are very similar to AT bone blocks, regarding structural stability and composition in terms of matrix and growth factors.

3 | FFB VERSUS AT BONE BLOCKS: SYSTEMATIC APPRAISAL OF PRE-CLINICAL IN VIVO AND CLINICAL STUDIES

For an objective evaluation of the potential of FFB blocks in comparison with AT bone blocks for alveolar ridge augmentation, a systematic search of the pre-clinical in vivo and clinical literature was conducted, following a PICO question structure:

I. for pre-clinical in vivo studies: (P) In animals, (I) subjected to bone augmentation, what is the effectiveness of (C) FFB blocks compared with that of AT bone blocks in terms of (O) healing/integration, and/or amount/volume of augmentation/block resorption, and/or dental implant integration.

II. for clinical studies: (P) In patients, (I) subjected to alveolar ridge augmentation, what is the effectiveness of (C) FFB blocks compared with that of AT bone blocks in terms of (O) healing/integration, and/or amount/volume of augmentation/block resorption, or dental implant survival and/or early/late post-surgical complication rate.

Three databases were searched (PubMed, EMBASE, and Scopus), with no time and language restrictions, independently by two evaluators (VXRO and CCM); in case of disagreement on an article, a third evaluator (GJO) decided whether to include or exclude the article. Details of the search as well as of the flowchart of search results are presented in Appendix A and Figure A1.

3.1 | Pre-clinical in vivo studies

Three publications from pre-clinical studies, on bone block augmentation with FFB versus AT bone, using different rabbit models (i.e., mandible,[42,43] tibia[44]) were identified as suitable for inclusion (Table 1). In two of the studies, bone block integration was assessed with histology and immunohistochemistry,[42,43] while in the third study, titanium implant osseointegration in conjunction with bone block grafting was assessed biomechanically and histologically.[44] In general, AT bone blocks showed faster resorption/remodeling and integration compared to FFB blocks, thus AT bone blocks showed some volume loss, while FFB blocks were more stable; further, the vital portion of AT bone blocks was much larger compared with that in FFB blocks, which were mainly acellular (necrotic) irrespective the observation time and integration grade.[42,43] In the single study involving implants, no differences in terms of amount of implant osseointegration, assessed histomorphometrically (i.e., amount of direct bone-to-implant contact; BIC) and with biomechanical testing (i.e., implant removal torque test) was observed.[44]

3.2 | Clinical studies—performance and histological results of FFB blocks versus AT bone blocks

Nine publications from clinical studies, on alveolar ridge augmentation with FFB blocks versus AT bone blocks were identified as suitable for inclusion. Seven publications focused on clinical, histological, and/or aspects of FFB blocks and AT bone blocks,[45–51] while the remaining 2 publications focused on safety and patient-related outcomes[52,53] (Table 2). Of these 9 publications, only 1 regarded a randomized controlled trial[46]; the remaining 8 publications were from non-randomized parallel-arm studies. Most of the studies report on aspects related to FFB block versus AT bone block grating only until implant installation, that is, they do not report on the outcome of implant therapy; only 2 publications refer to outcomes related to the implants installed.[45,51]

TABLE 1 Overview of pre-clinical in vivo studies on bone augmentation with FFB blocks versus AT bone blocks.

Author, year	Animal platform	Sample/design	Methods/analyses	Main outcomes
Hawthorne et al. (2013)[42]	Rabbit mandible	56 New Zealand White rabbits 20 animals, as donors 36 animals grafted FFB block and AT bone block as onlay, bilaterally on the mandible 6 animals sacrificed after 3, 5, 7, 10, 20, and 60 days post-op	Tomography for density and volume assessment Histology Immunochemistry	No differences between FFB and AT bone blocks regarding bone density and volume FFB blocks appeared intact at 20 and 60 days, while AT bone blocks underwent remodeling and were completely incorporated at Day 60
Garbin Junior et al. (2017)[43]	Rabbit mandible	25 New Zealand White rabbits 1 animal, as donor 24 animals grafted FFB block and AT bone block as onlay, bilaterally on the mandible 6 animals sacrificed after 15, 45, 120 and 180 days post-op	Histology Histomorphometry Immunohistochemistry	AT bone blocks presented faster graft integration and more vital bone than FFB blocks after 45 days (47% vs. 32%, respectively)
Ribeiro et al. (2018)[44]	Rabbit tibia	18 New Zealand White rabbits 6 animals, as donors 12 animals grafted Two implants with a block graft (FFB or AT bone), as onlay, on each tibiae All animals sacrificed at 18 weeks post-op	Implant stability (ISQ) Removal torque Histology Histomorphometry	No differences between FFB blocks and AT blocks regarding implant stability, removal torque, bone-to-implant contact, or bone area between the implant threads at 18 weeks

TABLE 2 Overview of clinical studies on alveolar ridge augmentation with FFB blocks versus AT bone blocks.

