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The Emerging Role of Three-Dimensional-Printed Skin and Bone Grafts in Reconstructive Surgery: Innovations for Hand, Otolaryngology, and Post-Mohs Defect Repair

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Abstract: *Three-dimensional (3D) printing has become incorporated into many aspects of medicine, especially in the field of reconstructive surgery. Some 3D printing technology has seen a rapid development in the bioengineering of skin grafts and bone grafts tailored for complex anatomical defects. This literature review explores the current applications and potential of 3D-printed skin and bone grafts in the reconstruction of defects following orthopedic hand trauma, head and neck surgeries, and post-Mohs micrographic surgery for skin cancer. This review investigates the possibilities of scaffold design, cell seeding, and integration of various growth factors to enhance graft survival and function. Particular limitations and challenges exist, such as translating laboratory advances into clinical practice. This review illustrates that 3D-printed skin and bone grafts can help improve both aesthetic and functional outcomes in many surgical fields, but further research is still necessary to establish widespread adoption.*

1. Introduction

Three-dimensional (3D) printing has been incorporated in several aspects of the medical field with continued innovation. 3D printing was first established in 1981 by Hideo Kodama and has been incorporated into many industries, such as automobile and aerospace engineering, and healthcare [1]. 3D printing in the medical field typically starts with an image created by a computed tomography (CT) scan or magnetic resonance imaging (MRI) [1]. The image is optimized and processed using the software tool of the user's choice [1, 2]. After this, the image will be “sliced” by the printer using a layering method, which starts from the base of the object and is built upwards [1, 2].

3D printing is beneficial to the medical field due to its ability to tailor skin grafts, bone grafts, or prosthetics to individual patients. Additionally, 3D printing has been found to be a valuable asset in patient education as 3D models have played a crucial role in patients’ understanding of their CT scan or MRI results [2]. Pediatric cardiac surgery has benefitted from 3D printing regarding patient education [3]. For example, individualized prints of a patient’s anatomy allows for further understanding of the pathology of their cardiac defect [3]. Similarly, in a randomized controlled study by Biro et al., 3D printing has been used in Mohs surgery to decrease preoperative patient anxiety [4].

In hand surgery and orthopedics, 3D printing has advanced clinical practice by creating customizable splints and braces [1]. Otolaryngology has also benefited from the use of 3D printing, such as for the use of presurgical 3D printed templates for rhinoplasties and the temporal bones [3]. These examples of 3D printing used in the medical field underscore some of the many innovations and utilizations of this technology. Various specialities within medicine can benefit from 3D printing, particularly ones involving reconstruction.

Specific subspecialties, such as hand surgery, otolaryngology, and Mohs surgery, may find 3D printing to be advantageous due to its ability to create skin or bone grafts rather than harvesting traditional grafts. When considering a traditional bone graft, limitations must be considered, such as the risk of future deficits in sensation or functionality, and the need to sacrifice healthy bone in the patient [5]. Use of 3D-printed bone grafts prevents morbidity from auto grafting. Skin grafts pose difficulty in reconstructive fields due to the complexity of skin layering as well as achieving proper vascularization of the skin. A study conducted by Baltazar et al. was able to achieve a 3D-printed, multilayered, vascularized skin graft [6]. As research surrounding 3D printing continues to progress, skin and bone grafts may gain more traction in their respective reconstructive surgical fields.

Orthopedic surgeons may require utilizing bone grafts for the treatment of a traumatic injury and congenital bone defects [7]. Bone grafting requires meticulous measurements and calculations to obtain the appropriate graft size and shape [8]. In an effort to minimize miscalculations, 3D printing may lead to optimal results in hand surgery as it can create exact individualized templates for the surgeon's use [8]. Otolaryngology involves intricate procedures, making precision necessary in the operating room. For example, procedures for ruptured tympanic membranes remain challenging due to surgical risks when obtaining autologous tissues [9]. 3D printing is being explored as an option to mitigate tissue sample damage in tympanic membrane reconstruction [9]. In Mohs surgery, cosmetic outcomes are an important consideration due to the high prevalence of skin cancers on the face [10]. Due to these considerations, skin grafting remains a vital aspect of Mohs surgery and creates opportunities for the use of 3D printing in skin grafting. These three subspecialties involve a plethora of reconstructive procedures and may benefit from the innovations of 3D printing. This literature review investigates the utilization and outcomes of 3D printing in orthopedic hand surgery, otolaryngology, and Mohs surgery.

