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Three-dimensional biofabrication strategies toward vascularized organoid and organoid-inspired models

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Abstract

Organoids are three-dimensional multicellular models generated through the intrinsic self-organization of stem cells and have emerged as powerful platforms for disease modeling, drug screening, and precision medicine. However, most organoids cultured *in vitro* lack a functional vascular interface, which restricts oxygen and nutrient transport, leading to central hypoxia and necrosis and ultimately limiting long-term maintenance, maturation, and translational applicability. To address this bottleneck, a range of three-dimensional bioprinting and biofabrication strategies have been developed to support vascularized organoid and organoid-inspired models. Importantly, current technologies do not yet routinely permit the direct fabrication of physiologically complete 1–10 μm capillary beds within organoids. Instead, their major contributions lie in the generation of perfusable mesoscale conduits, endothelialized hollow channels, multicellular architectures, microfluidic perfusion platforms, and self-organizing microenvironments that, together, facilitate vascular integration and maturation. In this review, we summarize the major biofabrication approaches relevant to vascularized organoid models, emphasizing their roles in vascular manufacturing, technical strengths, and limitations. We further discuss material systems specifically relevant to organoid vascular fabrication, including sacrificial materials, endothelialization-supportive matrices, mechanically stable, perfusion-compatible supports, and organ-specific ECM-derived bioinks. In addition, we analyze key vascularization-enabling strategies, such as endothelialized template formation, multicellular bioprinting, dynamic perfusion, microfluidic integration, and self-organization-assisted maturation. By comparing organ-specific requirements across brain, tumor, cardiac, hepatic, renal, pulmonary, pancreatic, and intestinal models, we further highlight how vascular scale, endothelial phenotype,

structural hierarchy, and functional endpoints differ by application. Finally, we discuss the major unresolved challenges, particularly the gap between printable mesoscale channels and physiological capillary networks, the mismatch between generic endothelial sources and organ-specific vascular phenotypes, and the lack of standardized functional criteria for evaluating vascularization. Overall, future progress should depend less on direct capillary-scale printing alone and more on integrating biofabrication, perfusion engineering, and developmental self-organization to achieve reproducible, functionally meaningful vascularized organoid models.

Keywords: Vascularized organoid models; Organoid-inspired models; Three-dimensional bioprinting; Biofabrication; Endothelialization; Microfluidics; Extracellular matrix; Vascular maturation

1. Introduction

In recent years, organoid technology has attracted widespread attention as an innovative three-dimensional (3D) cell culture system across multiple fields. Organoids are stem cell-derived 3D microstructures that self-organize under defined *in vitro* conditions and can partially recapitulate the morphology, architecture, and functions of native organs; therefore, they are often referred to as "mini-organs."[1] Organoid generation relies on diverse stem cell sources, including embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs), and adult tissue-resident stem/progenitor cells. Owing to their pluripotency, ESCs and iPSCs can differentiate into multiple lineages under appropriate cues, enabling the formation of organoids with complex tissue features. Notably, iPSCs—obtained by reprogramming somatic cells from individual donors—support the establishment of patient-specific disease models, thereby providing a powerful platform for personalized therapy and precision medicine. Adult stem cells are widely used to generate tissue-specific organoids (e.g., intestinal and hepatic organoids) and often better preserve organotypic physiological functions of the corresponding tissues.[2,3] Key characteristics of organoids include self-organization into 3D architectures, tissue-specific functional outputs, and cellular compositional complexity.[4] Beyond reproducing basic physiological functions—such as xenobiotic metabolism in liver organoids and nutrient absorption in intestinal organoids—organoids can also capture multicellular interactions among epithelial, stromal, and endothelial compartments at the cellular level.[5] Since 2010, substantial advances have been achieved in organoid derivation for the intestine, liver, brain, and other organs, catalyzing rapid growth of the field. A series of landmark studies have been published in leading journals, such as *Nature*, *Science*, and *Cell*, reflecting the progressive maturation of organoid technologies. These developments have enabled broad applications of organoids in drug screening, disease modeling, developmental biology, and regenerative medicine. Looking forward, organoids hold great promise as platforms for constructing human-relevant surrogate tissues. In particular, integration into multi-organ "human-on-a-chip" systems may enable simulation of inter-organ crosstalk, providing enhanced physiological relevance for drug discovery, mechanistic studies of disease, and individualized treatment evaluation.[6] With continued methodological advances, organoid technologies are expected to further propel precision medicine by facilitating personalized therapeutic decision-making and expanding their impact in translational and clinical settings.

Although organoid technologies have made substantial progress, challenges remain in scalability and long-term stability, with vascularization a particularly critical bottleneck. First, vasculature supplies oxygen and nutrients and removes metabolic waste, which is essential for tissue viability. This requirement is especially pronounced in metabolically demanding organs such as the liver, kidney, and pancreas, where a vascular network supports complex, energy-intensive metabolic processes. Second, vascular endothelial cells actively shape the organoid microenvironment through paracrine signaling and direct cell–cell contact, thereby influencing cell development and lineage specification and coordinating the functions of distinct cellular compartments within organoids.[7] However, insufficient vascular support imposes constraints, particularly as organoids increase in size. Organoid growth often outpaces the diffusion capacity of oxygen and nutrients; when tissue thickness exceeds 300 μm, cells in the core region can no longer receive an adequate supply and become prone to hypoxia and necrosis.[8,9] In addition, size limitations hinder sustained *in vitro* maintenance of organoid growth and function, resulting in reduced cellular

performance or progressive functional decline. This not only compromises experimental reproducibility but also restricts the use of organoids for long-term observation and repeated assays. A lack of effective vascularization further limits the applications of organoids. For example, the absence of a perfusable vascular network precludes prolonged drug perfusion studies, thereby limiting drug screening and toxicity evaluation. Moreover, organoids without vascular components cannot adequately recapitulate hemodynamic cues and vascular functions, thereby constraining investigations of flow-related and vascular-associated diseases (e.g., stroke and nephritis).[10,11] Collectively, these limitations partially diminish the value of organoids for both mechanistic research and translational applications.

To address the challenge of organoid vascularization, 3D bioprinting has been proposed as an effective solution. Compared to conventional approaches to vascular reconstruction, 3D bioprinting offers several distinct advantages. First, it provides high spatial resolution, enabling precise control over vessel diameter, branching patterns, and anastomotic junctions, thereby facilitating the fabrication of intricate and hierarchical vascular networks.[12] Second, 3D bioprinting supports the rational design of vascular architectures with high structural diversity, allowing the creation of biomimetic vascular trees, perfusable networks, and multilayered constructs that better emulate the organization and function of native vasculature within organs.[13] This design flexibility makes bioprinting adaptable to the heterogeneous requirements of different organoid types. In addition, the broad material compatibility of 3D bioprinting represents a major advantage. Researchers can select from a range of biofabrication materials, including hydrogels, bioinks, and scaffold-based supports, which not only meet biocompatibility requirements but also provide instructive cues to support cell survival, proliferation, and differentiation.[14,15] Through appropriate material selection and formulation, bioprinting can provide both mechanical support and a bioactive microenvironment, thereby enhancing the physiological relevance of organoids. Most importantly, 3D bioprinting enables cell-laden co-printing, achieving the synchronized manufacture of "structure and function." By integrating vascular networks with organoid-forming cells in a single biofabrication process, bioprinting can generate perfusion-controllable microvascular systems and organ-scale perfusion/oxygen delivery, thereby improving organoid stability and functional maturation and supporting long-term *in vitro* maintenance.[16] This technological advance substantially increases the physiological fidelity and translational potential of organoid platforms.

Taken together, this review does not equate current 3D bioprinting with the routine direct fabrication of fully physiological capillary beds inside organoids. Rather, we focus on how bioprinting and related printing-enabled biofabrication approaches support the development of vascularized organoid and organoid-inspired models through several complementary routes, including the fabrication of perfusable mesoscale templates, endothelialized hollow channels, multicellular patterning, microfluidic perfusion, and self-organization-assisted vascular maturation. By adopting this framework, we aim to define the field's current technical boundaries more precisely, distinguish direct organoid vascularization from broader vascular biofabrication in organoid systems, and summarize the key challenges that must be overcome to achieve physiologically relevant, functionally validated vascularized organoid models.

2. Technical framework for the biofabrication of vascularized organoid and organoid-inspired models

2.1. Bioprinting techniques

Because the present review focuses on vascularized organoid and organoid-inspired models rather than general-purpose biofabrication, not all printing modalities are equally relevant. In this context, the most informative techniques are those that directly contribute to perfusable channel generation, endothelialized conduit formation, multicellular vascular assembly, soft-matrix fabrication, or perfusion-enabled maturation. Accordingly, this section focuses on six vascular-relevant approaches: microextrusion bioprinting, digital light processing (DLP)/stereolithography (SLA)-based fabrication, freeform reversible embedding of suspended hydrogels (FRESH)/embedded printing, coaxial bioprinting, sacrificial-lumen printing, and microfluidic-integrated perfusion biofabrication.

2.1.1. Microextrusion bioprinting

Microextrusion bioprinting is one of the most widely used approaches for vascularized organoid-related constructs because it can handle relatively high-viscosity bioinks and supports continuous deposition of cell-laden filaments and lumen-like architectures.[17] Its principal value in vascular fabrication lies in its compatibility with multicellular bioinks, modular nozzle systems, and hydrogel formulations suitable for generating mesoscale perfusable templates.[18] Although its spatial resolution is modest compared with light-based systems, microextrusion remains highly practical for constructing vascular conduits, parenchyma–vascular interfaces, and organoid-

supporting bulk architectures. Its main limitation is that the achievable feature size generally remains insufficient for direct fabrication of physiological capillary beds, and shear stress during extrusion may reduce cell viability when printing conditions are not carefully optimized.[19,20]

2.1.2. Digital light processing/stereolithography-based fabrication

Digital light processing and SLA are particularly relevant when vascular fabrication requires higher geometric precision. By polymerizing photocurable materials layer by layer, these techniques enable the fabrication of finely patterned microchannels and structurally well-defined vascular templates.[21] Compared to extrusion-based approaches, DLP/SLA can achieve higher spatial resolution and faster layer-wise fabrication, making them attractive for the generation of small-diameter conduits and intricate vascularized geometries.[22] However, their applicability is restricted by the need for photopolymerizable materials, and light-induced cytotoxicity or thermal stress can compromise the viability and function of encapsulated cells.[23] Therefore, in organoid vascular fabrication, DLP/SLA are most valuable for precise template formation rather than for routine direct generation of fully mature cellular microvasculature.

2.1.3. Freeform reversible embedding of suspended hydrogels and embedded printing

Freeform reversible embedding of suspended hydrogels and related embedded-printing approaches are especially useful for vascularized organoid models because they enable the fabrication of soft, extracellular matrix (ECM)-rich structures that would otherwise collapse under their own weight. By printing within a support bath, these methods facilitate the formation of suspended channels, overhanging structures, and compliant vascular templates in materials such as collagen- or gelatin-based hydrogels.[24,25] This is particularly advantageous for organoid-based applications, where preservation of a soft, biologically permissive microenvironment is essential. In addition, embedded printing can support the positioning of cells or organoid building blocks within soft matrices, thereby improving the integration between vascular templates and surrounding tissue-like compartments.[26] The main drawbacks are workflow complexity, dependence on bath/ink rheological optimization, and limited throughput compared with simpler extrusion-based workflows.[27]

2.1.4. Coaxial bioprinting

Coaxial bioprinting is one of the most directly relevant strategies for vascular fabrication because it enables one-step generation of hollow, lumenized conduits. Using concentric nozzles, this method can spatially organize a core phase and a surrounding shell phase to fabricate vessel-like structures with predefined lumen geometry.[28,29] When combined with endothelial cells and supporting mural or stromal components, coaxial bioprinting provides an efficient means to construct endothelializable conduits and multilayer vascular architectures.[30] Its greatest strength lies in its operational simplicity for tubular fabrication and its suitability for building mesoscale perfusable channels.[31] However, like other printing-based methods, it primarily generates vessel-like conduits at the mesoscale and, by itself, does not resolve the challenge of constructing dense physiological capillary networks within organoids.[32,33]

2.1.5. Sacrificial-lumen printing

Sacrificial-lumen printing is another core approach for organoid vascular fabrication because it enables the flexible generation of open-channel networks within hydrogel matrices. In this strategy, a sacrificial template is first printed and then embedded in a secondary matrix; subsequent removal of the sacrificial material leaves behind a perfusable lumen.[32,34] This approach is particularly advantageous when complex branching geometries or multi-channel layouts are required. In vascularized organoid-related constructs, sacrificial-lumen printing provides a practical route to create perfusion pathways that enhance mass transport and support subsequent endothelialization.[35] Its limitations include the need for mild and well-controlled template removal, the risk of damaging surrounding cell-laden matrices, and the substantial case-by-case optimization often required to balance printing fidelity, structural stability, and cytocompatibility.[32,34,36]

2.1.6. Microfluidic-integrated perfusion biofabrication

Although microfluidic integration is not purely a printing modality in the narrow sense, it is highly relevant to vascularized organoid engineering because it provides the dynamic perfusion environment required for vascular maturation and long-term function. By coupling printed or bioprinted constructs with microfluidic devices, this approach enables controlled flow, nutrient transport, shear stress, and chemical gradients, thereby improving tissue viability and endothelial maturation.[37,38] In practice, microfluidic integration is especially important for converting printed vascular templates into functionally perfused systems. For this reason, it should be considered a vascular-relevant biofabrication strategy rather than merely a downstream culture add-on. Its main challenges are integration complexity, limited standardization, and the difficulty of simultaneously achieving microscale precision, long-term stability, and operational reproducibility.[39,40]

Taken together, vascular fabrication in organoid-related

systems currently relies less on a single "best" printing modality than on the complementary use of several techniques. Extrusion-based and coaxial bioprinting are practical for multicellular and lumenized constructs; DLP/SLA improve geometric precision; FRESH/embedded methods support soft-matrix fabrication; sacrificial-lumen printing provides flexible perfusion pathways; and microfluidic integration promotes functional maturation under flow (Table 1).

