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CAD/CAM Fabrication of Bone for Guided Bone Regeneration: A Narrative Review of Current Principles, Clinical Applications, Challenges and Future Perspectives

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ABSTRACT

Background: The computer-aided design/computer-aided manufacturing (CAD/CAM) workflow is state of the art for a plethora of oral- and maxillofacial reconstruction procedures. The workflow is well implemented in alveolar ridge preservation and segmental bone regeneration. Guided bone or guided tissue regeneration (GBR/GTR) are essential in stabilising and regenerating the alveolar ridge height and width and the surrounding soft tissue in segmental deficient situations. CAD/CAM-assisted GBR minimises surgical time, optimises bone volume preservation and provides predictable results in implantology and reconstructive procedures. Besides, the technique is crucial in planning and executing free microvascular anastomosed tissue transfer for continuity defects.

Methods: This review examines how CAD/CAM fabrication can further transform bony regeneration and reconstruction. Therefore, latest principles of CAD/CAM fabrication methods, manufacturing techniques in CAD/CAM bone fabrication, materials for CAD/CAM-fabricated bone in GBR, clinical applications of CAD/CAM bone in GBR, challenges and limitations as well as future perspectives are highlighted.

Results and Conclusions: In conclusion, CAD/CAM is poised to become a standard approach not only for segmental but also continuity defect situations in regenerative maxillofacial surgery as technology evolves.

1 | Introduction

Bone loss in the maxillofacial region due to trauma, pathology or congenital defects poses significant challenges for reconstructive surgery. To restore the functional and aesthetic craniofacial framework is the primary goal of reconstructive and regenerative maxillofacial surgery [1]. Currently, osteo-myocutaneous or osteomuscular free tissue transfer with microvascular anastomosis at the recipient site is considered the gold standard for continuity defects. Computer-aided design/computer-aided manufacturing (CAD/CAM) workflows have emerged as a state-of-the-art solution for precision reconstruction. Using patient imaging data, a three-dimensional (3D) model of the defect is generated, allowing virtual fitting of the chosen bony flap and design of cutting guides or patient-specific reconstruction plates (PSIs). Studies demonstrate that CAD/CAM-assisted procedures reduce operative time by 20%–35%, improve flap fitting accuracy and increase patient satisfaction compared with conventional freehand techniques [2]. Despite a success rate of 93%, flap loss due to hypoperfusion or venous congestion comes with severe functional and aesthetic impairments, re-operations and prolonged hospital stay [3]. Additionally, in cases of severe co-morbidity or vessel depletion, the free tissue transfer is not feasible in the first place. There is no equivalent alternative for

Clinical Relevance

The application of CAD/CAM technology in guided bone regeneration holds the potential to significantly improve patient outcomes in oral and maxillofacial surgery. CAD/CAM-assisted GBR minimises surgical time, optimises bone volume preservation and provides predictable results. By allowing for precise, patient-specific bone grafts, this technology enhances reconstruction, leading to better integration with native bone and reduced complication rates. Shortcomings are the increased planning time and direct costs for the device. In the future, translation of newly developed optimised materials and methods into the clinical workflow will pave the way for the regeneration of continuity bony defects.

reconstruction in these cases up to date [4]. Tissue engineering might overcome this limitation [5]. Tissue engineering is an interdisciplinary field combining biology, medicine and engineering. The goal is the fabrication of in vitro tissues or organs of interest by creating biomimetic scaffolds that mimic the native microenvironment of the respective tissue or organ for regeneration/replacement [6]. The use of scaffolds and biomaterials of autologous, allogeneic and xenogeneic origin combined with these principles and advanced technologies such as stem cell therapy concepts or additive manufacturing hold the promise to promote bone regeneration [7, 8].

The principles of guided bone or guided tissue regeneration (GBR/GTR) date back to experimental studies on the regeneration potential of periodontal tissues in the 1970s and 80s. They are essential in stabilising and regenerating the alveolar ridge height and width and the surrounding soft tissue in segmental deficient situations [9]. The GBR technique involves an absorbable or non-absorbable membrane or mesh, combined with bone substitutes and other biological materials such as growth factors, depending on bone defect features. The aim is to create a distinguished niche where osteoblasts can selectively enter the site of the defect, exclude connective and epithelial cells and stimulate bone regeneration [10]. CAD/CAM-assisted GBR minimises surgical time, optimises bone volume preservation and provides predictable results in implantology and reconstructive procedures compared with conventional bone grafting [11].