Author, year, study type	Sample/design	Methods/analyses	Main outcomes	Complications
Chiapasco et al. (2013)[45] Non-randomized prospective	12 patients, 18–84 years 6 patients received FFB blocks; 44 implants were installed 5–9 months after grafting 6 patients received AT bone blocks; 32 implants were installed 4–6 months after grafting Bone-core biopsies harvested during implant installation	Descriptive histology Histomorphometry regarding the relative bone composition in the bone-core biopsies	No differences in the relative bone composition between FFB blocks and AT bone blocks FFB Lamellar bone 24.7 ± 14.7% New bone 28.4 ± 13.3% Bone marrow 46.9 ± 16.9% AT Lamellar bone 25.3 ± 15.3% New bone 22.9 ± 11.0% Bone marrow 51.7 ± 15.7%	FFB 1 patient with early complication; graft loss due to infection 5 patients with late complications; soft tissue dehiscence with exposure of bone, bone sequestration, accelerated graft resorption with no apparent cause, peri-implantitis AT No complications
Spin Neto, Landazuri Del Barrio, et al., (2013)[47] Non-randomized prospective	12 patients, 25–60 years 6 patients received 17 FFB blocks 6 patients received 12 AT bone blocks Bone core biopsies harvested 7 months after grafting	Descriptive histology	All grafts were found to be firm in consistency and well-incorporated to the recipient bed. However, a more clear distinction was observed at the interface of the FFB block and the native bone Large amount of necrotic bone surrounded by few spots of newly formed bone in the FFB block group, suggesting low rate of graft remodeling	No complications
Spin Neto, Stavropoulos, et al., (2013)[50] Non-randomized prospective	26 patients, 21–70 years 13 patients received 19 FFB blocks 13 patients received 19 AT bone blocks CBCTs recorded prior to- and 14 days and 6 monhts after grafting	CBCT (i-CAT Classic) examinations Planimetric measurements on two-dimensional CBCT images of the grafted regions: CBA, changes in bone area; TBA, total maxillary or mandibular bone area	Larger bone graft resorption was seen in patients treated with FFB block than in those treated with AT bone block 6 months following alveolar ridge augmentation FBB TBA Baseline (mm^2) 140.20 ± 51.14 Grafted bone block area (mm^2) 54.39 ± 20.95 TBA 14 days (mm^2) 194.10 ± 56.88 TBA 6 months (mm^2) 182.60 ± 56.07 CBA% −9.33 ± 9.57 AT TBA baseline (mm^2) 165.30 ± 54.14 Grafted bone block area (mm^2) 24.19 ± 8.50 TBA 14 days (mm^2) 187.50 ± 56.65 TBA 6 months (mm^2) 195 ± 65.13 CBA% 2.57 ± 14.62	FFB 1 block exposed 2 blocks lost Survival rate (84.21%) AT No complications

TABLE 2 (Continued)

Author, year, study type	Sample/design	Methods/analyses	Main outcomes	Complications
Lumetti et al. (2014)[46] Randomized controlled trial	24 patients, 24–73 years 12 patients received 12 FFB blocks 12 patients received 12 AT bone blocks Bone-core biopsies harvested 6 months after grafting CBCTs recorded 7 days and 6 months after grafting	Descriptive histology CBCT (i-CAT Classic) examinations Volume change between 7 days- and 6 months after grafting	FFB blocks had lower density than AT bone blocks FBB Density T 7 days (HU) 619 ± 277 Density T 6 months (HU) 685 ± 385.1 Volume change (%) −52% ± 25.87 AT Density T 7 days (HU) 935 ± 250 Density T 6 months (HU) 1086 ± 202 Volume change (%) −25% ± 12.73 There were no differences regarding the new bone, residual bone graft, and bone marrow areas between the groups (no descriptive data were provided)	FFB 1 block totally resorbed. AT No complications
Spin Neto et al. (2014)[48] Non-randomized prospective	34 patients, 27–69 years 20 patients received 54 FFB blocks 14 patients received 20 AT bone blocks Bone-core biopsies harvested 6 months after grafting Mini-implants were placed during implant installation and harvested 4–6 months later	Histomorphometry of bone-core biopsies Evaluation of relative amounts (%) of viable bone (VB), necrotic bone (NcB), and soft tissues (ST) Histomorphometry of mini-implants Evaluation of the bone implant contact (BIC) and bone between the threads (BBT). Complications: Evaluated the blocks lost before the implants placement	Bone biopsies FFB NcB: 43.1 VB: 8.4 ST: 48.4 AT NcB: 55.9 VB: 27.6 ST: 16.4 Mini-implants FFB BIC: 38.1 BBT: 39.7 AT BIC: 47.1 BBT: 42.0	FFB 4 blocks losted (92.59% of FFB survival) AT No complications

(Continues)

TABLE 2 (Continued)