2.2. Bioprinting materials

For vascularized organoid and organoid-inspired systems, the relevance of a material should not be judged solely by its general biocompatibility or printability. Instead, candidate materials should be evaluated according to the specific functions they serve during vascular fabrication, including the generation of perfusable luminal structures, support of endothelial adhesion and maturation, maintenance of structural stability under dynamic culture, and provision of tissue-relevant biochemical cues for coordinated vascular–parenchymal development.[16] Accordingly, this section focuses on material systems that are directly or near-directly relevant to organoid vascular fabrication, rather than offering a broad overview of general-purpose

Table 1. Vascular-relevant printing and bioprinting approaches for vascularized organoid and organoid-inspired models

Approach	Vascular-relevant role	Main strengths	Main limitations	Reference
Microextrusion bioprinting	Deposition of cell-laden bulk constructs and mesoscale perfusable templates	Broad material compatibility; suitable for multicellular constructs; practical for parenchyma–vascular integration	Limited resolution for capillary-scale features; extrusion-induced shear stress may impair cell viability	17-20
DLP/SLA-based fabrication	High-fidelity fabrication of microchannels and vascular templates	High geometric precision; rapid layer-wise fabrication; suitable for patterned microchannel architectures	Restricted to photocurable formulations; potential phototoxicity; insufficient for routine direct fabrication of physiological capillary beds	21-23
FRESH/embedded printing	Fabrication of soft ECM-rich vascular templates and suspended hollow architectures	Compatible with soft biomaterials; preserves compliant microenvironments; useful for complex overhanging and lumenized structures	Workflow complexity; bath/ink optimization required; limited throughput	24-27
Coaxial bioprinting	One-step generation of hollow, endothelializable conduits	Efficient tubular fabrication; suitable for multilayer vessel-like architectures; supports lumen formation during printing	Mainly produces mesoscale conduits; limited ability to recreate dense capillary-scale vascular beds	28-33
Sacrificial-lumen printing	Fabrication of perfusable channel networks within hydrogels	Flexible control of lumen geometry and branching; effective for creating open perfusion pathways	Sacrificial removal must be mild and well controlled; structural collapse or matrix damage may occur during processing	32,34-36
Microfluidic-integrated perfusion biofabrication	Functional perfusion, endothelial maturation, and long-term dynamic culture of printed constructs	Reproduces shear stress and transport gradients; improves viability and vascular maturation; supports functional testing	High integration complexity; limited standardization; difficult to balance precision, stability, and scalability	37-40

Abbreviations: DLP: Digital light processing; ECM: Extracellular matrix; FRESH: Freeform reversible embedding of suspended hydrogels; SLA: Stereolithography.

bioinks. These material categories and their major roles in organoid vascular fabrication are summarized in Figure 1.

2.2.1. Sacrificial and template-forming materials for perfusable channel fabrication

A major material requirement in organoid vascular fabrication is the creation of open, perfusable channels that can subsequently be endothelialized or interfaced with self-organized microvascular networks. In this context, sacrificial materials are particularly valuable because they enable predefined hollow architectures to be generated while minimizing damage to surrounding cell-laden matrices during template removal.[41] Among them, Pluronic F127 remains one of the most widely used sacrificial inks due to its reversible sol–gel transition behavior. This thermoreversible property allows it to be deposited to define luminal geometry and then removed under relatively mild conditions after the surrounding matrix has stabilized, making it especially useful in perfusable biofabricated systems.[42] In kidney-related perfusion models, fugitive-ink strategies based on Pluronic-type templating have enabled the fabrication of embedded tubular architectures that better support flow and epithelial organization.[43]

However, sacrificial templating materials should not be evaluated in isolation. Their practical value depends not only on printability, but also on compatibility with the surrounding matrix, the mildness of template-removal conditions, and the extent to which lumen diameter, branching geometry, and interfacial integrity can be preserved after extraction. In organoid vascular fabrication, sacrificial materials are therefore best understood as enabling materials for the generation of perfusable architecture, rather than as matrices that directly promote vascular maturation.[36] Their contribution lies primarily in creating a structural framework that can later support endothelialization, perfusion, and integration with organoid tissue.[41]

2.2.2. Endothelialization-supportive matrices

Once a hollow or perfusable template has been established, the next material requirement is a matrix that supports endothelial cell attachment, spreading, migration, and barrier formation while remaining compatible with organoid growth. In current organoid vascularization studies, the most directly relevant matrices remain natural ECM-rich hydrogels, particularly Matrigel, fibrin, and collagen, as well as their combinations. For example, vascularized brain organoids have been generated by re-embedding organoids in Matrigel together with endothelial cells, while intestinal organoid vascularization has been optimized using fibrin–Matrigel co-gels, with further control of vascular organization achieved through matrix tuning and collagen-based structural guidance.[44,45] These findings indicate that endothelialization-supportive matrices should be selected not merely for cytocompatibility, but for their capacity to balance organoid morphogenesis with vascular network formation.

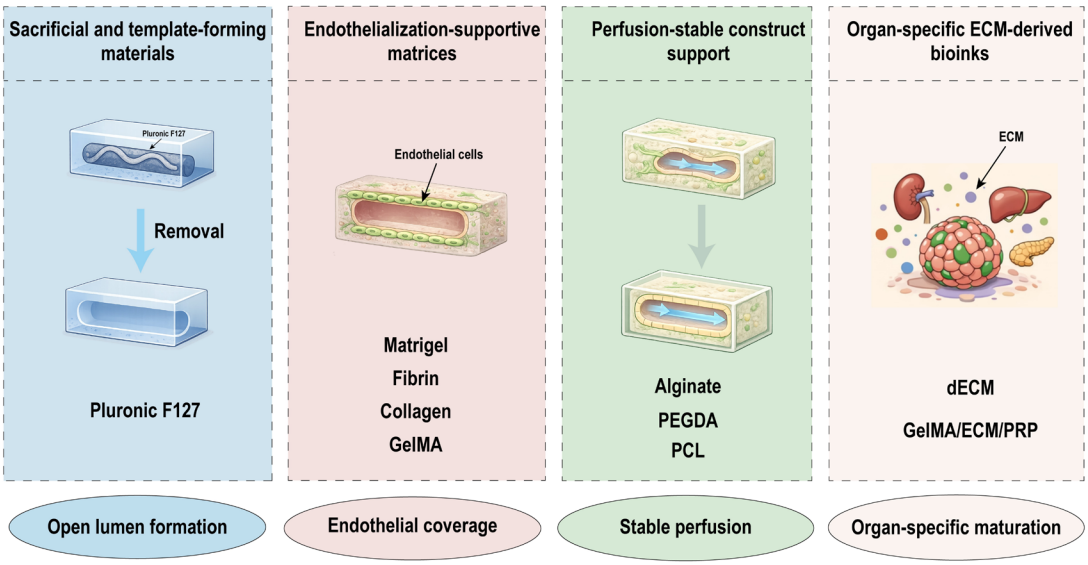

Figure 1. Functional material framework for organoid vascular fabrication
Abbreviations: ECM: Extracellular matrix; GelMA: Gelatin methacryloyl; PCL: Poly(ε-caprolactone); PEGDA: Poly(ethylene glycol) diacrylate; PRP: Platelet-rich plasma.

Nevertheless, each natural matrix presents trade-offs. Matrigel strongly supports organoid self-organization and early morphogenesis, but its batch-to-batch variability and poor standardization limit reproducibility.[46] Fibrin is highly favorable for endothelial migration and angiogenic remodeling, yet its rapid degradation can compromise long-term stability if used alone.[44] Collagen provides a more defined ECM-like environment and can offer structural guidance, but its mechanical properties may require optimization for sustained perfusion.[47] Accordingly, in organoid vascular fabrication, natural hydrogels are most effective when used in carefully tuned formulations that reconcile biological permissiveness with sufficient structural control.

Among modified hydrogels, gelatin methacryloyl (GelMA) is particularly valuable because it combines gelatin-derived cell-interactive motifs with photocrosslinkability, thereby allowing improved control over stiffness, geometry, and fabrication fidelity while retaining favorable endothelial compatibility.[48,49] Recent work has shown that mechanically tunable GelMA hydrogels can serve as stable, reproducible 3D supports for the growth and maturation of human iPSC-derived kidney organoids.[50]

2.2.3. Materials for perfusion stability and multicompartment vascular constructs

In vascularized organoid systems, a biologically favorable matrix alone is often insufficient to maintain long-term function under flow. Materials must also preserve channel geometry, resist collapse or interfacial delamination, and maintain overall construct integrity during extended dynamic culture.[51] For this reason, composite systems that combine soft bioactive matrices with mechanically supportive components are often more suitable than single-component hydrogels.[52] In this setting, materials such as alginate, poly(ethylene glycol) diacrylate (PEGDA), and poly(ε-caprolactone) (PCL) can be useful, but their roles should be carefully framed. Rather than being considered core organoid-vascularization matrices, they are more appropriately described as auxiliary structural materials that improve print fidelity, compartmentalization, dimensional stability, or macroscopic mechanical support.[53]

For example, alginate can improve shape fidelity and extrusion stability when combined with more bioactive hydrogels, whereas PEGDA can provide photocrosslinkable structural reinforcement and higher-resolution patterning.[54,55] Likewise, hybrid systems incorporating PCL may enhance macroscopic mechanical robustness in constructs that must resist deformation under perfusion.[56] However, these materials are generally less permissive to endothelial and organoid maturation unless they are biochemically modified or integrated with more cell-supportive matrices.[44] Therefore, in the context of organoid vascular fabrication, the importance of these materials lies primarily in engineering support, not in replacing the biological functions of permissive matrices such as fibrin, Matrigel, GelMA, or organ-specific ECM-derived hydrogels.

2.2.4. Organ-specific extracellular matrix-derived bioinks for vascularized organoid models

A further level of material refinement is required when vascularization must be coordinated with organ-specific maturation. In such settings, ECM-derived bioinks, especially tissue-specific decellularized ECM (dECM), are particularly attractive because they can provide biochemical signals that better resemble the native organ microenvironment than generic hydrogels.[57] The strongest direct evidence comes from kidney organoids, where kidney dECM hydrogels have been shown to enhance both vascularization and maturation, supporting the idea that organ-specific ECM cues can improve not only endothelial behavior but also vascular–parenchymal coordination within developing organoid systems.[58]

More broadly, the value of dECM-based materials in organoid vascular fabrication lies less in their use as universal stand-alone matrices and more in their ability to provide organ-instructive biochemical information when incorporated into composite, processable, and perfusion-compatible systems.[59] This principle is also reflected in organoid-specific composite bioinks, such as GelMA/ECM/platelet-rich plasma formulations developed for islet organoids, which have shown pro-angiogenic potential while improving handling and fabrication performance.[60] Despite these advantages, dECM materials still face limitations, including labor-intensive preparation, compositional variability, and incomplete standardization.[61] Thus, their most realistic application in current organoid vascular fabrication is as a biologically instructive component within hybrid material systems rather than as a universally optimal matrix.

2.3. Bioprinting strategies

Bioprinting strategies for organoid vascularization can be better understood when organized according to the sequential requirements for vascularized tissue construction. In general, these approaches progress from (i) the fabrication of perfusable vascular templates, to (ii) the spatial organization of multiple cell types and tissue compartments, and finally to (iii) post-printing maturation and higher-order optimization of vascular function. Based on this logic, current strategies can be broadly categorized

into endothelialized hollow-channel fabrication, multicellular co-printing, spatial compartmentalization, dynamic perfusion-assisted maturation, self-organization–assisted bioprinting, and biomimetic topological design, as summarized in Table 2.

2.3.1. Endothelialized hollow channels

Among current approaches, endothelialized hollow channels are among the most direct strategies for establishing perfusable vascular templates. This method typically begins with the fabrication of lumenized conduits by sacrificial printing or coaxial extrusion, followed by endothelial cell lining of the inner surface to generate vessel-like structures. A recently developed multi-axial co-extrusion microfluidic printhead enabled the rapid fabrication of bilayered and trilayered hollow channels within hydrogels and ECM-based matrices, while also supporting multimaterial integration and spatial loading of endothelial cells and fibroblasts in distinct layers.[62] By optimizing the fabrication parameters, channels with diameters ranging from 0.69 to 2.31 mm could be generated within seconds, demonstrating both scalability and flexibility for heterogeneous tissue construction. Similarly, Maggiotto *et al.*[63] used a CELLINK BioX™ platform to fabricate hollow channels by combining GelMA with a sacrificial material such as Pluronic; after ultraviolet crosslinking and removal of the sacrificial phase, the constructs were maintained under perfusion culture, leading to endothelial monolayer formation within 1–14 days and a marked reduction in vascular permeability. Together, these studies indicate that endothelialized hollow-channel engineering provides a robust structural basis for subsequent vascular maturation by coupling perfusable architecture with endothelial functionalization.

