



UNIVERSIDADE FEDERAL DE UBERLÂNDIA
FACULDADE DE ODONTOLOGIA



MARCELLA CUNHA CHIMIRRI

**APLICABILIDADE DOS ENXERTOS IMPRESSOS TRIDIMENSIONALMENTE NA
RECONSTRUÇÃO ÓSSEA: UMA REVISÃO DE ESCOPO**

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Trabalho de conclusão de curso apresentado a
Faculdade de Odontologia da Universidade
Federal de Uberlândia, como requisito parcial para
obtenção do título de Graduado em Odontologia

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RESUMO

Para solucionar os desafios associados à obtenção e adaptação de enxertos para reconstrução de defeitos ósseos complexos na região maxilofacial, tem sido proposto o desenvolvimento e criação de enxertos bioabsorvíveis customizados e impressos tridimensionalmente (3D). Esta revisão de escopo fornece uma visão geral dos avanços atuais no uso de enxertos bioabsorvíveis personalizados impressos em 3D em cirurgias reconstrutivas maxilofaciais. Pesquisas eletrônicas foram realizadas em cinco bases de dados para publicações até janeiro de 2024. Foram incluídos estudos que avaliaram pacientes submetidos à reconstrução de defeitos ósseos maxilofaciais utilizando planejamento virtual e enxertos bioabsorvíveis personalizados impressos em 3D. Foram coletados dados sobre complicações pós-operatórias, neoformação óssea, reabsorção do enxerto, sucesso/sobrevivência dos implantes dentários e satisfação do paciente. Dez estudos (5 relatos de casos, 4 séries de casos, 1 estudo clínico prospectivo) foram incluídos. Esses estudos avaliaram a eficácia dos enxertos impressos em 3D na reconstrução de defeitos maxilofaciais, no aumento ósseo para colocação de implantes dentários e na regeneração de defeitos ósseos periodontais. A maioria dos enxertos impressos em 3D foram considerados biocompatíveis e não causaram eventos adversos locais ou sistêmicos. Entretanto, algumas complicações pós-operatórias foram relatadas, incluindo exposição do enxerto, deiscência da ferida e infecção local. No geral, os enxertos impressos em 3D demonstraram compatibilidade dimensional com os defeitos ósseos, forneceram suporte para formação óssea, apresentaram uma união óssea adequada com as margens do defeito ósseo e permitiram a instalação de implantes dentários sem a necessidade de regeneração óssea guiada adicional. Conclui-se que os enxertos bioabsorvíveis personalizados impressos em 3D, guiados por planejamento virtual, apresentam uma opção promissora para reconstrução maxilofacial devido à sua precisão, osteocondutividade e propriedades biocompatíveis.

Palavras-chave: Impressão Tridimensional, Enxerto ósseo, Regeneração óssea, Materiais biocompatíveis.

ABSTRACT

Virtual planning and customized 3D-printed bioresorbable structures have been proposed as a solution to the challenges associated with obtaining and shaping grafts or implants for reconstructing complex geometric bone defects in the maxillofacial region. This scoping review provides an overview of the current advancements in virtual planning and custom-made 3D-printed bioresorbable scaffolds, along with their clinical outcomes in maxillofacial reconstructive surgeries. Electronic searches were conducted across five databases for publications up to January 2024. Included in the review were reports evaluating patients who underwent maxillofacial bone defect reconstruction using virtual planning and custom-made 3D-printed bioresorbable scaffolds. Data on postoperative complications, new bone formation, scaffold resorption, dental implant success/survival, and patient satisfaction were collected. Ten studies (5 case reports, 4 case series, one prospective clinical study) were included. These studies assessed the effectiveness of 3D-printed scaffolds in reconstructing maxillofacial defects, bone augmentation for dental implant placement, and regeneration of periodontal defects. Most of the 3D-printed scaffolds were biocompatible and did not cause local or systemic adverse events. However, some postoperative complications were reported, including graft exposure, wound dehiscence, and local infection. Overall, the 3D-printed scaffolds demonstrated favorable dimensional compatibility with deformities, provided durable support, promoted bone formation, achieved adequate bone union with host bone tissues, and supported dental implant placement without additional guided bone regeneration. In conclusion, custom-made 3D-printed bioresorbable scaffolds, guided by virtual planning, present a promising option for maxillofacial reconstruction due to their accuracy, osteoconductivity, and biocompatible properties.

Keywords: Three-Dimensional Printing, Bone graft, Bone regeneration, Biocompatible materials

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1 ARTIGO CIENTÍFICO

THREE-DIMENSIONAL PRINTED BIORESORBABLE SCAFFOLD FOR MAXILLOFACIAL BONE RECONSTRUCTION: A SCOPING REVIEW¹

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¹ Artigo Científico elaborado de acordo com as normas do periódico internacional Internacional Brazilian Dental Journal

ABSTRACT

The use of virtual planning and customized 3D-printed bioresorbable structures has been proposed as a solution to the challenges associated with obtaining and shaping grafts or implants for reconstructing complex geometric bone defects in the maxillofacial region. This scoping review provides an overview of the current advancements in virtual planning and custom-made 3D-printed bioresorbable scaffolds, along with their clinical outcomes in maxillofacial reconstructive surgeries. Electronic searches were conducted across five databases for publications up to January 2024. Included in the review were reports evaluating patients who underwent maxillofacial bone defect reconstruction using virtual planning and custom-made 3D-printed bioresorbable scaffolds. Data on postoperative complications, new bone formation, scaffold resorption, dental implant success/survival, and patient satisfaction were collected. Ten studies (5 case reports, 4 case series, 1 prospective clinical study) were included. These studies assessed the effectiveness of 3D-printed scaffolds in reconstructing maxillofacial defects, bone augmentation for dental implant placement, and regeneration of periosseous defects. Most of the 3D-printed scaffolds were found to be biocompatible and did not cause local or systemic adverse events. However, some postoperative complications were reported, including graft exposure, wound dehiscence, and local infection. Overall, the 3D-printed scaffolds demonstrated favorable dimensional compatibility with deformities, provided durable support, promoted bone formation, achieved adequate bone union with host bone tissues, and supported dental implant placement without the need for additional guided bone regeneration. In conclusion, custom-made 3D-printed bioresorbable scaffolds, guided by virtual planning, present a promising option for maxillofacial reconstruction due to their accuracy, osteoconductivity, and biocompatible properties.

Keywords: Custom-made synthetic scaffolds; synthetic bone graft; scaffold bone block; 3D printed scaffold; bone regeneration.

INTRODUCTION

Reconstructive surgeries of maxillofacial defects due to trauma or resulting from ablative procedures are crucial in restoring anatomic structures, appearance, and tissue functions (1). Similarly, in many cases, alveolar ridge deficiency resulting from bone resorption after tooth extraction requires primary augmentation before dental implant placement (2). Until now, autogenous bone grafts remain the “gold standard” for these procedures, providing their osteogenic, osteoinductive, and osteoconductive properties (3). However, the need for a second surgical site to harvest the grafts from an unaffected area drastically increases the procedure morbidity, including postoperative pain, infection risk, ambulatory difficulty, and sensory abnormalities. Associated with that, high graft resorption rate, limited availability, and anatomical limitations are deemed significant limitations (2). The need to manually sculpt the bone blocks into the complex tridimensional (3D) defect configuration is also highlighted as a significant disadvantage of autogenous bone grafts in these procedures, increasing its complexity and surgery time (4).

Allografts and synthetic bones have been used to treat craniofacial deformities as substitutes for autogenous bone grafts (5-7). Nonetheless, concerns over biological contamination and ethical considerations related to the trade of bodily tissues have restricted the use of allografts (5). Conversely, synthetic bones offer advantages over autografts and allografts regarding safety and invasiveness since they eliminate contamination risks and the need for bone harvesting. However, similarly to autogenous bone, both types of grafts require manual shaping during surgery, leading to diminished precision and suboptimal aesthetic results (6).