Author, year, study type	Sample/design	Methods/analyses	Main outcomes	Complications
Spin Neto et al. (2015)[49] Non-randomized prospective	Twenty-four patients, 18–69 years 8 patients received 20 cortical FFB blocks (C-FFB) 8 patients received 52 corticocancellous FFB blocks (CC-FFB) 8 patients received 20 AT bone blocks Bone biopsies were harvested 6 months after AT bone- and CC-FFB block grafting, and 8 months after C-FFB block grafting Tomographic images were obtained at baseline, 14 days, and 6 months after grafting for the AT bone- and CC-FFB block groups, and at baseline, 14 days and 8 months after grafting for the C-FFB block group	CBCT (i-CAT Classic) examinations Differences in alveolar ridge area among the various observation times were evaluated by planimetric measurements on two-dimensional CBCT images of the grafted regions: CBA, changes in bone area; TBA, total maxillary or mandibular bone area Histomorphometry of bone biopsies Evaluation of relative amounts (%) of viable bone (VB), necrotic bone (NcB), and soft tissues (ST)	C-FBB TBA Baseline (mm^2): 178.7 ± 35.4 Grafted bone block area (mm^2): 29.4 ± 10.4 TBA 14 days (mm^2): 204.6 ± 29.6 TBA 6 months (mm^2): 211.0 ± 37.8 CBA%: 1.3 ± 14.9 NcB: 83.7 ± 10.8 VB 3.9 ± 4.6 ST: 12.3 ± 8.5 CC-FBB TBA Baseline (mm^2): 136.4 ± 51.3 Grafted bone block area (mm^2): 56.8 ± 17.0 TBA 14 days (mm^2): 193.5 ± 63.9 TBA 6 months (mm^2): 181.2 ± 55.8 CBA%: −8.3 ± 7.1 NcB: 38.2 ± 12.1 VB: 9.3 ± 3.8 ST: 52.5 ± 11.7 AT TBA Baseline (mm^2): 182.9 ± 62.2 Grafted bone block area (mm^2): 27.5 ± 7.4 TBA 14 days (mm^2): 203.3 ± 63.3 TBA 6 months (mm^2): 215.5 ± 76.9 CBA%: 1.5 ± 20.6 NcB: 18.1 ± 17.1 VB: 25.1 ± 11.2 ST: 52.5 ± 11.7	No complications
Dellavia et al. (2016)[51] Non-randomized prospective	Twenty patients, 18–85 years 14 patients with FFB blocks; 69 implants installed 5–9 months after the grafting procedure 6 patients with AT bone blocks; 32 implants installed 5–9 months after the grafting procedure The patients received between 4 and 8 implants. The number of bone blocks placed in each patient was not clearly described	Histomorphometry of bone biopsies Evaluation of relative amounts (%) of lamellar bone (LB) - new bone (NB), and bone marrow spaces (BM)	FFB LB - 31.39% ± 19.41% NB- 21.60% ± 12.88% BM - 47.01% ±17.87% AT LB - 25.34% ± 15.33% NB - 22.92% ± 11.04% BM 51.75% ± 15.74%	FFB Peri-implantitis: 3 cases Implants lost: 5 cases Implant survival: 92.75% Implant success: 88.40% FFB block exposure: 1 case FFB block lost: 4 cases AT Implant survival and success: 100%

Noteworthy, the publications of Spin Neto et al. derive from the same group of patients. In all studies, the FFB blocks were brought to room temperature prior to use, then trimmed and adapted to fit, and fixed onto the perforated recipient bed, with screws; the gaps between the bone block and the recipient bed were commonly filled out with bone particles from the same type of bone as the block (i.e., FFB or AT bone), and everything was covered with a collagen membrane, and submerged; patients received, as standard, systemic antibiotics prophylactically and post-surgically; antiseptic chlorhexidine rinsing was used for several days post-operatively; implants were inserted after a period of 5–9 months of healing (Figure 1).

The histological results reported in the studies derive mainly from bone-core biopsies—harvested by means of trephine burs—during implant placement some months after the augmentation procedure, either from the implant site or from the buccal aspect of the block-augmented alveolar ridge. In 3 publications, from the same research group, the biopsies from the AT bone blocks presented with larger areas with vital bone compared with those from the FFD blocks, which were largely non-vital[47–49] (Figure 2). In particular, one of the publications looked specifically in the histological differences in FFB blocks depending on their spatial architecture in terms of cortical/cancellous bone.[49] In this study, it was observed that primarily cortical FFB blocks, retrieved from the tibia, presented significantly less areas of vital bone, compared with primarily corticocancellous FFB blocks retrieved from the femoral head and/or patella (4% vs. 9%, respectively); in contrast, AT bone blocks, harvested from the ramus (primarily cortical) showed 25% vital bone. Furthermore, higher amounts of non-vital bone were regularly observed in the part of the biopsies representing aspects of the FFB block distant to resident bone. These observations may explain the contradictory