2.3.2. Multicellular bioprinting

Once a perfusable framework has been established, the next requirement is to reproduce the multicellular composition of native vascularized tissues. Multicellular bioprinting addresses this need by simultaneously depositing multiple cell populations together with bioinks in a single fabrication process, thereby enabling coordinated assembly of parenchymal and vascular components. Using multi-nozzle systems, coaxial bioprinting platforms, and related modalities, this strategy can spatially organize endothelial cells, mural cells, stromal cells, and tissue-specific functional cells within predefined regions of the same construct.

For example, a four-layer coaxial nozzle was used to directly bioprint a co-culture model composed of a double-layer alginate hydrogel with dual hollow channels, into which human umbilical vein endothelial cells (HUVECs) and human umbilical vein smooth muscle cells were separately introduced. The resulting construct exhibited intact architecture and superior mechanical performance compared with single-layer hydrogels, supporting vascular-relevant multicellular co-culture.[64] In another study, Zhu *et al.*[65] combined GelMA with a microfluidic bioprinting system to spatially position human periodontal ligament fibroblasts together with hydroxyapatite, generating microscale structures that mimicked the periodontal bone repair interface; under dynamic perfusion, the constructs maintained high cell viability for more than seven days while preserving structural integrity and cellular organization. Therefore, multicellular bioprinting is important not only because it increases cellular complexity, but also because it better reconstructs the coordinated cell–cell and cell–matrix interactions required for organoid vascularization.

2.3.3. Dynamic perfusion and microfluidic integration for vascular maturation

After structural fabrication and spatial cellular organization, vascularized constructs must undergo functional maturation. At this stage, dynamic perfusion and microfluidic integration become essential because they provide physiologically relevant flow, nutrient transport, oxygen delivery, and shear stress. Microfluidic platforms are particularly valuable in this regard, as they enable precise control over flow rate, oxygen tension, chemical gradients, and multicellular interactions.[39,66]

Compared to static culture, such dynamic systems markedly improve organoid viability, reduce diffusion-limited necrosis, and promote vascular maturation. For instance, a microfluidic platform integrating cardiac and renal organoids supported long-term, stable co-culture of both tissues, with cardiac organoids maintaining contractility and renal organoids preserving proximal tubule marker expression together with measurable filtration-related function.[67] Quintard *et al.*[39] further developed a vascularized organoid-on-a-chip platform in which endothelial cells were pre-embedded within the scaffold and guided to form an endothelial network inside microfluidic channels; fluid shear stimulation significantly enhanced vascular-like maturation and prolonged organoid survival. Consistent with these observations, synthetic soft microfluidic architectures have also been used to establish dense capillary-like networks in millimeter-scale tissues, thereby alleviating core hypoxia and necrosis and improving tissue viability and morphological maturation.[68] More broadly, recent analyses have underscored that post-fabrication perfusion is not merely an auxiliary culture condition, but a central determinant of whether a printed or bioprinted vascular structure can transition into a functional vascular system.[69]

In this regard, predefined coaxial bioprinting combined with spontaneous endothelial sprouting represents an important hybrid strategy, because it bridges mesoscale conduits and microscale capillary formation within the same construct.[30] Overall, dynamic perfusion should be regarded as a key functional maturation step in vascularized organoid engineering.

2.3.4. Spatial compartmentalization

In addition to multicellular complexity, vascularized organoids require spatially defined tissue organization. Spatial compartmentalization addresses this challenge by dividing a construct into discrete functional regions, such as parenchymal, perfusion, and support layers, each of which can be fabricated using tailored bioinks and specific cell populations.[70,71] This strategy is particularly valuable for tissues whose function depends on regional specialization, including nephron-like architectures and multilayered vascular assemblies.

Recent studies have emphasized that compartmentalized biofabrication can be strengthened by integrating bioprinting with modular support baths and functionalized bioinks, thereby enabling more precise control over matrix mechanics, biochemical cues, multicellular coordination, and vascular network formation.[72] For example, the SPOT platform developed by Roth *et al.*[73] enabled accurate spatiotemporal positioning of multiple organoid building blocks, while cellulose nanofibers served as both an encapsulating material and a shear-thinning, self-healing support hydrogel to preserve the desired spatial arrangement. Likewise, magnetic-field-assisted printing using magnetic nanoparticle–chitosan hydrogels as transport beds enabled the controlled assembly of neural and tumor organoids into higher-order assembloids. These findings suggest that spatial compartmentalization serves as a critical intermediate strategy that links construct-level organization with functional tissue integration.

2.3.5. Self-organization-assisted Biofabrication

Although bioprinting can define the macroscopic geometry and initial cellular arrangement of a construct, it cannot by itself fully reproduce the emergent hierarchies observed during tissue development. Self-organization-assisted biofabrication has therefore emerged as an important complementary strategy. In this approach, stem/progenitor-derived organ building blocks (OBBs) are first positioned via bioprinting or guided assembly, after which intrinsic developmental programs drive their fusion, differentiation, and vascular network formation.[74]

Compared to conventional single-cell bioprinting, OBB-based approaches offer several advantages, including a preorganized architecture, preservation of biological functionality, and increased post-fabrication self-integration capacity.[75] Because these building blocks already contain cellular heterogeneity and early lineage specification cues, they are better able to generate lumenized structures, branched networks, and higher-order tissue organization after placement. Indeed, some studies have used stem cell-derived organoids as biofabrication units and, together with photocrosslinkable matrices such as Matrigel, achieved centimeter-scale tissue construction in which bioprinting established the initial geometry while subsequent self-organization generated microscale features such as lumens and branched networks.[76] This "bioprinting + self-organization" paradigm is particularly attractive because it combines the spatial precision of engineered cell placement with the developmental plasticity of organoids, thereby offering a more effective route toward tissues that more closely approximate *in vivo* architecture and function.

2.3.6. Biomimetic topological design

The final layer of optimization involves biomimetic topological design, aiming to enhance the anatomical realism and functional feasibility of vascularized constructs. Rather than focusing directly on cellular deposition, this strategy uses biomimetic principles and computational algorithms to reconstruct tissue-specific architectures, including hepatic lobular organization, alveolar geometry, and vascular branching patterns. By integrating medical imaging data, such as computed tomography or magnetic resonance imaging, with adaptive mesh generation and path-planning algorithms, researchers can generate tissue-featured anisotropic models and convert them into executable printing trajectories.[77,78] These algorithm-guided design methods improve fabrication efficiency, reduce layer-induced deformation, and enable more faithful reproduction of native tissue microarchitecture. For example, calcium phosphate-based materials have been combined with such computational design tools to fabricate customized bone-like architectures that recapitulate key structural and chemical features of native bone.[78] Similarly, algorithmic platforms for synthetic vascular-tree design have enabled the generation of printable vascular networks within complex tissue geometries, with perfusion performance further validated through hemodynamic simulations.[79] Thus, biomimetic topological design should be viewed primarily as an advanced structural design and path-planning strategy that supports subsequent printing or bioprinting, rather than as bioprinting per se.

3. Organ-specific vascular requirements and representative biofabricated vascularized organoid models

The relevance of vascular biofabrication differs substantially

across organoid applications. Therefore, this section is organized not simply as an organ-by-organ list of studies, but around the organ-specific vascular requirements that determine whether a given strategy is biologically meaningful. These requirements include the target vessel scale, the degree of structural hierarchy required, the endothelial phenotype needed for organ fidelity, and the physiological functions that define successful vascularization. The organ-specific vascular requirements discussed in this section, together with representative vascularized organoid and organoid-inspired models, are illustrated in Figure 2.

3.1. Brain organoids: Barrier-forming microvasculature and neurovascular support

For brain organoids, the vascular requirement is defined not simply by the presence of perfusable channels, but by the need to approximate a barrier-forming microvascular

Table 2. Key vascularization-enabling strategies for vascularized organoid and organoid-inspired models

Strategy	Primary role in organoid vascularization	Main advantage	Main bottleneck	Reference
Perfusable template formation (e.g., endothelialized hollow channels, coaxial or sacrificial-lumen approaches)	Establishes open conduits for transport and subsequent endothelial lining	Provides immediate perfusion pathways and controllable lumen geometry	Typically limited to mesoscale channels rather than physiological capillary beds	35,62,63,80,81
Multicellular bioprinting	Brings endothelial, mural, stromal, and organ-specific parenchymal cells into coordinated spatial organization	Improves cell–cell and cell–matrix interactions relevant to vascular maturation	Printing complexity increases substantially with cell-type number, ratio, and matrix heterogeneity	65,82-84
Dynamic perfusion and microfluidic maturation	Supplies shear stress, nutrient exchange, and controlled flow for endothelial stabilization and functional maintenance	Enhances vascular maturation, viability, and long-term culture performance	Integration complexity, limited standardization, and difficulty maintaining long-term perfusion stability	33,67,85,86
Spatial compartmentalization	Organizes constructs into functionally distinct vascular, parenchymal, and support regions	Improves regional fidelity and permits controlled tissue–vascular interfaces	Interfacial integration and hierarchical multiscale coordination remain difficult	71,87,88
Self-organization-assisted vascularization	Uses developmental self-assembly to generate microvascular-like features beyond direct printing resolution	Offers a realistic route toward capillary-like complexity and tissue-adaptive maturation	High variability, slower maturation, and limited reproducibility	74,76,89,90
Biomimetic topological design	Improves vascular-tree layout, branching logic, and anatomical plausibility before fabrication	Enhances structural realism and supports organ-specific design requirements	Design sophistication does not by itself solve the biological challenge of stable endothelialized microvasculature	33,77,78,91,92

environment. In terms of vessel size, the relevant target is not a large conduit system, but a microvascular-scale interface compatible with oxygen diffusion and blood–brain barrier (BBB)-related function.[85,93] Structurally, the key consideration is not channel formation alone, but the reconstruction of a neurovascular unit-like hierarchy involving endothelial cells together with neural and supporting cell compartments.[94] At the phenotypic level, endothelial cells must move beyond generic vascular identity toward BBB-relevant characteristics.[95] Functionally, successful vascularization should therefore be judged by improved internal transport, barrier-related

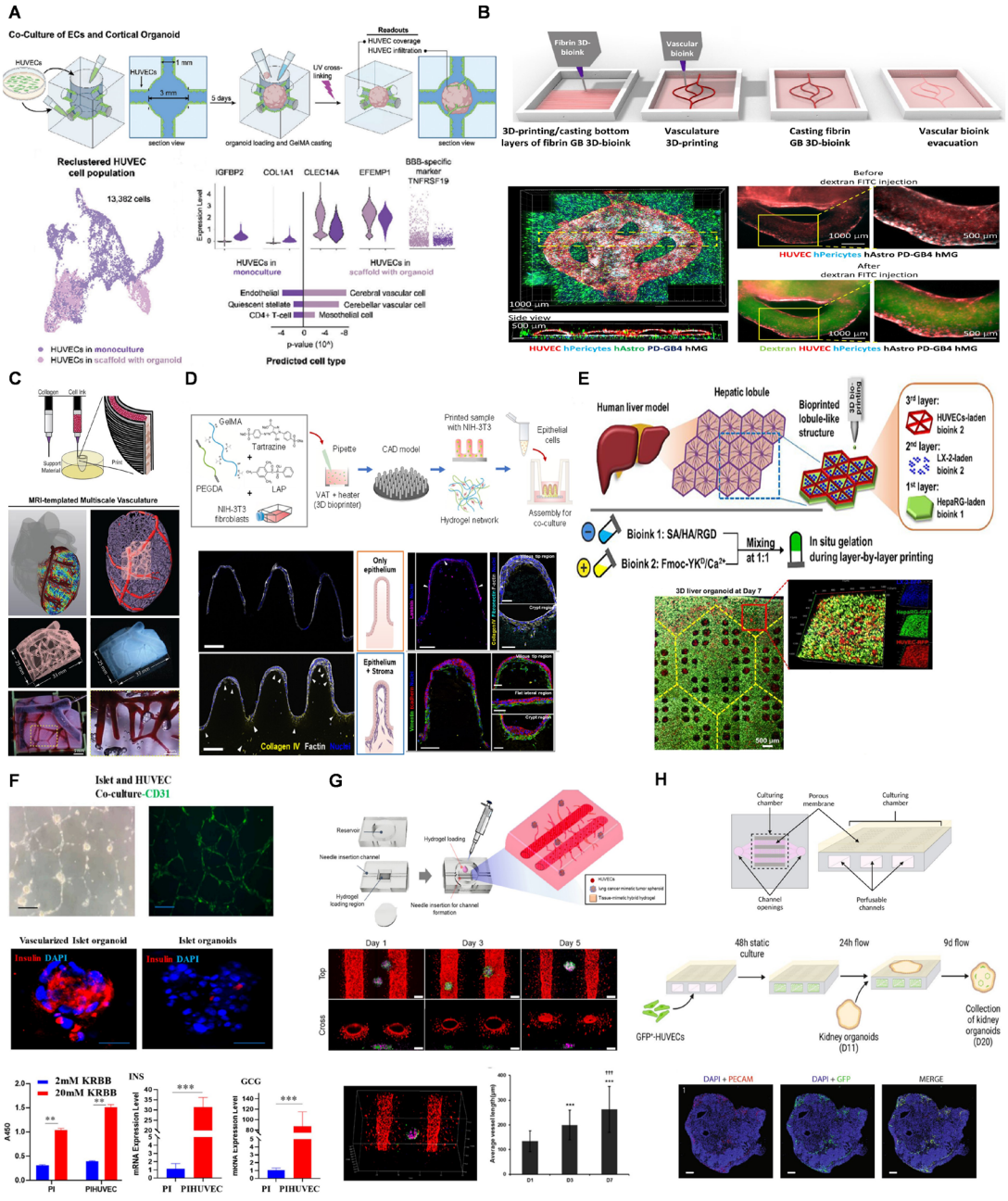

Figure 2. Organ-specific vascular requirements and representative examples of vascularized organoid and organoid-inspired models. (A) Three-dimensional-bioprinted cortical organoid platform based on a microchanneled gelatin methacryloyl scaffold for improved intratissue transport and early neurovascular organization.[84] (B) Glioblastoma-on-a-chip model with a perfusable vascular network for reconstruction of the tumor-associated microenvironment. Reprinted with permission from Ref.[124] Copyright © 2021 The American Association for the Advancement of Science. (C) Freeform reversible embedding of suspended hydrogels-printed organ-scale cardiac construct with multiscale perfusion pathways in thick myocardial tissue. Reprinted with permission from Ref.[25] Copyright © 2019 The American Association for the Advancement of Science. (D) 3D-bioprinted intestinal mucosa-like model with crypt–villus architecture, epithelial–stromal organization, and basement membrane-related extracellular matrix remodeling.[21] (E) Multicellular bioprinted liver organoid model with biomimetic lobular architecture for enhanced parenchymal–vascular coupling.[105] (F) *In vitro* vascularized pancreatic islet organoid model showing endothelial network formation around islet organoids under co-culture conditions.[125] (G) A representative biofabricated vascularized pulmonary tumor model. The platform integrates multicellular lung cancer spheroids with endothelialized perfusion channels within a lung decellularized extracellular matrix-based hydrogel microenvironment.[126] (H) Kidney organoid–vasculature interaction model on an organ-on-chip platform for endothelial integration and vascular association with renal organoids.[127]

properties, and neurovascular support rather than by morphology alone.[85,96]

