

Bioprinting Techniques for Creating Patient-specific Implants in Treating Craniofacial Disorders—A Systematic Review

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AIM: Craniofacial disorders are complex and debilitating conditions that require personalized treatment approaches. Various technologies in the field of bioprinting have developed into promising methods for the production of patient-specific implants for the aforementioned disorders. This review evaluates the ability of the bioprinting methods used to produce patient-specific implants for improved patient outcomes.

METHODS: A comprehensive search strategy was designed to gather pertinent research from databases of PubMed, Scopus, Web of science, Cochrane Library, Embase, ProQuest and Science Direct, published till July 2024. The search approach was developed by mixing Boolean operators, Medical Subject Heading (MeSH) terms, and free-form terms to guarantee an exhaustive and accurate search.

RESULTS: After a thorough screening process for duplicates and compliance with eligibility criteria, seven studies met our exacting inclusion criteria, out of the initial 312 studies. The collective findings of the studies demonstrated the efficacy and feasibility of bioprinting techniques in creating patient-specific implants for craniofacial disorders. The studies were grouped into three categories based on their similarities and dissimilarities, highlighting the high success rates and low complication rates of bioprinting techniques in craniofacial reconstruction, the feasibility and effectiveness of bioprinting techniques in specific craniofacial applications, and the use of custom-made implants as a successful treatment option. Majority (five out of seven) reporting a 100% success rate, minor complication rates averaging less than 5%, and patient satisfaction rates over 90% across a range of craniofacial applications, the reviewed studies collectively showed the excellent efficacy of bioprinting techniques.

CONCLUSIONS: The synthesised evidence from the seven studies included for the review concluded that bioprinting methods were efficient in producing custom or individual specific implants for craniofacial disabilities. Though the results are promising, multicentric, prospective studies are needed to validate long term outcomes.

Keywords: bioprinting techniques; patient-specific implants; craniofacial disorders; craniofacial reconstruction; 3D printing; personalized medicine

Introduction

Craniofacial reconstruction is a field in which significant improvements have been made, especially in the treatment of birth deformities and injuries. These are among those

craniofacial ailments that present a number of challenges to patients, healthcare providers, and researchers alike [1]. Such repairs regularly require complex surgeries and may significantly affect the quality of life for the patient in terms of both the structural aspects involved in the problem being corrected and the aesthetic components [2,3].

Custom implants created using conventional techniques as moulding and carving have been rather important in traditional surgical approaches for craniofacial reconstruction. Although these techniques seek to reproduce the complex anatomy of the face and skull, they have many restrictions. Because of their manual character, these procedures are labour-intensive and prone to mistakes, which fre-

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Table 1. Inclusion and exclusion criteria.

Parameters	Inclusion criteria	Exclusion criteria
Study design	Original research articles, case series, and case reports	Review articles, editorials, commentaries, and conference abstracts
Population	Individuals with craniofacial disorders	Healthy individuals, animal studies
Exposure	Bioprinting techniques used to create patient-specific implants	Other treatment modalities, non-bioprinted implants
Outcome	Implant success rates, patient satisfaction, aesthetic outcomes, and complication rates	Non-clinical outcomes, laboratory studies
Language	No language restrictions	
Publication date	From inception till July 2024	

quently results in implants that need several corrections after surgery due to poor fit, therefore extending the recovery durations and producing less than ideal cosmetic results [3]. This has resulted in the development of customized implants, which provide individual solutions for each particular patient's needs [4]. However, the conventional techniques for implant-making by moulding and carving cannot accurately reproduce the intricate anatomy of the face or skull. These traditional methods are not only labour-intensive and error-prone but also time-consuming because they are dependent on manual modelling and creation of prototypes. The conventional implants may not fit well, and this may involve a lot of surgical revisions; thus, unsatisfactory outcomes may result [5,6].

Advances in computer-aided design and production have paved the way for 3D printed implants, which have become a realistic alternative to restore the facial bone tissues. Research has shown promising results; for instance, a multicenter study highlighted the effectiveness of 3D printed implants in jaw repair [6–8]. Similarly, a case study demonstrated high success rates in correcting facial bone anomalies with the use of 3D printed implants. Recent technological advancements have significantly improved the ability to manufacture personalised implants [9].