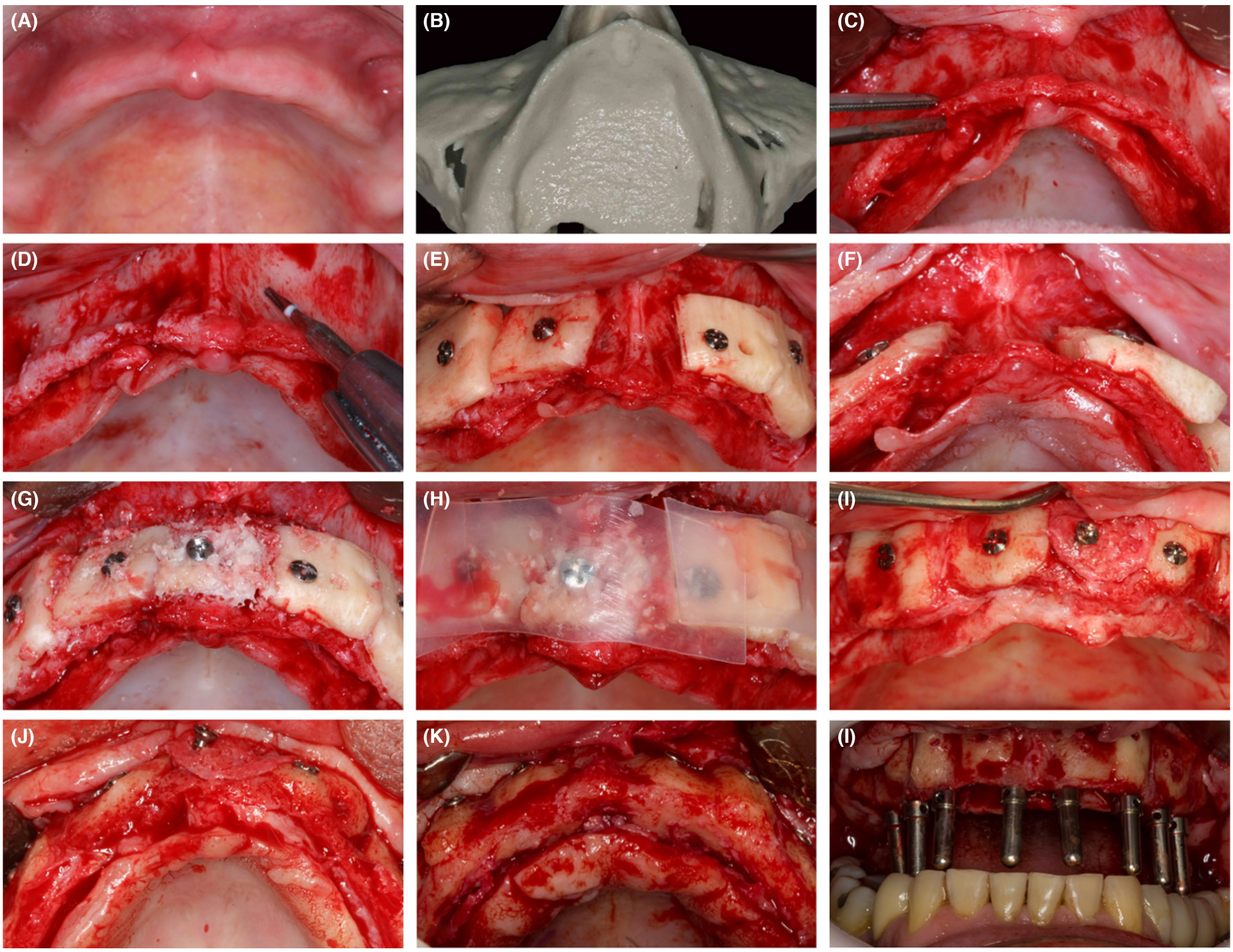

FIGURE 1 Representative case of a patient with a very thin alveolar ridge in the maxilla, treated with FFB block grafting (case provided by Prof. Elcio Marcantonio Jr.). Clinical view (A), 3-D printed model of the maxilla (B), and intra-surgical clinical view (C). First the bone bed was wounded with a bur to provide access to induce bleeding and/or provide access to the marrow (D), then FFB blocks were trimmed and adapted, and fixed in place with screws (E, F), and the gaps in-between the blocks and the bed were filled with particulated FFB (G) and covered with a collagen membrane (H). After about 6 months, the blocks appear well integrated (I) and the alveolar ridge is clearly wider (J), except from the area between tooth 11–21, where the block was loose and had to be removed (K); this event, however, did not preclude installation of implants in the planned position. FFB, fresh-frozen bone.

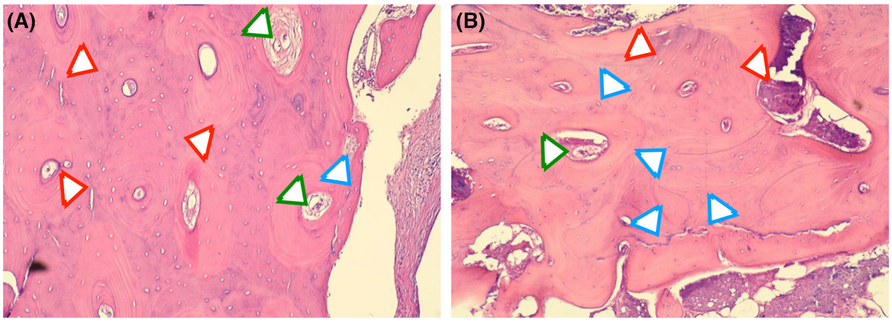

FIGURE 2 Representative aspects from bone-core biopsies from FFB and AT bone blocks, harvested at the timepoint of implant installation, about 6 months post-grafting. (A) The FFB blocks were often largely non-vital, as evident from the empty ostocyte lacunae (red arrowheads), although signs of revitalization could be observed at the periphery of the graft, as evident by the presence of vascular elements within the haversian channels (green arrowheads) and new bone apposition (blue arrowheads). (B) The AT bone blocks were largely vital, as evident from the presence of ostocytes and areas of new bone formation (blue arrowheads), and by the presence of vascular elements within the haversian channels (green arrowheads). Areas where the block was non-vital, as evident from the empty ostocyte lacunae (red arrowheads), were also observed. FFB, fresh-frozen bone.

findings in the remaining 3 publications reporting histological data, where no differences in the amount of vital bone between the two types of bone blocks were observed.[45,46,51] Indeed, in the studies reporting no differences in terms of vitality between FFB blocks and AT bone blocks, corticocancellous blocks from hip were used.[45,46] Nevertheless, the difference in vitality between FFB and AT bone blocks seems not to have a major negative impact on osseointegration; in one of the studies, where mini-implants were intentionally placed perpendicularly to the bone block during the grafting procedure, in order to be retrieved later for histomorphometrical assessment, no significant differences in terms of BIC were observed between implants placed in FFB blocks and AT bone blocks (38.1% vs. 47.1%, respectively).[48]

In terms of block graft volume stability, a larger resorption during the integration face was reported for the FFB blocks compared with the AT bone blocks.[46,49,50] The extent of volume loss seems related to the relative amount of the cancellus component of the graft, that is, more volume loss, the more cancellous the block is[45,49]; however, this property (drawback) of FFB blocks did not compromise implant installation significantly, that is, no big changes in terms of patient rehabilitation were reported in those studies due to bone block resorption. In two of the publications, the impact of FFB block grafting on the immune system was addressed by assessing various inflammatory markers in the systemic circulation of patients receiving either FFB blocks or AT bone blocks, 2 weeks after the grafting procedure[52,53]; these studies showed, that irrespectively from the number of bone blocks used (from 1 to 6 blocks), FFB block grafting seem not to challenge the immune system significantly.