A representative step in this direction was reported by Cadena *et al.*,[84] who developed an embedded 3D-bioprinted cortical organoid platform using GelMA to fabricate microchannel-containing scaffolds that guided human iPSCs toward brain-like structures while incorporating endothelial cells to model vascularization. This strategy improved architectural controllability and structural reproducibility, indicating that bioprinting can provide a useful framework for introducing vascular guidance into otherwise self-organized neural systems. However, the vascular features remained non-perfusable, and the system did not yet reproduce a mature neurovascular unit. Thus, its significance lies in improving spatial organization and diffusion support rather than in establishing a fully functional brain microvasculature.

Xu *et al.*[97] approached the problem from another angle by using two-photon polymerization to fabricate an artificial reticular scaffold that supported the expansion and long-term growth of brain organoids. The microporous architecture improved internal mass transport, reduced central hypoxia, and facilitated communication among region-specific organoid components. This work is relevant because it shows that, in brain organoids, one practical role of high-resolution printing is to relieve transport limitations and create a more permissive environment for later neurovascular maturation. Even so, the printed structures were still not perfusable and did not reproduce a true BBB-like endothelial interface.

Taken together, current biofabrication efforts in brain organoids have primarily improved internal transport and preliminary neurovascular organization, but have not yet achieved integrated, perfusable, and barrier-forming microvasculature. Future studies should therefore move beyond vascular-like geometry alone and focus on endothelial specialization, the incorporation of astrocytic and pericytic support, and functional validation using BBB-relevant endpoints, such as permeability control and barrier stability.

3.2. Tumor organoids: Perfusable but pathologically permeable vasculature

For tumor organoids, the vascular requirements differ from those of healthy organ models, as the goal is not to reproduce a stable barrier-forming vasculature but to capture a pathologically relevant tumor vascular microenvironment. With respect to vessel size, the key need is a vascular scale that generates local perfusion and transport gradients rather than a fully physiological capillary bed.[11,74] In terms of structural hierarchy, tumor vasculature is typically irregular, heterogeneous, and incompletely organized, and this abnormality itself is biologically meaningful.[98] At the phenotypic level, endothelial cells are expected to display a more permeable, tumor-associated behavior than those in tightly regulated healthy tissues.[99] Functionally, the main criteria are therefore drug penetration, hypoxia patterning, nutrient heterogeneity, and stromal or immune interaction, rather than structural channel formation alone.[33]

Shi *et al.*[100] provided an early example by using an embedded printing strategy to co-fabricate breast cancer cells and cancer-associated fibroblasts within a collagen-based bioink and silk fibroin support bath. The addition of endothelial cells promoted microvessel formation and improved the physiological relevance of the reconstructed tumor microenvironment (TME). The importance of this study lies in demonstrating that vascularization in tumor organoids can be advanced through multicellular spatial organization rather than solely through vascular geometry. At the same time, the model still lacked truly perfusable vasculature, and printing-associated cell viability loss limited the extent to which dynamic tumor behavior could be recapitulated.

A more directly relevant example was reported by Choi *et al.*,[101] who developed a 3D-printed vascularized lung cancer organoid platform integrating patient-derived lung cancer organoids, fibroblasts, and vascular channels using decellularized porcine lung ECM as the bioink. Compared to conventional Matrigel-based culture, this system provided improved physiological relevance, better representation of fibrosis-associated microenvironmental effects, and stronger performance in drug-response evaluation. Their study is particularly important because it links vascularization to clinically meaningful tumor behavior, rather than treating vascularization as an isolated structural feature. Nevertheless, the platform still did not fully reproduce long-term vascular stability or the full complexity of immune-cell participation under flow.

Overall, the most meaningful direction for tumor organoid vascularization is not simply the addition of endothelial cells or the creation of printed channels, but the reconstruction of a functionally relevant vascularized TME. In this setting, the critical requirements are partially perfusable yet pathologically leaky vasculature, controllable nutrient and drug gradients, and coordinated stromal integration. Future work should therefore focus on linking vascular architecture with functional endpoints such as drug penetration, endothelial permeability, hypoxia distribution, and immune-cell trafficking, so that vascularization becomes a determinant of tumor model fidelity rather than a secondary design feature.

3.3. Liver organoids: Sinusoid-like exchange networks and metabolic support

For liver organoids, vascularization is required not only to supply oxygen but also to reproduce a highly specialized exchange interface. In contrast to organs in which barrier integrity is the dominant vascular endpoint, the liver depends on a sinusoid-like microenvironment that supports efficient mass transfer, close parenchyma–endothelium interaction, and sustained metabolic activity.[102,103] Accordingly, the most relevant vascular features in liver organoid models are not simply hollow channels or bulk perfusion routes, but spatially organized exchange networks that can support hepatocyte function, multicellular crosstalk, and long-term metabolic stability.[104]

A representative study in this direction was reported by Jian and colleagues, who used a multicellular bioprinting strategy to fabricate liver-like organoids with biomimetic lobular organization.[105] By spatially arranging hepatocytes, liver sinusoidal endothelial cells, and hepatic stellate cells, they reconstructed aspects of the radial architecture extending from the central vein to the portal region. This design improved albumin secretion and urea synthesis, suggesting that a vascularly informed spatial organization can enhance metabolic performance beyond that achieved in less structured liver organoid systems. The importance of this study lies less in the direct recreation of physiological sinusoidal capillaries than in demonstrating that vascularized liver organoids require coordinated spatial coupling between parenchymal and vascular compartments.

Lekkala *et al.*[106] further addressed the transport problem by developing a vascularized liver organoid platform incorporating predefined micropillar-based microstructures. This strategy improved oxygen transport and promoted vascular network formation, thereby extending organoid survival and enhancing drug-metabolism-related performance. Compared to simple static culture, this work better captured the functional significance of vascular support in liver models. Nevertheless, the resulting system still fell short of reproducing the full structural and functional complexity of the hepatic sinusoidal network, particularly with regard to long-term perfusion stability and the fine-scale exchange interface characteristic of native liver tissue.

From the perspective of reproducibility and screening utility, Shrestha *et al.*[107] established a controllable human liver organoid platform using microarray-based bioprinting. The value of this approach lies in improved standardization and organoid-to-organoid consistency, which are important for drug testing and disease modeling. At the same time, its limited construct size and architectural complexity mean it does not yet resolve the broader challenge of recreating hierarchical sinusoidal organization together with durable vascular perfusion.

Taken as a whole, current biofabrication studies on liver organoids have made the greatest progress in three areas: spatially organizing hepatic parenchymal and vascular components, improving internal transport, and extending metabolic function *in vitro*. However, the central unresolved issue remains the reconstruction of a sinusoid-like exchange system rather than simply adding channels. Future work should therefore focus on organ-specific endothelial phenotypes, tighter coupling between vascular and biliary architectures, and functional validation using exchange-relevant endpoints, such as metabolic output, drug processing, and sustained mass transport under perfusion.

3.4. Kidney organoids: Filtration-oriented vascular interfaces

Kidney organoids pose a different vascular challenge than liver or tumor systems, as vascularization must support not only nutrient delivery but also filtration-related architecture and segmental functional coupling. In this context, the biologically meaningful target is not a generic vascular network, but a renal vascular interface capable of supporting glomerular filtration, tubular exchange, and sustained fluid transport.[108,109] As a result, the relevant design requirements include an appropriate microvascular scale at the filtration interface, structural coordination between glomerular and tubular compartments, and endothelial functionality compatible with renal transport physiology.

A representative organoid-relevant example was provided by Valverde *et al.*,[108] who used a multicellular bioprinting strategy to generate kidney organoids containing glomerulus-like structures. By patterning tubular epithelial cells, endothelial cells, and fibroblasts, they reproduced aspects of nephron-related organization and achieved a level of functional relevance for drug screening. This study is important because it shows that vascularization in kidney organoids cannot be considered separately from nephron architecture: the value of vascular integration lies in its ability to support glomerular–tubular functional coupling. However, as in many current systems, limited vascular maturity and insufficient long-term perfusion remained major constraints.

Singh *et al.*[110] further improved physiological relevance by using 3D cell-printing to generate microfluidic hollow renal tubular/vascular constructs, thereby introducing luminal flow and more realistic transport-related functions into engineered renal systems. This advance is particularly

important for kidney applications, where fluid handling and solute exchange are central to tissue function. Even so, incomplete intercellular crosstalk and limited perfusion capacity indicate that current printed renal platforms still reproduce only part of the vascular contribution required for sustained renal physiology.

A particularly relevant advance was reported by Feng *et al.*, who developed a pump-free printed perfusion platform for tubular tissues.[111] By engineering a microchannel architecture that supports long-term flow, this system improved perfusion stability and created a more kidney-relevant culture environment. In parallel, Homan *et al.*[112] showed that sustained fluid stimulation in a microfluidic culture system promoted vascular network formation and enhanced metabolic capacity in kidney organoids. Together, these studies suggest that functional perfusion in kidney organoids may be at least as important as static structural vascularization. In other words, a renal vascular model is meaningful only if it supports transport, exchange, and filtration-related maturation under dynamic conditions.

Collectively, the kidney field has made progress in integrating vascular thinking into nephron-oriented organoid design, but current models still fall short of reproducing a stable and physiologically credible filtration interface. The major challenge is not simply adding endothelial cells or channels, but establishing vascular structures that are functionally coupled to glomerular and tubular compartments. Future work should therefore prioritize endothelial specialization at the renal interface, more robust perfusion-linked maturation, and functional assessment based on transport, filtration, and segment-specific renal readouts rather than on structural vascular markers alone.

3.5. Pancreatic organoids: Vascular support for endocrine survival and function

In pancreatic organoids, the value of vascularization lies less in reproducing a complex hierarchical vascular tree and more in sustaining endocrine viability, oxygen supply, and stimulus-responsive secretion. This is especially important for islet-like systems, in which insufficient transport rapidly leads to functional decline.[113,114] For this reason, the most relevant vascular targets in pancreatic organoid models are local microvascular support, effective mass exchange, and a microenvironment that preserves glucose responsiveness and insulin release, rather than large perfusable conduits alone.

A representative example was provided by Wang *et al.*,[115] who engineered islet organoids using a composite hyaluronic acid methacrylate (HAMA)/processed ECM hydrogel. In this system, the HAMA component contributed to printing fidelity, whereas the pancreatic ECM component supplied tissue-relevant biological cues. The resulting constructs maintained islet cell function and, after implantation into diabetic mice, supported improved glycemic control. Importantly, compared with HAMA alone, the composite formulation also promoted more robust angiogenesis, indicating that material choice can affect not only construct formation but also the vascular support required for endocrine function. This study is particularly relevant because it links vascularization to a meaningful pancreatic endpoint rather than treating vascularization as a structural feature in isolation.

A related advance was reported in a system combining GelMA, pancreas-derived ECM, and platelet-rich plasma to construct islet organoids with improved pro-angiogenic and immunoregulatory properties.[60] This approach enhanced capillary-like behavior in endothelial cells, increased expression of vascular markers, and supported stable function of pancreatic β cells. The importance of this work lies in showing that pancreatic vascular support is not purely a matter of flow or geometry. Instead, it depends on a microenvironment that coordinates angiogenic signaling, immune modulation, and endocrine-cell maintenance.

