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International Journal of Bioprinting

ACCEPTED PAPER · SUPPLEMENTARY FILE

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Article ID: IJB026210207

Citation: Guo L, Niu X, Bux N, Li Y, Xu T, Guo D. Recent advances and challenges in 3D bioprinting for skin tissue regeneration. *Int J Bioprint*. 2026. doi: 10.36922/IJB026210207

AccScience Publishing
REVIEW ARTICLE
Volume X Issue X (2026)
doi: 10.36922/IJB026210207

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Running title: 3D bioprinting for skin regeneration

Supplementary File

Table S1. Unified materials-design framework for skin bioprinting.

Material class	Target skin layer	Healing phase activity	Compatible technology	Key functional requirement	Primary limitation
Collagen type I	Dermis	Proliferative, remodeling	Inkjet, LAB, extrusion	Fiber alignment, mechanotransduction	Rapid degradation, poor printability alone
GelMA	Dermis, DEJ	All three phases	Extrusion, DLP, LAB	Tunable stiffness, inflammatory modulation	Photoinitiator toxicity

Fibrinogen/fibrin	Dermis	Inflammatory, proliferative	Inkjet, extrusion	Provisional scaffold, hemostasis	Weak mechanics, rapid degradation
dECM	Dermis	All three phases	Extrusion	Full signaling complexity	Batch variability, immune risk
Alginate	Structural support	Structural only	Extrusion	Gelation control	No cell adhesion without modification
Chitosan	Epidermis, wound surface	Inflammatory	Inkjet, extrusion	Antimicrobial, hemostatic	Immunostimulatory risk
PEG	Structural / mechanical	Remodeling	DLP, extrusion	Tunable mechanics, low immunogenicity	No bioactivity without functionalization
PCL	Structural scaffold	Remodeling	Extrusion	Mechanical strength, slow degradation	Poor cell adhesion
Tropoelastin	Dermis	Remodeling	Extrusion	Elastic recoil, cyclic load	Largely unexplored in

				resistance	skin bioprinting
Platelet biologics/GelMA	Dermis	Inflammatory → proliferative	Extrusion, inkjet	Phase-matched growth factor release	Release kinetics control; cost

Table S2 Comparative Analysis of Natural Polymer Biomaterials for 3D Bioprinting Applications

Material	Properties	Advantages	Limitations	Applications	Ref:
Collagen	High biocompatibility Natural ECM mimicry Low mechanical strength	Supports cell adhesion and proliferation Biodegradable and non-toxic	Rapid degradation in vivo Poor structural stability High cost	Epidermal/dermal layer fabrication Vascularized constructs	[1,2]
Gelatin	Thermoresponsive gelation RGD motifs for cell adhesion	Low immunogenicity Cost-effective Tunable viscosity	Weak mechanical properties Requires chemical crosslinking (e.g GelMA)	Sacrificial microchannels Multi-layered skin models	[3,4]
Fibrinogen	Natural role in wound healing Polymerizes to fibrin via thrombin	Enhances cell migration and angiogenesis Biodegradable	Rapid degradation Batch-to-batch variability	Wound dressings Vascular network integration	[5,6]
Alginate	Ionic crosslinking (Ca^{2+}) High printability	Rapid gelation Structural support for thick tissues	Lacks cell-adhesive motifs Requires RGD modification	Temporary scaffolds Hybrid bioinks for mechanical reinforcement	[6,7]
Chitosan	Antibacterial properties Positively charged polysaccharide	Hemostatic and antimicrobial effects Enhances wound healing	Poor solubility in neutral pH Low cell adhesion	Antimicrobial wound dressings Composite bioinks for infection-prone wounds	[8,9]
Hyaluronic Acid	High hydrophilicity ECM component in skin	Promotes tissue hydration Supports fibroblast migration	Low mechanical strength Fast degradation	Anti-scarring hydrogels Epidermal regeneration	[9,10]
Decellularized ECM (dECM)	Native ECM composition Growth factor retention	High bioactivity Patient-specific compatibility	Complex preparation Risk of pathogen transmission	Full-thickness skin substitutes Vascularized and innervated constructs	[11,12]
Silk Fibroin	High tensile strength Tunable degradation rate	Excellent mechanical properties Biocompatible	Requires harsh processing solvents	Load-bearing skin scaffolds Nerve conduit fabrication	[13,14]

Slow gelation

Table S3 The Main Cell Types and Functions of 3D Bioprinting for Skin Repair.

Cell Type	Characteristics	Primary Functions	Applications	Advantages	Limitations	Ref:
Keratinocytes	Epidermal progenitor cells Express cytokeratins	Re-epithelialization Barrier formation Wound closure	Epidermal layer reconstruction Chronic wound healing (e.g., burns, ulcers)	Rapid proliferation Autologous sourcing possible	Limited ECM production Sensitive to shear stress during printing	[15,16]
Fibroblasts	Dermal ECM-producing cells Secrete collagen, fibronectin, and growth factors	ECM synthesis Granulation tissue formation Scar modulation	Dermal regeneration Hypertrophic scar reduction	Enhance mechanical stability Promote angiogenesis	Risk of fibrosis if overactivated	[5,17]
Endothelial Cells (ECs)	Line blood vessels Express CD31 and vWF	Vascular network formation Nutrient/oxygen delivery	Vascularized skin substitutes Diabetic wound healing	Enable perfusion of thick constructs Reduce necrosis	Low survival in hypoxic conditions Complex co-culture requirements	[18,19]
Melanocytes	Melanin-producing cells Localized in the epidermal basal layer	Skin pigmentation UV protection	Pigmentation restoration Cosmetic reconstruction (e.g., vitiligo)	Improve aesthetic outcomes Patient-specific matching	Limited proliferation capacity Sensitive to oxidative stress	[20,21]
Mesenchymal Stem Cells (MSCs)	Multipotent stromal cells; paracrine signaling; may be derived from bone marrow (BM-MSCs), adipose tissue (ADSCs), umbilical cord, or other sources	Anti-inflammatory effects ECM remodeling Differentiation into skin cells	Chronic wound healing Scarless regeneration	Immunomodulatory properties Versatile differentiation potential	Heterogeneous cell populations Risk of uncontrolled differentiation	[22,23]

Adipose-Derived Stem Cells (ADSCs) [MSC subtype]	MSC subtype isolated from adipose tissue; fulfills ISCT MSC criteria (plastic adherence, surface markers CD73/CD90/CD105+, multipotent differentiation); easily accessible; high proliferative capacity	Secrete angiogenic factors (e.g., VEGF); support nerve regeneration; anti-inflammatory and immunomodulatory effects consistent with MSC lineage	Diabetic ulcers Burn repair with appendage regeneration	Abundant source (adipose tissue); low immunogenicity; superior accessibility compared to BM-MSCs	Variable efficacy based on donor age/health	[24-26]
Schwann Cells	Glial cells of the peripheral nervous system	Axonal guidance Neurotrophic factor secretion (e.g., NGF, BDNF)	Innervated skin substitutes Peripheral nerve repair	Critical for sensory recovery Enhance neurite outgrowth	Difficult to isolate and expand in vitro	[27,28]

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