This review focuses on how CAD/CAM fabrication is transforming bony regeneration and reconstruction. It highlights advances over traditional approaches, addresses current limitations and explores future directions for segmental and continuity defect reconstruction.

2 | Principles of CAD/CAM Fabrication

CAD/CAM (computer-aided design/computer-aided manufacturing) technology refers to a digital workflow that integrates software-based design with automated manufacturing processes. It comprises digital imaging, virtual modelling and computer-controlled manufacturing [12]. In maxillofacial reconstruction, CAD/CAM provides significant advantages over conventional freehand techniques, including improved precision, reduced intraoperative modifications and shorter surgical times [13, 14]. Compared with traditional methods, CAD/CAM-assisted procedures have demonstrated a significant reduction in surgical time, improved flap fit and geometry and reduced complication rates [15, 16]. It is standardly used to restore segmental defects. Bone augmentation techniques with GBR with barrier membranes are a common method, but emerging techniques are expanding the possibilities for effective treatment [17]. Up to date, the CAD/CAM workflow for personalised scaffolds consists of five stages (Figure 1):

1. Image acquisition with a Computed Tomography (CT) or cone-beam computed tomography (CBCT) cone-beam CT scan for hard tissue and intraoral scan for soft tissue.
2. Image pre-processing: conversion of the DICOM file into STL file for preparing 3-D printable condition.
3. Image post-processing: 3-D volume visualisation for optimisation of scaffold shape.
4. Rapid prototyping: based on image processing, scaffolds are manufactured by the 3-D printer.
5. Clinical application: custom-fit scaffold is applied at the time of reconstructive surgery. Depending on the material, the approach is implemented with autologous, alloplastic or xenogeneic material [18].

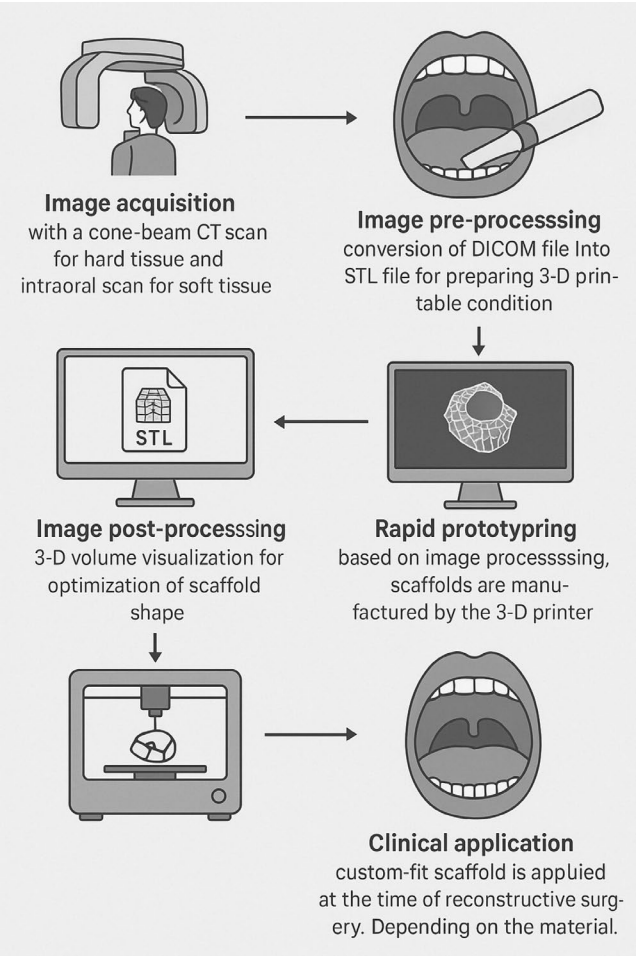

FIGURE 1 | This figure summarises the five stages in the CAD/CAM process: Image acquisition, Image pre-processing, Image post-processing, Rapid prototyping and clinical application.