Soltanian *et al.*[116] further moved the field toward a transplantation-oriented setting by developing a 3D-printed "tissue trapper" for pancreatic progenitors. The printed macroporous pouch permitted nutrient diffusion while limiting immune-cell infiltration, and implanted cells matured *in vivo* into endocrine clusters that improved glycemic control. Although this platform is not a direct model of fully vascularized pancreatic organoids *in vitro*, it remains relevant because it highlights a central issue in pancreatic vascularization: the construct must simultaneously support mass transport, functional maturation, and host compatibility. The fibrotic response observed over time also underscores how difficult it remains to maintain a favorable vascular interface in longer-term applications.

In summary, current work suggests that pancreatic organoid vascularization should be judged primarily by whether it supports endocrine survival and function. The key issue is therefore not simply the formation of channels, but the establishment of a transport-supportive and pro-angiogenic niche that preserves glucose sensing, insulin secretion, and long-term viability. Future efforts should place greater emphasis on microvascular support around islet-like structures, more stable perfusion strategies, and functional evaluation based on endocrine performance rather than morphology alone.

3.6. Intestinal organoids: Epithelial–vascular interfaces under luminal gradients

For intestinal organoids, vascularization is meaningful only when it supports a physiologically relevant epithelial–vascular interface rather than simply adding channels to a printed construct. Unlike tissues in which the main goal is bulk perfusion, the intestine requires vascular support that is closely coupled to the crypt–villus axis, nutrient transport, barrier maintenance, and responses to luminal or inflammatory gradients.[117-119] Accordingly, the relevant vascular requirements in intestinal organoid models include an appropriate local vessel scale for epithelial exchange, a spatial hierarchy compatible with crypt–villus organization, and functional integration sufficient to sustain long-term epithelial homeostasis under dynamic conditions.

A representative example was reported by Huang *et al.*,[120] who developed an intestinal organoid-on-a-chip platform with embedded artificial microvessels using coaxial microfluidic fabrication and a pH-responsive zeolitic imidazole framework 8/sodium alginate scaffold. This system recapitulated oxygen gradient dynamics during intestinal ischemia–reperfusion injury and showed that dynamic perfusion improved long-term viability and physiological relevance. Its significance lies in directly linking vascular integration to a biologically meaningful intestinal function, namely the response of the epithelial compartment to changing oxygen and transport conditions. In this sense, the study demonstrates that vascularization in intestinal organoids should be judged not only by structural incorporation of vessels, but also by whether vascular support enables functionally relevant epithelial behavior under dynamic stress.

A second important advance was reported by Li *et al.*,[121] who used embedded 3D bioprinting to fabricate a large-scale intestinal tissue construct with continuous crypt–villus architecture and predefined vessel-guidance channels. Using a composite bioink of alginate methacrylate, PEGDA, and GelMA, they generated a multilevel intestinal structure in which Caco-2 cells formed a barrier-forming epithelial layer with microvillus- and crypt–villus-like features, while HUVECs embedded in the surrounding matrix gradually developed capillary-like networks. This study is particularly valuable because it addresses several intestinal vascular requirements simultaneously: the need for structural hierarchy, the need for guided vascular organization within the supporting matrix, and the need for improved mass transport during longer-term culture. Although the resulting vasculature does not fully reproduce the complexity of native intestinal microcirculation, it represents a more integrated step toward vascularized intestinal organoid-related models than static topographic scaffolds alone.

In conclusion, current progress in intestinal organoid vascularization has moved beyond simple epithelial culture toward systems that begin to couple epithelial organization, perfusion support, and vascular guidance. However, the central challenge remains the reconstruction of a stable epithelial–vascular interface that can preserve crypt–villus organization, barrier function, and long-term viability under dynamic luminal conditions. Future work should therefore prioritize coordinated vascular support, controlled perfusion, and multicellular integration rather than structural complexity alone.

3.7. Cardiac and lung organoid-inspired models: Emerging directions and current limitations

Compared to the brain, liver, kidney, or pancreatic systems, the literature on direct vascularized cardiac and lung organoids remains limited. Numerous available studies are more accurately described as organoid-inspired models or engineered tissue constructs rather than classical organoids.[33,122,123] For this reason, these two fields are considered together here as emerging directions in which vascular biofabrication is clearly important, but in which the boundary between organoid vascularization and broader tissue engineering remains less clearly defined.

In cardiac models, the main vascular requirement is maintaining oxygen delivery and cellular viability within thick, contractile tissue, while supporting electromechanical stability during prolonged culture. Printed cardiac constructs with lumenized channels or multicellular organization have shown that perfusable mesoscale pathways can improve tissue survival and functional maintenance. Likewise, FRESH-based fabrication of vessel-like channels within collagen-rich cardiac constructs has demonstrated the practical value of perfusion routes in thicker engineered tissues.[25] However, these advances still do not fully reproduce a mature myocardial microvascular bed, and many current examples are better regarded as vascularized cardiac tissue models than as organoids in the strict sense.

In lung-related models, the key requirement is not merely vascular presence, but a vascular interface compatible with airway or alveolar architecture and exchange-related function. Some printed lung cancer organoid models incorporating vascular channels have begun to address this issue, particularly in the context of TME reconstruction.[101] Yet a large part of the broader lung-printing literature remains centered on airway chips, epithelial patterning, or non-organoid constructs. These systems are valuable for pulmonary bioengineering, but

only a subset is directly relevant to vascularized lung organoid modeling.

On the whole, the cardiac and lung fields illustrate an important boundary in the current literature: vascular biofabrication has clear value, but the number of examples that genuinely qualify as organoid vascularization remains limited. At present, the most defensible way to discuss these systems is as organoid-inspired models that highlight future opportunities rather than as fully established organoid vascularization platforms. Future work in both areas will need to move beyond bulk perfusion routes and toward more organ-relevant endothelial phenotypes, better integration with tissue-specific cellular organization, and clearer functional criteria for what constitutes meaningful vascularization.

4. Current technical bottlenecks and unmet challenges

Although substantial progress has been made in vascularized organoid biofabrication, the central challenge is no longer simply whether vascular structures can be introduced, but whether those structures are appropriate for the intended biological use.[11] At present, the main limitations concern not only fabrication itself, but also the mismatch between printable structures and physiological microvasculature, the absence of shared perfusion standards, the lack of application-specific maturation criteria, and the unresolved question of which vascular cell sources are suitable for different organoid systems.[117,128]

A first and persistent bottleneck is the gap between fabrication feasibility and physiological vascular scale. Most current printing-based strategies can reproducibly generate mesoscale conduits, endothelialized channels, or perfusion routes, but they do not yet routinely recreate the dense capillary beds that dominate transport in native tissues. In practice, increasing spatial precision often comes at the expense of cell viability, material flexibility, or manufacturing robustness.[80,129-131] For this reason, the most workable strategy at present is often a hybrid one: printing is used to establish larger perfusion pathways or spatial guidance, whereas finer vascular features arise through endothelial sprouting, self-organization, or remodeling after fabrication.[80,129,132]

A second major issue is perfusion standardization. Even when vascular channels are successfully established, long-term performance remains highly variable across systems.[133] Channel geometry, flow profile, shear stress, oxygen delivery, and media turnover are rarely standardized in a way that allows direct comparison across studies. This is not a minor methodological issue, because vascular stability under flow determines whether endothelial coverage is maintained, whether lumens remain patent, and whether the construct can support sustained transport rather than just short-term appearance.[38,134,135] Recent organoid-on-chip and vascularized bioprinted models have shown that even relatively simple perfusion systems can improve organoid growth, metabolic support, and assay performance, but these gains are easier to demonstrate in controlled *in vitro* platforms than in larger or more translational constructs.[33,136]

A third problem is that maturation metrics are still too loosely defined. In many studies, vascularization is inferred solely from morphology, such as channel presence, CD31 staining, or endothelial sprouting. These readouts are useful, but they are not sufficient on their own.[137] More importantly, the relevant maturation benchmark depends on the intended use of the model. For *in vitro* analytical platforms, such as drug screening or disease modeling, a construct may already be valuable if it shows reproducible perfusion, stable endothelial coverage, improved transport, and application-relevant functional outputs.[71,138] In contrast, implantable constructs must meet a much higher standard, including durable perfusion, structural stability, host integration, and preservation of tissue-specific function after transplantation. These two use scenarios should not be judged using the same threshold.[139,140]

A fourth bottleneck concerns the selection of vascular cells. Many current vascularized models still rely on HUVECs because they are experimentally robust and readily available. However, a generic endothelial source is not necessarily adequate for organoids that require tissue-specific vascular behavior. Brain, liver, kidney, and intestinal organoids differ not only in parenchymal composition but also in endothelial phenotype and vascular function.[87,117] This point is now difficult to ignore, given growing evidence for organotypic vascular heterogeneity across human tissues. The issue is even clearer for immortalized endothelial lines, such as EA.hy926.[141] These cells remain useful as research tools, but they are somatic hybrid lines rather than clinically deployable endothelial sources, and transcriptomic analyses have shown clear differences between EA.hy926 and primary endothelial cells.[11,142] Future progress should therefore require more deliberate choices regarding organ-matched endothelial cells, perivascular support cells, and stem-cell-derived vascular components.

A fifth unresolved issue is the balance between universality and organ specificity in vascular design. Some engineering principles are broadly useful, including perfusion-compatible matrices, endothelial pre-patterning, sacrificial templating, and dynamic flow conditioning. Yet it is increasingly clear that vascularization cannot be

treated as a single generic endpoint across all organoids.[143] Brain-like barrier vasculature, liver sinusoidal exchange networks, and glomerular filtration interfaces represent fundamentally different targets.[33,38] Recent discussions of *in vitro* vascularization have emphasized that capillary organization itself varies markedly across tissues, including branched, bifurcated, and glomerulus-like architectures.[144] A central question for the next stage of the field is therefore not whether one universal vascularization strategy exists, but which parts of vascular design can be standardized and which must remain organ-specific.

Finally, scaling and translation remain difficult because vascular complexity increases disproportionately with construct size. As organoids grow larger or become more functionally ambitious, diffusion limitations, perfusion instability, and multicompartment failure become more pronounced.[128] At the same time, translational intent brings additional concerns, including manufacturability, biosafety, and ethical oversight. For this reason, scaling cannot be treated as a purely engineering problem.[145] It also determines the level of vascular maturity genuinely required and whether a given platform should be judged as an *in vitro* test system or a translational tissue construct .

5. Future perspectives

Future progress in this field will likely depend less on a single leap in printing resolution than on better integration between fabrication, vascular maturation, and application-specific evaluation. In practical terms, the most promising near-term path is not the direct printing of complete physiological capillary beds, but the coupling of reproducible mesoscale perfusion routes with post-printing endothelial remodeling, sprouting, and self-organization.[53,128] This hybrid logic already underlies several of the more convincing recent platforms and is likely to remain the most realistic route for improving both reproducibility and biological relevance.

A second priority is the establishment of clear maturation criteria aligned with the intended use. For *in vitro* pharmacology or mechanistic studies, the goal should not necessarily be full anatomical fidelity. In numerous cases, it is sufficient—and experimentally meaningful—to achieve controlled perfusion, stable endothelialization, improved oxygen and nutrient delivery, and reproducible functional readouts. This is precisely why relatively simple vascularized systems have already proved useful for drug testing, including vascularized tumor and liver models.[33,146] In contrast, for implantation-oriented constructs, partial vascularization is insufficient. These systems must sustain flow over longer periods, resist structural failure, and support tissue-specific function after implantation.[147] A stronger distinction between these two endpoints would make the field more coherent and would prevent *in vitro* screening platforms from being judged by unrealistic translational standards.

A third direction concerns cell-source upgrading. If organoid vascularization is to move beyond proof-of-concept, greater attention will need to be paid to endothelial identity. The accumulating evidence for organotypic vascular diversity suggests that future models will benefit from replacing generic endothelial inputs with organ-matched endothelial cells, stem-cell-derived endothelial populations, or better-defined vascular organoids when the biological question requires tissue specificity.[141,148] This will be especially important in systems such as the brain, kidney, and liver, where endothelial function is closely tied to organ-specific physiology rather than simple nutrient transport.[144]

A fourth priority is the development of modular and comparable perfusion platforms. Many current systems remain highly customized, making it difficult to compare results across laboratories or organ types. More standardized modules for channel interfacing, shear control, oxygenation, and online monitoring would help define more reproducible vascular maturation conditions.[38] This is particularly relevant for organoid-on-chip systems, where moderate levels of vascular complexity can already yield substantial gains in assay performance, maturation, and long-term culture stability.[38,39]

A fifth and broader issue is how to combine shared engineering strategies with organ-specific vascular targets. The field is unlikely to advance through purely generic vascularization recipes. Instead, progress will probably come from a layered design strategy: a common engineering backbone for fabrication and perfusion, combined with organ-specific modules that reflect the structural and functional demands of brain, liver, kidney, pancreas, intestine, or tumor tissue.[128,145] This is likely to be more productive than asking whether one vascularization method can serve all organoid types equally well.

Finally, a few noncanonical oxygen-support strategies may deserve cautious discussion in future perspectives. One recent example outside the organoid field is the incorporation of symbiotic microbes into bioprinted constructs to locally supply oxygen. This is not yet an established strategy for organoid vascularization, and it should not be presented as such. Even so, it is worth mentioning briefly because it addresses the same biological problem from a different angle: in some settings, relieving hypoxia may require not only better vasculature, but also complementary approaches to oxygen management. Used carefully, such examples can broaden the future outlook without diluting the central theme of vascularization.[149,150]

In summary, the next stage of vascularized organoid biofabrication depends on a shift in emphasis: from demonstrating that vascular structures can be introduced into organoid systems to showing that these structures are fit for purpose. That shift requires sharper maturation criteria, better endothelial choices, more comparable perfusion systems, and a clearer distinction between broadly useful engineering principles and organ-specific vascular requirements.