In a recent scenario, virtual planning and 3D fabrication of custom prototypes, surgical guides, templates, implants, grafts, and scaffolds have become tools of interest in cranio-maxillofacial surgeries to overcome these limitations (7). Using a 3D computed tomography (CT) scan, it's possible to create a 3D prototype of the patient's maxillofacial structure by transferring the files to specific reconstruction software (Figure 1). Advanced computer-aided design (CAD) software can design a custom-made bone graft based on this 3D model, ensuring it fits precisely into the intended site. This approach guarantees a more effective, patient-specific treatment with a simplified surgical procedure that consumes less time (8).

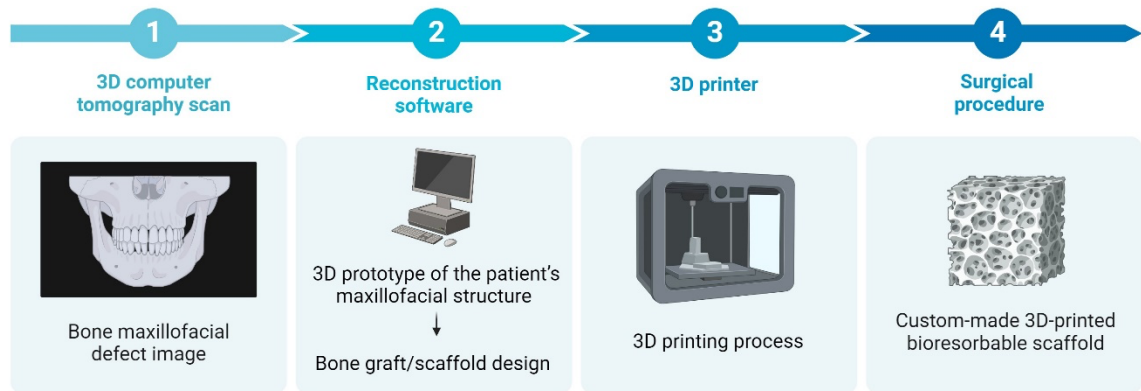


Figure 1: Three-dimensional printed bioresorbable scaffold obtention sequence

Three common 3D fabrication methods include cutting, casting, and layer manufacturing (6). In particular, layer manufacturing (such as fused deposition modeling, selective laser sintering, stereolithography, and inkjet printing) involves the fabrication of objects through material deposition, allowing the construction of objects layer-by-layer from a digital CAD file (8). Unlike the other two methods, layer manufacturing techniques can mimic complex external shapes and internal structures to be reconstructed from maxillofacial deformities. Moreover, the possibility of manufacturing internal interconnective pores and vessels in personalized scaffolds, medical implants, and grafts allows the possibility of vascularization and cell invasion of these synthetic biomaterials (9).

Layer manufacturing technology holds the potential to offer reduced surgical time, morbidity, and highly customized grafts for reconstructing maxillofacial defects in a convenient, rapid, and cost-effective manner (10). Various materials and processes have been investigated and documented for this purpose. Nonbiodegradable scaffolds have been reported, made of titanium or polyetherketoneketone, using 3D fabrication technology (11). Nonetheless, the implanted nonbiodegradable scaffolds are enduring and could potentially induce inflammation and infection at the implantation site (10). In response to these constraints, biodegradable or bioabsorbable materials have garnered attention for their ability to possess rigidity and biocompatibility, promote bone regeneration, and reduce the risk of foreign body reactions (12). However, concerns about material resistance, vascularization, resorption, fixation methods, indications, and host responses are some of the topics under review.

Thus, this scoping review presents the current ‘state of the art’ about virtual planning and custom-made 3D-printed bioresorbable scaffolds and their reported clinical results applied to maxillofacial reconstructive surgeries.

MATERIALS AND METHODS

1. Protocol

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) guidelines (13) were used for reporting this study. A specific review question was elaborated by PICO (population; intervention; comparator; outcome): "Does the utilization of 3D-printed bioresorbable scaffolds effectively promote bone regeneration in maxillofacial bone defects?"

2 Eligibility criteria

The following inclusion criteria were adopted based on the following PICO criteria: (P) Population: patients with maxillofacial bone defects; (I) Intervention: maxillofacial bone defects reconstruction using virtual planning and custom-made 3D-printed bioresorbable scaffolds; (C) Comparator: bone defects reconstruction using different types of bone grafts; (O) Outcomes: postoperative complications, new bone formation, scaffold resorption, dental implant success/survival and patients satisfaction; (S) Study design: clinical studies [including randomized clinical trials (RCTs), controlled clinical studies, cohort studies (prospective or retrospective), case series, case reports] reporting data about using 3D-printed bioresorbable scaffolds for the reconstruction of maxillofacial bone defects. Moreover, only articles in the English language were included.

Original research articles that did not follow the above criteria were excluded from this scoping review. Moreover, letters to the editor, conference proceedings, protocol articles, historical reviews, preclinical studies, and unpublished articles were also excluded.

3. Information source and search

Electronic searches of PubMed, EMBASE, Web of Science, Scopus, and Cochrane Library databases were conducted for publications up to January 2024. The search strategies were created using the Medical Subject Headings (MeSH) and Embase Subject Headings (Emtree). Boolean operators (AND and OR) combined the descriptors and improved the search strategy through different combinations, respecting each database syntax rule (Table 1). Grey

literature (Google Scholar database) was also searched. No filters were utilized in the search strategy.

Table 1: Strategies for database search

Database	Search Strategy (January 2024)
PubMed/ MEDLINE	#1 ("3D printed"[All Fields] OR "3D printed scaffold"[All Fields] OR ("3d"[All Fields] AND ("printed"[All Fields] OR "printing"[MeSH Terms] OR "printing"[All Fields] OR "print"[All Fields] OR "printings"[All Fields] OR "prints"[All Fields]) AND ("bone and bones"[MeSH Terms] OR ("bone"[All Fields] AND "bones"[All Fields]) OR "bone and bones"[All Fields] OR "bone"[All Fields]) AND ("scaffold"[All Fields] OR "scaffold s"[All Fields] OR "scaffolded"[All Fields] OR "scaffolder"[All Fields] OR "scaffolders"[All Fields] OR "scaffolding"[All Fields] OR "scaffoldings"[All Fields] OR "scaffolds"[All Fields])) OR "3D printing"[All Fields] OR "three-dimensional printings"[All Fields] OR "additive manufacturing"[All Fields] OR "computer aided design computer aided manufacturing"[All Fields] OR "CAD/CAM"[All Fields] OR "computer aided design computer aided manufacturing"[All Fields] OR ("custom made"[All Fields] AND ("computer aided design"[MeSH Terms] OR ("computer aided"[All Fields] AND "design"[All Fields]) OR "computer aided design"[All Fields] OR ("cad"[All Fields] AND "cam"[All Fields]) OR "CAD/CAM"[All Fields]) AND ("scaffold"[All Fields] OR "scaffold s"[All Fields] OR "scaffolded"[All Fields] OR "scaffolder"[All Fields] OR "scaffolders"[All Fields] OR "scaffolding"[All Fields] OR "scaffoldings"[All Fields] OR "scaffolds"[All Fields])) OR "Custom-Made Synthetic Scaffolds"[All Fields])
	#2 (((("scaffold"[All Fields] OR "scaffold s"[All Fields] OR "scaffolded"[All Fields] OR "scaffolder"[All Fields] OR "scaffolders"[All Fields] OR "scaffolding"[All Fields] OR "scaffoldings"[All Fields] OR "scaffolds"[All Fields]) AND ("bone and bones"[MeSH Terms] OR ("bone"[All Fields] AND "bones"[All Fields]) OR "bone and bones"[All Fields] OR "bone"[All Fields]) AND ("block"[All Fields] OR "blocked"[All Fields] OR "blocking"[All Fields] OR "blockings"[All Fields] OR "blocks"[All Fields])) OR "synthetic bone graft"[All Fields] OR "bone graft"[All Fields] OR "scaffold tissue"[All Fields] OR "scaffolds tissue"[All Fields] OR "tissue scaffold"[All Fields] OR "tissue scaffolds"[All Fields] OR "grafting bone"[All Fields] OR "bone grafting"[All Fields] OR "bone transplantation"[All Fields] OR "transplantation bone"[All Fields] OR "scaffolds"[All Fields] OR "scaffold"[All Fields])
	#3 ("bone formation"[All Fields] OR "new bone formation"[All Fields] OR "bone regeneration"[All Fields] OR "implant survival"[All Fields] OR "survival rate"[All Fields] OR "implant stability"[All Fields])
	#1 AND #2 AND #3
Embase	#1 '3d printed' OR '3d printed scaffold' OR '3d printed bone scaffold' OR '3d printing'/exp OR '3d printing' OR 'three-dimensional printings' OR 'additive manufacturing'/exp OR 'additive manufacturing' OR 'cad/cam'/exp OR 'cad/cam' OR 'computer-aided design/computer-aided manufacturing'/exp OR 'computer-aided design/computer-aided manufacturing' OR 'custom-made cad/cam scaffolds' OR 'custom-made synthetic scaffolds'
	#2 'scaffold bone block' OR 'synthetic bone graft'/exp OR 'synthetic bone graft' OR 'bone graft'/exp OR 'bone graft' OR 'scaffold, tissue'/exp OR 'scaffold, tissue' OR 'scaffolds, tissue' OR 'tissue scaffold'/exp OR 'tissue scaffold' OR 'tissue scaffolds'/exp OR 'tissue scaffolds' OR 'grafting, bone' OR 'bone grafting'/exp OR 'bone grafting' OR 'bone transplantation'/exp OR 'bone transplantation' OR 'transplantation, bone'/exp OR 'transplantation, bone' OR 'scaffolds' OR 'scaffold'/exp OR 'scaffold'
	#3 'bone formation'/exp OR 'bone formation' OR 'new bone formation' OR 'bone regeneration'/exp OR 'bone regeneration' OR 'implant survival'/exp OR 'implant survival' OR 'survival rate'/exp OR 'survival rate' OR 'implant stability'/exp OR 'implant stability'
	#1 AND #2 AND #3
Web of Science	#1 (((((((ALL=("3D printed")) OR ALL=("3D printed scaffold")) OR ALL=("3D printed bone scaffold")) OR ALL=("3D printing")) OR ALL=("three-dimensional printings")) OR ALL=("additive manufacturing"))

