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Vascularized bioprinting for neuroischemic diabetic foot ulcers and selected ischemic lower-limb wounds: A proposed vascular-surgery design framework

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Supplementary File

Table S1. Study-level technical evidence crosswalk for the primary studies summarized in Table 2

The table summarizes the printing modality, principal matrix or bioink, cells or payload, model and disease match, comparator or control, and highest vascular evidence level for the primary studies listed in Table 2. Evidence levels follow the hierarchy defined in Section 4.2: Level 1, endothelial organization or marker-positive structures; Level 2, a lumenized network shown to be perfusable within the construct; Level 3, anastomosis or direct connection with host vessels; and Level 4, functional tissue perfusion demonstrated by flow-sensitive imaging, tracer delivery, oxygenation or an equivalent physiological measure. Level 0/indirect indicates that no direct vascular endpoint at Levels 1-4 was established in the evidence summarized for this review.

Study	Printing modality	Principal matrix/bioink	Cells or payload	Model and disease match	Comparator/control	Highest vascular evidence demonstrated
Vascularized perfusable skin graft [34]	Layered bioprinting	Collagen/fibrin-based skin matrix	Keratinocytes, fibroblasts, pericytes and endothelial cells	Human skin-equivalent construct; implantation-oriented testing; not DFU/CLTI	Non-vascularized and component controls	Level 2: a perfusable network was demonstrated within the construct; host-vessel anastomosis and disease-matched functional tissue perfusion were not established.
Spatiotemporal growth-factor patterning [38]	3D bioprinting of spatial cue fields	Printable hydrogel carrier	Patterned growth factors	Regenerative tissue-patterning model; not DFU-specific	Patterned versus non-patterned cues	Level 0/indirect: angiogenic cue delivery was studied, but endothelial organization, a perfusable network and host connection were not demonstrated.
In situ autologous skin-cell printing [37]	In situ bioprinting	Fibrin/collagen-type wound matrix	Autologous skin cells	Extensive full-thickness excisional wounds; acute non-DFU model	Standard wound or non-printed comparisons	Level 0/indirect: wound closure and tissue repair were reported; vascular detail was limited and functional perfusion was not established.
Placental-derived printed bioink [40]	Extrusion-style printing	Placental-derived dECM-like bioink	Skin-relevant cells and matrix cues	Skin regeneration and wound-healing models; not neuroischemic DFU	Bioink and material controls	Level 1: angiogenic or endothelial organization was supported; construct perfusability and host-vessel connection were not established.
Microfluidic/coaxial diabetic wound dressing [42]	Microfluidic plus coaxial printing	Core-shell hydrogel fibres	Therapeutic payloads rather than a full skin-cell system	Diabetic wound-dressing concept; infection and perfusion context limited	Fibre and formulation controls	Level 0/indirect: the architecture was relevant to angiogenic delivery, but a vascular network, host connection and functional perfusion were not demonstrated.
Photosynthetic in situ scaffold [43]	In situ printing	Photosynthetic living scaffold	Oxygen-generating biological component	Oxygen-supportive wound-healing model; DFU/CLTI status not established	Non-photosynthetic and scaffold controls	Level 0/indirect: oxygen support and wound repair were assessed without direct vascular-network or perfusion evidence.
Immunomodulatory exosome bioprinted biomaterial [44]	3D bioprinting	Immunomodulatory biomaterial	Engineered exosomes from M2-polarized macrophages	In vivo wound-healing and angiogenesis model; DFU disease match uncertain	Biomaterial and exosome controls	Level 1: angiogenic markers or organization were reported; a perfusable network, host anastomosis and functional perfusion were not established.