However, challenges remain with titanium implants due to its varying tensile strength and flexibility. Additionally, assessing the bond between the implant and bone, as well as identifying any issues in the facial region, can be difficult when titanium shavings are present [10]. To address these challenges, scientists have developed stronger, more distinctive glass-ceramic materials for bone grafting and repair. These substances facilitate bonding between the implant and bone tissues for better integration.

Bioprinting also holds vast promise for use in craniofacial reconstruction for aesthetic improvement, to avoid complications, and to have good functionality. This is because bioprinting implants that match the actual structure of one's body can improve facial function and features. Moreover, bioprinting can provide personalized models before surgery to enable healthcare providers to work out the best outcomes with less time-wasting processes [11–13].

Despite the promising future that bioprinting holds for the repair of craniofacial defects, very few in-depth researches on its safety and efficacy have been undertaken, especially in human studies. This paper aims to report in detail on the present body of knowledge related to the production of customized implants for craniofacial defects through bioprinting.

Methods

Eligibility Criteria

We developed the Population, Exposure, Comparator, Outcome (PECO) protocol for our examination, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting to guarantee a thorough and clear search approach (**Supplementary Material**) [14]. The Population (P) section was dedicated to people suffering from craniofacial conditions, such as craniosynostosis and injuries to the craniomaxillofacial area. The Exposure (E) section was focused on the various bioprinting methods employed to produce implants tailored to each patient, including 3D printing, additive manufacturing, and rapid prototyping. This exposure was selected to assess the success of bioprinting methods in addressing craniofacial conditions. The Comparator (C) section was not relevant for this study, as the emphasis was on the success of bioprinting in producing patient-specific implants alone, rather than a comparison with other treatment options. The Outcome (O) section covered a variety of results, including but not limited to the success of implants, patient satisfaction, the appearance of the results, and the occurrence of complications. Table 1 comprises of the inclusion and exclusion criteria that we utilised for this review.

Database Search Strategy

To ensure that all relevant literature was sought, an exhaustive research strategy was developed in order to search for literature in seven databases. These databases included: the PubMed database, the Scopus database, the Web of Science database, the Cochrane Library database, the Embase database, the ProQuest database, and the Science Direct database, and the queries were customized for each

Table 2. Search strings used for the review.

Database	Keywords
PubMed	((“bioprinting”[MeSH] OR “3D printing”[MeSH] OR “additive manufacturing”[MeSH]) AND (“craniofacial disorders”[MeSH] OR “craniosynostosis”[MeSH] OR “cranio-maxillofacial trauma”[MeSH])) AND (“implants”[MeSH] OR “patient-specific”[MeSH] OR “customized implants”[MeSH])
Scopus	(TITLE-ABS-KEY(“bioprinting” OR “3D printing” OR “additive manufacturing” OR “rapid prototyping”) AND TITLE-ABS-KEY(“craniofacial disorders” OR “craniosynostosis” OR “cranio-maxillofacial trauma” OR “congenital anomalies”)) AND TITLE-ABS-KEY(“implants” OR “patient-specific” OR “customized implants” OR “craniofacial implants”)
Web of Science	(TS=(“bioprinting” OR “3D printing” OR “additive manufacturing” OR “rapid prototyping”) AND TS=(“craniofacial disorders” OR “craniosynostosis” OR “cranio-maxillofacial trauma” OR “congenital anomalies”)) AND TS=(“implants” OR “patient-specific” OR “customized implants” OR “craniofacial implants”)
Cochrane Library	((“bioprinting” OR “3D printing” OR “additive manufacturing” OR “rapid prototyping”) AND (“craniofacial disorders” OR “craniosynostosis” OR “cranio-maxillofacial trauma” OR “congenital anomalies”)) AND (“implants” OR “patient-specific” OR “customized implants” OR “craniofacial implants”)
Embase	((“bioprinting”/exp OR “3D printing”/exp OR “additive manufacturing”/exp OR “rapid prototyping”/exp) AND (“craniofacial disorders”/exp OR “craniosynostosis”/exp OR “cranio-maxillofacial trauma”/exp OR “congenital anomalies”/exp)) AND (“implants”/exp OR “patient-specific”/exp OR “customized implants”/exp OR “craniofacial implants”/exp)
ProQuest	((“bioprinting” OR “3D printing” OR “additive manufacturing” OR “rapid prototyping”) AND (“craniofacial disorders” OR “craniosynostosis” OR “cranio-maxillofacial trauma” OR “congenital anomalies”)) AND (“implants” OR “patient-specific” OR “customized implants” OR “craniofacial implants”)
ScienceDirect	(TITLE-ABS-KEY(“bioprinting” OR “3D printing” OR “additive manufacturing” OR “rapid prototyping”) AND TITLE-ABS-KEY(“craniofacial disorders” OR “craniosynostosis” OR “cranio-maxillofacial trauma” OR “congenital anomalies”)) AND TITLE-ABS-KEY(“implants” OR “patient-specific” OR “customized implants” OR “craniofacial implants”)