6. Conclusion

The convergence of 3D bioprinting and organoid technologies has opened unprecedented avenues in tissue engineering, making it increasingly feasible to construct complex tissues that exhibit both structural and functional biomimicry. To date, this field has evolved into a diversified technological landscape encompassing multiscale printing, perfusion-enabled culture systems, and self-organization-assisted strategies, with an expanding repertoire of application paradigms. However, substantial differences in anatomical architecture, physiological function, and microenvironmental context across organ systems necessitate that biofabrication approaches be precisely tailored and matched to organ-specific requirements. Looking forward, deeper interdisciplinary integration—linking bioprinting, biomaterials science, and developmental biology—alongside the establishment of standardized manufacturing workflows and unified evaluation frameworks, will be pivotal for enabling scalable organoid production and accelerating clinical translation.

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All the authors confirm that there are no conflicts of interest.

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Not applicable.

References

1. Li J, Li Y, Song G, *et al*. Revolutionizing cardiovascular research: Human organoids as a Beacon of hope for understanding and treating cardiovascular diseases. *Mater Today Bio*. 2025;30:101396.

   doi: 10.1016/j.mtbio.2024.101396

2. Huch M, Koo BK. Modeling mouse and human development using organoid cultures. *Development*. 2015;142(18):3113-3125.

   doi: 10.1242/dev.118570

3. Corrò C, Novellasdemunt L, Li VSW. A brief history of organoids. *Am J Physiol Cell Physiol*. 2020;319(1):C151-C165.

   doi: 10.1152/ajpcell.00120.2020

4. Yi SA, Zhang Y, Rathnam C, Pongkulapa T, Lee KB. Bioengineering Approaches for the Advanced Organoid Research. *Adv Mater*. 2021;33(45):e2007949.

   doi: 10.1002/adma.202007949

5. Fang Z, Li P, Du F, Shang L, Li L. The role of organoids in cancer research. *Exp Hematol Oncol*. 2023;12(1):69.

   doi: 10.1186/s40164-023-00433-y

6. Man Y, Liu Y, Chen Q, *et al*. Organoids-On-a-Chip for Personalized Precision Medicine. *Adv Healthc Mater*. 2024;13(30):e2401843.

   doi: 10.1002/adhm.202401843

7. Strobel HA, Moss SM, Hoying JB. Vascularized Tissue Organoids. *Bioengineering (Basel)*. 2023;10(2).

   doi: 10.3390/bioengineering10020124

8. Abdulla A, Chen S, Chen Z, *et al*. Three-dimensional microfluidics with dynamic fluidic perturbation promotes viability and uniformity of human cerebral

organoids. *Biosens Bioelectron*. 2023;240:115635.

doi: 10.1016/j.bios.2023.115635

9. Park S, Cho SW. Bioengineering toolkits for potentiating organoid therapeutics. *Adv Drug Deliv Rev*. 2024;208:115238.

doi: 10.1016/j.addr.2024.115238

10. Kobayashi Y, Hashizume H, Takiguchi S, *et al*. A microfluidics platform for simultaneous evaluation of sensitivity and side effects of anti-cancer drugs using a three-dimensional culture method. *Sci Rep*. 2025;15(1):39.

doi: 10.1038/s41598-024-84297-0

11. Du Y, Wang YR, Bao QY, *et al*. Personalized Vascularized Tumor Organoid-on-a-Chip for Tumor Metastasis and Therapeutic Targeting Assessment. *Adv Mater*. 2025;37(6):e2412815.

doi: 10.1002/adma.202412815

12. Su SP, Lee YC, Lin SL, *et al*. Realization of NIR-II 3D whole-body contour and tumor blood vessels imaging in small animals using rotational stereo vision technique. *J Biomed Opt*. 2023;28(9):094807.

doi: 10.1117/1.Jbo.28.9.094807

13. Fang Y, Guo Y, Wu B, *et al*. Expanding Embedded 3D Bioprinting Capability for Engineering Complex Organs with Freeform Vascular Networks. *Adv Mater*. 2023;35(22):e2205082.

doi: 10.1002/adma.202205082

14. Zhang J, Wehrle E, Rubert M, Müller R. 3D Bioprinting of Human Tissues: Biofabrication, Bioinks, and Bioreactors. *Int J Mol Sci*. 2021;22(8).

doi: 10.3390/ijms22083971

15. Zhao C, Lv Q, Wu W. Application and Prospects of Hydrogel Additive Manufacturing. *Gels*. 2022;8(5).

doi: 10.3390/gels8050297

16. Nwokoye PN, Abilez OJ. Bioengineering methods for vascularizing organoids. *Cell Rep Methods*. 2024;4(6):100779.

doi: 10.1016/j.crmeth.2024.100779

17. Placone JK, Engler AJ. Recent Advances in Extrusion-Based 3D Printing for Biomedical Applications. *Adv Healthc Mater*. 2018;7(8):e1701161.

doi: 10.1002/adhm.201701161

18. Li Z, Li K, Zhang C, *et al*. Bioprinted Organoids: An Innovative Engine in Biomedicine. *Adv Sci (Weinh)*. 2025;12(33):e07317.

doi: 10.1002/advs.202507317

19. Nasehi R, Schieren J, Grannemann C, *et al*. Bioprinting-associated pulsatile hydrostatic pressure elicits a mild proinflammatory response in epi- and endothelial cells. *Biomater Adv*. 2023;147:213329.

doi: 10.1016/j.bioadv.2023.213329

20. Navara AM, Kim YS, Xu Y, *et al*. A dual-gelling poly(N-isopropylacrylamide)-based ink and thermoreversible poloxamer support bath for high-resolution bioprinting. *Bioact Mater*. 2022;14:302-312.

doi: 10.1016/j.bioactmat.2021.11.016

21. Torras N, Zabalo J, Abril E, Carré A, García-Díaz M, Martínez E. A bioprinted 3D gut model with crypt-villus structures to mimic the intestinal epithelial-stromal microenvironment. *Biomater Adv*. 2023;153:213534.

doi: 10.1016/j.bioadv.2023.213534

22. Li X, Wang M, Davis TP, Zhang L, Qiao R. Advancing Tissue Culture with Light-Driven 3D-Printed Microfluidic Devices. *Biosensors (Basel)*. 2024;14(6).

doi: 10.3390/bios14060301

23. Platania V, Lamprou A, Bugueno IM. Living Tissues by Design: The Rise of Hybrid Models in Biofabrication. *J Funct Biomater*. 2026;17(3).

doi: 10.3390/jfb17030135

24. Budharaju H, Sundaramurthi D, Sethuraman S. Embedded 3D bioprinting - An emerging strategy to fabricate biomimetic & large vascularized tissue constructs. *Bioact Mater*. 2024;32:356-384.

doi: 10.1016/j.bioactmat.2023.10.012

25. Lee A, Hudson AR, Shiwarski DJ, *et al*. 3D bioprinting of collagen to rebuild components of the human heart. *Science*. 2019;365(6452):482-487.

doi: 10.1126/science.aav9051

26. Cho WW, Park W, Cho DW. Recent trends in embedded 3D bioprinting of vascularized tissue constructs. *Biofabrication*. 2025;17(2).

doi: 10.1088/1758-5090/adafdd

27. Yogeshwaran S, Goodarzi Hosseinabadi H, Gendy DE, Miri AK. Design considerations and biomaterials selection in embedded extrusion 3D bioprinting. *Biomater Sci*. 2024;12(18):4506-4518.

doi: 10.1039/d4bm00550c

28. Yu Y, Xie R, He Y, *et al*. Dual-core coaxial bioprinting of double-channel constructs with a potential for perfusion and interaction of cells. *Biofabrication*. 2022;14(3).

doi: 10.1088/1758-5090/ac6e88

29. Stankey PP, Kroll KT, Ainscough AJ, *et al*. Embedding Biomimetic Vascular Networks via Coaxial Sacrificial Writing into Functional Tissue. *Adv Mater*. 2024;36(36):e2401528.

doi: 10.1002/adma.202401528

30. Kim JH, Park M, Shim JH, Yun WS, Jin S. Multi-scale vascularization strategy for 3D-bioprinted tissue using coaxial core-shell pre-set extrusion bioprinting and

biochemical factors. *Int J Bioprint*. 2023;9(4):726.

doi: 10.18063/ijb.726

31. Simińska-Stanny J, Nicolas L, Chafai A, *et al*. Advanced PEG-tyramine biomaterial ink for precision engineering of perfusable and flexible small-diameter vascular constructs via coaxial printing. *Bioact Mater*. 2024;36:168-184.

doi: 10.1016/j.bioactmat.2024.02.019

32. Wang K, Lan X, Chen J, *et al*. One-Step Coaxial 3D Printing of Pre-Vascularized Skin Organoid Models with ADSC Microspheres for Enhanced Wound Healing. *Adv Sci (Weinh)*. 2026;13(9):e17409.

doi: 10.1002/advs.202517409

33. Gao Q, Wang J, Zhang H, Wang J, Jing Y, Su J. Organoid Vascularization: Strategies and Applications. *Adv Healthc Mater*. 2025;14(20):e2500301.

doi: 10.1002/adhm.202500301

34. Liu Y, Liu X, Zhang Y, *et al*. Interpenetrating Polymer Network HA/Alg-RGD Hydrogel: An Equilibrium of Macroscopic Stability and Microscopic Adaptability for 3D Cell Growth and Vascularization. *Biomacromolecules*. 2023;24(12):5977-5988.

doi: 10.1021/acs.biomac.3c01022

35. Jäger J, Berger P, Morrison AI, *et al*. A Sacrificial 3D Printed Vessel-on-Chip Demonstrates a Versatile Approach to Model Granulation Tissue. *Adv Healthc Mater*. 2026;15(7):e03081.

doi: 10.1002/adhm.202503081

36. Ren B, Song K, Sanikommu AR, *et al*. Study of sacrificial ink-assisted embedded printing for 3D perfusable channel creation for biomedical applications. *Appl Phys Rev*. 2022;9(1):011408.

doi: 10.1063/5.0068329

37. Li Y, Huang D, Zhang Y, Xiao Y, Zhang X. Microfluidic-assisted engineering of hydrogels with microscale complexity. *Acta Biomater*. 2025;199:1-17.

doi: 10.1016/j.actbio.2025.05.023

38. Menzani B, De Gea P, Gidrol X, Tubbs E. Vascularizing organoids-on-chip for perfused and personalized models. *Lab Chip*. 2026;26(6):1798-1819.

doi: 10.1039/d5lc00890e

39. Quintard C, Tubbs E, Jonsson G, *et al*. A microfluidic platform integrating functional vascularized organoids-on-chip. *Nat Commun*. 2024;15(1):1452.

doi: 10.1038/s41467-024-45710-4

40. Liu H, Gan Z, Qin X, Wang Y, Qin J. Advances in Microfluidic Technologies in Organoid Research. *Adv Healthc Mater*. 2024;13(21):e2302686.

doi: 10.1002/adhm.202302686

41. Shi J, Wang C, Mei X, *et al*. Sacrificial Biofabrication for Vascularization: Concept, Materials, Technologies, and Applications. *Adv Mater*. 2026;38(2):e07747.

doi: 10.1002/adma.202507747

42. Zhang C, Hao J, Shi W, *et al*. Sacrificial scaffold-assisted direct ink writing of engineered aortic valve prostheses. *Biofabrication*. 2023;15(4).

doi: 10.1088/1758-5090/aceffb

43. Homan KA, Kolesky DB, Skylar-Scott MA, *et al*. Bioprinting of 3D Convoluted Renal Proximal Tubules on Perfusable Chips. *Sci Rep*. 2016;6:34845.

doi: 10.1038/srep34845

44. Wen Z, Orduno M, Liang Z, Gong X, Mak M. Optimization of Vascularized Intestinal Organoid Model. *Adv Healthc Mater*. 2024;13(31):e2400977.

doi: 10.1002/adhm.202400977

45. Pham MT, Pollock KM, Rose MD, *et al*. Generation of human vascularized brain organoids. *Neuroreport*. 2018;29(7):588-593.

doi: 10.1097/wnr.0000000000001014

46. Gan Z, Qin X, Liu H, Liu J, Qin J. Recent advances in defined hydrogels in organoid research. *Bioact Mater*. 2023;28:386-401.

doi: 10.1016/j.bioactmat.2023.06.004

47. Gopinathan J, Noh I. Recent trends in bioinks for 3D printing. *Biomater Res*. 2018;22:11.

doi: 10.1186/s40824-018-0122-1

48. He J, Sun Y, Gao Q, *et al*. Gelatin Methacryloyl Hydrogel, from Standardization, Performance, to Biomedical Application. *Adv Healthc Mater*. 2023;12(23):e2300395.

doi: 10.1002/adhm.202300395

49. Vanhove L, Van Gansbeke T, Devriendt B, Van der Meeren R, Dmitriev RI, Okkelman IA. Lack of biochemical signalling in GelMA leads to polarity reversion in intestinal organoids independent from mechanoreciprocity. *J Tissue Eng*. 2025;16:20417314251345000.

doi: 10.1177/20417314251345000

50. Clerkin S, Singh K, Davis JL, *et al*. Tuneable gelatin methacryloyl (GelMA) hydrogels for the directed specification of renal cell types for hiPSC-derived kidney organoid maturation. *Biomaterials*. 2025;322:123349.