3.3 | Clinical studies—complications with FFB versus AT bone block grafting

A relevant aspect when considering FFB blocks as an alternative to AT bone blocks is potential differences in the rate of early/late complications, either associated with the grafting procedure itself (e.g., block exposure and/or loss) or implant-related complications (e.g., early/late implant loss or peri-implantitis). Indeed, early complications were seldom with AT bone blocks, which seem to almost never fail when the grafting procedure is performed by experienced surgeons. In contrast, FFB block grafting seems to be more prone for early post-operative complications compared with AB blocks grafting. Specifically, wound dehiscence and FFB block exposure was the commonly reported complication, while FFB block loss was a rather rare event and occurred in only a few patients, and regarded only a few of the grafts.[45,48,51] Lack of FFB block integration, is more often a late complication, discovered during second stage surgery for implant installation (Figure 1I–K). Management of wound dehiscence depends on the size of block exposure and the quality of fixation of the block. Smaller exposures with properly fixed blocks can be treated with removal/trimming of the exposed necrotic part of the block and application of chlorhexidine locally; in cases of large wound dehiscence and poor block fixation, the block must be removed.[48,51] When lack of bone block integration is discovered at second stage, then the procedure may need to be repeated or the prosthetic plan revised.[51] In this context, recipient bed perforation to the bone marrow and good adaptation and fixation of the FFB block on the bed, similarly to the standard procedure for AT bone block grafting,[54] are factors considered reducing the risk for block failure.

In the only 2 publications reporting about the implants installed,[45,51] late complications were observed in several patients treated with FFB blocks (e.g., soft tissue dehiscence and bone sequestration, graft resorption, implant associated infection/loss of osseointegration, peri-implantitis), while no remarkable late complications were reported regarding AT bone blocks. The reported implant survival and success rates ranged from 89%–93% and 82%–88%, respectively, regarding the implants installed in the FFB block-augmented sites; no late complications were reported regarding implants inserted in AT bone block-augmented ridges in these studies. Nevertheless, the timeframe the complications occurred, or the implant survival/success rates are referring to, is unclear in these 2 publications. In this context, several, non-comparative studies (i.e., studies not including a direct comparison with AT bone blocks), mostly with short- or medium-term observation time, report high survival rates for implants in FFB block-augmented jaws. For example, in a study with 16 patients and 34 implants, all implants survived from 18 to 30 months,[55] while in another, retrospective, study with an average follow-up of 23 months a survival rate of 99.2% was reported for 133 implants installed in 41 patients.[56] In contrast, relatively low survival rates have been presented in other studies, reporting on long-term outcomes of implants installed in FFB block-augmented jaws. For example, in a study including 45 patients with 262 implants, an implant survival rate of about 91% after an average follow-up time of about 4 years was reported; most of the losses occurred after 3.5 years from implant installation.[57] Similarly, in a retrospective study of 262 implants installed in 45 patients, an implant survival rate of 91% after an average observation time of 5 years was reported; implant losses were due to loss of osseointegration and occurred between 2.5 and 7 years (the majority of implants were lost after 4–5 years of loading).[58] In yet another publication on 69 patients with 287 implants, a survival rate of 98% over an average follow-up time of 26 months was observed; however, increased marginal peri-implant bone loss (>2.1 mm) at 4 years post-op was observed, resulting in a success rate of only 40%.[59] In this context, a recently published systematic review on survival rates of implants placed in connection all types of AL bone blocks, concluded that FFB blocks are associated with in rather unfavorable outcomes compared with AT bone blocks; in this review, an average implant survival rate of 96% after an average follow-up of 3 years was calculated from 77 publications including 6861 implants placed in connection with 2397 AT bone blocks in 2195 patients.[60] The increased rates of complications and/or failures associated with FFB block grafting—especially regarding the early complications—has been attributed partly on the fact that in most studies, patients were fully edentulous and in the need of large augmentations, which in turn increases the risks of complications; indeed, in several studies, lack of enough autogenous bone for harvesting was the reason for patient inclusion in the FFB block group (e.g., Spin Neto et al.). Another explanation, however, for the increased rate of implant loss and/or failures should be attributed in the lack of complete integration of the FFB blocks. This results into larger portions of the block remaining non-vital, and thus, being more prone to develop microcracks during implant loading compared to vital bone; consequently, as there is basically no capacity for microcrack repair in non-vital bone, these propagate and result in complete fractured bone pieces that exfoliate (bone sequestration) or loss of implant osseointegration.

4 | CONCLUDING REMARKS

Based on the histological observations in the pre-clinical studies, together with the histological observations from the bone-core biopsies in the clinical studies herein, and considering the long-term complications reported, it seems reasonable to conclude that a FFB block graft: (a) cannot be considered as a reliable replacement of a AT bone block, and (b) should only be considered in cases where the amount of necessary augmentation—in a lateral direction—is relatively limited, so that the main portion of the body of the implant lies within the inner (i.e., the vital) aspect of the block.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

No conflict of interest related to this manuscript.