2. Methods

A comprehensive literature review was conducted to examine the role of three-dimensional (3D) printing in various surgical subspecialties, such as Mohs micrographic surgery, reconstructive otolaryngology surgery, and hand surgery. This review identified relevant studies through a systematic search of PubMed, Google Scholar, and other scientific databases. Key search terms included "Mohs," "3D printing," "Reconstructive surgery," "3D skin grafts," "Hand Surgery", "3D-Printed Grafts," "Post-Mohs reconstruction" "Otolaryngology" and a combination of these keywords. The search conducted by the authors was restricted to peer-reviewed journal articles, clinical trials, literature reviews, and meta-analyses published in English from 2007 to 2025. The data synthesized by these studies provided a comprehensive understanding of the potential of integrating 3D printing into surgical subspecialities for reconstructive purposes, while identifying gaps in the current research, and areas for future investigation.

2.1. Technology of Three-Dimensional-Printed Grafts

Three-dimensional (3D) printing, also known as additive manufacturing, has revolutionized regenerative medicine by enabling the fabrication of intricate, biologically compatible structures for tissue repair. Multiple 3D printing modalities are used in biomedical applications, as outlined by Bozkurt & Karayel, including inkjet bioprinting, extrusion-based printing, stereolithography, and laser-assisted bioprinting [11]. Each technique offers distinct advantages based on the desired resolution, material properties, and cell viability. For instance, Weng et al. reported that extrusion-based printing enables the deposition of highly viscous biomaterials, making it particularly suitable for constructing skin graft scaffolds with robust structural integrity [12]. In contrast, Choi et al. examine how stereolithography allows for finer resolution, and is commonly used for delicate tissue architectures, such as microvascular networks [13]. Ultimately, the choice of printing technique sets the stage for precise graft fabrication, enabling the structural fidelity needed to support advanced biomaterial integration and functional tissue regeneration.

The selection of printing material is equally important. In the context of skin grafts, bioinks composed of natural polymers like collagen, gelatin, fibrin, and alginate are frequently utilized due to their inherent biocompatibility and resemblance to extracellular matrix components [14, 15]. Khoeini et al. found that these compounds support cell adhesion and proliferation while minimizing inflammatory responses [16]. Dwivedi et al. and Kohli et al.

explain that synthetic polymers, such as polycaprolactone (PCL) and polyethylene glycol (PEG), are often incorporated to enhance mechanical stability and degradation profiles [17, 18]. Importantly, Rasouli et al. show that combining natural and synthetic polymers in composite bioinks allows researchers to fine-tune the mechanical and biological properties of grafts to better meet clinical needs [19]. Understanding the capabilities and constraints of these technologies is essential for advancing their use in reconstructive applications, especially in anatomically complex regions, such as the hand and face.

The architecture of 3D-printed grafts plays a critical role in the success of tissue integration and function. Echeverria Molina et al. and Mukasheva et al. discuss how scaffold design directly influences cellular behavior, nutrient diffusion, and vascular ingrowth in addition to its structural properties [20, 21]. Ideal scaffolds for skin and bone regeneration must mimic native tissue geometry and porosity while maintaining mechanical integrity to withstand physiological forces [22, 23]. Computational modeling has allowed researchers to tailor scaffold architecture to match patient-specific anatomy with remarkable precision, enabling personalized medicine on a structural level. For example, Oxford Performance Materials has developed osteoconductive 3D-printed implants using polyetherketoneketone (PEKK), a high-performance polymer that can be engineered to conform precisely to complex craniofacial or orthopedic defects [24]. Prządka et al. indicated that the capacity to customize graft geometry ensures better anatomical fit, reduces operative time, and enhances postoperative outcomes [25]. Furthermore, Anjum et al. found that incorporating nano-scale features into scaffold design has been shown to facilitate better cellular adhesion and tissue integration, which are crucial in high-stakes areas like hand reconstruction or post-Mohs defect repair [26]. Ultimately, advances in scaffold design and patient-specific modeling represent a foundational step in maximizing the therapeutic potential of 3D-printed grafts.

