Biological and physical properties of bone block grafting biomaterials for alveolar ridge augmentation

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Abstract

Objective

Bone resorption of maxillary ridges is an unavoidable process that occurs after tooth extraction. Many treatment alternatives have been proposed to facilitate implant placement in these scenarios. Drawbacks such as morbidity, cost and excessive resorption owing to the procedure have prompted clinicians to seek biomaterials as an alternative to autogenous bone. The objective of this article was to review the current state of the art by means of the biological and physical properties of biomaterials used for block grafting in atrophic maxillary ridges. Secondly, it was aimed herein at presenting the clinical and histological findings when using these biomaterials.

Materials and methods

An electronic and manual literature search was conducted by two independent reviewers using several databases, including MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and Cochrane Oral Health Group Trials Register databases, for articles written in English up to June 2016. Owing to the heterogeneity of the findings, quantitative assessment could not be conducted. As such, a narrative review was carried out on the biological and physical aspects of biomaterials used for block grafting.

Results

Both allogeneic and xenogeneic block grafts have been developed to overcome deficiencies of autogenous grafts. Allogeneic block grafts have been widely investigated, but there is a lack of long-term follow-up. On the contrary, xenogeneic block grafts have only limited scientific evidence of their suitability for ridge reconstruction.

Conclusion

Allogeneic and xenogeneic bone block grafts represent a promising alternative to autogenous bone for ridge augmentation. Nonetheless, the evidence supporting xenogeneic block graft usage remains minimal; hence, more long-term human studies are needed to validate their effectiveness. In addition, using prefabricated scaffolds impregnated with growth factors provides an interesting field to be further explored.

Keywords

Bone grafting, bone biomaterials, allogeneic, xenogeneic, bone substitutes.

Introduction

After tooth extraction, bone remodeling that leads to bone resorption is a common phenomenon. Ridge resorption has made grafting procedures popular in implant and restorative therapy.[1–4] These procedures aim at restoring width and height for proper 3-D implant placement. Numerous treatment alternatives have been proposed (e.g., distraction osteogenesis and guided bone regeneration with particulated bone materials).[5] Nonetheless, for extensive or severely atrophic ridges, block grafting has been advocated to be the most predictable approach.[6, 7]

Autogenous bone has been regarded as the gold standard for bone reconstruction.[8] This can be harvested from different locations based upon the extension of the atrophic area.[8] While intraoral bone block grafts (mandibular ramus or mental symphysis) can be harvested with a less traumatic approach, the amount is often limited. However, extraoral bone block grafts (calvaria or iliac crest) fulfill the requirements in terms of quantity, but they increase the cost and lead to some sequelae for the donor site. Regardless of the harvesting location, autogenous block grafts might be further classified depending on their origin. For example, intramembranous grafts (mandibular ramus and calvaria bone) have less bone resorption and the process of bone remodeling or "creeping substitution" takes longer[9] compared with endochondral bone (iliac crest).[10] Hence, it is important to take this into consideration when planning implant treatment so that it will not cause extensive bone remodeling that threatens the final adequate prosthetically driven implant position.[11, 12]

Indeed, autologous bone has osteogenic capacity;[8] in other words, bone can potentially grow in between the interface of the graft and the host bone. Nevertheless, as already mentioned, the drawbacks associated with this approach have encouraged clinicians to use alternatives, such as allogeneic or xenogeneic bone blocks.[13, 14] These treatment modalities not only reduce the possibility of experiencing morbidity, but also shorten the treatment and, hence, increase patient acceptance and satisfaction. The mechanism of forming new mineralized tissue is mediated by the mesenchymal cells, which differentiate into osteoblasts that are coordinated by glycoproteins (bone morphogenetic proteins).[15] Hence, after an inflammatory process that ends in gradual substitution, the newly formed bone is obtained,[16] or in this case hard tissue capable of obtaining first implant stability and subsequently osseointegration.

In general, allogeneic and xenogeneic block grafts do not contain osteoprogenitor cells and, consequently, integration with the native bone might be arduous. Promising results have been shown in the literature with application of these block grafts for bone regeneration.[17, 18] Depending on their origin, they can be either from human (cadaver), known also as allografts, or from animal origin (equine and bovine), which are also called xenografts. Once harvested, the grafts must be preserved, and each manufacturing company has developed its own process that can potentially determine the properties of the respective biomaterial.

The objective of this article was to review the biological and physical properties of block grafting biomaterials available for bone regeneration in atrophic maxillary ridges. Furthermore, the aim was to present the human and animal clinical and histological findings of biomaterials used for maxillary reconstructions.

Materials and methods

Information sources

An electronic literature search was conducted by two independent reviewers (AM and HLW) of several databases, including MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and Cochrane Oral Health Group Trials Register databases, for articles written in English up to June 2016.