Study	Printing modality	Principal matrix/bioink	Cells or payload	Model and disease match	Comparator/control	Highest vascular evidence demonstrated
Endothelial-patterned skin patches [48]	In-bath, light-activated printing	Light-activated bioink	Patterned endothelial cells	Wound-healing skin-patch model; not DFU/CLTI	Patterned versus less-patterned patch controls	Level 1: spatial endothelial organization was demonstrated; perfusability and host-vessel connection were not established.
Lipoaspirate-derived cell-laden skin constructs [60]	3D bioprinting	Cell-laden skin-construct hydrogel	Human lipoaspirate-derived cells	Full-thickness skin-defect repair; not diabetic or ischemic	Scaffold and cell controls	Level 0/indirect: tissue repair was the principal endpoint and vascular readouts were secondary; functional perfusion was not established.
Gel/dECM/Qcs DFU scaffold [19]	Extrusion printing	Gelatin, decellularized ECM and quaternized chitosan	Antibacterial scaffold with exosome-loading rationale	DFU-oriented scaffold-repair study	Material and formulation controls	Level 0/indirect: fibroblast compatibility and wound-repair rationale were reported, while direct perfusion validation was limited.
Xeno-free vascularized human skin graft [20]	3D bioprinting	Xeno-free skin bioink system	Human skin and vascular cells	Implantable vascularized human skin graft; not DFU/CLTI	Non-vascularized or comparator-graft logic	Level 3: host-connected, perfused human microvessels were reported after implantation; disease-matched functional tissue perfusion in DFU/CLTI was not shown.

Abbreviations: CLTI, chronic limb-threatening ischemia; dECM, decellularized extracellular matrix; DFU, diabetic foot ulcer; Qcs, quaternized chitosan.

Table S2. Literature search, priority scoring and citation reconciliation

Supplementary Table S2 reconciles the automated search-prioritization workflow with the final narrative bibliography. Final references were selected through expert-led narrative synthesis for their direct relevance to the review questions. The additive score and top-180 cap therefore served as literature-prioritization and organization tools rather than a PRISMA-style study-inclusion set.

Component	Operational definition	Count or score
Raw retrieval	Twelve topic queries spanning DFU/chronic wounds, vascularized skin, angiogenic bioinks, neurovascular repair, CLTI/revascularization and related biofabrication contexts.	608 records: OpenAlex, 577; PubMed, 31
Deduplication	Records were merged by DOI, then PMID, then normalized title when persistent identifiers were unavailable.	466 unique records; 142 duplicate records merged
Threshold eligibility	The additive priority score described below was applied to titles and available abstracts or metadata. A score of at least 7 defined eligibility for ranking.	371 eligible; 95 below threshold
Working evidence map	Eligible records were ordered by priority score, citation count and publication year. The first 180 formed the working evidence map; the cap was a narrative-review prioritization device.	180 mapped (score range 10-19); 191 eligible records below rank cut-off
Final citation selection	Manual citation decisions required direct support for biofabrication mechanisms, disease/wound context, vascular or neural integration, infection/safety constraints, or translational and clinical-scope arguments. Redundant or peripheral records were not cited.	78 cited references; full text consulted for each
Citation reconciliation: map	Final references matched to the 180-record map by DOI first and normalized title second.	44 of 78
Citation reconciliation: pool	Final references present in the 466-record deduplicated pool but outside the top-180 rank cut-off.	3 of 78
Citation reconciliation: targeted updates	References introduced through subsequent targeted citation checking and scope updates and therefore absent from the original automated search library.	31 of 78
Bioprinting/biofabrication	Any match to bioprinting, biofabrication, bioink, 3D/three-dimensional printing or additive manufacturing.	+4
Vascular-surgery/DFU/CLTI	Any match to diabetic foot, chronic/critical limb ischemia, peripheral artery disease, limb salvage, vascular surgery, ischemic/neuroischemic wound or revascularization.	+4
Wound/repair	Any match to wound, ulcer, skin/tissue defect, repair, regeneration or healing.	+3
Vascularization/perfusion	Any match to vascularization/vascularisation, angiogenesis, endothelial, microvascular, perfusion, vascularized/vascularised or blood vessel.	+3
Neural/neurovascular	Any match to neural, nerve, neurovascular, Schwann, reinnervation, innervation or neural regeneration.	+3
Review article	Any match to review, systematic review, meta-analysis or perspective.	+1
Publication year	Recency signal used only for prioritization.	2021 onward: +2; 2018-2020: +1; earlier: 0
Citation count	Citation signal recorded at the time of search and used only for prioritization.	At least 200: +2; 50-199: +1; below 50: 0

Notes: Records could satisfy more than one scoring feature, and feature weights were additive. The score supported literature prioritization and was not intended as a risk-of-bias or methodological-quality assessment. The working evidence map and final bibliography served different purposes: the former organized a broad narrative evidence landscape, whereas the latter contains only sources cited to support statements in the manuscript.