The workflow for continuity defects involves digital imaging such as a CT or CBCT that generates a high-resolution 3-D model of the defect site. With this DICOM data, segmentation of a virtual model of the defect situation and the possible donor bone is possible. In order to achieve optimal oncological margins, reconstructive geometry, bone-to-bone contact or preservation of blood supply to soft tissue portions of the free flap via perforator vessels, osteotomies are defined for both the ablative segment and the donor graft. Specialised planning software allows the clinician and the technical medical designer to create the best-fitted bone grafts or scaffolds tailored to the patient's anatomy. With the use of 3-D printing techniques, printing of anatomic models of both the native anatomy as well as the reconstructive plan and cutting guides using biocompatible materials is feasible [1]. The incorporation in this workflow of additively manufactured patient-specific reconstruction plates (Patient-specific implant, 'PSI') for flap fixation is now standard of care. With decreased surgery time, higher surgical precision and efficiency as well as higher mechanical integrity, the PSI's outperform the intraoperatively manually bended plates [19]. Main advantages of the CAD/CAM workflow in bony continuity reconstruction procedures are the high precision with defined osteotomy lines and tailored grafts that fit impeccably, reducing intraoperative modifications and overall a reduced surgical time that can promote faster patient recovery. Additionally, the CAD/CAM workflow is of great value for alloplastic reconstruction procedures: If a free flap is not feasible, titanium osteosynthesis plates remain the only treatment option today. The implemented CAD/CAM workflow and use of PSI supersede the pre- and operative bending of the plate that leads to material fatigue and plate fractures consequently. However, more studies have to strengthen that evidence [4].

Overall, CAD/CAM technology provides quantifiable improvements over traditional techniques in both segmental and continuity defect reconstructions. Its advantages include standardised planning, improved precision, reduced operative time and potential for better long-term outcomes. While free flap transfer remains the gold standard for large defects, CAD/CAM offers future alternatives for cases where traditional approaches are limited or not feasible.

3 | Manufacturing Techniques in CAD/CAM Bone Fabrication

Production of scaffolds using a range of conventional manufacturing techniques, such as gas foaming, solvent casting, milling, melt moulding, is feasible. Conventional methods are limited in reproducing complex microarchitecture, such as pore interconnectivity, geometry and spatial material distribution, which are critical for osteoconduction and vascularisation [20]. In contrast, additive manufacturing or 3-D printing techniques have the ability to design any complex structure with precise control over the dimensions, offering significant advantages over traditional approaches. Among a variety of solid freeform fabrication methods, fused filament fabrication, selective laser sintering, stereolithography and digital light processing, as well as direct ink writing techniques are the most widely adopted (Figure 2) [20]. For instance, computer numerical control milling is used for solid bone blocks, titanium frameworks and ceramic scaffolds. It provides high accuracy but is limited in complex microarchitecture replication. Selective Laser Sintering produces porous titanium scaffolds for GBR. With stereolithography, polymer-based scaffolds with precise layer-by-layer deposition can be designed. Fused Deposition Modelling can cost-effectively print biodegradable polymer scaffolds [21]. Beside these achievements, there exist certain drawbacks of adopting 3-D printing technology to fabricate computationally generated scaffolds. Since the scaffold microstructure is typically in the range of micrometres or even nanometres while various 3-D printing techniques lack the precision required at that resolution. In addition, the usage of support structures for printing topologically optimised scaffolds with highly interconnected pores can further complicate the fabrication process. Alternatively, such scaffold structures can be efficiently using laser-based techniques, although limited to the use of photopolymers only, can fabricate such scaffold structures. To conclude, despite the advantages and achievements, no single 3-D printing technique can fully serve the purpose of fabricating computationally optimised scaffold designs [20].