Screening process

Combinations of controlled terms (MeSH and EMTREE) and keywords were used whenever possible:

(((((((Alveolar bone atrophy[MeSH Terms])
OR alveolar bone loss[MeSH Terms])
AND bone grafting[MeSH Terms])
OR allograft[MeSH Terms])
OR xenograft[MeSH Terms])
OR biomaterials[MeSH Terms])
AND block)
OR onlay

OR

((((((("alveolar bone loss"[MeSH Terms]
OR "alveolar bone loss"[MeSH Terms])
AND bone graft[Title/Abstract])
AND block[Title/Abstract])
OR onlay[Title/Abstract])
AND biomaterial[Title/Abstract])
OR allogeneic[Title/Abstract])
OR allograft[Title/Abstract])
OR xenogeneic[Title/Abstract])
OR xenograft[Title/Abstract]
AND "humans"[MeSH Terms]

Additionally, a manual search of periodontics- and implantology-related journals, including the *Journal of Dental Research*, *Journal of Clinical Periodontology*, *Journal of Periodontology*, and *International Journal of Periodontics and Restorative Dentistry*, from January 2015 up to June 2016, was performed to ensure a thorough screening process. Furthermore, references of included articles were screened to check all available articles.

Biomaterials' properties

"Biomaterial" refers, generally speaking, to material that has been developed to interact with the biological system, acting as a scaffold for replacement and repair of, in this case, lost bone. Firstly, a biomaterial must be biocompatible, which is defined as the capacity that the material has to elicit an appropriate biological response and, thus, not be detected as a foreign body by the host. In addition, it must have sufficient durability to carry out the task for which it was developed. Further, it must be chemically stable (neither toxic nor carcinogenic for the host).

For block grafts used in regeneration, an ideal biomaterial, from the cellular and molecular standpoint, must have the following properties:

- Its design enables osteogenic cells to reach the entire block by osteoconduction and osteoinduction in order to complete the turnover process. In order to permit osteoblastic growth and mineralized tissue production, the ideal size of the micropores should be within 180–600 μ.[19] This is of crucial importance inasmuch as osteoblasts (15–50 μ) and stem cells (5–12 μ) have to proliferate guided through the pores.[20] The biomaterial itself must be replaced by vital bone (newly formed bone). Therefore, the biomaterial's degradation must be in accordance with the remodeling process.
- The trabeculae-like structures that form the scaffold must leave enough space for the formation of new vessels by the endothelial cells that will supply of all the nutrients and osseous cells to the scaffold.

Therefore, as occurs in autogenous bone blocks, biomaterials undergo three steps: (1) colonization of host cells; (2) degradation of the biomaterial while turnover is occurring; and (3) maturation of the newly formed bone and integration with the recipient site's bone **(Fig. 1)**.

However, biomaterials in bone grafting must fulfill other properties besides biological ones. This will allow the material to interact with the host environment and, thus, increase the possibility of bone formation and long-term stability. These properties should include:

- Mechanical properties: Among these properties are resistance, resilience, stiffness, fragility, tenacity, ductility and malleability. The result of the combination of these mechanical properties will determine the handling of the material more than its capacity as scaffold for bone regeneration.[21] However, it is important to note that, generally, the stiffer the biomaterial is, the longer it lasts due to the more rigid element.
- Surface phenomena: It is important to take into consideration the internal energy, surface tension, wettability, and adhesion and cohesion of the biomaterial to be used for bone regeneration. These properties are in part responsible for the aggregation and attachment of vital osteogenic cells in a nonvital structure (scaffold).[21]
- Physical properties: Three main properties are included within this group:
  - Thermals: thermal expansion, thermal contraction, thermal insulation, melting point and interval;
  - Electrics: electric conductivity, electrical resistivity and oral galvanism; and
  - Optics: color and appearance.
- Chemical properties: toxicity, chemical stability, half-life, flammability or enthalpy of formation among others.
- Rheological properties: apparent viscosity, normal force coefficients, storage modulus, complex viscosity and complex functions of nonlinear viscoelasticity.