doi: 10.1016/j.biomaterials.2025.123349

51. Li C, An N, Song Q, *et al*. Enhancing organoid culture: harnessing the potential of decellularized extracellular matrix hydrogels for mimicking microenvironments. *J Biomed Sci*. 2024;31(1):96.

doi: 10.1186/s12929-024-01086-7

52. Su X, Wang M, Yuan R, *et al*. Organoids in Dynamic Culture: Microfluidics and 3D Printing Technologies. *ACS Biomater Sci Eng*. 2025;11(6):3165-3181.

doi: 10.1021/acsbiomaterials.4c02245

53. Zhou R, Brislinger D, Fuchs J, *et al*. Vascularised organoids: Recent advances and applications in cancer research. *Clin Transl Med*. 2025;15(3):e70258.

doi: 10.1002/ctm2.70258

54. Ahn SH, Rath M, Tsao CY, Bentley WE, Raghavan SR. Single-Step Synthesis of Alginate Microgels Enveloped with a Covalent Polymeric Shell: A Simple Way to Protect Encapsulated Cells. *ACS Appl Mater Interfaces*. 2021;13(16):18432-18442.

doi: 10.1021/acsami.0c20613

55. Hakim Khalili M, Zhang R, Wilson S, Goel S, Impey SA, Aria AI. Additive Manufacturing and Physicomechanical Characteristics of PEGDA Hydrogels: Recent Advances and Perspective for Tissue Engineering. *Polymers (Basel)*. 2023;15(10).

doi: 10.3390/polym15102341

56. Kim D, Kim YH, Lee G, Lee EC, Bhang SH, Lee K. Multidimensional nanofibrous hydrogels integrated triculture system for advanced myocardial regeneration. *Biofabrication*. 2025;17(1).

doi: 10.1088/1758-5090/ad9cc3

57. Zhu L, Yuhan J, Yu H, Zhang B, Huang K, Zhu L. Decellularized Extracellular Matrix for Remodeling Bioengineering Organoid's Microenvironment. *Small*. 2023;19(25):e2207752.

doi: 10.1002/smll.202207752

58. Kim JW, Nam SA, Yi J, *et al*. Kidney Decellularized Extracellular Matrix Enhanced the Vascularization and Maturation of Human Kidney Organoids. *Adv Sci (Weinh)*. 2022;9(15):e2103526.

doi: 10.1002/advs.202103526

59. Cui X, Liu H, Liu Y, *et al*. Tissue-specific decellularized extracellular matrix rich in collagen, glycoproteins, and proteoglycans and its applications in advanced organoid engineering: A review. *Int J Biol Macromol*. 2025;315(Pt 2):144469.

doi: 10.1016/j.ijbiomac.2025.144469

60. Zhu B, Wang D, Pan H, *et al*. Three-in-one customized bioink for islet organoid: GelMA/ECM/PRP orchestrate pro-angiogenic and immunoregulatory function. *Colloids Surf B Biointerfaces*. 2023;221:113017.

doi: 10.1016/j.colsurfb.2022.113017

61. Guo X, Liu B, Zhang Y, *et al*. Decellularized extracellular matrix for organoid and engineered organ culture. *J Tissue Eng*. 2024;15:20417314241300386.

doi: 10.1177/20417314241300386

62. Attalla R, Puersten E, Jain N, Selvaganapathy PR. 3D bioprinting of heterogeneous bi- and tri-layered hollow channels within gel scaffolds using scalable multi-axial microfluidic extrusion nozzle. *Biofabrication*. 2018;11(1):015012.

doi: 10.1088/1758-5090/aaf7c7

63. Maggiotto F, Bova L, Micheli S, *et al*. 3D bioprinting for the production of a perfusable vascularized model of a cancer niche. *Front Bioeng Biotechnol*. 2025;13:1484738.

doi: 10.3389/fbioe.2025.1484738

64. He J, Shao J, Li X, Huang Q, Xu T. Bioprinting of coaxial multicellular structures for a 3D co-culture model. *Bioprinting*. 2018;11:e00036.

doi: 10.1016/j.bprint.2018.e00036

65. Zhu Y, Yu X, Liu H, *et al*. Strategies of functionalized GelMA-based bioinks for bone regeneration: Recent advances and future perspectives. *Bioact Mater*. 2024;38:346-373.

doi: 10.1016/j.bioactmat.2024.04.032

66. Papamichail L, Koch LS, Veerman D, Broersen K, van der Meer AD. Organoids-on-a-chip: microfluidic technology enables culture of organoids with enhanced tissue function and potential for disease modeling. *Front Bioeng Biotechnol*. 2025;13:1515340.

doi: 10.3389/fbioe.2025.1515340

67. Gabbin B, Meraviglia V, Angenent ML, *et al*. Heart and kidney organoids maintain organ-specific function in a microfluidic system. *Mater Today Bio*. 2023;23:100818.

doi: 10.1016/j.mtbio.2023.100818

68. Grebenyuk S, Abdel Fattah AR, Kumar M, *et al*. Large-scale perfused tissues via synthetic 3D soft microfluidics. *Nat Commun*. 2023;14(1):193.

doi: 10.1038/s41467-022-35619-1

69. Yeo M, Sarkar A, Singh YP, Derman ID, Datta P, Ozbolat IT. Synergistic coupling between 3D bioprinting and vascularization strategies. *Biofabrication*. 2023;16(1).

doi: 10.1088/1758-5090/ad0b3f

70. Matai I, Kaur G, Seyedsalehi A, McClinton A, Laurencin CT. Progress in 3D bioprinting technology for tissue/organ regenerative engineering. *Biomaterials*. 2020;226:119536.

doi: 10.1016/j.biomaterials.2019.119536

71. Sanchez-Rubio A, Jayawarna V, Maxwell E, Dalby MJ, Salmeron-Sanchez M. Keeping It Organized: Multicompartment Constructs to Mimic Tissue Heterogeneity. *Adv Healthc Mater*. 2023;12(17):e2202110.

doi: 10.1002/adhm.202202110

72. Rhee S, Puetzer JL, Mason BN, Reinhart-King CA, Bonassar LJ. 3D Bioprinting of Spatially Heterogeneous Collagen

Constructs for Cartilage Tissue Engineering. *ACS Biomater Sci Eng*. 2016;2(10):1800-1805.

doi: 10.1021/acsbiomaterials.6b00288

73. Roth JG, Brunel LG, Huang MS, *et al*. Spatially controlled construction of assembloids using bioprinting. *Nat Commun*. 2023;14(1):4346.

doi: 10.1038/s41467-023-40006-5

74. Zhou Y, Wu Y, Paul R, Qin X, Liu Y. Hierarchical Vessel Network-Supported Tumor Model-on-a-Chip Constructed by Induced Spontaneous Anastomosis. *ACS Appl Mater Interfaces*. 2023;15(5):6431-6441.

doi: 10.1021/acsami.2c19453

75. Baptista LS, Mironov V, Koudan E, *et al*. Bioprinting Using Organ Building Blocks: Spheroids, Organoids, and Assembloids. *Tissue Eng Part A*. 2024;30(13-14):377-386.

doi: 10.1089/ten.TEA.2023.0198

76. Brassard JA, Nikolaev M, Hübscher T, Hofer M, Lutolf MP. Recapitulating macro-scale tissue self-organization through organoid bioprinting. *Nat Mater*. 2021;20(1):22-29.

doi: 10.1038/s41563-020-00803-5

77. Li C, Chen J, Jie T, *et al*. Construction of Biomimetic Tissues with Anisotropic Structures via Stepwise Algorithm-Assisted Bioprinting. *Small*. 2022;18(46):e2204316.

doi: 10.1002/smll.202204316

78. Huang D, Li Z, Li G, *et al*. Biomimetic structural design in 3D-printed scaffolds for bone tissue engineering. *Mater Today Bio*. 2025;32:101664.

doi: 10.1016/j.mtbio.2025.101664

79. Sexton ZA, Rütsche D, Herrmann JE, *et al*. Rapid model-guided design of organ-scale synthetic vasculature for biomanufacturing. *Science*. 2025;388(6752):1198-1204.

80. Seymour AJ, Westerfield AD, Cornelius VC, Skylar-Scott MA, Heilshorn SC. Bioprinted microvasculature: progressing from structure to function. *Biofabrication*. 2022;14(2).

doi: 10.1088/1758-5090/ac4fb5

81. Parkhideh S, Calderon GA, Janson KD, *et al*. Perfusable cell-laden matrices to guide patterning of vascularization in vivo. *Biomater Sci*. 2023;11(2):461-471.

doi: 10.1039/d2bm01200f

82. Krajewska U, Chechlińska M, Kurzyk A. Vascularisation in 3D bioprinted models: emerging solutions engineering functional tissues and tumour models. *Biofabrication*. 2026;18(2).

doi: 10.1088/1758-5090/ae2f02

83. Zhu H, Guo K, Feng J, *et al*. Rethinking Neuroregenerative Microenvironments: Synergy Between Bioengineering and Organoids. *Adv Healthc Mater*. 2026:e71115.

doi: 10.1002/adhm.202471115

84. Cadena MA, Sing A, Taylor K, *et al*. A 3D Bioprinted Cortical Organoid Platform for Modeling Human Brain Development. *Adv Healthc Mater*. 2024;13(27):e2401603.

doi: 10.1002/adhm.202401603

85. Song Y, Jo H, Jeong S, Kim I, Lee SS. Vascularised Brain Organoids: Engineering Strategies and Neurobiological Applications. *Cell Prolif*. 2026;59(3):e70161.

doi: 10.1111/cpr.70161

86. Ko PL, Wang CK, Hsu HH, Lee TA, Tung YC. Revealing anisotropic elasticity of endothelium under fluid shear stress. *Acta Biomater*. 2022;145:316-328.

doi: 10.1016/j.actbio.2022.03.040

87. Werschler N, Quintard C, Nguyen S, Penninger J. Engineering next generation vascularized organoids. *Atherosclerosis*. 2024;398:118529.

doi: 10.1016/j.atherosclerosis.2024.118529

88. Salmon I, Grebenyuk S, Abdel Fattah AR, *et al*. Engineering neurovascular organoids with 3D printed microfluidic chips. *Lab Chip*. 2022;22(8):1615-1629.

doi: 10.1039/d1lc00535a

89. Morizane R, Lamers MM. Organoids in disease modeling and regenerative medicine. *Cell Mol Life Sci*. 2025;82(1):169.

doi: 10.1007/s00018-025-05692-y

90. Bosmans C, Ginés Rodriguez N, Gutiérrez Hernández UJ, *et al*. A Quantitative Printability Framework for Programmable Assembly of Pre-Vascular Patterns via Laser-Induced Forward Transfer. *Adv Healthc Mater*. 2026;15(8):e03665.

doi: 10.1002/adhm.202503665

91. Wang J, Huang D, Chen H, Zhao Y. Biomimetic hepatic lobules from three-dimensional imprinted cell sheets. *Sci Bull (Beijing)*. 2024;69(10):1448-1457.

doi: 10.1016/j.scib.2024.02.030

92. Byrne O, Coulter F, Roche ET, O'Cearbhaill ED. *In silico* design of additively manufacturable composite synthetic vascular conduits and grafts with tuneable compliance. *Biomater Sci*. 2021;9(12):4343-4355.

doi: 10.1039/d0bm02169e

93. Yan L, Moriarty RA, Stroka KM. Recent progress and new challenges in modeling of human pluripotent stem cell-derived blood-brain barrier. *Theranostics*. 2021;11(20):10148-10170.

doi: 10.7150/thno.63195

94. Wang Q, Zheng J, Pettersson S, Reynolds R, Tan EK. The link between neuroinflammation and the neurovascular unit in synucleinopathies. *Sci Adv*. 2023;9(7):eabq1141.

doi: 10.1126/sciadv.abq1141

95. Jezierski A, Huang J, Haqqani AS, *et al*. Mouse embryonic stem cell-derived blood-brain barrier model: applicability to studying antibody triggered receptor mediated transcytosis. *Fluids Barriers CNS*. 2023;20(1):36.

doi: 10.1186/s12987-023-00437-0

96. Fan S, Du H, Yao Y, *et al*. Protection against stroke-induced blood-brain barrier disruption by Guanxinning injection and its active-component combination via TLR4/NF-κB/MMP9-mediated neuroinflammation. *Phytomedicine*. 2025;147:157162.

doi: 10.1016/j.phymed.2025.157162

97. Xu L, Ding H, Wu S, *et al*. Artificial Meshed Vessel-Induced Dimensional Breaking Growth of Human Brain Organoids and Multiregional Assembloids. *ACS Nano*. 2024;18(38):26201-26214.

doi: 10.1021/acsnano.4c07844

98. Ascheid D, Baumann M, Funke C, *et al*. Image-based modeling of vascular organization to evaluate anti-angiogenic therapy. *Biol Direct*. 2023;18(1):10.

doi: 10.1186/s13062-023-00365-x

99. Stankovic I, Notaras M, Wolujewicz P, *et al*. Schizophrenia endothelial cells exhibit higher permeability and altered angiogenesis patterns in patient-derived organoids. *Transl Psychiatry*. 2024;14(1):53.

doi: 10.1038/s41398-024-02740-2

100. Shi W, Mirza S, Kuss M, *et al*. Embedded Bioprinting of Breast Tumor Cells and Organoids Using Low-Concentration Collagen-Based Bioinks. *Adv Healthc Mater*. 2023;12(26):e2300905.