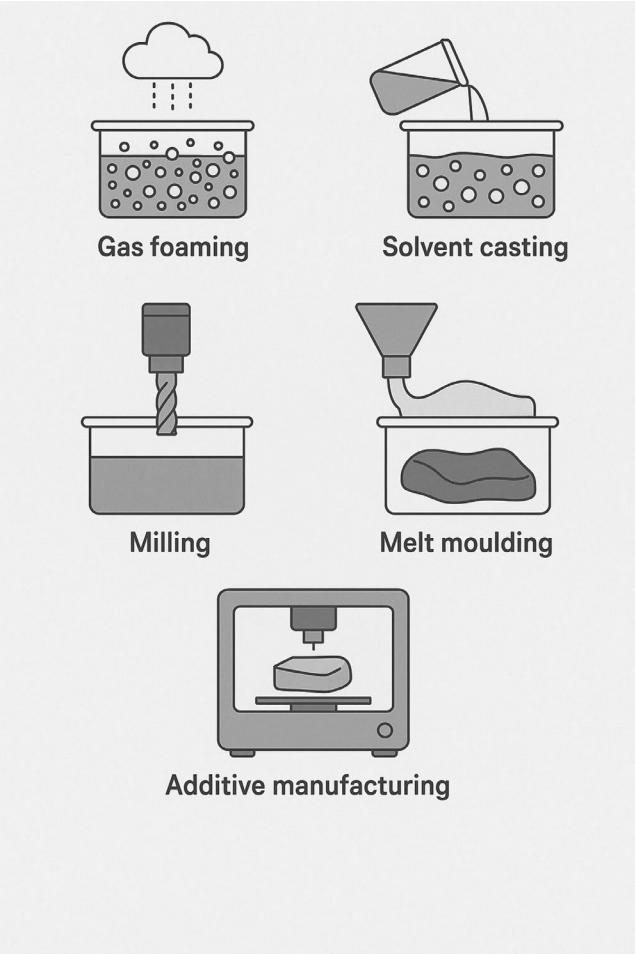

FIGURE 2 | Common Methods for Scaffold Fabrication. This diagram illustrates various techniques used for fabricating scaffolds in tissue engineering, including gas foaming, solvent casting, milling, melt moulding and additive manufacturing (3-D printing). These methods allow precise control over scaffold structure and properties.

To sum up, recent studies demonstrate that 3-D printed scaffolds can be tailored to patient-specific defects with enhanced mechanical and biological properties, outperforming traditional graft shaping methods. However, challenges remain [22, 23]:

- Achieving micro- and nano-scale precision for highly porous scaffolds.
- Managing support structures for complex topologies.
- Material limitations, particularly for load-bearing applications.

In addition, the 3-D bio printing is an emerging technique that can create 3-D living artificial bio implants or complex tissues by simultaneous deposition of living cells and extracellular matrix in a predefined pattern inside a controlled environment [20]. With integration of live cells into 3-D printed matrices, this approach potentially enables vascularised and osteoinductive scaffolds for GBR [24].

4 | Materials for CAD/CAM-Fabricated Bone in GBR

Besides the poor availability, donor-site morbidity and prolonged operation time, autografts are still the gold standard for bone substitution [25]. The implementation of CAD/CAM techniques can partly overcome this limitation. Computer-guided procedures for harvesting autologous bone enable clinicians to obtain sufficient autogenous bone to manage segmental defects with high accuracy and technical predictability [26, 27]. Recently, precise, minimally invasive, individualised jawbone milling in a variety of oral and maxillofacial surgeries is achievable by robotic systems [28]. The applications of allografts or xenografts as alternatives are also limited because of notable drawbacks such as immune response complications, risk of disease transmission and lack of osteogenetic properties. This can result in bone absorption, non-union and graft failure [25]. Consequently, recent advances in tissue engineering have emerged. A variety of biological materials and non-biological but modified scaffolds such as bioactive glasses, ceramics or titanium were exploited for bone defect repairs [25].