	OR ALL=("Computer-aided design/computer-aided manufacturing")) OR ALL=("CAD/CAM")) OR ALL=("computer-aided design/computer-aided manufacturing")) OR ALL=("custom-made CAD/CAM scaffolds"))
	#2 ((((((((((ALL=("scaffold bone block")) OR ALL=("synthetic bone graft")) OR ALL=("bone graft")) OR ALL=("scaffold, tissue")) OR ALL=("scaffolds, tissue")) OR ALL=("tissue scaffold")) OR ALL=("tissue scaffolds")) OR ALL=("grafting, bone")) OR ALL=("bone grafting")) OR ALL=("bone transplantation")) OR ALL=("transplantation, bone")) OR ALL=("scaffolds")) OR ALL=("scaffold"))
	#3 (((((ALL=("bone formation")) OR ALL=("new bone formation")) OR ALL=("bone regeneration")) OR ALL=("implant survival")) OR ALL=("survival rate")) OR ALL=("implant stability"))
	#1 AND #2 AND #3
Scopus	#1 (("3d printed bone scaffold") OR ("three-dimensional printings") OR ("additive manufacturing") OR ("computer-aided design/computer-aided manufacturing") OR ("cad/cam") OR ("computer-aided design/computer-aided manufacturing") OR ("custom-made cad/cam scaffolds") OR ("custom-made synthetic scaffolds"))
	#2 (("scaffold bone block") OR ("synthetic bone graft"))
	#3 (("bone formation") OR ("new bone formation") OR ("bone regeneration") OR ("implant survival") OR ("survival rate") OR ("implant stability"))
	#1 AND #2 AND #3
The Cochrane Library	#1 "3D printed" OR "3D printed scaffold" OR "3D printed bone scaffold" OR "3D printing" OR "three-dimensional printings" OR "additive manufacturing" OR "Computer-aided design/computer-aided manufacturing" OR "CAD/CAM" OR "computer-aided design/computer-aided manufacturing" OR "custom-made CAD/CAM scaffolds" OR "Custom-Made Synthetic Scaffolds"
	#2 "scaffold bone block" OR "synthetic bone graft" OR "bone graft" OR "scaffold, tissue" OR "scaffolds, tissue" OR "tissue scaffold" OR "tissue scaffolds" OR "grafting, bone" OR "bone grafting" OR "bone transplantation" OR "transplantation, bone" OR "scaffolds" OR "scaffold"
	#3 "bone formation" OR "new bone formation" OR "bone regeneration" OR "implant survival" OR "survival rate" OR "implant stability"
	#1 AND #2 AND #3

4. Selection of sources of evidence

The studies were selected by two independent researchers (CMAM and JAO). Titles and abstracts of retrieved articles were screened for eligibility, considering the inclusion/exclusion criteria described above, and irrelevant studies were excluded. Full texts of the studies that met the eligibility criteria were accessed by both authors for inclusion. Disagreements between the investigators were resolved by consensus or were referred to a third review author (SCP) for the final decision. Studies that met the selection criteria were processed for data extraction. The articles excluded in the full-text analysis were listed separately, and the reasons for exclusion were specified.

5. Data charting and synthesis of results

Two investigators (CMAM and JAO) independently read all studies and extracted the following data from all included studies using a standardized spreadsheet: (a) study design; (b) sample size; (c) patients' gender and mean age; (d) maxillofacial defect region; (e) alloplastic material type; (f) graft pore size and porosity; (g) graft dimension; (h) software and printer type; (i) fixation type; (j) postoperative complications; (k) Follow-up and (l) Outcomes (bone regeneration, dental implant success/survival and patients satisfaction).

6. Synthesis of results

A logical and descriptive summary of the results was made based on the review objective and question. A table was developed describing the characteristics of the included studies and the key information relevant to the review question.

RESULTS

1. Selection of sources of evidence

The electronic search in the databases found 5323 results, being 3150 unique citations. A total of 51 publications (45 publications obtained from the database search and 6 publications obtained through other search methods) were evaluated for full-text reading, of which 41 were subsequently excluded based on the inclusion criteria (Figure 2). The exclusion motivation for each study is shown in Table 2. The remaining 10 studies were included in the scoping review (Table 3).

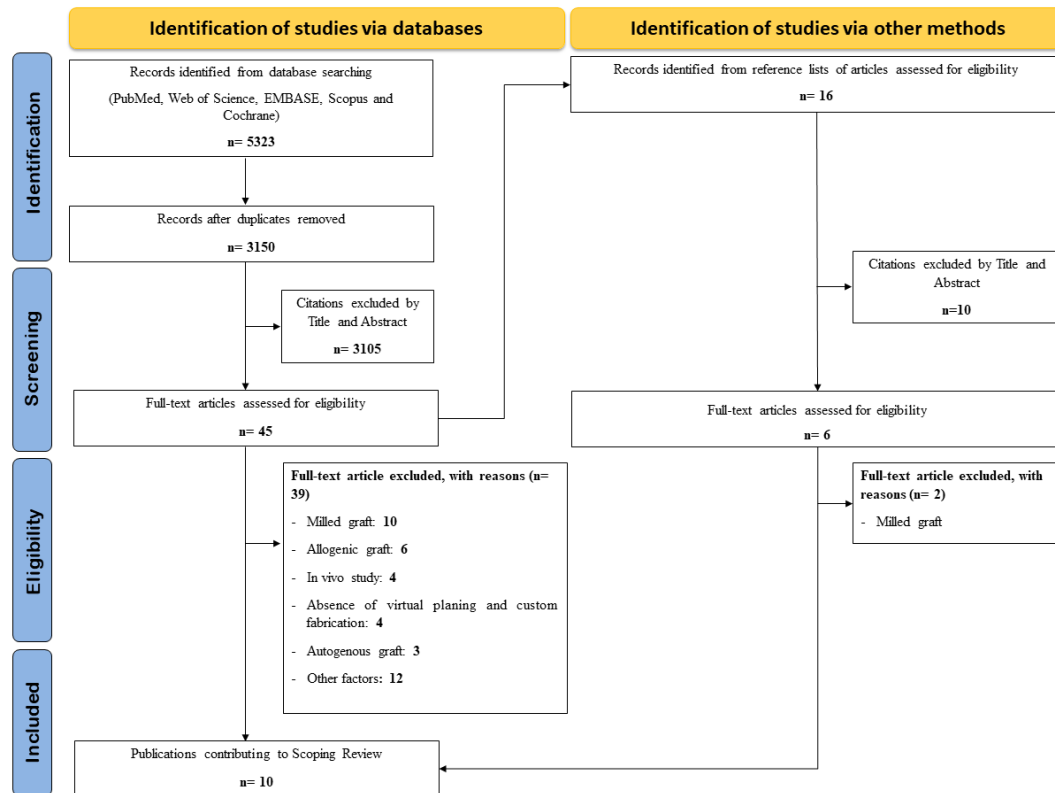


Figure 2: Literature search flowchart.