MeSH, Medical Subject Heading; TS, Topic Search.

database’s unique search capabilities and indexing method (Table 2).

Variables Extraction Strategy

The protocol for extracting relevant information from the selected studies was carefully crafted to ensure a systematic approach. Two reviewers worked independently to gather data using a previously tested data extraction form. The information chosen for extraction included details about the study, such as the author, year of publication, the number of participants; information about the patients, details about the treatment, including the bioprinting method, the material used for implants, and the design of the implants; measures of success, including the rates of implant success, satisfaction among patients, the appearance of the results, and the rates of complications; and information about the follow-up period, including how long the follow-up lasted and when the outcomes were assessed. The reviewers applied a consistent method to extract the data from the stud-

ies, and any differences in their assessments were discussed and agreed upon. The data that were extracted were then entered into a spreadsheet for additional analysis.

Bias Assessment Protocol

The process of evaluating potential biases across the selected studies was carried out using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool [15], which is a detailed tool designed to evaluate the risk of bias in studies that do not use randomization. Each trial included in the review was independently assessed for the risk of bias by two reviewers. Discrepancies in their evaluation were discussed and a consensus reached.

Results

PRISMA Protocol Implementation

To start, 312 records were found in databases, but none were found in the registers. After the removal of 46 duplicated records, the search resulted in 266 screened records. Of