CAD/CAM principles revolutionise the clinical workflow. Customised allografts such as demineralised freeze-dried bone and/or xenografts such as bovine-derived materials can now be milled to fit specific defects, offering predictable resorption and remodelling [29]. 3-D printing enables the mould-free fabrication of patient-specific bone substitutes with complex configuration directly from biomaterials. The structures at the macro- and micro-scales that provide optimal in vivo responses can be designed. The application is currently limited to the critical-sized defects of non-weight-bearing bones, regarding the poor mechanical property and failure of anatomically fitting the individual defect situation. Biocompatibility, biodegradability, microstructure, osteoconductivity and mechanical properties are critical characteristics of tissue-engineered scaffolds for bone defect repair [25]. On the macro-scale, the combination of natural (e.g., alginate, chitosan, collagen, hyaluronic acid, bioceramic scaffolds such as hydroxyapatite, calcium phosphate scaffolds, bioactive glasses and polymer scaffolds such as polylactide or polyetheretherketone) and synthetic polymer-based materials (e.g., metallic scaffolds, biodegradable metallic scaffolds such as porous magnesium) is promising to create novel tissue-engineered scaffolds that combine the advantages of both materials [25]. On the micro-scale, 3-D printing is capable of defining porosity, pore size and interconnected pore structure of the printed constructs, influencing cell viability and fostering tissue ingrowth (Table 1) [30]. Using existing materials, 3-D printing approaches seek to develop innovative scaffolds that provide enhanced mechanical properties for load-bearing applications [25, 31]. Up to date, these approaches are limited to in vitro and in vivo research on total bone replacement.

To conclude, CAD/CAM-milled autografts and 3D-printed scaffolds reduce operative time improve defect-specific fit and are associated with higher predictability of bone regeneration in comparison to traditional bone grafting. Current CAD/CAM-fabricated scaffolds are limited to non-load-bearing defects, as many biomaterials lack sufficient mechanical strength. Bioinks and composite scaffolds are still under investigation, with translation to clinical practice limited by regulatory and cost considerations.

5 | Clinical Applications of CAD/CAM Bone in GBR

Currently, clinical implementation of CAD/CAM procedures in GBR is (still) limited to a few indications. The most significant use of CAD procedures is for alveolar ridge preservation in segmental bony defects (Figure 3). Individually shaped and 3-D printed titanium meshes that perfectly fit the defect are regularly used in combination with autologous and/or xenogeneic bone substitute material in GBR [33]. Furthermore, experimental studies and case reports describe other methods and material combinations: GBR with reinforced polytetrafluoroethylene mesh is feasible and reliable [34]. The use of 3-D printed synthetic bone blocks seems to represent a valuable and predictable surgical alternative technique for the reconstruction of extensive alveolar ridge defects [35]. For horizontal ridge augmentation, a fully digital workflow is more accurate and effective in intraoral bone block harvesting [36]. Another clinical application of CAD/CAM in GBR is the production of custom-made scaffolds obtained from porous hydroxyapatite or other allogeneic or xenogeneic materials [37]. With these possibilities in mind, a decision tree can be proposed to help clinical decision-making (Figure 3) in segmental bony defects. However, this should be understood as a subjective recommendation as every decision-making process includes individual local/systemic factors and incision designs that heavily impact the choice of materials, grafting techniques, as well as donor site morbidity [32]. For a 3-wall defect situation, GBR can lead to sufficient horizontal augmentation. In a 1- and 2-wall defect, horizontal and vertical augmentation can be achieved with block augmentation, the use of mesh and shell techniques such as Koury's technique and sinus floor elevation. With bone splitting, horizontal augmentation can be realised. This is also the case for the inlay technique to enhance vertical dimension.

In complex cases, vascularised bone augmentation with free flap transfer is superior to alloplastic alternatives. There are CAD/CAM grafts that restore mandibular continuity post-resection,

TABLE 1 | Key properties of tissue-engineered scaffolds for bone defect repair. This table summarises the critical characteristics, material examples and their relevance to scaffold design, highlighting the combination of natural and synthetic materials to optimise bone regeneration.

Property	Relevance for scaffold design	Material examples	Remarks
Biocompatibility	Prevents immune reactions, supports cell adhesion and proliferation	Natural polymers: alginate, chitosan, collagen, hyaluronic acid Synthetic polymers: polylactide (PLA), polyetheretherketone (PEEK)	Combining natural and synthetic materials enhances biocompatibility and functionality
Biodegradability	Enables natural tissue remodelling without additional intervention	Bioceramics: calcium phosphate, hydroxyapatite Biological polymers and biodegradable metals (e.g., porous magnesium)	Degradation rate must match tissue regeneration
Microstructure	Influences cell migration, nutrient diffusion, and tissue integration	Depends on the manufacturing process (e.g., 3-D printing)	Microarchitecture (porosity, pore size, interconnectivity) is crucial for cell behaviour
Osteoconductivity	Promotes bone cell growth along the scaffold	Hydroxyapatite, calcium phosphate, bioactive glasses	Especially important in bone regeneration
Mechanical properties	Must meet the mechanical requirements of the target tissue	Synthetic polymers (e.g., PEEK), metals (e.g., magnesium, titanium)	Balance between stability and biodegradability is crucial
Macroscale structure	Enables structural integrity and shaping of the defect replacement	Combination of natural and synthetic polymers, metal structures	Material combination utilises the benefits of both classes
Microscale control (3-D printing)	Controls porosity, pore size, and interconnectivity – influences cell viability	3-D printed structures based on the above materials	Allows precise adaptation to the requirements of cell colonisation and tissue ingrowth