Table 2: Articles excluded with the reasons after evaluating the full text.

Author/Year	Exclusion reasons
Abbate, Togo (13)	Autogenous graft
Abdelazeem, Mattar (14)	Event annals
Alshammari, Alabdah (15)	In vivo study
Ambrosio, Azimi (16)	Allogeneic graft
Averianov, Stepanova (17)	Communication
Benady, Meyer (18)	Wrong region
Blume, Back (19)	Allogeneic graft
Bugiolachi, Bontá (20)	Allogeneic graft
Cianci (21)	Milled graft
Cristalli, La Monaca (22)	Milled graft
de Almeida Malzoni, Gonçalves (23)	Study protocol
Di Emidio, Cardinelli (24)	Used human cadaver
El Chaar, Urtula (25)	Allogeneic graft
Figliuzzi, Mangano (26)	Milled graft
Finelle and Lee (27)	Milled graft
Ghayor, Bhattacharya (28)	In vivo study
He, Dong (29)	In vivo and in vitro studies
Kijartorn, Wongpairojpanich (30)	Absence of virtual planning and custom fabrication
Kritzas, Uhrich (31)	Event annals

Lee, Kengla (32)	In vivo study
Li, Zhang (33)	In vitro study
Li, Zhang (34)	Guide printing
Luongo, Mangano (35)	Milled graft
Malmström, Slotte (36)	Absence of virtual planning and custom fabrication
Mangano, Macchi (37)	Milled graft
Mangano, Zecca (38)	Milled graft
Mangano, Luongo (39)	Milled graft
Milovanovic, Stojkovic (40)	Characterization study
Mirković, Budak (41)	Milled graft
Montero, Becerro (42)	Absence of virtual planning and custom fabrication
Pfaffeneder-Mantai, Meller (43)	Milled graft
Pham Dang, Lafarge (44)	Allogeneic graft
Perez, Lazzarotto (45)	Absence of virtual planning and custom fabrication
Rodríguez-Tizcareño, Barajas (46)	Full text not found
Tang, Zhai (47)	Autogenous graft
Tuna, Yilmaz (48)	Milled graft
Warnke, Springer (49)	Milled graft
Wu, Shi (50)	Wrong region
Zhang, Shi (51)	Allogeneic graft and wrong region
Zheng, Wang (52)	Characterization study
Zheng, Chen (53)	Autogenous graft

2. Characteristics of sources of evidence

Out of the 10 studies included, 5 were case reports, 4 were case series, and only one was classified as a prospective clinical study. A total of 58 patients with maxillofacial defects underwent treatment using custom-made 3D-printed bioresorbable scaffolds. Five studies (6, 10, 12, 54, 55) assessed the effectiveness of the 3D scaffolds for reconstructing maxillofacial defects in various regions, including the maxilla (15 partial or total defects and one alveolar cleft defect), mandible (21 defects), chin (10 defects), and frontal bone (1 defect). Four studies (2, 8, 56, 57) utilized the 3D scaffolds for bone augmentation before dental implant placement, while one study (9) employed the 3D scaffolds for regenerating periosseous defects. The minimum postoperative follow-up duration was 6 months, while the maximum was 7 years.

Regarding the type of alloplastic material used for 3D-printed bioresorbable scaffold production, polycaprolactone (PCL) polymer was the most commonly utilized, without any other alloplastic material (3 studies). PCL was also used in combination with beta-tricalcium phosphate (β -TCP) (1 study) or hydroxyapatite (HA) (1 study). Other alloplastic materials

utilized included α -TCP alone (2 studies), nano-HA (1 study), calcium phosphate cement (1 study), and HA associated with TCP (1 study). Some studies reported the use of additional biomaterials/biological agents in conjunction with 3D-printed scaffolds to enhance the biological response, including demineralized bone matrix (2 studies), calcium phosphate (1 study), collagen membrane (1 study), bone marrow mesenchymal stem cells (BMSCs; 1 study), platelet-rich fibrin (PRF; 1 study), platelet-rich plasma (PRP; 1 study), concentrated growth factors (CGFs; 1 study), recombinant human platelet-derived growth factor-BB (rhPDGF-BB; 1 study), and recombinant human bone morphogenetic protein-2 (rhBMP-2; 1 study). Only 6 studies provided data on the pore size of the 3D-printed scaffolds, with sizes ranging from 300 to 500 μm in 4 studies and 900 to 2250 μm in 2 studies. Additionally, four studies reported the porosity of the 3D-printed scaffolds, with values of 50% in 2 studies, 60% in 1 study, and 75% in 1 study. The fixation of the 3D-printed scaffolds typically involved the use of plates, screws, pins (constructed from titanium, hydroxyapatite/poly-L-lactide, or poly-D and L-lactic acid), and/or wire steel, as reported in 5 studies. Three studies used sutures, while two did not employ any fixation methods.

3. Synthesis of results

Most 3D-printed scaffolds utilized in the included studies were biocompatible and did not induce local or systemic adverse events. However, some postoperative complications were reported, including graft exposure (3 studies; 8 of 14 sites), wound dehiscence (1 study; 1 of 8 sites), and local infection (1 study; 4 of 20 sites). In five studies, the defects were repaired without any abnormal findings.

Overall, the 3D-printed scaffolds utilized in maxillofacial defect reconstruction (five studies) exhibited favorable dimensional compatibility with deformities, provided durable support, enhanced bone formation (assessed through computed tomography (CT) images), and achieved adequate bone union between the artificial bones and host bone tissues. Two studies (6, 55) reported that the patients were satisfied with the treatment outcomes. In addition, using 3D scaffolds for bone augmentation in the maxilla (2, 8, 56) and anterior mandible defects (57) promoted bone formation (confirmed by histological analysis and CT images). It allowed dental implant placement without additional guided bone regeneration. On the other hand, only one case report (9) described the treatment of a periosseous defect using 3D-printed scaffolds; after 13 months the site showed a larger dehiscence and wound failure, necessitating entire scaffold removal.

Table 3: Characteristics of the studies and participants included in the review.

Author (Year)	Study design	Sample size	Mean Age	Gender	Maxillofacial defect region	Alloplastic material type	Graft dimensions, pore size and porosity	Software/ Printer type	Fixation type	Postoperative complications	Follow-up	Outcomes
Ahn, Lee (10)	Case report	1	10	M	Alveolar cleft defect	Medical - grade PCL (Evonik Industry, Pharma Polymers, Essen, Germany) + Bone marrow-derived MSCs	Graft dimensions: NI Pore size: 300µm Porosity: 50%	Software: 3D medical image editing software (Materialise) Printer: Micro-extrusion-based 3D bioprinter (T&R Biofab Co, Ltd, Siheung, Republic of Korea)	2-hole titanium mini-plate (2 mm in thickness; Jeil Medical Co, Seoul, Republic of Korea) + Mini-screws (2 mm in diameter and 6 mm in length; Jeil Medical Co)	Exposition of the plate fixing the graft 4 months after the surgery. The plate and screws were removed.	6 months	The bone volume of the newly regenerated bone accounted for 45% of the total defect volume (evaluated by radiodensity analysis of CT images). The bone mineral density of the regenerated bone measured approximately 604.8 HU, compared to about 806 HU for the normal bone surrounding the defect. The left maxillary canine erupted, and orthodontic treatment started 8 months after surgery.
Han, Shim (54)	Case series	3	P1: 43 P2: 45 P3: 18	F: 1 M: 2	P1: left radial maxillectomy; P2: radical maxillectomy and partial mandibulectomy; P3: right partial maxillectomy	Medical - grade PCL (Evonik Industries, Essen, Germany)	Graft dimensions: NI Pore size: 900 µm Porosity: NI	Software: 3D medical image editing software (Materialise Mimics; Materialise NV, Leuven, Belgium)	NI	No wound dehiscence or signs of infection	2 years	Follow-up evaluation revealed that the pores had indeed become filled with soft tissue, and the facial contour was well maintained. Eye height with an acceptable degree of symmetry (compared with that note