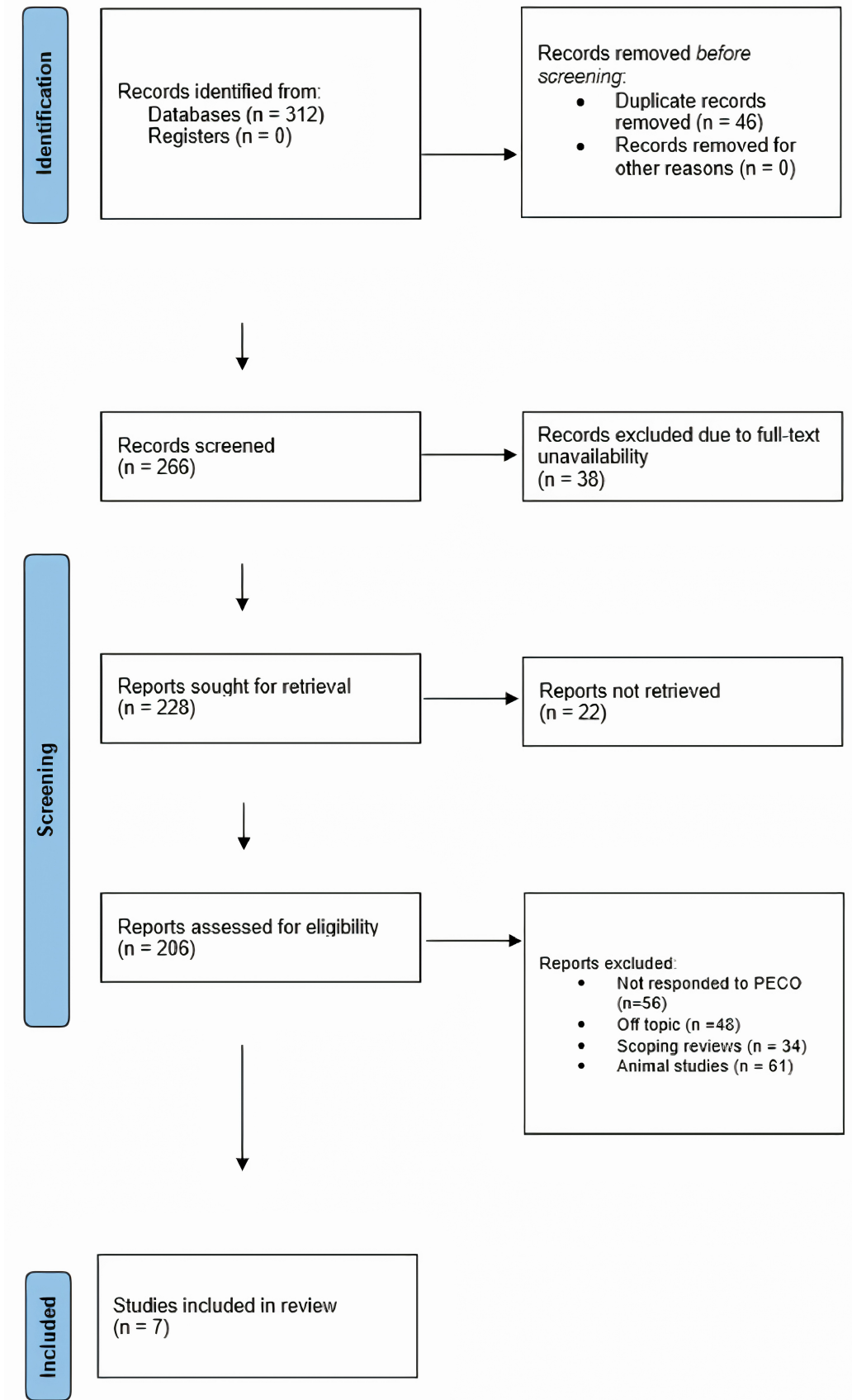


Fig. 1. Description of the different stages of article selection process for the review. PECO, Population, Exposure, Comparator, Outcome.

these, 38 were excluded due to full-text unavailability, leaving 228 records sought for retrieval. Of those, 22 could not be retrieved, resulting in 206 reports assessed for eligibility. After looking over them, 56 reports were not included because they didn't meet the PECO criteria, 48 were considered not relevant, 34 were reviews to see what was needed, and 61 were studies on animals. In the end, only 7 studies [16–22] fit the requirements and were added to the review, as shown in Fig. 1.

Bias Levels Evaluated

Fig. 2 shows the bias domain evaluation across the included trials [16–22]. Overall, the reported risk of bias was low as seen in 5 out of 7 studies. The studies of da Silva Júnior *et al.* [17], Kim DH *et al.* [18], Kim YC *et al.* [19], Lee *et al.* [20] and Scerrati *et al.* [22] showed low risk of bias. Moderate risk of bias was seen in Csámer *et al.* [16] and Park *et al.* [21].

Demographic Variables Assessed

Table 3 lists the included trials [16–22] and their observed inferences. 52 patients with a mean age of 40.2 years (SD \pm 13.41) and a male-to-female ratio of 2.46 were included in the study conducted by Csámer *et al.* [16]. While Kim DH *et al.* [18] examined 20 patients, 20% of whom were female and 80% of whom were male, with a mean age of

34.95 years (SD: 11.96), da Silva Júnior *et al.* [17] included 16 patients with major cranial abnormalities. Kim YC *et al.* [19] reported ten cases consisting of seven males and three females. The average age was 47 years (range 19–65 years). Lee *et al.* [20] studied ten patients. Their average age was 34.8 years. Nine females and one male were included. Park *et al.* [21] noted an average patient age of 28.6 years (range 8–62 years). Scerrati *et al.* [22] studied seven patients. Their average duration of follow-up was six months.