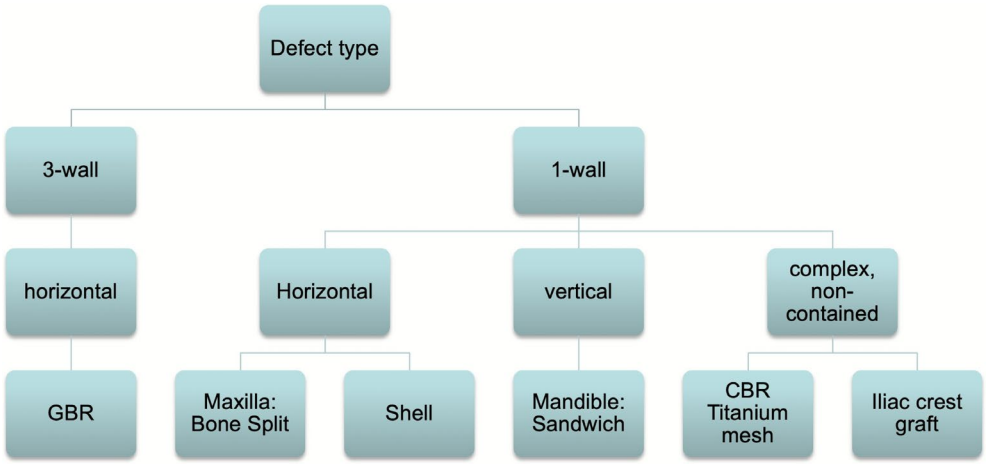

FIGURE 3 | Classification of Bone Defect Types and Associated Treatment Approaches. This diagram illustrates the categorisation of bone defects based on complexity, with specific treatment options including GBR (Guided Bone Regeneration), bone split in the maxilla, and CAD/CAM methods. Adapted from: Kämmerer and Al-Nawas [32].

but it is still limited to alloplastic material such as titanium or PEEK. The integration of finite element analyses in the manufacturing process partly overcomes material weaknesses and helps lower fatigue material fractures. With this, the implementation in the clinical workflow is feasible [4, 38]. However, large clinical trials are missing as the gold standard remains the autologous bony free flap transfer.

The development of the CAD/CAM workflow and use of tissue scaffolds is of great interest for periodontal regeneration, as they can be designed to compartmentalise and spatiotemporally coordinate periodontal regeneration, better controlling concomitant and overlapping cementogenesis, neo-ligament formation and osteogenesis. Hence, multi-compartment fibre-guiding 3-D scaffolds can direct the regeneration of periodontal tissues that result in a functional three-phase structure with load-bearing properties similar to those of the native periodontium [39]. A recent review describes two clinical studies that use 3-D printed scaffolds for periodontal regeneration [40], large clinical trials are missing. Furthermore, in cleft, palate and craniofacial defects 3-D printed grafts can provide patient-specific solutions for congenital anomalies [41]. Favourable results with bone morphogenetic protein 2 (BMP-2)-aided bone tissue engineering have been reported for the reconstruction of the alveolar cleft in defect situations. However, more studies are necessary to assess the quality of bone and long-term outcomes [42].