								Printer: In-house 3D printer (T&R Biofab Co. Ltd., Seoul, Korea)				preoperatively) was maintained throughout the follow-up period.
Jeong, Kim (12)	Case series	8	36.4 ±13.7	F: 4 M: 4	Maxillary defects	PCL (Evonik Industries, Essen, Germany) + β-TCP (Foster corporation, Putnam, CT, USA) (8:2 ratio) + Bone regeneration material [Ca ₃ (PO ₄) ₂ bone substitute (n=1); DBM (n=2); none (n=5)]	Graft dimensions: NI Pore size: 500 μm Porosity: 50%	Software: 3D modeling software (3- Matic Research 9.0, Materialise, Leuven, Belgium) Printer: NI	HA-PLLA resorbable plate and screws (n=1) Titanium miniplate and screws (n=5) Wire steel (n=2)	Secondary fat graft (n=4) and wound dehiscence (n=1)	6 months	The PCL/β-TCP scaffold provided durable support and enhanced bone formation (evaluated by CT: mean bone fraction volume of 23.34%, ranging from 7.81% to 66.21% and mean tissue density of 188.84 HU, ranging from 151.48 HU to 291.74 HU). The Young's modulus of the standardized scaffold with 50% porosity was 162.7 ±12.8 MPa
Kanno, Nakatsuka (55)	Prospect ive clinical study	20 (23 sites)	31.7 ±11	F: 14 M: 6	Facial bone deformities localized in maxilla (n=3), mandible (n=12), chin (n=7), and frontal bone (n=1)	Sprayed hardening liquid (5% sodium chondroitin sulfate, 12% disodium succinate and 83% distilled water) +	Graft dimensions: NI Pore size: NI Porosity: NI	Software: NI Printer: 3D inkjet printer (Z4606 3D color printer, Z- Corporation, MA, USA)	Absorbable sutures [2-0 Vicryl®, Johnson & Johnson, USA; (n=15)] No fixation (n=5)	Bone graft removal due to local infection [after 1-2 years (3 cases); after 5 years (1 case)]	1 to 7 years and 3 months	The grafts were confirmed to be easily installed onto the recipient sites. In 18 out of 21 sites, the patients were satisfied with their results at 1 year postoperatively. Sufficient bone union was confirmed in 19 sites. No chronological change was seen in the

						α -TCP powder (Taihei Chemical Industrial, Osaka, Japan)						graft shape (CT analysis). The inner CT values of the graft increased in all the sites.
Mekcha, Wongpairojp anich (2)	Case series	12	53.5 $\pm$ 9.26	M: 6 F: 6	Dental implant therapy for horizontal bone defects	3D bone block of nHA alone (n=3) or 3D bone block of nHA + CGFs + DBM + collagen membrane + PRF membrane (n=9)	Graft dimensions: NI Pore size: ranged between 1.47 and 2.25 mm Porosity: NI	Software: 3D design software (Geomagic Freeform®, 3D Systems, USA) + professional haptic device (The Touch™ Haptic Device, 3D Systems, USA) Printer: ProJet160 3D printer (3D systems, USA)	No fixation	Mucosa perforation resulting in partial or total bone graft failure (two cases treated only with HA block grafts) Partial bone block graft failure (one case treated with HA block + CFG + PRF)	6 months	The 3DHA block graft was successful in 10 of 12 patients. Graft adjustment was not required. All 3DHA adapted and fit well at all defect sites. Maximum mean horizontal bone gains were 3.06 $\pm$ 1.02 and 3.56 $\pm$ 0.23 mm from the DICOMs and STL data sets, respectively. The volume gain was 229.8 $\pm$ 82.96 mm ³ . A low pain score after surgery was reported of 1.41 $\pm$ 0.51, while the healing index score increased with a maximum mean of 4.7 $\pm$ 0.67. New bone formation was observed around the graft particles in all harvested bone cores (28.6 $\pm$ 1.88%). Thirteen implants were placed with good primary stability (ISQ = 65 $\pm$ 4.08), without

												additional guided bone regeneration.
Mangano, Giuliani (8)	Case report	1	NI	NI	Maxilla buccal plate defect	HA (30%) + TCP (70%)	Graft dimensions: NI Pore size: $370 \pm 25\mu\text{m}$ Porosity: 60%	Software: NI Printer: Industrial robot (GLT, Pforzheim, Germany)	Sutures	No complications	7 years	The biomaterial volume decreased by over 23%, with the newly formed bone volume representing more than 57% of the overall mineralized tissue (microcomputed tomography biopsy analysis). In comparison to unloaded controls or peri-dental bone, the test sample appeared significantly more mineralized and bulkier. Histological evaluation revealed complete integration of the scaffold and signs of particle degradation. The percentage of bone, biomaterials, and soft tissues was 59.2%, 25.6%, and 15.2%, respectively.

Rasperini, Pilipchuk (9)	Case report	1	53	M	Periosseous defect (lower right canine)	PCL powder (Polysciences Inc., Warrington, PA, USA) + 4% HA (4%) + rhPDGF-BB (0.3 mg/mL)	Graft dimensions: NI Pore size: NI Porosity: NI	Software: Magics 15 (Materialise Inc., Leuven, Belgium), NX 7.5 (Siemens PLM Software, Plano, TX, USA) and Mimics (Materialise Inc) Printer: Selective laser sintering (Formiga P100 System; EOS e-Manufacturing Solutions)	Ultrasound-activated resorbable poly-D and L-lactic acid pins (SonicWeld, KLS Martin Group, Tuttlingen, Germany)	The scaffold became exposed and was removed after 13 months.	13 months	For 12 months, the scaffold stayed concealed, showing a 3-mm increase in clinical attachment and partial root coverage. The 3D scaffold implanted successfully filled the human periodontal osseous defect, with no evidence of chronic inflammation or dehiscence. Nonetheless, by the 13th month, the scaffold became exposed.
Saijo, Igawa (6)	Case Series	10	35 ± 12.3	F: 9 M: 1	Maxilla (n=1), Mandible (n=7), Chin (n=3)	α-TCP powder (Taihei Chemical Industrial, Osaka, Japan) + Curing solution (5% sodium chondroitin sulfate, 12% disodium succinate and 83%	Graft dimensions: NI Pore size: NI Porosity: NI	Software: NI Printer: 3D inkjet printer (Z406 3D color printer, Z Corporation, Burlington, MA, USA)	Resorbable sutures	No local or systemic adverse events	12 months	The graft had good dimensional compatibility to deformities, requiring minimal dimension adjustment and minimum fixation. Initial clinical evidence of bone union between the artificial bones and host bone tissues was seen as early as 6 months, and all patients had partial union at 12 months. All the patients were satisfied with the esthetic facial appearance.

						distilled water)						
Schuckert, Jopp (57)	Case report	1	71	F	Peri-implant bone defect in the anterior mandible	PCL (Osteopore International Pte Ltd. Singapore) + PRP + rhBMP-2 (Induct0s, Wyeth, 1.2 mg)	Graft dimensions: NI Pore size: NI Porosity: 75%	Software: NI Printer: NI	No fixation	Complication-free wound healing	6 months	The radiological control demonstrated de novo-grown bone in the anterior mandible 6 months postoperatively (CT images). Dental implants were inserted in a third operation. All histological analyses, of the local bone as well as of the newly grown bone, showed vital laminar bone.
Schulz, Holtzhausen (56)	Case report	1	62	M	Bilateral severely atrophied posterior maxilla	Calcium-phosphate cement paste	Graft dimensions: 10 × 10 × 8 mm (right maxilla) and 10 × 14 × 8.5 mm (left maxilla) Pore size: 330 µm Porosity: NI	Software: SolidWorks software of Dassault Systèmes (SolidWorks Deutschland GmbH, München, Germany) + CTinA software Printer: NI	One micro screw (1.5 × 7 mm; Gebrüder Martin, Tuttlingen, Germany).	Any abnormal finding	9 months	After nine months, the scaffolds integration was evident. The trephine core revealed dense structures of the bone substitute closely associated with mature bone. In the interface bone substitute/mature bone, areas of osteoid deposition were present. Implant placement was feasible with adequate primary stability, and after 3 months, the implants were fully integrated.