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ETHICS STATEMENT

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CONSENT

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PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not relevant.

CLINICAL TRIAL REGISTRATION

Not relevant.

ORCID

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APPENDIX A

Search strategy for PubMed, Embase and Scopus

Database	Search strategy
Main databases	
PubMed http://www.ncbi.nlm.nih.gov/pubmed	**#1** "Allografts"[Mesh] OR "Allograft" OR "Allogeneic Transplants" OR "Allogeneic Transplant" OR "Transplant, Allogeneic" OR "Transplants, Allogeneic" OR "Allogeneic Grafts" OR "Allogeneic Graft" OR "Graft, Allogeneic" OR "Grafts, Allogeneic" OR "Homografts" OR "Homograft" OR "Homologous Transplants" OR "Homologous Transplant" OR "Transplant, Homologous" OR "Transplants, Homologous" OR "Transplantation, Homologous"[Mesh] OR "Allogeneic Transplantation" OR "Transplantation, Allogeneic" OR "Homografting" OR "Homologous Transplantation" OR "Allogeneic Grafting" OR "Grafting, Allogeneic" OR "Allografting" **#2** "Autografts"[Mesh] OR "Autograft" OR "Autologous Transplants" OR "Autologous Transplant" OR "Transplant, Autologous" OR "Transplants, Autologous" OR "Autotransplants" OR "Autotransplant" OR "Transplantation, Autologous"[Mesh] OR "Autotransplantation" OR "Autotransplantations" OR "Autografting" OR "Autograftings" OR "Autologous Transplantation" OR "Autologous Transplantations" OR "Transplantations, Autologous" OR "Heterografts"[Mesh] OR "Heterograft" OR "Xenografts" OR "Xenograft" OR "Transplantation, Heterologous"[Mesh] OR "Heterografting" OR "Xenotransplantation" OR "Xenograft Transplantation" OR "Transplantation, Xenograft" OR "Xenografting" OR "Heterograft Transplantation" OR "Transplantation, Heterograft" OR "Heterologous Transplantation" OR "Bone Substitutes"[Mesh] OR "Replacement Material, Bone" OR "Replacement Materials, Bone" OR "Materials, Bone Replacement" OR "Bone Substitute" OR "Substitute, Bone" OR "Substitutes, Bone" OR "Bone Replacement Material" OR "Material, Bone Replacement" OR "Bone Replacement Materials" **#3**"Alveolar Ridge Augmentation"[Mesh] OR "Alveolar Ridge Augmentations" OR "Augmentation, Alveolar Ridge" OR "Augmentations, Alveolar Ridge" OR "Ridge Augmentation, Alveolar" OR "Ridge Augmentations, Alveolar" OR "Mandibular Ridge Augmentation" OR "Augmentation, Mandibular Ridge" OR "Augmentations, Mandibular Ridge" OR "Mandibular Ridge Augmentations" OR "Ridge Augmentation, Mandibular" OR "Ridge Augmentations, Mandibular" OR "Maxillary Ridge Augmentation" OR "Augmentation, Maxillary Ridge" OR "Augmentations, Maxillary Ridge" OR "Maxillary Ridge Augmentations" OR "Ridge Augmentation, Maxillary" OR "Ridge Augmentations, Maxillary" OR "Alveolar Bone Grafting"[Mesh] OR "Alveolar Cleft Grafting" OR "Graft Survival"[Mesh] OR "Graft Survivals" OR "Survival, Graft" OR "Survivals, Graft" OR "Bone Transplantation"[Mesh] OR "Grafting, Bone" OR "Bone Grafting" OR "Transplantation, Bone" OR "Dental Implants"[Mesh] OR "Implant, Dental" OR "Implants, Dental" OR "Dental Implant" OR "Dental Implants, Mini" OR "Dental Implant, Mini" OR "Mini Dental Implant" OR "Mini Dental Implants" OR "Dental Prostheses, Surgical" OR "Dental Prosthesis, Surgical" OR "Surgical Dental Prostheses" OR "Surgical Dental Prosthesis" OR "Prostheses, Surgical Dental" OR "Prosthesis, Surgical Dental" **#1 AND #2 AND #3**
Embase http://www.embase.com	**#1** 'allograft'/exp OR 'allo inplant' OR 'allogeneic graft' OR 'allografts' OR 'alloplastic graft' OR 'alloplastic implant' OR 'allotransplant' OR 'graft, allogenic' OR 'graft, homologous' OR 'homograft' OR 'homograft sensitivity' OR 'homologous graft' OR 'homotransplant' OR 'transplant, homo' OR 'allograft' OR 'bone allograft'/exp OR 'allogenic bone graft' OR 'AlloQuent' OR 'fiberFUSE' OR 'fiberFUSE Advanced' OR 'maxgraft' OR 'Trinity ELITE (bone allograft)' OR 'Trinity Evolution (bone allograft)' OR 'bone allograft' OR 'allotransplantation'/exp OR 'allogeneic transplantation' OR 'allogenic transplantation' OR 'allograft transplantation' OR 'homoiotransplantation' OR 'homologous transplantation' OR 'homotransplantation' OR 'transplantation, homologous' OR 'allotransplantation' **#2** 'autograft'/exp OR 'autogenous graft' OR 'autografts' OR 'autotransplant' OR 'autotransplants' OR 'graft, auto' OR 'autograft' OR 'autotransplantation'/exp OR 'autologous transplantation' OR 'transplantation, auto' OR 'transplantation, autologous' OR 'autotransplantation' OR 'xenograft'/exp OR 'graft, heterologous' OR 'graft, xenogeneic' OR 'heterogenous graft' OR 'heterograft' OR 'heterografts' OR 'heterologous graft' OR 'heterologous transplantation' OR 'heterotransplant' OR 'peritoneum heterograft' OR 'system xenograft' OR 'transplantation, heterologous' OR 'xenogeneic graft' OR 'xenograft system' OR 'xenografts' OR 'xenotransplant' OR 'xenograft' OR 'bone prosthesis'/exp OR 'bone endoprosthesis' OR 'bone prosthesis (physical object)' OR 'bone substitute' OR 'bone substitutes' OR 'Hydroset' OR 'bone prosthesis' OR 'bone graft'/exp OR 'autograft, bone' OR 'autograft, spongy bone' OR 'autologous bone graft' OR 'bone autograft' OR 'bone flap' OR 'bone flaps' OR 'bone grafts' OR 'bone transplant' OR 'BoneCeramic' OR 'compact bone autograft' OR 'free bone graft' OR 'graft, bone' OR 'osseous flap' OR 'osseous flaps' OR 'osseous graft' OR 'osseous grafts' OR 'osteoarticular graft' OR 'rib autograft' OR 'spongy bone autograft' OR 'Straumann XenoGraft' OR 'viable bone graft' OR 'bone graft' **#3** 'alveolar ridge augmentation'/exp OR 'ridge augmentation procedure' OR 'alveolar ridge augmentation' OR 'alveolar bone grafting'/exp OR 'graft survival'/exp OR 'allograft survival' OR 'graft survival prolongation' OR 'homograft survival' OR 'survival, graft' OR 'transplant survival' OR 'transplantation survival' OR 'graft survival' OR 'bone transplantation'/exp OR 'bone grafting' OR 'bone reimplantation' OR 'transplantation, bone' OR 'bone transplantation' **#4** 'tooth implant'/exp OR 'Bicon' OR 'dental implant' OR 'dental implants' OR 'Grafton' OR 'implant, teeth' OR 'implant, tooth' OR 'implants, teeth' OR 'implants, tooth' OR 'intramucosal dental implant' OR 'Straumann Mini' OR 'Straumann PURE' OR 'Swish Active' OR 'Swish Tapered' OR 'teeth implant' OR 'teeth implants' OR 'tooth implants' OR 'Variobase' OR 'tooth implant' OR 'histology'/exp OR 'bone demineralization technique' OR 'comparative histology' OR 'decalcification technique' OR 'histocytological preparation techniques' OR 'histologic stain' OR 'histologic studies' OR 'histologic study' OR 'histologic technique' OR 'histological diagnosis' OR 'histological method' OR 'histological staining' OR 'histological studies' OR 'histological study' OR 'histological technique' OR 'histological techniques' OR 'histology, comparative' OR 'neurohistology' OR 'replica techniques' OR 'histology' ' **#1 AND #2 AND #3 AND #4**