Taken together, the most widely documented applications include:

1. Alveolar ridge preservation:
   a. Individualised 3D-printed titanium meshes and PSIs are used with autologous or xenogeneic bone substitutes.
   b. Studies report reduced surgical time, improved defect fit and higher patient satisfaction compared to conventional block grafting.
2. Horizontal and vertical ridge augmentation:
   a. CAD/CAM-guided block grafts and mesh techniques improve precision in one- and two-wall defects.
   b. Fully digital workflows enable more accurate intraoral bone block harvesting, with significantly reduced intraoperative adjustments.
3. Continuity defect reconstruction:
   a. PSIs and custom scaffolds allow reconstruction of mandibular continuity post-resection.
   b. Compared to manually bent titanium plates, CAD/CAM solutions improve mechanical stability and reduce operative time.
   c. Autologous free flap remains gold standard for large defects, but CAD/CAM-assisted alloplastic reconstructions provide valuable alternatives when free flap is not feasible.
4. Periodontal and cleft regeneration:
   a. Multi-compartment 3D scaffolds guide spatially coordinated regeneration of cementum, ligament and bone.
   b. Early clinical reports in alveolar cleft repair demonstrate promising bone formation using BMP-2 functionalised 3D-printed scaffolds, though long-term data remain limited.

6 | Challenges and Limitations

The CAD/CAM workflow in GBR has revolutionised current practice. However, plenty of challenges and limitations exist that hinder the transfer into daily clinical routine but for segmental defect reconstruction. Foremost, regulatory and ethical considerations are intricate. Standardisation and approval processes for CAD/CAM bone substitutes in continuity defect situations remain complex [43]. Availability, ethical considerations and regulatory requirements need to be balanced against the materials' performance as a biomimetic bone substitute [44]. The scaffold micro- and nano-topography, cell source, optimal cell number, growth factor dosage and mode of application, and their exact mechanisms of action, remain unclear in most engineered scaffolds. The choice of scaffold material, manufacturing process, the addition of cells and the incorporation of growth factors must be addressed in the specific indication [44]. Unlike conventional drugs or therapeutics, engineered scaffolds and 3-D bioprinted tissues are novel therapeutics and need different regulatory protocols for clinical trials and commercialisation processes. However, the current legislation and standards are more suited for conventional drugs/therapeutics. Hence, it is imperative for the regulatory authorities and other parties to learn the background of these advanced products and adapt the complexities to facilitate the approval processes. Furthermore, clinicians and researchers should learn the scientific requirements, background of standards, necessary training on clinical trials to fulfil the needs of regulatory bodies and global standards [45]. Despite the achievements in the tissue engineering process, material limitations still limit the indications for CAD CAM designed bone substitutes. For example, synthetic biomaterials lack ideal osteoinductive properties [46]. In terms of biological integration, engineered grafts require optimised surface modifications to enhance cellular response and vascularisation. To minimise the risk of disease transmission and cope with immunological reactions, decellularisation of allogeneic or xenogeneic material is crucial. This, in turn, compromises the osteoinductivity of the material [44]. Due to the lack of standardised protocols, the production of large-scale decellularised materials for commercialisation remains challenging [6]. Additionally, advanced CAD/CAM fabrication remains expensive compared to traditional grafting. Extra fees provided by statutory health insurance may provide financial compensation, so the technique is for wide application nonetheless [47].

Regulatory and ethical considerations, material limitations, technical and clinical barriers hamper the clinical use of the advanced CAD/CAM workflow. Translational bottlenecks exist for moving from bench to bedside for bioprinting, AI-optimised scaffold design and 4D printing in terms of extensive preclinical testing, regulatory approvals and clinical trials. Overall, the limited long-term clinical outcome data constrain widespread adoption.

7 | Future Perspectives

Novel concepts hold the promise to overcome the current challenges and limitations. With advances in bioprinting, a 3-D fitting of the graft to the actual defect and the simultaneous deposition of different materials, cells and growth factors seems possible. In a personalised medicine approach,