Fig. 1

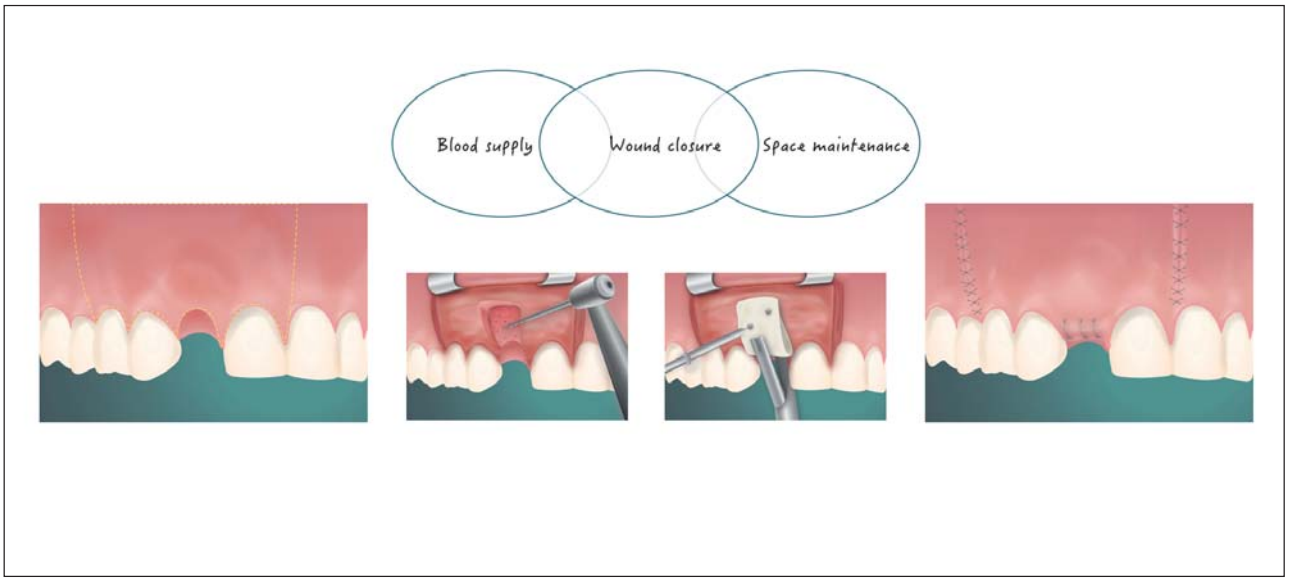


Fig. 1
Descriptive illustration of the onlay bone grafting procedure. In order to be successful, the three elements must be achieved to ensure a proper creeping substitution process.

Vascularization

Biomaterials used in bone regeneration lack cells, proteins and vessels. In this manner, risk of disease transmission is minimized. Therefore, cells from the recipient site of the graft carry out the process of neoangiogenesis, an essential step for successful bone regeneration.[22] Neovascularization indeed is fundamental because it supplies the avascular scaffold with oxygen and the nutrients required for cell growth and differentiation.[23] Accordingly, newly formed bone and resorption of the block graft rely upon the neoangiogenesis process. Numerous growth factors, such as vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), some subgroups of the transforming growth factor beta family (TGF-β), transcription factor to induce hypoxia (HIF), angiopoietin (Ang-1), hepatocyte growth factor (HGF), platelet-derived growth factor (PDGF-BB), insulin-like derived growth factor (IGF-1, IGF-2) and neurotrophic growth factor (NGF) are involved in the process.[24] Accordingly, VEGFs and their receptors are in charge of the molecular and cellular cascade inasmuch as they lead the development of the endothelial system by vasculogenesis, angiogenesis and the lymphatic net. Additionally, VEGFs play a meaningful role in skeletal growth and in bone repair and regeneration.[25] Likewise, FGFs are in charge of promoting proliferation and differentiation of endothelial cells and fibroblasts. On the contrary, TGFs increase extracellular matrix development. HIFs mediate the effects of hypoxia on the cells. Ang-1 stabilizes the vessels. However, HGFs act on epithelial and endothelial cells for organ regeneration and wound healing. Commonly used as exogenous growth factors in bone regeneration, the PDGF family plays an important role in angiogenesis. IGFs in contrast have endocrine effects upon the host. Lastly, NGFs, also known as neurotrophins, maintain nerve cells within the horizontal newly formed bone.[26, 27]

In bone regeneration using block grafts as scaffolds, new tendencies are arising, since, contrary to autogenous grafts, early neoangiogenesis is essential for biomaterial survival and integration. In consequence, techniques such as the delivery of stem cells and growth factors in order to accelerate the process have been closely examined recently with promising results.[28] However, there is still a lack of results to make any conclusive statement in this regard.

Types of block graft biomaterials

1. Allogeneic block grafts

The use of allografts represents a fair alternative to autogenous block grafts, since the blocks are harvested from the same species as that of the recipient. The first bone allografts were performed in late 19th century by a group of surgeons who reconstructed an infected humerus with a graft harvested from the tibia of the same

patient.[29] The establishment of the U.S. Navy Tissue Bank in 1990 was a significant influencing factor for the wide use of bone allografts. The use of allografts has continued to increase since then.[30]

Properties

The properties of allograft material are directly related to its processing and its precedence.[31] Allogeneic block grafts may be prepared as fresh, frozen and freeze-dried. Nowadays, the vast majority of grafts are carefully screened, harvested, processed and distributed, and this is governed by the American Association of Tissue Banks. The risk of disease transmission is often minimized through the above processes.[32, 33] In addition, during graft preparation, the antigenic components are carefully removed to eliminate any potential host immune response.[32]

Fresh or frozen allografts retain both osteoinductive and osteoconductive capacities, allowing a slightly faster bone turnover than that of freeze-dried allografts. However, the risks of disease transmission and host reactions are slightly increased,[34] whereas the immune response is reduced in freeze-dried allografts.[34] This is due to the elimination of the cells by embedding the graft in antibiotic wash twice for 1 h and then storing it at -70 °C to dry up to 5% of the water.[35, 36] Another issue to bear in mind is that, because of the drying, mechanical properties are weakened. Hence, microfracture of the grafts might easily occur. Consequently, for this type of block allograft, rehydration is suggested prior to placement in order to regain some of the mechanical properties.[37] Currently, Zimmer Biomet Dental (Carlsbad, Calif., U.S.) has patented its suitable preparation sequence **(Fig. 2)**. This is the Tutoplast process, which includes cleaning and ultrasonic lipidization in acetone, an osmotic and later oxidative treatment, ending with dehydration in sequential acetone baths and gamma irradiation.[38] The result of this process is a greater preservation of the minerals and collagen matrix, leading to rapid bone turnover.[39]