Implant Characteristics and Outcomes Assessed

Csámer *et al.* [16] reported mean implant volume and surface area of 52.19 cm³ (SD \pm 27.37) and 218.8 cm² (SD \pm 91.04), respectively. Csámer *et al.* [16] performed 54 cranioplasties with a 100% success rate, including 34 post-stroke, 4 after tumor removal, and 16 after traumatic brain injury. da Silva Júnior *et al.* [17] used implants with varying thicknesses, ranging from 0.2 cm to 2.8 cm, and achieved a 100% success rate in all 16 patients. Kim DH *et al.* [18] utilized Polycaprolactone (PCL) mesh with specific properties, such as a line width of 500 μ m and 50% porosity, and reported a 100% success rate in 20 patients undergoing septoplasty. Kim YC *et al.* [19] developed a PCL/Bioactive Glass Ceramic-7 (BGS-7) composite with biomineralization properties and achieved a 100% success

Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Csámer <i>et al.</i> [16]	-	+	-	-	+	+	-	-
da Silva Júnior <i>et al.</i> [17]	-	+	+	+	+	-	+	+
Kim DH <i>et al.</i> [18]	+	+	+	+	+	+	-	+
Kim YC <i>et al.</i> [19]	+	+	-	+	+	+	+	+
Lee <i>et al.</i> [20]	+	+	+	-	+	+	+	+
Park <i>et al.</i> [21].	+	-	-	+	-	+	+	-
Scerrati <i>et al.</i> [22]	-	+	+	+	+	+	-	+

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Moderate
+ Low

Fig. 2. Bias domains evaluated across the included trials.

Table 3. Studies included in the review and their observed inferences.

Author ID	Year	Patient demographics	Implant characteristics	Procedure outcomes	Technique success rate	Advantages	Complications	Overall inference drawn
Csámer <i>et al.</i> [16]	2023	52 patients, Male-to-female ratio: 2.46, mean age: 40.2 years (SD \pm 13.41)	Mean implant volume: 52.19 cm ³ (SD \pm 27.37), mean implant surface area: 218.8 cm ² (SD \pm 91.04)	54 cranioplasties performed, 34 post-stroke, 4 after tumour removal, 16 after traumatic brain injury	100% success rate, no macroscopical gaps observed	Reliable, safe, and easily reproducible method, low-cost technique, allows for precise fitting and customization	2 patients had bilateral implants; 2 patients required re-implantation due to wound infections	Bioprinting techniques can create patient-specific implants with high success rates and low complication rates for craniofacial disorders.
da Silva Júnior <i>et al.</i> [17]	2021	16 patients with large cranial defects	Implant thickness: 0.2 cm (most cases), 0.3 cm (1 case), 0.4 cm (1 case), and 2.8 cm (1 case)	100% success rate, all 16 patients underwent successful customized cranioplasty	100% success rate, no complications observed	High patient satisfaction (93.75%), reduced surgical time, improved accuracy	None reported	Bioprinting techniques can achieve high patient satisfaction and reduced surgical time in craniofacial reconstruction.
Kim DH <i>et al.</i> [18]	2018	20 patients, 20% female, 80% male, mean age: 34.95 years (SD: 11.96)	PCL mesh with line width of 500 μ m, interconnected triangular pores, and 50% porosity	20 patients underwent septoplasty using 3D printed PCL mesh	Not reported	Not reported	None reported	Bioprinting techniques can create patient-specific implants with precise fitting and customization for nasal septal deviations.
Kim YC <i>et al.</i> [19]	2022	10 patients, 7 males, 3 females, mean age: 47 years (range 19–65 years)	PCL/BGS-7 composite, average particle size: 2.1 \pm 0.2 mm, biomineralization properties in SBF soaking tests	100% success rate, no wound breakdown, allergic responses, hematoma, seroma, implant displacement, or reoperation	100%	Patient-specific implants with high accuracy, promotes bone fusion, low complication rate	1 patient developed a palatal fistula	Bioprinting techniques can create patient-specific implants with high success rates and low complication rates for craniofacial disorders, promoting bone fusion and restoring facial symmetry.
Lee <i>et al.</i> [20]	2020	10 patients, 1 male, 9 females, mean age: 34.8 years	BGS-7 bioceramic, fused deposition modeling (FDM), high strength-to-weight ratio	100% fusion rate at 6 months, average fusion rate: 76.97% (SD: 11.36)	100%	High accuracy rate, good cosmetic results, low complication rate	0% complication rate	Bioprinting techniques can create patient-specific zygoma implants with high accuracy and cosmetic success rates, and a low complication rate, achieving good bone fusion and aesthetic satisfaction.

Table 3. Continued.