advances in bioprinting and tissue engineering could lead to fully patient-specific, bioengineered bone grafts in both, segmental and continuity defect situations. This graft will show optimised mechanical and biological properties, mimic natural bone architecture and enhance osteoconduction and -induction. On the same page, this will minimise donor-site morbidity with the reduction of reliance on autogenous bone harvesting. Despite this promise, bioprinting is still a rather novel concept that needs further research, especially into the formulation of adequate bioinks. But with regulatory aspects in mind, it seems more likely that well-characterised materials, already proven in clinical application, will be further functionalised, used in composites or in bioink formulations to improve the treatment of bone defects [44]. Combining vascular and bone-engineered entities into a composite to create a living tissue bed in the bony niche to allow differentiation into vascularised bone remains a great challenge [46]. The integration of growth factors in this concept seems promising, especially the incorporation of Bone morphogenetic protein (BMP), vascular-endothelial growth factor (VEGF) and stem cells can principally enhance osteogenesis [48, 49]. The discussed regulatory restrictions are here of utmost importance and hinder the implementation of these concepts in the clinical workflow. On the same page, nanotechnology enables researchers to conduct scaffolds that contain small extracellular vesicles with specific sets of proteins and RNA that enhance bone regenerative ability significantly [13]. With the development of 4D printing, smart materials that adapt to biological cues for enhanced healing seem possible. Mediated by an external or internal trigger via pressure, temperature, vibration or pH value, the printed materials can change their surface modification or release active ingredients [14]. Within this concept, the optimised bone regeneration mimics the physiological healing cascade [50, 51]. Today, artificial intelligence (AI), including machine learning (ML), can provide alternative routes for materials development and optimisation. This technique streamlines prediction of implantation cases, selection of candidate materials, construction shaping, visualisation, modelling of biodegradation and screening of bone scaffolds [52]. Together, AI-driven design optimisation can improve scaffold efficiency.

Taken together, the following processes hold the promise to overcome current limitations of CAD/CAM bone regeneration:

1. Bioprinting:
   - Enables simultaneous deposition of living cells, growth factors and biomaterials into 3D constructs tailored to patient-specific defects
     - Translational steps: preclinical in vitro and in vivo testing for biocompatibility, vascularisation and mechanical stability; scale-up for reproducible manufacturing; regulatory approval for clinical trials.
     - Bottlenecks: formulation of stable bioinks, achieving sufficient mechanical strength for load-bearing defects and long-term functional integration.
2. AI-driven scaffold design:
   - Machine-learning algorithms optimise scaffold architecture, material selection and biodegradation profiles [53].
     - Translational pathway: validation against preclinical models, integration with CAD/CAM workflow, regulatory review for AI-assisted medical devices.
     - Bottlenecks: requirement for large, high-quality data sets, standardisation across patient populations and clinician training.
3. 4D printing and smart materials:
   - 4D printing produces scaffolds that adapt to biological cues via external or internal triggers (temperature, pH, mechanical stress) [51].
     - Translational steps: preclinical testing of material responsiveness, safety evaluation and demonstration of enhanced healing outcomes in vivo.
     - Bottlenecks: limited material availability, complex fabrication processes and regulatory uncertainties.
4. Growth factor and stem cell integration:
   - Incorporation of BMPs, VEGF or stem cells into CAD/CAM scaffolds can enhance osteogenesis and vascularisation [49].
     - Clinical translation requires standardised protocols for cell sourcing, dosing and delivery methods.
5. Nanotechnology:
   - Functionalised scaffolds with extracellular vesicles or nanoparticles can further promote bone regeneration [31].

8 | Conclusion

CAD/CAM fabrication represents a significant advancement in guided bone regeneration, offering precise, patient-specific solutions with measurable improvements over traditional techniques, including reduced operative time, improved defect fit and lower complication rates. While autologous free flap transfer remains the gold standard for large continuity defects, CAD/CAM-assisted approaches provide valid alternatives, particularly when traditional methods are limited or not feasible.

Emerging technologies—such as bioprinting, AI-driven scaffold optimisation and 4D printing—hold the potential to further personalise bone regeneration, enhance osteogenesis and minimise donor-site morbidity. Translational hurdles remain, including regulatory approval, material limitations and clinical validation. Nonetheless, ongoing research and integration of advanced biomaterials suggest that CAD/CAM-assisted bone regeneration is poised to become a standard, patient-centered approach in maxillofacial reconstructive surgery.

Author Contributions

Bilal Al-Nawas: conceptualization, writing – original draft, writing – review and editing, visualization, project administration, supervision, resources. **Sebastian Blatt:** conceptualization, writing – original draft, writing – review and editing.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no data sets were generated or analysed during the current study.

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