Database	Search strategy
Scopus http://www.scopus.com/	**#1** TITLE-ABS-KEY "Allografts" OR "Allograft" OR "Allogeneic Transplants" OR "Allogeneic Transplant" OR "Transplant, Allogeneic" OR "Transplants, Allogeneic" OR "Allogeneic Grafts" OR "Allogeneic Graft" OR "Graft, Allogeneic" OR "Grafts, Allogeneic" OR "Homografts" OR "Homograft" OR "Homologous Transplants" OR "Homologous Transplant" OR "Transplant, Homologous" OR "Transplants, Homologous" OR TITLE-ABS-KEY "Transplantation, Homologous" OR "Allogeneic Transplantation" OR "Transplantation, Allogeneic" OR "Homografting" OR "Homologous Transplantation" OR "Allogeneic Grafting" OR "Grafting, Allogeneic" OR "Allografting" **#2** TITLE-ABS-KEY ("Autografts" OR "Autograft" OR "Autologous Transplants" OR "Autologous Transplant" OR "Transplant, Autologous" OR "Transplants, Autologous" OR "Autotransplants" OR "Autotransplant") OR TITLE-ABS-KEY ("Transplantation, Autologous" OR "Autotransplantation" OR "Autotransplantations" OR "Autografting" OR "Autograftings" OR "Autologous Transplantation" OR "Autologous Transplantations" OR "Transplantations, Autologous") OR TITLE-ABS-KEY ("Heterografts" OR "Heterograft" OR "Xenografts" OR "Xenograft") OR TITLE-ABS-KEY ("Transplantation, Heterologous" OR "Heterografting" OR "Xenotransplantation" OR "Xenograft Transplantation" OR "Transplantation, Xenograft" OR "Xenografting" OR "Heterograft Transplantation" OR "Transplantation, Heterograft" OR "Heterologous Transplantation") OR TITLE-ABS-KEY ("Bone Substitutes" OR "Replacement Material, Bone" OR "Replacement Materials, Bone" OR "Materials, Bone Replacement" OR "Bone Substitute" OR "Substitute, Bone" OR "Substitutes, Bone" OR "Bone Replacement Material" OR "Material, Bone Replacement" OR "Bone Replacement Materials") OR TITLE-ABS-KEY ("Bone Transplantation" OR "Grafting, Bone" OR "Bone Grafting" OR "Transplantation, Bone") **#3** TITLE-ABS-KEY ("Alveolar Ridge Augmentation" OR "Alveolar Ridge Augmentations" OR "Augmentation, Alveolar Ridge" OR "Augmentations, Alveolar Ridge" OR "Ridge Augmentation, Alveolar" OR "Ridge Augmentations, Alveolar" OR "Mandibular Ridge Augmentation" OR "Augmentation, Mandibular Ridge" OR "Augmentations, Mandibular Ridge" OR "Mandibular Ridge Augmentations" OR "Ridge Augmentation, Mandibular" OR "Ridge Augmentations, Mandibular" OR "Maxillary Ridge Augmentation" OR "Augmentation, Maxillary Ridge" OR "Augmentations, Maxillary Ridge" OR "Maxillary Ridge Augmentations" OR "Ridge Augmentation, Maxillary" OR "Ridge Augmentations, Maxillary") OR TITLE-ABS-KEY ("Alveolar Bone Grafting" OR "Alveolar Cleft Grafting") OR TITLE-ABS-KEY ("Graft Survival" OR "Graft Survivals" OR "Survival, Graft" OR "Survivals, Graft") OR TITLE-ABS-KEY ("Dental Implants" OR "Implant, Dental" OR "Implants, Dental" OR "Dental Implant" OR "Dental Implants, Mini" OR "Dental Implant, Mini" OR "Mini Dental Implant" OR "Mini Dental Implants" OR "Dental Prostheses, Surgical" OR "Dental Prosthesis, Surgical" OR "Surgical Dental Prostheses" OR "Surgical Dental Prosthesis" OR "Prostheses, Surgical Dental" OR "Prosthesis, Surgical Dental") **#1 AND #2 AND #3**