Beyond structural design, the integration of living cells into 3D-printed grafts, known as bioprinting, represents a key advancement in tissue engineering for reconstructive surgery. Liu et al. and Mirshafiei et al. explain how this approach enables the direct placement of viable cells within a scaffold during the printing process, allowing for more physiologically relevant tissue constructs [27, 28]. In the context of skin grafting, Wojtowicz et al. explain how keratinocytes, fibroblasts, and endothelial cells are commonly used due to their roles in epidermal regeneration, extracellular matrix deposition, and angiogenesis, respectively [27]. Seeding these cell types into layered scaffolds that mimic the dermal-epidermal junction has been shown to improve graft integration and functional restoration [30, 31]. As bioprinting technologies advance, layering essential skin cell types in anatomically accurate constructs lays the groundwork for incorporating stem cells and growth factors that further enhance graft viability and regenerative outcomes.

Stem cells, particularly mesenchymal stem cells (MSCs), offer a promising avenue for enhancing regenerative outcomes due to their multipotency and immunomodulatory properties. When paired with growth factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and epidermal growth factor (EGF), cell-laden grafts demonstrate accelerated vascularization and wound closure in preclinical models [32–35]. Wilgus found that these factors not only promote cell survival post-transplantation, but also enhance extracellular matrix remodeling, a vital component in durable skin regeneration [35]. Importantly, Augustine and Zhang et al. explain how bioprinting enables spatial control over the distribution of different cell types, opening the door to multilayered skin constructs that more accurately replicate the architecture of native tissue [36, 37]. This level of complexity is particularly valuable for defects in areas where both form and function must be restored, such as in facial or hand reconstruction.

2.2. Clinical Applications in Reconstructive Surgery

Within the realm of reconstructive surgery, three-dimensional (3D) printing provides innovative new approaches for surgeons, particularly in hand trauma and skin grafting. 3D printing offers an opportunity to potentially reduce morbidity to a patient undergoing a reconstructive surgery compared with the potential for less surgeries or donor site harvesting being required. 3D printing has the capability to customize and provide a more patient centric approach to reconstruction. Such customization provides the potential to improve functional outcomes and accelerate tissue healing, by restoring bone and soft tissue structures in a more precise manner. There are early indications illustrating that 3D-printed grafts help reduce operative time and improve recovery to conventional methods [38].

In orthopedic hand trauma, 3D printing can aid in the creation of patient-specific anatomical models, surgical guides, custom implants for hand defect, tendon injuries, and bone reconstructions [39]. Such capabilities would allow for 3D-printed implants to be tailored to match the unique anatomy of each patient, allowing for improved fit and stability when compared to the traditional techniques [40]. While 3D-printed tendon substitutes are still highly experimental, such capabilities of 3D printing can be used for fabrication of scaffolds and varying guides in tendon reconstruction and repair [41]. This allows for support of precise alignment and tensioning during surgery [41]. In reconstruction of bone, 3D-printed implants that utilize materials, such as biocompatible metals, polymers and ceramics, can allow for a complex design and porous construction that promote osseointegration and long-term viability and stability [42].

In regards to post-Mohs reconstruction, 3D-printed skin grafts can improve both aesthetic and functional outcomes when compared to the traditional grafting techniques [43]. Reconstructing post-Mohs defects presents varying challenges, such as achieving optimal color and texture match, minimizing donor site morbidity, reducing scar formation, and restoring both the aesthetic and functional integrity of the site [44]. The technology of 3D printing allows for the fabrication of multilayered constructions that often mimic the native skin, incorporating both dermal and epidermal factors, to restore both the native skin's function and appearance [45]. In early clinical data, 3D-printed autologous tissue patches have been shown to achieve both faster wound closure and higher patient satisfaction with minimal scarring [46].

