# 3D Bioprinting: A Review and Potential Applications for Mohs Micrographic Surgery


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## Background

- Mohs Micrographic Surgery (MMS) is a well-recognized treatment modality for various cutaneous malignancies, known for high cure rates and tissue preservation.
- 3D bioprinting has emerged as an approach that holds future potential for advancing skin tissue engineering in MMS, especially in complex reconstructions.
  - Uses rapid prototyping to mimic natural tissue or organs by layering cells, growth factors, and biomaterials via computer-aided design/computer-aided manufacturing (CAD/CAM) technology.[1]
    - Patient-derived cells expand in culture before adhering to the scaffold, proliferating, and producing the extracellular matrix, promoting tissue regeneration.[2,3]
    - Adding biomaterial scaffolds and cells to structures like vasculature, muscle, cartilage, and bone also yields regenerative benefits.[2,3]
  - Classified into 3 techniques based on the molding principle and printing material:
    - **Droplet-based-**
      - Inkjet bioprinting employs thermal or piezoelectric methods for pressure generation but faces challenges like droplet directionality and nozzle clogging.[4,5]
      - Acoustic bioprinting ejects droplets using an acoustic field, avoiding heat and high pressure.[1]
      - Micro-valve bioprinting has shown potential for skin regeneration by generating droplets via an electromechanical valve.
    - **Extrusion-based-**
      - A modified inkjet printing method, enabling printing of highly viscous biomaterials through continuous bead dispensation.[5,6]
      - Widely recognized for its compatibility with various biomaterials and ability to produce high cell density bioscaffolds, making it the most prevalent 3D bioprinting method.[6]
    - **Photocuring-based-**
      - Uses a laser pulse to vaporize a metallic ribbon film, ejecting bioink droplets onto the substrate with precise control over dimensions and surface properties.[7]
      - While offering precise control, particularly in small scales, PBB requires costly and time-consuming integration of materials with the metallic film, limiting its applicability in tissue engineering.[7]

## Objectives

1. Examine the applications of 3D bioprinting in medical settings, particularly within dermatologic surgery.
2. Assess the potential benefits, challenges, and logistics of integrating 3D bioprinting into clinical practice.
3. Identify research gaps in the field of dermatology related to 3D bioprinting technology.
4. Propose avenues for future investigation to address challenges and optimize the integration of 3D bioprinting in dermatologic surgery.

## Methods

- We conducted a comprehensive PubMed search using keywords "Three-dimensional bioprinting" OR "3-D printing" AND "Mohs" OR "Mohs surgery" OR "Surgery."
  - Inclusion criteria: peer-reviewed English articles discussing 3D bioprinting in medical contexts
  - Exclusion criteria: non-peer-reviewed sources, conference abstracts, and non-English articles

## Results

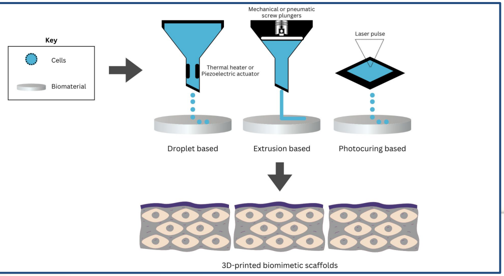
**Current applications of 3D bioprinting:**

| Education | Surgery | Reconstruction |
|---|---|---|
| • Medical professionals/trainees:<br>3D printed models for easier diagnostic processes, simulation models for experiential learning.[8-10, 11]<br>• Patient/Caregivers:<br>3D models to demystify complex surgeries and help comprehension of medical condition.[12] | • Procedural rehearsal, patient-specific surgical cutting guides, 3D-based preoperative planning.[13]<br>→ Operational time reduction<br>→ Cost savings<br>→ Enhanced patient outcomes | • Skin grafts for burn victims or those with chronic wounds.[14]<br>• Bone and cartilage structures for patients with bone defects or osteoarthritis. |

**Potential applications of 3D bioprinting in MMS:**

| Benefits | Challenges |
|---|---|
| Medical and Patient Educational Models<br>- 3D-printed facial model realistically demonstrated flap reconstruction in MMS[11]<br>- 3D MMS model reduced anxiety and increased understanding in patients[12]<br>**- Significantly larger reductions in anxiety scores (3.00 to 1.7, $p < 0.0001$) compared to the those receiving standard education (2.5 to 2.0, $p < 0.04$)**<br>**- On a MMS knowledge assessment, the model group averaged significantly higher scores (5.59 or 93.25% correct responses) than the standard education group (5.15 or 85.83% correct responses)**<br>Surgical Guides and Stimulation<br>- Improved surgical techniques[11]<br>**- Improvement in both banner ($p$=0.002) and bilobed flaps ($p$=0.04) among surgical residents**<br>**- Medical students using the 3D model outperformed those learning through reading ($p$=0.001)**<br>- Increased comfort levels in flap design and execution increased after model use[11]<br>Implants or Grafts for Reconstruction<br>- Personalized fabrication of skin scaffolds with precise control over depth, shape, size, and thickness<br>- Reduced wound contraction, shorter healing time,and improved scar appearance compared to autograft[15-18] | - Cost-effectiveness[19]<br>- High costs of different bioink components, biomaterials, and printers<br>- Difficulties in scaling and integrating 3D printing into existing medical systems<br>- Affordability and efficiency in smaller healthcare settings<br>- Regulatory & ethical frameworks[20]<br>- Stringent safety standards limiting widespread implementation<br>- Need for reassessment of regulations for a rapidly growing field of 3D printing<br>- Reproducibility and precision[19]<br>- Necessity for specialized training among medical professionals<br>- Complex optimization of cell and biomaterial printing, particularly in cell quantification |

**Figure 1.** 3D Bioprinting Methods




## Discussion

- 3D bioprinting may eliminate autografting needs, reducing pain and infection risks associated with donor sites.
- 3D-printed skin scaffolds stimulate granulation tissue production, accelerate healing, and minimize scarring which contributes to improved cosmetic outcomes and patient satisfaction.
- In contrast to traditional tissue engineering methods, 3D bioprinting introduces precision in creating anatomically correct microstructures, enabling the fabrication of more complex and customizable biomimetic tissues.
- Limitations of 3D bioprinting integration in MMS:
  - Specialized training required for its use
  - High costs associated with bioink and printers
  - Technological constraints in replicating complex tissue structures like glandular tissue and vasculature
  - Practicality in the outpatient setting
- **Future implications:**
  - Integration with optical coherence tomography (OCT) may expedite the process by providing real-time information for precise identification of tumor boundaries.
  - Regulatory and ethical frameworks need reassessment due to decentralization of manufacturing process.
  - Comprehensive patient discussions regarding use of stem cells in 3D bioprinting are essential if utilized.
  - More extensive investigation needed on the following:
    - Long-term effects of synthetic tissue incorporation, especially in human subjects
    - Comprehensive assessments of cost-effectiveness are essential for widespread adoption, particularly in smaller healthcare settings

## Conclusion

- 3D bioprinting may be a beneficial adjunct to conventional skin cancer therapies, enhancing wound healing and aesthetic outcomes.
- Further research is needed on long-term effects, cost-effectiveness, and human skin studies to address current challenges and limitations.
- Significant technological advancements and research efforts required prior to widespread adoption in integration into clinical practice.

Scan for references: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