NI: not informed; MSCs: mesenchymal stem cells; PCL: polycaprolactone; HU: hounsfield unit; β -TCP: beta tricalcium phosphate; α -TCP: alfa tricalcium phosphate; HA-PLLA: Hydroxyapatite/poly-l-lactide; DBM: Demineralized bone matrix; CGFs: concentrated growth factors; PRF: platelet-rich fibrin; ISQ: implant stability quotient; nHA: nanohydroxyapatite; HA: hydroxyapatite; TCP: tricalcium phosphate; rhPDGF-BB: recombinant human platelet-derived growth factor BB; PRP: platelet-rich plasma; rhBMP-2: recombinant human bone morphogenetic protein-2.

DISCUSSION

Managing complex maxillary defects with traditional reconstruction approaches is challenging when restoring the original 3D bone structure is necessary (12). As an alternative to conventional methods, this review showed that the use of custom-made artificial bones using a 3D layered manufacturing (3D printing) process enables the fabrication of scaffolds with customized patient- and site-specific forms, geometries, and porosity using biocompatible and bioresorbable materials. Collectively, findings from the included studies indicate that biodegradable printing materials are now viable for the personalized reconstruction of complex maxillofacial defects, yielding satisfactory outcomes by providing durable support and enhancing bone formation.

One of the most important characteristics of scaffolds is their chemical composition. It is recognized that using non-biodegradable materials heightens the risk of inflammation, infection, and potential implant protrusion (54). The utilization of biodegradable and clinically safe polymers has been proposed to address these constraints. In this review, PCL, either alone or in conjunction with other biomaterials and/or biological agents, was the most employed material in 3D-printed scaffold fabrication. PCL safely degrades into carbon dioxide and water and offers a suitable scaffold for guided bone regeneration due to its favorable mechanical properties and biocompatibility, with a slower degradation rate (2-3 years) (12). In this review, the utilization of PCL 3D-printed scaffold proved unsuccessful in one case report of periosteal defect regeneration (9). According to the authors, the slow resorption profile of the PCL scaffold, associated with a bulky design, restricted bone regeneration, leading to dehiscence, exposure, and subsequent microbial contamination around teeth after 12 months.

Incorporating β -TCP into PCL has been demonstrated to enhance the mechanical properties of the scaffold and promote osteogenic cell proliferation, differentiation, and mineralization (58). The fabrication of a scaffold with a ratio of 80:20 PCL: β -TCP, 50% porosity, and 500 μ m pore size was found to be effective in promoting early bone growth and ensuring durability in 8 cases of maxillary defects in this review (12). TCP is a bioceramic material with chemical properties resembling bone minerals and exhibits excellent osteoconductivity (12). Additionally, TCP displays an unpredictable biodegradation profile lasting 6 to 24 months. According to Yeo, Rai (59), the PCL–20% TCP scaffold gradually degraded within 6 months while maintaining pore interconnectivity for the formation of the newly mature bone. This initial degradation releases calcium ions, which enhance

mineralization by facilitating the osteogenic differentiation of adipose-derived stem cells. Saijo, Igawa (6) reported 10 successful cases of maxillofacial reconstruction using 3D-printed scaffolds containing α -TCP, wherein partial union between host bone and graft was observed at 12 months.

The use of synthetic HA in the fabrication of 3D-printed scaffolds was also reported in this review. HA demonstrates favorable biocompatibility and osteoconductive characteristics owing to its chemical similarity to alveolar bone. It is the least soluble form among naturally occurring calcium phosphate salts, providing an osteoconductive scaffold with notable resistance to physiological resorption (2). Following HA implantation, forming a thin apatite layer on the material surface facilitates the integration between the host bone and the material. Mangano, Giuliani (8) described the fabrication of a 3D-printed scaffold using HA (30%) combined with TCP (70%) for regenerating maxillary buccal plate defects. Assessment via microcomputed tomography revealed a decrease in biomaterial volume of over 23%, with newly formed bone accounting for more than 57% of the overall mineralized tissue after a 7-year follow-up period. The utilization of biphasic calcium phosphate in scaffold production is advantageous, as the rapid dissolution of TCP creates more space for new bone formation. At the same time, HA maintains the proper microarchitecture during the repair process (8).

In a case series reported by Mekcha, Wongpairojpanich (2), the utilization of a 3D bone block for horizontal bone defects was documented. This involved employing a combination of a 3D powder printing process and a low-temperature phase transformation to generate a unique low-crystalline nano-HA structure. The authors described a high complication rate in the early 2 months as soft tissue perforation for the HA block graft alone (two out of three cases). To address this issue, the authors utilized CGFs and PRF membranes to promote soft tissue healing, resulting in no complications in the other cases. After 6 months, cone beam computed tomography (CBCT) images showed sufficient bone volume for implant placement in all patients. The mean maximum horizontal bone gain reported (3.56 ± 0.45 mm) was comparable to that achieved with autologous bone block grafts combined with particulate xenografts covered with a resorbable membrane (4.8 ± 0.79 mm) (60) and allogeneic blocks (2.6 ± 2.5 mm) (61).

Another material utilized in the fabrication of 3D-printed scaffolds for bone regeneration is calcium phosphate cement (CPC). CPCs are hydraulic cement comprising one or more calcium orthophosphate powders and a liquid phase (56). This material is biologically active and osteoconductive, facilitating the migration and proliferation of osteoblasts, while its

slow biodegradability ensures high volume stability over many years (56). Moreover, calcium phosphate cements can be a carrier for specific agents to promote bone regeneration. Another advantage of CPC lies in its moldability and printability, allowing for base material modifications (56). Schulz, Holtzhausen (56) evaluated a 3D-printed CPC scaffold for sinus grafting. Nine months post-implantation, evident scaffold integration was observed, and implant placement was feasible with sufficient primary stability. According to the authors, one notable advantage of utilizing 3D-printed scaffolds is the ability to customize pore size according to biological and mechanical demands, which vary between non-load-bearing regions such as the maxillary sinus and load-bearing areas in the mandible. A recent histomorphometric analysis of human biopsies revealed that increased packing density reduced the integration of bone substitute particles in sinus floor augmentation (62). This issue could be addressed using a 3D-printed scaffold, as pore size is adjustable to optimize bone ingrowth (56).

It has been suggested that the scaffold's ideal degradation rate aligns with the osteogenesis rate. Consequently, the scaffold's framework would be substituted by newly formed bone (56). However, the studies reviewed found that the scaffolds were not entirely replaced by new bone within a short follow-up period (ranging from 6 months to 2 years). For instance, a complete replacement was not found even in the case 7 years and 3 months of the longest follow-up, although new bone formation was partly seen inside of the scaffolds (8). Nevertheless, the 3D-printed scaffolds reported in this review provided durable support and achieved adequate bone union between the artificial bones and host bone tissues. This outcome may be attributed to the ability of 3D-printed scaffolds to be customized to fit the defect site, facilitating close bone-scaffold contact. Unlike conventional artificial bones, which typically require considerable surgical time and expertise for dimensional adjustment and fixation (6), the 3D-printed scaffolds necessitated minimal or no dimensional adjustment (several minutes) and fixation, as reported by all included studies.

Porosity and pore size play crucial roles in cell attachment, differentiation, and proliferation. While increased material porosity can enhance cell adhesion and proliferation through interconnected pores, higher pore size or porosity may compromise mechanical resistance (56). Ideally, scaffolds should possess an interconnected macroporous structure (>100 μm in diameter) to facilitate cell infiltration, bone growth, and neovascularization (42). Moreover, incorporating microporosities into the macroporous structure can enhance permeability and cell migration, facilitating faster bone ingrowth and reducing patient healing time (56). Notably, 3D manufacturing technology allows for scaffold customization to address

the needs of each bone defect (42). Conversely, allogeneic and xenogeneic materials have predetermined properties and lack adjustability (56). In this review, pore sizes ranged from 300 to 2250 μm , with the porosity of 3D-printed scaffolds varying from 50 to 75%.