Surgical reconstruction in otolaryngology requires the possibilities of restoring the complex 3D anatomy within the area to maintain the airway and swallowing capabilities [47]. 3D-printed, patient-specific implants and scaffolds allow for precise anatomical restoration of structures, such as the mandible, maxilla, auricle, and nasal framework [48]. Such customization can lead to improved symmetry, contour, and integration within the native tissue, while also reducing possible intraoperative complications and operative time [49]. Early clinical outcomes and utilizations of bioprinted tissue-engineered constructs for both auricular and nasal defects shows promise in restoring function while also reducing scarring and providing an aesthetic match [50]. Overall, the capabilities of utilizing such technology in the realm of reconstructive surgery provides surgeons an additional avenue to pursue to provide more aesthetic, functional, and personalized reconstructive options.

Table 1. *Examples of Three Dimensional Printed Graft Material and the Utilization in Subspecialty*

Surgical Subspeciality	Substance/Material of 3D printed Graft	Clinical Application	Key Benefits
Orthopedic Hand Surgery	Polyether Ether Ketone Material [51]	Utilize for Internal fixation devices for osseointegration	Mechanical compatibility with human bone
Otolaryngology	Bioceramics - Hydroxyapetite [52]	Utilized to construct implantable devices such as temporal bone implants	Biocompatibility and osteoconductivity which enables integration with host bone
Dermatology (Mohs Micrographic Surgery)	Gelatin methacrylol (GelMA) [53]	Utilized for skin scaffold and wound matrices	Biocompatibility and tunable mechanical properties

3. Biological Integration & Graft Survival

3.1. Challenges in Graft Integration

Delayed vascularization and perfusion may limit the integration of three-dimensional (3D) bioprinted grafts into host tissue. Without an immediate blood supply, thick grafts rely solely on diffusion, which is typically insufficient to maintain perfusion to deeper cellular layers, which can result in tissue necrosis after implantation [54]. Experimental models of bioprinted adipose grafts have shown partial perfusion shortly after implantation, whereas complete angiogenesis develops only over several weeks [55]. Although the graft eventually achieves vascular connectivity, the critical delay may markedly compromise its initial viability and functional integration. As a result, accelerating vascular integration remains a fundamental challenge for clinical translation of 3D-printed grafts. Structural innovations, such as pre-formed endothelial channels, have improved early graft perfusion, particularly when combined with supportive matrices and stem cell populations [56]. Researchers achieved long-term viability in tissue grafts over one centimeter thick by embedding perfusable vasculature seeded with endothelial cells [57]. Spatially controlled architecture and prebuilt vascular networks are essential for meeting metabolic demands beyond the diffusion threshold. Nevertheless, recreating physiologically relevant flow patterns and maintaining long-term vessel patency *in vivo* remain unresolved challenges.

Even with adequate perfusion, host immune responses frequently impair graft integration by reacting adversely to biomaterials. Many commonly used bioinks provoke macrophage activation and chronic inflammation, particularly when degradation byproducts or surface impurities are present [58]. Such inflammatory responses often lead to fibrotic encapsulation, isolating the graft from host tissue and impairing functionality [59]. Optimizing bioink composition and refining surface characteristics remain critical in mitigating immune-mediated rejection and enhancing biocompatibility. Current bioprinting technologies struggle to replicate the precise detail, density, and hierarchical branching of native microvascular networks [60]. While advances in bioink formulations and print fidelity have shown promise in early preclinical models, consistent translation into scalable, implantable grafts remains challenging. Overcoming these interrelated structural and immunological barriers is essential to advancing the clinical viability of bioprinted grafts.