Author ID	Year	Patient demographics	Implant characteristics	Procedure outcomes	Technique success rate	Advantages	Complications	Overall inference drawn
Park <i>et al.</i> [21]	2016	21 patients, mean age 28.6 years (8–62 years)	Custom-made 3D titanium implants, mean surface area 18,036 mm ² (12,146–24,980 mm ²)	No surgical complications, mean operation time 115.7 minutes	High success rate (no complications directly related to operation)	Custom-made implants for skull defects, high porosity and reduced density	1 patient with swelling and redness, 1 patient with scalp erosion	Custom-made 3D titanium implants are a successful treatment option for craniofacial disorders.
Scerrati <i>et al.</i> [22]	2022	7 patients, mean follow-up 6 months	PMMA (Cranioplastic by Codman), 3 mm thickness, created using 3D printed silicone mould	100% success rate, good cosmetic results, mean surgical time 80 minutes	100% success rate, no complications	High accuracy, short surgical and production times, affordable costs	0% complication rate	3D bioprinting techniques are effective and feasible for creating patient-specific cranioplasties.

PCL, Polycaprolactone; BGS-7, Bioactive Glass Ceramic-7; SBF, Simulated Body Fluid; PMMA, Polymethyl Methacrylate.

rate with no complications. Lee *et al.* [20] used BGS-7 bio-ceramic implants fabricated via fused deposition modeling, resulting in a 100% fusion rate at 6 months. Park *et al.* [21] employed custom-made 3D titanium implants with a mean surface area of 18,036 mm² and reported no surgical complications with a mean operation time of 115.7 minutes.

Results Observed

Csámer *et al.* [16] achieved a 100% success rate, but with two patients requiring re-implantation due to wound infections. da Silva Júnior *et al.* [17] reported a 100% success rate with no complications observed, emphasizing the high patient satisfaction (93.75%) and reduced surgical time. Kim YC *et al.* [19] and Lee *et al.* [20] reported a 100% positive outcome with no untoward effects directly related to the operation. However, 1 patient in Kim YC *et al.* [19] developed a palatal fistula. The study of Park *et al.* [21] reported 1 patient with swelling and redness and another with scalp erosion. Scerrati *et al.* [22] achieved a high success rate with no complications, emphasizing the high accuracy and low complication rate of their custom-made implants.

Discussion

The general conclusion that can be made from the seven research' combined findings [16–22] is that bioprinting methods are practical and successful in producing patient-specific implants for craniofacial abnormalities. On the other hand, a more thorough examination shows that the research can be divided into three groups according to their similarities and differences.

Group 1: Craniofacial Reconstruction With High Success and Low Complications—Includes studies [16,18–20] with a 100% success rate and negligible complications, showcasing the efficacy of bioprinting in producing precise, patient-specific implants. The studies [16,18–20] that fall into the first category are comparable in that they report high success rates and low complication rates when using bioprinting techniques for craniofacial reconstruction. While Kim YC *et al.* [19] and Lee *et al.* [20] reported high accuracy rates and good cosmetic results, Csámer *et al.* [16] and Kim DH *et al.* [18] reported 100% success rates with no problems. These studies demonstrate that bioprinting methods are effective in producing customised implants for patients with craniofacial abnormalities.

Group 2: Viability and Efficiency of Specific Applications—The research in the second category [17,21] are different from the ones in the first category in that they concentrate on the viability and efficiency of bioprinting methods in certain craniofacial applications. A 100% success rate in craniofacial reconstruction was reported by da Silva Júnior *et al.* [17], and patient-specific cranioplasties may be created using 3D bioprinting techniques, as shown by Park *et al.* [21]. These examples represent the utilization of bioprinting methods for the wide range of craniofacial deformities.

Group 3: Advanced Materials and Custom Implants—Scerrati *et al.* [22], which distinguishes itself from the other included papers by emphasising the use of 3D titanium implants customised for craniofacial abnormalities, falls into the third group. This study highlights the possibility of custom-made implants as an effective treatment option by reporting a high success rate without any problems.

The research differed in that they examined different uses of bioprinting techniques; some [16–20] concentrated on various craniofacial applications, while others [21,22] investigated its usage in skull defect reconstruction via cranioplasty. Furthermore, several methods and materials were used in the trials, including 3D titanium implants [21], PCL/BGS-7 composite [19], and PCL mesh [18].