According to Saijo, Igawa (6), inkjet printing technology stands out compared to other layer manufacturing methods due to its capability to process biocompatible and biodegradable materials at room temperature. This capability enables the creation of porous scaffolds with precisely controlled internal structures and excellent resolution. In contrast, the current stereolithography approach relies on photosensitive resin and photoinitiators, which typically lack biocompatibility or biodegradability. Additionally, this method generates radicals that can pose toxicity risks to human tissues (6). Similarly, although less precise, fused deposition modeling utilizes thermoplastics that are often neither biocompatible nor biodegradable and may require support structures in specific scenarios (6).

Some postoperative complications were described in the studies, including wound dehiscence, graft exposure, and local infection. The 3D-printed scaffold should be covered with a durable and thick flap to prevent these complications. A meticulous debridement of remaining unhealthy tissue inside the defect should also be carried out to avoid wound complications (12). Moreover, Kanno, Nakatsuka (55) it noted that the excessive height of the 3D-printed scaffold in contact with the recipient bone led to unexpected mobility and instability of the graft, increasing susceptibility to infection associated with friable granulation tissue. According to these authors, fixation of the 3D-printed scaffold to the recipient's bones helped reduce the incidence of postoperative infection.

Although the included studies reported promising results with the use of 3D-printed scaffolds in maxillofacial defect reconstruction, caution should be exercised in their evaluation. This is due to the predominance of case series and case reports with short follow-up periods among the included studies. Additionally, no randomized controlled trials have been identified in the literature thus far. Furthermore, bone formation was primarily assessed solely by CT images in most of the studies. Therefore, experimental studies with larger sample sizes are necessary to validate the efficacy of 3D-printed scaffolds in bone regeneration. Variations in the scaffold's porosity and long-term examinations of the scaffold resorption characteristics are also needed to optimize stability and bone ingrowth.

In conclusion, custom-made 3D-printed bioresorbable scaffolds, seem to offer a promising alternative for maxillofacial reconstruction due to their accuracy, osteoconductivity,

and biocompatible properties. However, further clinical studies with larger sample sizes and long-term results are needed to determine the clinical efficacy of 3D-printed scaffolds.

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ANEXO I – Normas do Periódico Internacional Brazilian Dental Journal

INSTRUCTIONS FOR AUTHORS

The Brazilian Dental Journal is a peer-reviewed (double-blind system) scientific journal that publishes Original Full-Length Papers, Short Communications, Case Reports and Invited Reviews, dealing with the several fields of dentistry or related areas, with open access. Only original papers will be considered for publication. In submitting a manuscript, the authors should state in the cover letter that the material has not been published previously and is not under consideration by another journal in either electronic or printed versions.

ELECTRONIC ADDRESS FOR SUBMISSION

MANUSCRIPTS MUST BE SUBMITTED IN ENGLISH. Authors whose primary language is not English must have their manuscript reviewed by someone proficient in English. Manuscripts accepted for publication will be submitted to the Technical Review for revision of English grammar and scientific writing and to fit the text into the Journal's standards. The cost of the Technical Review will be charged to the authors. Submission of a manuscript to BDJ implies the acceptance of these terms. The decision of acceptance for publication relies on the Editors and is based on the recommendation of the Editorial Board and/or ad hoc reviewers. Authors of manuscripts not recommended for publication will receive an email explaining the decision. The concepts emitted in the papers published in the BDJ are the sole responsibility of the authors, not necessarily reflecting the Editorial Board's opinion.

All manuscripts will be submitted to peer-review. Authors and referees will be kept anonymous during the review process. Articles accepted for publication become property of the journal. Brazilian Dental Journal is an open access journal, which means that all published articles are freely available on the Internet immediately upon publication.

The Brazilian Dental Journal shall retain the copyright and publishing rights of all published articles, including translations. Users can use, reuse and build upon the material published in the journal but only for non-commercial purposes and provided the source is clearly and properly mentioned.

The Journal adopts plagiarism identification system (AntiPlagiarist - ACNP Software)

The Brazilian Dental Journal is indexed by DOAJ database for public access.

Registration and publication of Errata

Errata are corrections of errors identified in an article or other type of document already published. The publication of an erratum is necessary when the author(s) of the article or the editor identifies one or more errors in the already published article. The procedure for

publishing an erratum follows the guidelines of the international databases and aims to preserve the original record of the manuscript, informing, however, about eventual corrections. Corrections should be identified and informed to the Editor-in-Chief of the Brazilian Dental Journal by e-mail sousanet@forp.usp.br. The Editor-in-Chief will then initiate the publication process in SciELO informing about the error located in an already published article.

Retraction of published articles

Retraction is a public instrument to register problems in a published article (Partial Retraction) or to communicate its cancellation (Full Retraction) and it is an integral part of the scientific communication system. The procedure to register the withdrawal of an article published by the Brazilian Dental Journal is initiated after receiving a formal communication to the Editor-in-Chief of the journal, through the e-mail sousanet@forp.usp.br, who will communicate it to SciELO. The communication should be accompanied by the retraction text informing the reasons for which the article will be retracted. The retracted article will not be deleted from the journal where it was originally published. In the XML version for full retraction cases, only the text of the retraction with the justification sent by the editor and the article's basic data, such as title, author, affiliation, and abstract, will be published. Only the part in which the problem was identified will be suppressed for partial retraction. In both cases, the original PDF is kept, but with the text of the retraction aggregated before the original full text and with watermark stripes identifying it as a retracted article.

Publication of Addendum

The publication of an Addendum is carried out in cases where there are no text corrections or digital assets, but when there is the inclusion of information about a document already published. Addenda do not contradict the original publication and are not used to correct errors; they should be used when the addition of the information is beneficial to the reader's understanding of a significant part of the published contribution. Addenda may be peer-reviewed in accordance with the journal's editorial policy. All addenda are linked to the published article to which they relate. In this case, the added information is not effectively inserted in the already published document as it occasionally happens with an erratum, for example. The addendum publication procedure follows the guidelines of the international databases and aims at preserving the original record of the manuscript, informing, however, about eventual additions. The process of addendum publication can be initiated by a communication to the Editor-in-Chief of the Brazilian Dental Journal, through the e-mail

sousanet@forp.usp.br, who will communicate SciELO informing about the need for an addendum in an already published article.

Good practice guide for strengthening ethics in scientific publishing

The Brazilian Dental Journal follows the good practice guide for strengthening ethics in scientific publication standards for all the journals of the SciELO Network collections. The SciELO Program follows norms and recommendations of standards of ethics and responsibility in scholarly communication established by national and international institutions, among which we highlight: COPE, CSE, Equator Network, ICMJE, CNPq, FAPESP, and the SciELO Manual of Good Practices for Strengthening the Ethics in Scientific Publication. This guide promotes integrity and transparency in the process of manuscript evaluation and in the reproducibility of research, about the occurrence of manipulation or invention of data, the unreferenced copy of data or of another author's text, the duplicate publication of the same text or research, conflicts of interest or authorship. Everything that is published in the journal, as well as the corrective actions that may be necessary, are the responsibility of the editor-in-chief. In this sense, this guide explains concepts and actions that promote integrity in the publication process and referrals in cases of suspected or proven misconduct. Further information can be obtained through formal contact with the Editor-in-Chief of the journal via e-mail: sousanet@forp.usp.br.

Form and preparation of manuscripts

THE FOLLOWING GUIDELINES MUST BE FOLLOWED CAREFULLY.

General

- The authors must submit the manuscript in Word and in PDF, comprising the title page, text, tables, figure captions and figures (photographs, micrographs, radiographs, schematic drawings, graphs, computer-generated images, etc).
- The manuscript must be typed in Times New Roman 12 font, with 1.5 spacing, 2.5-cm margins at each side. DO NOT USE bold letters, watermarks or other resources to make the text visually attractive.
- Pages should be numbered consecutively, starting with the summary.
- Full-length manuscripts are assembled in the following sections:
 1. Title Page
 2. Summary and Key Words
 3. Introduction; Material and Methods; Results; Discussion

4. Summary in Portuguese (an item necessary for Latin American Indexing Services that will be provided for non-Brazilian authors by the Journal)

5. Acknowledgements (if any)

6. References

7. Tables

8. Figure captions

9. Figures

- All titles of sections (Introduction, Material and Methods, etc) must be capitalized in regular font type (not bold).
- Results and Discussion **MUST NOT** be joined in a single section.
- Short Communications and Case Reports should be divided into appropriate sections.
- Products, equipments and materials: the trade name must be followed by the manufacturer's name, city, state and country, within parentheses upon first mention. For further mentions, only the manufacturer's name is required.
- All abbreviations must be explained at first mention.