Clinical outcomes

Bone block allografts are a relatively novel alternative to autogenous grafts for horizontal and/or vertical bone augmentation of the atrophic maxilla **(Table 1)**. In 1999, the first case of using an allogeneic block bone graft for bone regeneration was reported. In that case, dental implants for oral rehabilitation were successfully placed three months after the grafting procedure.[18] Since then, multiple prospective human clinical trials have been published demonstrating proof of principle for this human allograft block usage.[40–56]

From our clinical experience and others', when the human allograft is exposed to the oral cavity, it often leads to graft failure.[42, 57] Moreover, it has much higher failure rate in the mandible than in the maxilla owing to difficulty in flap advancement and a thinner soft-tissue biotype.[58] Failure of a block graft generally occurs in the early stages of graft healing.[41, 45, 52, 55] In addition, bone graft resorption occurs during healing, which is the same as with autogenous grafts. However, greater bone loss occurs at six months after placement compared with autogenous bone harvested from the mandibular ramus (52.00 ± 25.87% vs. 25.00 ± 12.73%, respectively).[46] A recent systematic review found promising results on the use of allogeneic bone grafts for horizontal bone augmentation in maxillae.[59] It was shown that not only high graft and implant survival rates had been achieved (98.0% and 96.9%, respectively), but also that a weighed mean of 4.79 mm of horizontal bone had been gained over a mean follow-up period of 23.9 months.

Histological and histomorphometric outcomes

Indeed, allogeneic block grafts do not behave like autogenous bone from the cellular standpoint because of the lack of osteogenic potential; notwithstanding, respecting a proper healing time (more than six months), this biomaterial results in similar clinical healing to that of native bone[40–56] **(Figs. 3a–c & 4)**. Acocella et al. showed that, after nine months, a high number of empty osteocyte lacunae were still present and that more fibrous tissue was present than in the samples taken previously.[40] Additionally, newly formed bone (61.96 ± 11.77%) was surrounded by nonvital bone with empty osteocyte lacunae. At the same time after healing, Contar et al. demonstrated a lamellar arrangement around Haversian canals interspersed with osteocytes in lacunae.[43] They also observed that the central portions of the grafts showed osteocytes with a higher number of empty lacunae.

When histological results are compared between groups (allogeneic vs. autogenous), behavioral dissimilarities are displayed. Lumetti et al. showed that, after six months of healing, osteocyte lacunae were mostly empty for the

Fig. 2

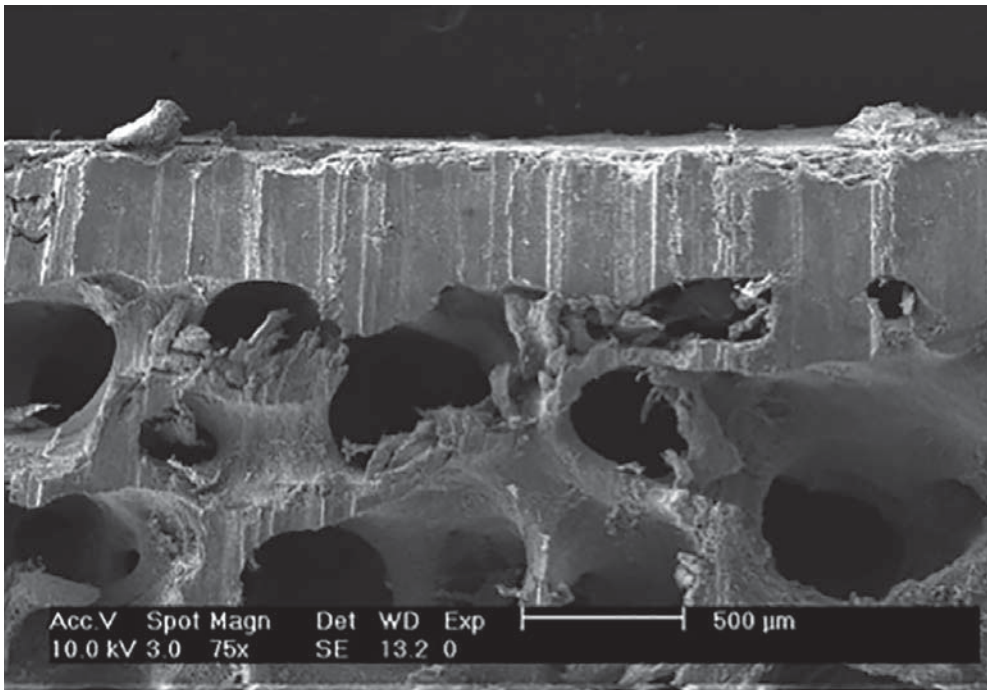


Fig. 2

Scanning electron microscopy image of the Puros Block Allograft (Zimmer Biomet Dental) microarchitecture (75× magnification). (Courtesy of Zimmer Dental).