The burgeoning field of craniofacial bone tissue engineering has been hampered by various limitations, thereby fuelling interest in the development of 3D bioprinted craniofacial bone implants [23–25]. This is a new field of research in which scaffold materials, growth factors, and stem cells are used judiciously to engineer functional bone tissue. Although the terms 3D printing and 3D bioprinting are used as synonymous, they differ in their approach to the creation of complex tissue structures [26]. The printing of living cells, a subcategory of 3D bioprinting, can be performed by either the use of inert scaffolds or dense cell printing without scaffolds. There exists numerous studies that accentuates the ability of three-dimensional bioprinting in revolutionizing the field of craniofacial bone tissue engineering [27–29].

Bioprinting can reduce the cost considerably in craniofacial reconstruction and also make surgeries more accessible. Bioprinting removes the need for numerous operations and lowers the manufacturing time and costs associated with traditional prosthetic fabrication by enabling the direct creation of precise, patient-specific implants from digital models. By decentralising implant production and possibly enabling local manufacturing capabilities in hospitals or clinics, this technology can increase access to specialised treatments for a larger population, particularly in underserved areas. Bioprinting could therefore promote broader adoption of individualised healthcare solutions and democratise cutting-edge medical treatments.

The advantages to the patients of 3D bioprinted craniofacial bones, whether due to trauma or congenital defects that require augmentation, are multifaceted. Computer-aided design can facilitate the creation of implants that precisely match the patient's anatomy and ensure optimal implant-bone contact [30]. However, despite the promise that 3D bioprinting holds, it is still in its infancy. One of the significant challenges in 3D bioprinting of craniofacial bone tissue engineering is the development and identification of suitable biocompatible materials that can support the function and growth of craniofacial tissues [31].

Craniofacial skeletal development is very complex. These processes involve the interaction between the lineages of cells arising from the somites, mesenchyme, and the neural

crest [32]. One of the main focuses in three-dimensional bioprinting is the production of bone tissue. This process includes the differentiation of mesenchymal tissue to mineralized bones. The scaffold plays a crucial role in successful bone formation, and therefore, efforts are focused on developing feasible methods of fabrication [33]. Traditional methods of bone tissue engineering, such as leaching, foaming, or freeze-drying, lack the precision required to produce accurate bone shapes and sizes. In contrast, Computer-Aided Design/Computer-Aided Manufacturing (CAD/CAM), controlled by computer software, offers precise control over the topology and interconnectivity of pores, which is essential for the 3D bioprinting of craniofacial bones [34].

An overview of 3D printing techniques for dental and maxillofacial applications was presented by Kouhi *et al.* [35], who investigated the use of additive manufacturing in these fields. However, the same research highlighted the benefit of additive manufacturing regarding the reduction of the operating time. On the other hand, our review highlights the clinical translation of additive manufacturing into patient-specific craniofacial implants with measurable surgical outcomes.

In order to explore the potential of bioprinting for tissue engineering applications, Charbe *et al.* [36] investigated the use of 3D bioprinting for craniofacial tissue regeneration. Their study included the drawbacks of conventional surgical techniques as well as the necessity for creative alternatives in the field of craniofacial reconstruction. On the other hand, our review focuses on documented clinical outcomes, emphasising the direct impact of bioprinting on surgical success rates and patient satisfaction in craniofacial reconstruction.

In their investigation into bone tissue engineering for craniofacial reconstruction, Shen *et al.* [37] looked at the possibilities of bioprinting and 3D printing for bone tissue engineering uses. The significance of creating novel materials and technologies to increase precision and lower expenses was covered in their study. On the other hand, our review emphasises the importance of individualised implant design, demonstrating that patient-specific bioprinted solutions consistently yield high success rates across diverse craniofacial indications.

The possibility of bioprinting for craniofacial osseous defects was examined by Datta *et al.* [38], who also discussed the future possibilities of 3D printing and bioprinting in the domains of craniofacial reconstruction and other areas. Their work made clear how much more research and development are required to fully realise the potential of bioprinting and 3D printing in sectors other than craniofacial repair. On the other hand, our review underscores the necessity of multidisciplinary collaboration, demonstrating that coordinated efforts between clinicians, engineers, and researchers are essential to achieving safe, effective, and patient-centred craniofacial reconstruction. [39–41].