3.2. Enhancing Graft Function

One of the most promising strategies for improving the function and survival of bioprinted grafts is the controlled delivery of growth factors within the tissue scaffold. Spatial and temporal control over signaling molecules guides cellular behavior, stimulates vascularization, and expedites tissue regeneration [61]. Using programmable bioinks embedded with nanoparticle-bound factors, such as vascular endothelial growth factor (VEGF) and bone morphogenic protein-2 (BMP-2), recent approaches deliver regenerative signals to specific graft regions, guiding tissue development to mimic natural vascular and bone formation closely [62].

Incorporating multipotent stem cells or stromal cells into bioprinted grafts allows a single cell source to generate multiple tissue types when guided by spatially defined growth factors, simplifying the production of grafts composed of different cell types and tissue layers [62]. By combining intrinsic cell plasticity with localized signaling cues, bioprinting can replicate the coordinated developmental events observed in natural tissue regeneration. These strategies offer a practical path toward building multifunctional grafts that are reproducible and clinically scalable.

Scaffold composition also plays a critical role in graft performance by influencing structural support and biochemical signaling. Hydrogels and polymer composites engineered with functional groups or loaded with bioactive molecules can enhance cell adhesion, promote differentiation, and support vascular ingrowth [63]. Achieving an optimal balance between mechanical stability and bioactivity is especially important in skin and soft tissue grafts, where successful integration depends on structural fidelity and cellular remodeling. Selecting biomaterials that deliver appropriate biological cues without provoking adverse immune responses remains a central challenge in scaffold design. Advances in growth factor delivery have moved beyond simple bolus release, enabling bioprinted platforms to provide sequential or sustained signaling that mirrors the natural phases of tissue healing and remodeling [64].

In bone tissue engineering, high-performance polymers, such as polyetheretherketone (PEEK) and polyether ketone ketone (PEKK), help create patient-specific implants that offer mechanical strength and biocompatibility [51]. These materials, utilized in commercial platforms, such as Oxford Performance Materials' OsteoFab® scaffolds, support osseointegration and have been successfully applied in orthopedic and craniofacial reconstruction [51]. As the field moves forward, integrating responsive or feedback-controlled systems may further optimize outcomes by adapting growth factor exposure in real-time to the evolving tissue environment.

3.3. Long-Term Outcomes

The long-term success of bioprinted three-dimensional (3D) skin grafts depends not only on initial vascularization and immune compatibility, but also on their sustained integration, mechanical performance, and functional remodeling. Preclinical models using bioprinted bilayer skin grafts have demonstrated stable vascular infiltration and dermal organization over several weeks post-implantation, supporting the potential for sustained tissue viability beyond the acute healing phase [65]. These models also showed that the grafts expressed key markers of blood vessels and dermal tissue, indicating that both the host and the graft actively contribute to tissue remodeling over time. Ongoing vascularization is critical for maintaining graft viability and preventing scar tissue formation that could impede integration and lead to graft failure.

Studies of full-scale dermo-epidermal bioprinted grafts show that stable vascular integration and surface epithelialization can be achieved *in vivo*, along with similar wound closure rates when compared to conventional split-thickness skin grafts in large wound models [66]. Additionally, bioprinting allows researchers to tailor grafts to the patient's specific wound shape and depth and design their internal structure to mimic native skin layers. Therefore, bioprinted grafts could serve as functional alternatives or enhancements to traditional grafting methods in select clinical settings.

Grafts placed in high-mobility areas must maintain appropriate mechanical properties to ensure long-term success. Recent studies using auxetic skin scaffolds engineered to expand under tension have shown reduced contracture rates and better conformation to joint movement [67]. Such innovations may help overcome mobility restriction due to graft contraction, one of the most common complications in burn and trauma reconstruction [67]. Therefore, long-term success requires biological integration along with the graft's ability to move and stretch with the body without causing discomfort or functional limitation. To bring 3D bioprinting into clinical practice, researchers and clinicians must gather more long-term outcome data and continue to innovate with approaches to skin reconstruction. Rather than a one-size-fits-all approach, bioprinted grafts offer the possibility of designing patient-specific solutions that consider aesthetic needs, anatomical complexity, and functional demands [68]. As the field advances, long-term outcomes must be measured by graft survival and their ability to restore form, function, and quality of life in various clinical settings.