doi: 10.1002/adhm.202300905

101. Choi YM, Lee H, Ann M, Song M, Rheey J, Jang J. 3D bioprinted vascularized lung cancer organoid models with underlying disease capable of more precise drug evaluation. *Biofabrication*. 2023;15(3).

doi: 10.1088/1758-5090/acd95f

102. Zhang LF, Wang XH, Zhang CL, *et al*. Sequential Nano-Penetrators of Capillarized Liver Sinusoids and Extracellular Matrix Barriers for Liver Fibrosis Therapy. *ACS Nano*. 2022;16(9):14029-14042.

doi: 10.1021/acsnano.2c03858

103. Zhang LF, Ru JW, Liang SQ, *et al*. Nanotherapy targeting liver sinusoidal endothelial cells in liver fibrosis. *J Control Release*. 2026;394:114864.

doi: 10.1016/j.jconrel.2026.114864

104. Gao J, Lan T, Kostallari E, *et al*. Angiocrine signaling in sinusoidal homeostasis and liver diseases. *J Hepatol*. 2024;81(3):543-561.

doi: 10.1016/j.jhep.2024.05.014

105. Jian H, Li X, Dong Q, Tian S, Bai S. In vitro construction of liver organoids with biomimetic lobule structure by a multicellular 3D bioprinting strategy. *Cell Prolif*. 2023;56(5):e13465.

doi: 10.1111/cpr.13465

106. Lekkala VKR, Shrestha S, Al Qaryoute A, *et al*. Enhanced Maturity and Functionality of Vascular Human Liver Organoids through 3D Bioprinting and Pillar Plate Culture. *ACS Biomater Sci Eng*. 2025;11(1):506-517.

doi: 10.1021/acsbiomaterials.4c01658

107. Shrestha S, Lekkala VKR, Acharya P, Kang SY, Vanga MG, Lee MY. Reproducible generation of human liver organoids (HLOs) on a pillar plate platform via microarray 3D bioprinting. *Lab Chip*. 2024;24(10):2747-2761.

doi: 10.1039/d4lc00149d

108. Valverde MG, Mille LS, Figler KP, *et al*. Biomimetic models of the glomerulus. *Nat Rev Nephrol*. 2022;18(4):241-257.

doi: 10.1038/s41581-021-00528-x

109. Maggiore JC, LeGraw R, Przepiorski A, *et al*. A genetically inducible endothelial niche enables vascularization of human kidney organoids with multilineage maturation and emergence of renin expressing cells. *Kidney Int*. 2024;106(6):1086-1100.

doi: 10.1016/j.kint.2024.05.026

110. Singh NK, Han W, Nam SA, *et al*. Three-dimensional cell-printing of advanced renal tubular tissue analogue. *Biomaterials*. 2020;232:119734.

doi: 10.1016/j.biomaterials.2019.119734

111. Zhang F, Lin DSY, Rajasekar S, Sotra A, Zhang B. Pump-Less Platform Enables Long-Term Recirculating Perfusion of 3D Printed Tubular Tissues. *Adv Healthc Mater*. 2023;12(27):e2300423.

doi: 10.1002/adhm.202300423

112. Homan KA, Gupta N, Kroll KT, *et al*. Flow-enhanced vascularization and maturation of kidney organoids in vitro. *Nat Methods*. 2019;16(3):255-262.

doi: 10.1038/s41592-019-0325-y

113. Yang J, Yan Y, Yin X, *et al*. Bioengineering and vascularization strategies for islet organoids: advancing toward diabetes therapy. *Metabolism*. 2024;152:155786.

doi: 10.1016/j.metabol.2024.155786

114. Huang H, Karanth SS, Guan Y, *et al*. Oxygenated Scaffolds for Pancreatic Endocrine Differentiation from Induced Pluripotent Stem Cells. *Adv Healthc Mater*. 2024;13(3):e2302275.

doi: 10.1002/adhm.202302275

115. Wang D, Guo Y, Zhu J, *et al*. Hyaluronic acid methacrylate/pancreatic extracellular matrix as a potential 3D printing

bioink for constructing islet organoids. *Acta Biomater*. 2023;165:86-101.

doi: 10.1016/j.actbio.2022.06.036

116. Soltanian A, Ghezelayagh Z, Mazidi Z, *et al*. Generation of functional human pancreatic organoids by transplants of embryonic stem cell derivatives in a 3D-printed tissue trapper. *J Cell Physiol*. 2019;234(6):9564-9576.

doi: 10.1002/jcp.27644

117. Naderi-Meshkin H, Cornelius VA, Eleftheriadou M, Potel KN, Setyaningsih WAW, Margariti A. Vascular organoids: unveiling advantages, applications, challenges, and disease modelling strategies. *Stem Cell Res Ther*. 2023;14(1):292.

doi: 10.1186/s13287-023-03521-2

118. Uckeley ZM, Kee C, Ramirez C, *et al*. Hypoxia Affects Stem Cell Fate in Patient-Derived Ileum Enteroids in a HIF-1α-Dependent Manner. *Cells*. 2025;15(1).

doi: 10.3390/cells15010031

119. Sharma A, Jin L, Wang X, Wang YT, Stresser DM. Developing an adult stem cell derived microphysiological intestinal system for predicting oral prodrug bioconversion and permeability in humans. *Lab Chip*. 2024;24(2):339-355.

doi: 10.1039/d3lc00843f

120. Huang J, Xu Z, Jiao J, *et al*. Microfluidic intestinal organoid-on-a-chip uncovers therapeutic targets by recapitulating oxygen dynamics of intestinal IR injury. *Bioact Mater*. 2023;30:1-14.

doi: 10.1016/j.bioactmat.2023.07.001

121. Li Y, Cheng S, Shi H, *et al*. 3D embedded bioprinting of large-scale intestine with complex structural organization and blood capillaries. *Biofabrication*. 2024;16(4).

doi: 10.1088/1758-5090/ad5b1b

122. Xia X, Hu M, Zhou W, Jin Y, Yao X. Engineering cardiology with miniature hearts. *Mater Today Bio*. 2025;31:101505.

doi: 10.1016/j.mtbio.2025.101505

123. Joo H, Min S, Cho SW. Advanced lung organoids for respiratory system and pulmonary disease modeling. *J Tissue Eng*. 2024;15:20417314241232502.

doi: 10.1177/20417314241232502

124. Neufeld L, Yeini E, Reisman N, *et al*. Microengineered perfusable 3D-bioprinted glioblastoma model for in vivo mimicry of tumor microenvironment. *Sci Adv*. 2021;7(34).

doi: 10.1126/sciadv.abi9119

125. Song P, Wang Y, Peng J, Liu L, Du L. A Protocol for the In Vitro Culturing of Vascularized Pancreatic Islet Organoids. *Bioengineering (Basel)*. 2025;12(11).

doi: 10.3390/bioengineering12111222

126. Park S, Kim TH, Kim SH, You S, Jung Y. Three-Dimensional Vascularized Lung Cancer-on-a-Chip with Lung Extracellular Matrix Hydrogels for In Vitro Screening. *Cancers (Basel)*. 2021;13(16).

doi: 10.3390/cancers13163930

127. Bas-Cristóbal Menéndez A, Du Z, van den Bosch TPP, *et al*. Creating a kidney organoid-vasculature interaction model using a novel organ-on-chip system. *Sci Rep*. 2022;12(1):20699.

doi: 10.1038/s41598-022-24945-5

128. Shin YJ, Safina D, Zheng Y, Levenberg S. Microvascularization in 3D Human Engineered Tissue and Organoids. *Annu Rev Biomed Eng*. 2025;27(1):473-498.

doi: 10.1146/annurev-bioeng-103023-115236

129. Lu B, Ye M, Xia J, Zhang Z, Xiong Z, Zhang T. Electrical Stimulation Promotes the Vascularization and Functionalization of an Engineered Biomimetic Human Cardiac Tissue. *Adv Healthc Mater*. 2023;12(19):e2300607.

doi: 10.1002/adhm.202300607

130. Hooper R, Cummings C, Beck A, Vazquez-Armendariz J, Rodriguez C, Dean D. Sheet-based extrusion bioprinting: a new multi-material paradigm providing mid-extrusion micropatterning control for microvascular applications. *Biofabrication*. 2024;16(2).

doi: 10.1088/1758-5090/ad30c8

131. Le HT, Phan HL, Lenshof A, *et al*. Ultrasound standing wave spatial patterning of human umbilical vein endothelial cells for 3D micro-vascular networks formation. *Biofabrication*. 2023;16(1).

doi: 10.1088/1758-5090/ad03be

132. Son J, Kim D, Choi J, *et al*. Triple-Scale Endothelialized Tubular Networks via Hybrid Biofabrication for Scalable Vascular Tissue Engineering. *Adv Healthc Mater*. 2026;15(9):e03334.

doi: 10.1002/adhm.202503334

133. Yang R, Qi Y, Zhang X, Gao H, Yu Y. Living biobank: Standardization of organoid construction and challenges. *Chin Med J (Engl)*. 2024;137(24):3050-3060.

doi: 10.1097/cm9.0000000000003414

134. Deng H, Eichmann A, Schwartz MA. Fluid Shear Stress-Regulated Vascular Remodeling: Past, Present, and Future. *Arterioscler Thromb Vasc Biol*. 2025;45(6):882-900.

doi: 10.1161/atvbaha.125.322557

135. Xiao Z, White NA, Wen J, *et al*. Exploring the link between disturbed flow and endothelial cell function in an in vitro arteriovenous fistula model. *Acta Biomater*. 2026;213:328-340.

doi: 10.1016/j.actbio.2026.01.044

136. Minahan DJ, Nelson KM, Ribeiro F, *et al*. Democratizing

Organ-On-Chip Technologies With a Modular, Reusable, and Perfusion-Ready Microphysiological System. *Adv Healthc Mater*. 2026;15(1):e02202.

doi: 10.1002/adhm.202502202

137. Koganemaru S, Fuchigami H, Yamashita H, *et al*. Quantitative Analysis of the Concentration of Trifluridine in Tumor Hypoxic Regions Using a Novel Platform Combining Functional Endoscopy and Mass Spectrometry. *Clin Pharmacol Ther*. 2024;115(1):62-70.

doi: 10.1002/cpt.3066

138. Hao D, Lin J, Liu R, *et al*. A bio-instructive parylene-based conformal coating suppresses thrombosis and intimal hyperplasia of implantable vascular devices. *Bioact Mater*. 2023;28:467-479.

doi: 10.1016/j.bioactmat.2023.06.014

139. Sesa M, Holthusen H, Lamm L, *et al*. Mechanical modeling of the maturation process for tissue-engineered implants: Application to biohybrid heart valves. *Comput Biol Med*. 2023;167:107623.

doi: 10.1016/j.compbiomed.2023.107623

140. Chatzopoulou E, Bousaidi N, Guilbert T, *et al*. Multiscale Imaging to Monitor Functional SHED-Supported Engineered Vessels. *J Dent Res*. 2024;103(13):1392-1402.

doi: 10.1177/00220345241271122

141. Barnett SN, Cujba AM, Yang L, *et al*. An organotypic atlas of human vascular cells. *Nat Med*. 2024;30(12):3468-3481.

doi: 10.1038/s41591-024-03376-x

142. Wang D, Chen Z, Wai Kan Yeung A, Atanasov AG. Differences between common endothelial cell models (primary human aortic endothelial cells and EA.hy926 cells) revealed through transcriptomics, bioinformatics, and functional analysis. *Curr Res Biotechnol*. 2021;3:135-145.

doi: 10.1016/j.crbiot.2021.05.001

143. Ryan AR, Cleaver O. Plumbing our organs: Lessons from vascular development to instruct lab generated tissues. *Curr Top Dev Biol*. 2022;148:165-194.

doi: 10.1016/bs.ctdb.2022.02.013

144. Huang YH, Ono A, Sudo R. Advances in In Vitro Vascularization of Engineered Tissues: From Microvessel Formation to Hepatic Tissue Integration. *Regen Ther*. 2026;32:101086.

doi: 10.1016/j.reth.2026.101086

145. O'Connor C, Brady E, Zheng Y, Moore E, Stevens KR. Engineering the multiscale complexity of vascular networks. *Nat Rev Mater*. 2022;7(9):702-716.

doi: 10.1038/s41578-022-00447-8

146. Han S, Kim S, Chen Z, *et al*. 3D Bioprinted Vascularized Tumour for Drug Testing. *Int J Mol Sci*. 2020;21(8).

doi: 10.3390/ijms21082993

147. Liao L, Meng Y, Shi Y, *et al*. Engineering strategies for the clinical translation of organoids. *J Adv Res*. 2026.

doi: 10.1016/j.jare.2026.03.049

148. Fitzsimmons RL, Hudson JE. Endothelial specialization and angiocrine factors are critical for vascularized organoid models. *Cell Rep*. 2025;44(10):116410.

doi: 10.1016/j.celrep.2025.116410

149. Lin K, Xu H, Liu H, *et al*. Bioprinted dressing with symbiotic microbes for oxygen supply and antibacterial therapy for enhanced diabetic wound healing. *J Control Release*. 2026;392:114653.

doi: 10.1016/j.jconrel.2026.114653

150. Ortega JS, Corrales-Orovio R, Ralph P, Egaña JT, Gentile C. Photosynthetic microorganisms for the oxygenation of advanced 3D bioprinted tissues. *Acta Biomater*. 2023;165:180-196.

doi: 10.1016/j.actbio.2022.05.009