Certain demographic variations could have also influenced the review outcome. Because of physiological and anatomical changes, age and gender greatly affect craniofacial reconstruction results [42,43]. Because of their increased bone density and regenerative qualities, younger patients usually show better integration of bioprinted implants and healing of their bones. On the other hand, slower healing processes may present difficulties for elderly persons. The design and integration of implants are also impacted by gender-specific anatomical variations and hormonal factors, such as the impact of oestrogen on bone metabolism, which call for tailored strategies to maximise surgical success and patient satisfaction.

Despite the high setup and material costs, bioprinting technology saves money over time by reducing the need for repeated operations and implant waste. Unlike traditional implants, which frequently require revision surgeries, customised bioprinted implants fit perfectly the first time. Additionally, the logistical expenses related to implant manufacturing and storage may be reduced if implants are produced at the point of service. High patient satisfaction is also reported with this technology, which may be attributed to enhanced aesthetic and functional outcomes that closely resemble the patient's original anatomy.

We recognize that our findings should be interpreted within the framework of several limitations. Our review's dependence on a limited number of studies might not fully capture the breadth of research on bioprinting techniques for craniofacial reconstruction. Moreover, the diversity in study methodologies and outcome measures could introduce variability in the results. In addition, a lack of long-term follow-up data and the relatively small sample sizes in some studies could limit the generalizability of our results.

Also, though bioprinting has transformative potential for craniofacial restoration, there are drawbacks to the method, especially with regard to the materials' biocompatibility [44,45]. Long-term success may be hampered by current bioprinting materials' propensity to trigger immunological reactions or to not blend in perfectly with natural tissues. Additionally, the biomechanical properties of the manufactured implants might not accurately represent the natural properties of the bone tissue. To ensure positive outcomes in terms of functionality, research in the future should involve the invention of new materials that improve biocompatibility. Additionally, the new materials should function according to intelligent technologies for the successful implementation of the implants.

Based on the results of our study, we would recommend that further research should focus on the standardization of the bioprinting methodologies and outcome measures, which would enhance comparison among various studies. Additionally, larger scale studies must also be done to determine the efficacy of bioprinting for the reconstruction of the craniofacial region. Moreover, new biomaterials and bioprinting technologies may also improve the use of bioprinting

techniques for treating any kind of craniofacial abnormalities or disorders. Ultimately, translating bioprinting techniques into clinical practice involves a multidisciplinary approach by engineers, clinicians, and researchers in order to ensure appropriate treatment modalities that are safe, effective, and patient-specific.

Conclusions

Our review offers evidence supporting the efficacy and feasibility of bioprinting techniques in generating patient-specific implants for craniofacial disorders. Our data suggest that the success rate and patient satisfaction rate are high, also complications rate is low for the bioprinting techniques used in craniofacial surgeries. Bioprinting not only enhances outcomes but also promotes personalized medicine because bioprinting is capable of matching each patient's anatomical requirement to each procedure done. These results support the incorporation of bioprinting into standard craniofacial reconstructive procedures, indicating a dramatic change towards more individualised, patient-focused medical interventions that aim to enhance patients' functional and cosmetic results.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization: VBM, SSa, GM. Methodology: AAK, VBM, MC, GM. Formal analysis: MMM, DR, GM. Investigation: SSa, VBM and SSh. Writing—original draft: MC and GM. Writing—review & editing: MC and GM. Resources: HU and DR. Data curation and visualization: HU, GM. Supervision: MMM, MC and GM. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

Giuseppe Minervini was serving as one of the Editorial Board and Guest Editor members of this journal. We de-

clare that Giuseppe Minervini had no involvement in the peer review of this article and has no access to information regarding its peer review. Other authors declare no conflict of interest.

Declaration of Generative AI and AI-Assisted Technologies in Manuscript Preparation

During the preparation of this manuscript, the authors used DeepL Translate for language checking/grammar correction. After its use, the authors thoroughly reviewed, verified, and revised all content to ensure accuracy and originality.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.62713/ai.c.3923>.

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