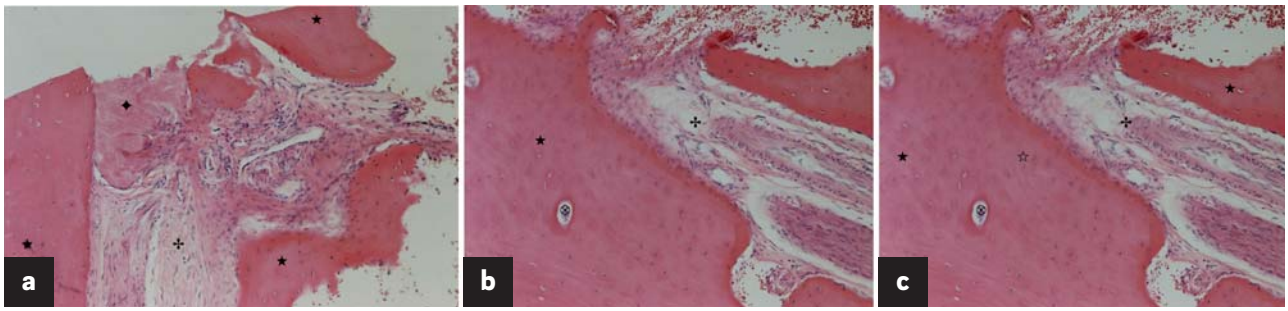
Figs. 3a–c

Histological samples of Puros Block Allograft six months after a regenerative procedure of the atrophic maxillae (100× magnification [a] and 400× magnification [b & c]).

Fig. 4

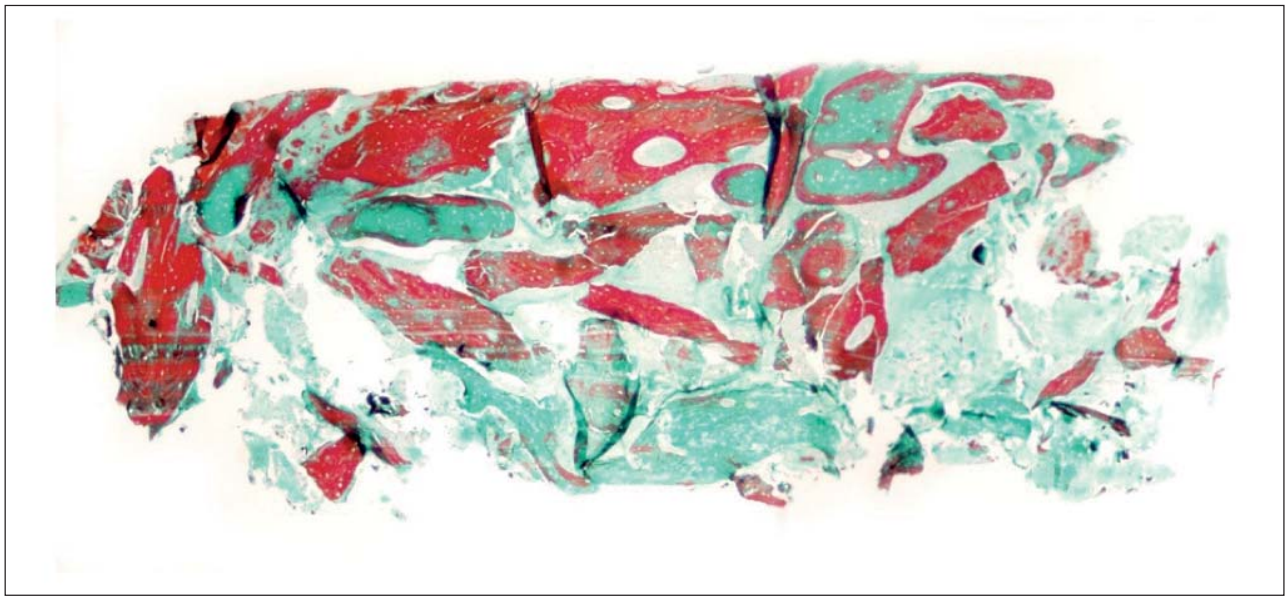
Histological sample of J-Block Puros Allograft six months after a regenerative procedure for horizontal augmentation in atrophic maxillae. Note the high amount of newly formed bone present, while the percentage of remaining material is decreased.

Figs. 3a–c



★ Newly-formed bone
✦ Remaining allogeneic grafting material
✢ Non-mineralized tissue
⊗ Osteocyte lacunae