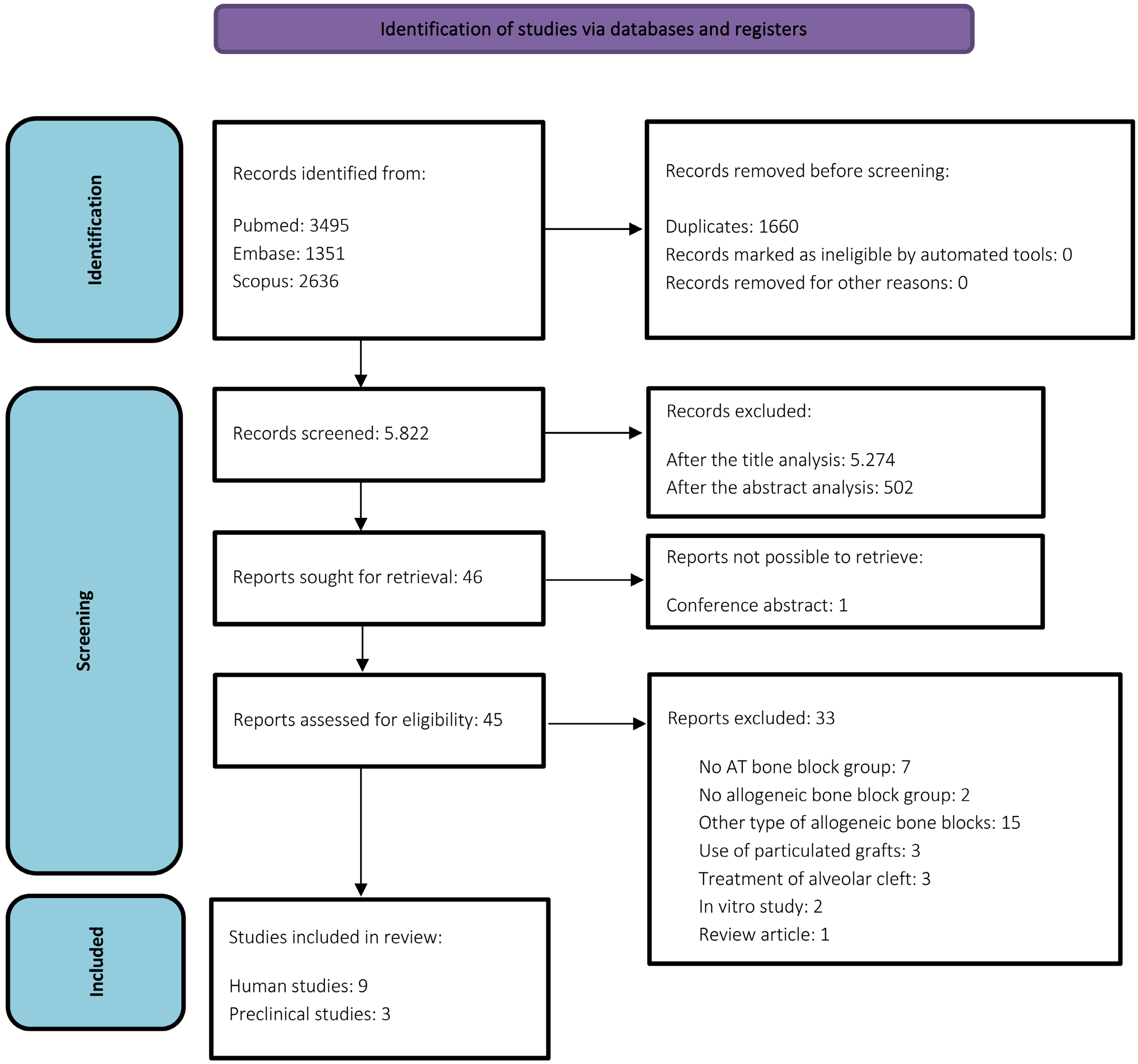

FIGURE A1 Flowchart of the search of the studies.