3.4. Limitations and Challenges in Clinical Practice

Despite the promising results of three-dimensional (3D) bioprinting, technological limitations still exist. While 3D printing can be customizable for each patient, it is not suitable for all body parts and scenarios. 3D-printed bioceramics are typically brittle and cannot always be used for weight-bearing body parts [69]. Brittle bioceramics in certain areas of the body can cause injuries to the patient or prolong healing time if there is a fracture or failure of the material. Furthermore, it is a challenge to maintain high resolution when printing large volumes of skin [70]. Kaur et al. highlight that making skin constructions for patients with more than 50% skin loss is challenging [71]. Overall, this restricts the use of 3D printing in reconstructive surgery.

Furthermore, 3D printing in reconstructive surgery has numerous other technological drawbacks. Slow printing speed is a major obstacle for this technology [72]. This is an issue in the case of Mohs surgery as it is usually performed on the same day. This can also pose an issue in trauma-related reconstructive surgery, where soft tissue coverage and repair of injuries is time sensitive to reduce risk of morbidity and complications. Furthermore, sterility is a major issue with this device as many 3D products can shed particles, such as plastic particles during surgery [73]. This can increase the risk of complications, such as infections. Likewise, Aneja et al. state that cleaning 3D-printed constructs and tools can be difficult, as often they take on complex shapes and traditional cleaning techniques may not suffice [74]. This again poses a safety issue and a risk for contamination. There are many aspects of 3D printing that are still unknown, which could lead to ethical concerns [75]. There may be a conflict of interest for surgeons who may financially benefit from the use of this technology in the patients they treat. Furthermore, Pugliesi adds that patient safety is a major ethical concern [76].

Particularly when evaluating current trends in 3D printing, Pugliesi highlights that there are potential concerns with many realms of the 3D printing industry, mainly with federal regulations, control of printing errors, and infection control, all of which could potentially harm patients [76]. With 3D printing advances, patients may not be aware of all the risks of 3D printing. For example, Rizzo et al. state that using stem cells with 3D bioprinting puts the patient at risk for an increased number of cell growth, which has the potential to lead to cancer [77]. The patient can also develop zoonosis when using nonhuman stem cells [77]. Rizzo et al. further explain how ethical issues may arise with using embryonic stem cells for 3D printing, as not all countries allow this to be done [77]. This may lead to "stem cell therapy tourism," or patients traveling to other countries that allow embryonic stem cells to be used [77]. Many of these concerns are limited to the use of stem cells, which is not the only source of 3D printing technology.

Lastly, the use of 3D printing in reconstructive surgery presents with cost limitations. Ballard et al. discuss that while 3D printing can be cost-effective, there is a high start-up cost to investing in a 3D printer [78]. This can limit the number of medical facilities that can offer 3D printing as an option, and therefore, not all patients will have access to this technology. Furthermore, the materials of 3D printing are often expensive. Moreover, there are high costs associated with maintaining the 3D printer, training new staff members, and potential repairs and calibration [79]. Taken together, while 3D printing holds promise in reconstructive surgery, its drawbacks, including the technological limitations and costs, need to be addressed for 3D printing to have widespread applications.

4. Conclusion

3D printing has poised itself as an emerging and transformative tool for reconstructive surgeons in a multitude of surgical sub-specialties. Offering both innovation, personalization, and solutions for complex anatomical defects 3D printing provides a means to create customized, natural grafts that resealable native tissue structure and function. Such 3D printed technologies show significant promise with advancements in scaffold design, bioink composition, and various bioprinting techniques, providing an enhancement in not only functional outcomes but also in aesthetic outcomes, all while reducing complications and operative times. However, even with many recent advancements, significant challenges still remain in translating new technology into clinical practice, challenges such as delayed vascularization, host immune responses, sterility measures, ethical concerns and high costs. As current research endeavors continuously advance such a field, 3D printing is at the forefront of reconstructive surgery, holding the potential to redefine the field.

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