Fig. 4



Author (year)	Study design	Groups	No. of patients	No. of sites grafted	Location of grafted sites	Bone augmentation (V/H)	Type of bone block graft
Acocella et al. (2012)[40]	Prospective case series	NCG	16	18	Anterior/posterior	H	Monocortical fresh-frozen
Barone et al. (2009)[41]	Prospective case series	NCG	13	24	Anterior (13)/ posterior (9)	H (19)/V (5)	Corticocancellous deep-frozen
Chaushu et al. (2010)[42]	Prospective case series	NCG	101	90	Anterior (58)/ posterior (32)	NC	Cancellous fresh-frozen
Contar et al. (2009)[44]	Prospective case series	NCG	15	34	Anterior/posterior	H	Cancellous/cortical fresh-frozen
Contar et al. (2011)[43]	Prospective case series	NCG	18	39	Anterior/posterior	NC	Cancellous/cortical fresh-frozen Cortical fresh-frozen
Wallace & Gellin (2010)[56]	Prospective case series	NCG	12	16	Anterior/posterior	H	Cancellous fresh-frozen
Spin-Neto et al. (2013)	Prospective case series	AL	13	17	Anterior (14)/posterior (3)	H	Corticocancellous deep-frozen
		AT	13	17			Mandibular ramus
Novell et al. (2012)[52]	Prospective case series	NCG	12	20	Anterior/posterior	H/H + V	Cortical/cancellous fresh-frozen
Deluiz et al. (2013)[45]	Prospective case series	NCG	24	24	Anterior/posterior	H	Corticocancellous fresh-frozen
Nissan et al. (2011)[51]	Prospective case series	NCG	20	28	Anterior	H (27)/V (12)	Cancellous fresh-frozen
Nissan et al. (2011)[51]	Prospective case series	NCG	31	46	Anterior	H (42)/V (27)	Cancellous fresh-frozen
Nissan et al. (2008)[50]	Prospective case series	NCG	11	11	Anterior	H/V	Cancellous fresh-frozen
Lumetti et al. (2012)[46]	RCT	AL	12	12	Anterior/posterior	H	Corticocancellous fresh-frozen
		AT	12	12			Mandibular ramus
Spin-Neto et al. (2013)[55]	Prospective case series	AL	6	17	Anterior/posterior	H	Cortical fresh-frozen
		AT	6	12			Mandibular ramus
Peleg et al. (2010)[53]	Prospective case series	NCG	34	38	Anterior (31)/ posterior (7)	H/H + V	Corticocancellous fresh-frozen

RCT = randomized controlled trial; AL = allogeneic graft; AT = autogenous graft; H = horizontal; V = vertical; Y = yes; N = no; MCA = mineralized cortical allograft;
BBM = bovine bone mineral; NC = not clear; NM = not mentioned; NCG = no control group.

Table 1

	Membrane (Y/N)	Additional grafting material/growth factor	Healing period (months)	Resorption (%)	Histological analysis	
					Newly formed bone (%)	Characteristics
	N	N	9	11.45 ± 8.37	61.96 ± 11.77	A high number of empty osteocyte lacunae were still present and more fibrous tissue was present than in the samples taken previously. Newly formed bone was surrounded by nonvital bone with empty osteocyte lacunae.
	N	Cancellous allograft particles	5	NM	NM	NM
	Y	N	6	NM	NM	NM
	N	N	NC	NM	NM	Mature and compact osseous tissue surrounded by marrow spaces
	N	N	9	NM	NM	Lamellar arrangement around Haversian canals interspersed with osteocytes in lacunae. No evidence of inflammatory infiltrate. The central portions revealed osteocytes with a higher number of empty lacunae.
	Y	MCA + rhPDGF-BB	5	NM	NM	NM
	Y	N	6	NC	NM	NM
	Y	Freeze-dried allograft particles	NM	NM	NM	NM
	N		8	13.02 ± 3.86	NM	Newly formed bone with osteocytes was observed at all of the time points. Osteocyte presence was higher at 4 months. Vessels were also detected abundantly in the samples.
	Y	Particulate BBM	6	NM	NM	NM
	Y	Particulate BBM	6	10.00 ± 1.00	NM	NM
	Y	Particulate BBM	6	NM	NM	NM
	Y	Particulate fresh-frozen	6	52.00 ± 25.87	NC	Osteocyte lacunae were mostly empty. Newly formed bone contained viable osteocytes. Bone-forming osteoblasts and fluorescent labeling were detected. Dense connective tissue with the presence of inflammatory cells (WM score = 1.67) and eroded areas.
				25.00 ± 12.73	NC	Osteocyte lacunae were mostly empty. Newly formed bone contained viable osteocytes. Bone-forming osteoblasts and fluorescent labeling were detected. WM inflammatory score = 1.
	Y	N	7	NM	NM	Large segments of necrotic bone with empty osteocyte lacunae and little osteoclastic activity. Blood vessels were invading the Haversian canals of the material. No direct contact was found between remodeled and grafted bone. Some osteoclastic activity surrounded by connective tissue with no presence of inflammatory cells by newly formed bone failed to invade the graft.
				NM	NM	Small areas of necrotic bone with abundant presence of osteocytes. No difference between the grafted and the host bone.
	Y	N	4	NM	NM	NM

Table 1

Studies demonstrating the clinical and histological characteristics of the prospective (cohort and case series) testing of allograft block grafts for horizontal and /or vertical bone augmentation of the atrophic maxilla.

allogeneic block graft group[46] and that newly formed bone contained viable osteocytes. In these samples, bone-forming osteoblasts were detected. Dense connective tissue with the presence of inflammatory cells and eroded areas were also reported. Minimal differences were shown for the autogenous block graft group, in which no connective tissue was found and the presence of inflammatory cells was low. However, Spin-Neto et al. found major differences between groups.[55] The following histological characteristics were found to be associated with allogeneic bone block grafts: (a) large segments of necrotic bone with empty osteocyte lacunae and little osteoclastic activity; (b) blood vessels invading the Haversian canals of the material—no direct contact was found between remodeled and grafted bone; and (c) some osteoclastic activity surrounded by connective tissue with no presence of inflammatory cells by newly formed bone failed to invade the graft. On the contrary, autogenous block grafts presented small areas of necrotic bone with a higher number of osteocytes and a smoother junction between the graft and host bed. Therefore, from the cellular standpoint, allogeneic block grafts in the early stages of healing behave in a different manner to autogenous block grafts. However, the long-term outcome and differences remain to be determined.