Title page

- The first page must contain the title of the manuscript, a short title (maximum of 40 characters, to be used as a running head), author(s) name(s) (no more than 6) and their Department(s), School(s) and/or University (s). **DO NOT INCLUDE** the author's titles (DDS, MSc, PhD, etc.) or position (Professor, Graduate student, etc.).
- Provide the name and complete address of the corresponding author (inform email, telephone and fax numbers).
- The title page must be uploaded at the website as a separate file (not included in the body of the manuscript).

Manuscript

- The first page of the manuscript must contain: title of the manuscript, short title with no more than 40 characters, and **NO** authors' names or identification.

Summary

- The second page should contain a summary of no more than 250 words, stating the aims, methods, results, and any conclusions drawn from the study. Do not use topics and paragraphs and do not cite references in the Summary.
- A list of key words (no more than 5) should be included below the summary in lowercase letters, separated by commas.

Introduction

- Summarize the purpose of the study, giving only pertinent references. Do not review existing literature extensively. State clearly the working hypothesis.

Material and Methods

- Material and methods should be presented in sufficient detail to allow confirmation of the observations. Indicate the statistical methods used, if applicable.

Results

- Present the results in a logical sequence in the text, tables and figures, emphasizing the important information.
- Do not repeat in the text data contained in the tables and illustrations. The important observations should be emphasized.
- Do not repeat the same data in tables and figures.
- Describe the statistical data in this section.

Discussion

- Summarize the findings without repeating in detail the data given in the Results section.
- Relate your observations to other relevant studies and point out the implications of the findings and their limitations. Cite pertinent studies.
- Present your conclusions at the end of the Discussion, indicating how your study is pertinent and/or its clinical implications. Presentation of the conclusions in topics should be avoided.

Summary in Portuguese (for Brazilian authors only)

- The Summary in Portuguese should be IDENTICAL to the English version (Summary). DO NOT INCLUDE title and key words in Portuguese.

Acknowledgements

- Financial support by government agencies should be acknowledged. If appropriate, technical assistance or assistance from colleagues may be acknowledged.

References

- References must follow the Journal's style. Authors should refer to a current issue of the Brazilian Dental Journal (BDJ) for guidance on reference citation and presentation of the reference list.
- References must be numbered consecutively in the text in order of citation, within parentheses, without space between numbers: (1), (3,5,8), (10-15). DO NOT USE superscript numbers.

- For papers with two authors, cite both authors in the text, as follows: Ex: "According to Santos and Silva (1)...". If there are more than 3 authors, cite only the first author and add "et al.". Ex: "Pécora et al. (2) reported that..."
- All authors of each paper should be included in the Reference List unless there are 7 or more. In this case, the first 6 authors should be given, followed by "et al.".
- The reference list must be typed at the end of the manuscript in numerical sequence. No more than 25 references may be cited.
- Citation of abstracts and books, as well as articles published in non-indexed journals should be avoided, unless absolutely necessary. Do not cite references in Portuguese.
- Abbreviations of journal titles should conform to those used in Dental Index. The style and punctuation of references must follow the format illustrated below:

Journal articles

1. Lea SC, Landini G, Walmsley AD. A novel method for the evaluation of powered toothbrush oscillation characteristics. *Am J Dent* 2004;17:307-309.

Book

2. Shafer WG, Hine MK, Levy BM. *A Textbook of Oral Pathology*. 4th ed. Philadelphia: WB Saunders; 1983.

Chapter in a Book

3. Walton RE, Rotstein I. Bleaching discolored teeth: internal and external. In: *Principles and Practice of Endodontics*. Walton RE (Editor). 2nd ed. Philadelphia: WB Saunders; 1996. p 385-400.

Tables

- Each table with its title must be typed after the text. Tables should be numbered with Arabic numerals. DO NOT USE vertical lines, bold letters and capital letters (except the initials).
- The corresponding title should appear at the top of each table.
- Tables must contain all necessary information and be understandable without allusions to the text.

Figures

- BDJ WILL NOT ACCEPT FIGURES EMBEDDED IN FILES ORIGINATED IN TEXT-EDITING SOFTWARE (WORD OR SIMILAR) OR FIGURES ORIGINATED IN POWER POINT.
- The digital files of the images should be generated in Photoshop, Corel or any other image-editing software and saved in the CD-ROM. Image files should have TIFF extension and 300

dpi minimum resolution. Only BLACK & WHITE figures are accepted. Save the figures in the CD-ROM.

- Lettering and identifying marks must be clear and sharp, and the critical areas of x-rays and photomicrographs must be demarcated and/or isolated.
- Separate parts of composite figures must be labeled with capital letters (A, B, C, etc). Single figures and composite figures must have minimum width of 8 cm and 16 cm, respectively.
- Figure captions should be numbered with Arabic numerals and typed on a separate page, after the lists of references or after the tables (if any)

Policies on Conflict of Interest, Human and Animal rights, and Informed Consent

CONFLICT OF INTEREST

The Brazilian Dental Journal reassures the principles incorporated in the Helsinki Declaration and insists that all research involving human beings, in the event of publication in this journal, be conducted in conformity with such principles and others specified in the respective ethics committees of authors' institution. In the case of experiments with animals, the same ethical principles must also be followed. When surgical procedures in animals were used, the authors should present, in the Methodology section, evidence that the dose of a proper substance was adequate to produce anesthesia during the entire surgical procedure. All experiments conducted in human or animals must accompany a description, in the Methodology section, that the study was approved by the respective Ethics Committee of authors' affiliation and provide the number of the protocol approval.

The papers presenting experimental studies in human volunteers or in animals must contain the Ethical Committee approval of the reports as mandatory supplementary file. The Ethics Committee certificate written in different languages from English, Spanish and Portuguese must be full translated into English.

All authors and co-authors are required to disclose any potential conflict of interest when submitting their article (e.g. employment, consulting fees, research contracts, stock ownership, patent licenses, advisory affiliations, etc.). If the article is subsequently accepted for publication, this information should be included in the end section.

HUMAN AND ANIMAL RIGHTS

All research must have been carried out within an appropriate ethical framework. If there is suspicion that work has not taken place within an appropriate ethical framework, Editors will follow may reject the manuscript, and/or contact the author(s)' ethics committee. On rare

occasions, if the Editor has serious concerns about the ethics of a study, the manuscript may be rejected on ethical grounds, even if approval from an ethics committee has been obtained.

- Articles conducting any animal or clinical studies should contain a statement in accordance with the animal and human ethics committee.
- Research should be carried out in a manner that animals do not get affected unnecessarily.
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INFORMED CONSENT

In the Brazilian Dental Journal, patients have a right to privacy that should not be violated without informed consent. Identifying information, including names, initials, or hospital numbers, should not be published in written descriptions, photographs, or pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication.

Informed consent for this purpose requires that an identifiable patient be shown the manuscript to be published. Authors should disclose to these patients whether any potential identifiable material might be available via the Internet as well as in print after publication. Patient consent should be written and archived either with the journal, the authors, or both, as dictated by local regulations or laws. Nonessential identifying details should be omitted. Informed consent should be obtained if there is any doubt that anonymity can be maintained. When informed consent has been obtained, it should be indicated in the published article.

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2. Title page.
3. Manuscript file (text, tables, figure captions).
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 - tables, figure captions and figures at the end of the manuscript.
5. Digital files of figures, black & white, saved in TIFF format with minimum resolution of 300 dpi.

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The Technical Review Fee is R\$ 550,00 Reais Brasileiros (for Brazilian authors) or U\$300 American dollars (for foreign authors) and will be charged to the corresponding author, even if only minor corrections to the manuscript are needed.