2. Xenogeneic block grafts

Xenografts, which are derived from a genetically different species than the host, represent another potential alternative to autogenous block grafts for bone augmentation. Similar to human allografts, the lack of osteogenic capacity makes them less predictable in terms of graft incorporation into host bone. In addition, lack of human cells turns xenografts into scaffolds with no osteoinductive potential. Despite its novel applicability as block grafts for augmenting severely atrophied bone, this type of biomaterial has been widely used as particulate bone graft, showing excellent outcomes by means of space maintenance.[60–62] Thus far, there is a scarcity of literature regarding this biomaterial for onlay grafts, and xenogeneic block grafts have been used more commonly as inlay grafts. As mentioned above, vascularity for this biomaterial is even more critical for success and, consequently, a three-wall defect (as displayed by host bone for inlay grafts) often makes this approach more reliable. However, an advantage of using xenogeneic biomaterial is that, owing to its slow rate of resorption, space is better maintained over the long term **(Fig. 5)**.[63, 64]

Currently, two types of xenografts are available as blocks for bone augmentation: bovine and equine. While deproteinized bovine bone relies on its acceptability by clinicians, equine bone has shown to be less fragile to fracture.[65] However, as mentioned, more studies are needed to verify the viability of this type of biomaterial in comparison to autogenous or allogeneic block grafts.

Properties

In contrast to human-derived bone, xenogeneic grafts do not have osteoinductive potential. Therefore, they are used only as scaffolds for space maintenance and cell migration guidance. Geistlich Bio-Oss (Geistlich Pharma, Wolhusen, Switzerland), a bovine-derived biomaterial, is the most widely used xenogeneic graft. This biomaterial is claimed to have all organic material removed, so is nonantigenic. A modified Geistlich Bio-Oss block that contains more collagen components for improving its manageability has also been introduced.[66] Equine bone blocks have recently been introduced and have shown to provide an improved scaffold for cases of severe atrophy owing to this bone's natural trabecular structure.[67]

Xenogeneic biomaterials, albeit not posing osteoinductive potential, are claimed to serve as slow-resorption scaffolds capable of promoting bone formation.[68, 69] Nonetheless, more studies on this material are still needed to better understand its overall properties and long-term results.

Clinical outcomes

As mentioned before, studies on xenogeneic block grafts are limited.[8] At this point, only a few *in vivo* studies have been carried out on this biomaterial.[66, 67, 70–72] The xenogeneic block graft has been advocated for bone augmentation. Steigmann presented the first human case report that used this biomaterial for horizontal bone augmentation in the maxillary anterior region.[85] Li et al. successfully used Geistlich Bio-Oss blocks for horizontal bone augmentation via a subperiosteal tunneling approach.[70] This might represent an alternative approach for placing this specific biomaterial owing to the success rate it achieved. Despite these preliminary results, we still need more evidence to support the use of xenogeneic materials for onlay block grafting.

Fig. 5

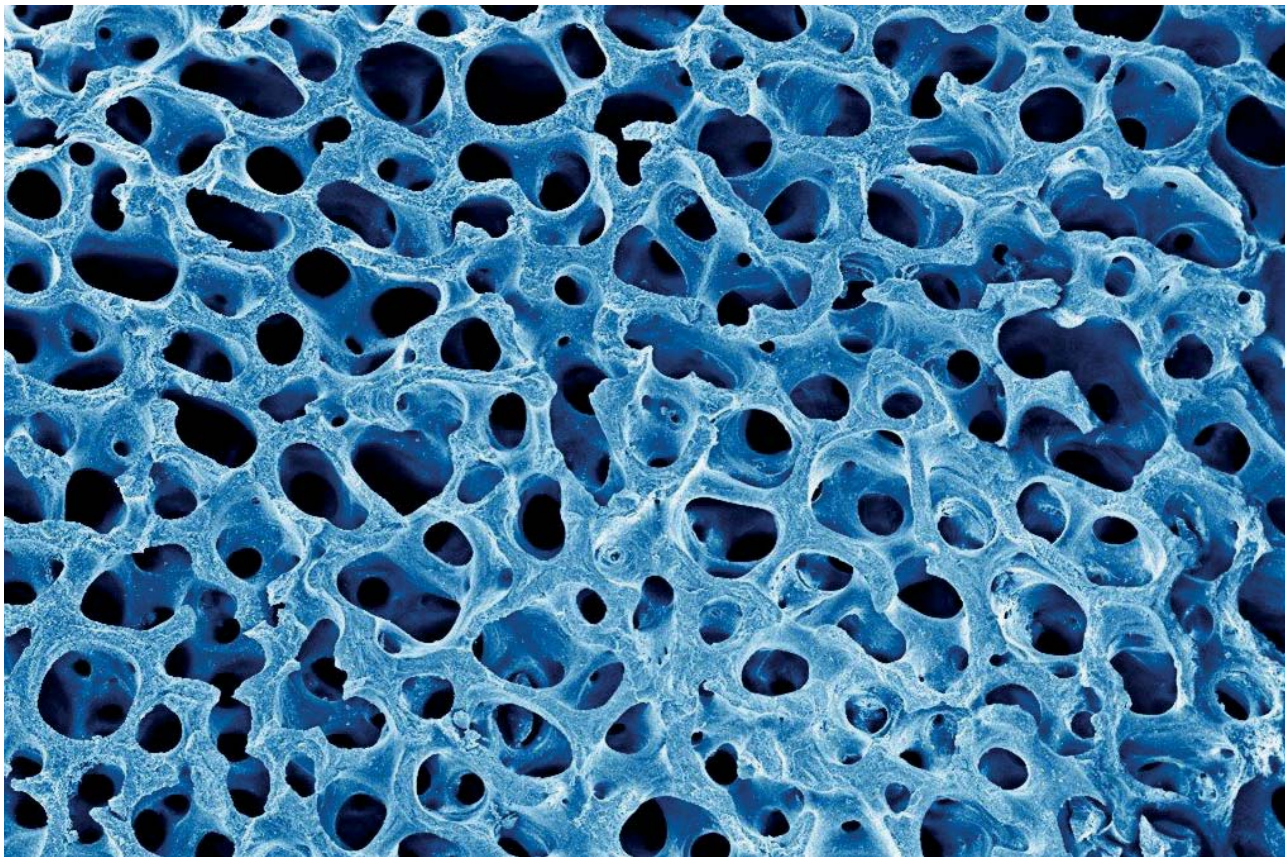


Fig. 5
Scanning electron microscopy image of pore morphology of cancellous bovine bone (50× magnification) by Dr. Michael Bufler. (Courtesy of Geistlich Pharma, 2014)

Regarding xenogeneic graft resorption, Araújo et al. in a dog study showed that the Geistlich Bio-Oss block graft is capable of retaining its dimension with moderate amounts of new bone formed at the base of the graft, while autogenous block grafts undergo 30% and 50% graft resorption.[71] Likewise, De Santis et al. demonstrated superior volumetric stability of deproteinized bovine bone mineral compared with autogenous block grafts harvested from the mandibular ramus in a dog study (0.2 mm vs. 0.9 mm of horizontal resorption, respectively).[73]

Histological and histomorphometric outcomes

Animal studies have shown that both bovine Geistlich Bio-Oss and equine eHac (Geistlich Pharma) blocks demonstrated similar histological results. In the early stages of healing, the grafts were surrounded by fibrovascular connective tissue with no signs of necrosis, osteolysis or tissue degeneration.[66] In contrast, Schwarz et al. showed that, after 12 weeks of healing, bovine bone had no signs of degradation, while equine bone presented with an increase in osteoclasts and multinucleate giant cells.[67] Additionally, it was shown that the amount and extent of bone ingrowth was higher for equine bone blocks, although this was not of statistical significance. Moreover, Araújo et al. evidenced the lesser osteogenic capacity of xenogeneic blocks, compared with autogenous grafts, by means of mineralized tissue (47.5 ± 5.0% vs. 23.3 ± 3.0%, respectively).[17] Similarly, findings by De Santis et al. illustrated the poor incorporation of the block graft into the pristine bone for horizontal ridge augmentation, demonstrating that, while 77% of the autogenous bone presented with vital mineralization, only 5.9% of the deproteinized bovine bone could be identified as new bone formation.[73] Therefore, it depends upon the clinician's judgment regarding whether it is preferable to maintain the space or improve predictability by ensuring faster bone turnover.

Future directions

In order to facilitate bone graft adaptation, speed up the surgical procedure and limit any potential graft mobility or dead space, prefabrication of graft scaffolds using advanced computed

tomography is the next wave of bone regeneration and repair.[74, 75] The idea of these scaffolds for bone regeneration is based upon their ability not only to maintain space, but also to create a 3-D graft structure that mimics the body's own extracellular matrix into which cells attach, migrate and proliferate.[76, 77] The porosity in such a scaffold biomaterial is important because it allows the transport of nutrients and facilitates tissue ingrowth. Hollister et al. proposed that the ideal scaffold should possess the following four properties: form, function, fixation and formation.[74] Wagoner Johnson and Herschler further pointed out that scaffolds should possess biocompatibility, conductivity, bioactivity, osteoinductive and interconnected porosity.[78] Hence, synthetic scaffolds are currently being studied in animal models and *in vitro*.[79–84] The application of gene therapy (mesenchymal stem cells or human-derived growth factors) via prefabricated scaffolds is the focus of much research at present because growth factors can be used to accelerate the wound-healing process and to promote mesenchymal stem cell migration and maturation.

Conclusion

Allogeneic and xenogeneic bone block grafts represent promising alternatives to autogenous bone for ridge augmentation. Nonetheless, the evidence supporting the use of xenogeneic block grafts remains minimal; hence, more long-term human studies are needed to validate their effectiveness. In addition, using prefabricated scaffolds impregnated with growth factors provides an interesting field to be further explored.

Competing interests

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

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