

Perfusable Vascular-Network Biofabrication: Channel Formation, Endothelialisation, Leakage, Flow and Remodelling

From printable lumen geometry to functional perfusion and evolving vascular barrier behaviour

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Abstract

Perfusable vascular networks are required for transport through thick engineered tissues, but a hollow printed channel is not yet a functional vessel. Channel formation, endothelial lining, barrier integrity, flow resistance, leakage, thrombogenic response and long-term remodelling are distinct qualification layers. Biofabrication strategies include sacrificial writing, coaxial printing, embedded printing and light-patterned channels, often combined with photocurable supporting matrices. This review organises these approaches around function rather than fabrication modality. It distinguishes geometric patency from hydraulic performance and hydraulic performance from biological vascular function. Particular attention is given to endothelial coverage and junction formation, because a channel can remain physically open while leaking or exposing non-endothelial matrix to flow. Time-dependent remodelling can improve barrier function or cause narrowing, delamination and collapse. A qualification framework is proposed that integrates channel geometry, pressure-flow response, permeability, endothelial coverage, branch connectivity and tissue maturation under perfusion.

Keywords: vascular biofabrication; perfusable channels; endothelialisation; leakage; flow; remodelling; bioprinting

1. Significance and scope

Perfusable networks enable convective transport and are central to thick-tissue biofabrication. Sacrificial writing into dense cellular matrices has demonstrated embedded vascular channels that support long-term perfusion and maturation [1], while more recent coaxial sacrificial writing has generated hierarchically branching multilayered vascular networks with endothelialised lumens [2].

1.1 Corpus boundary

ER-330 owns perfusable vascular-network biofabrication: channel formation, endothelialisation, barrier/leakage behaviour, flow, hydraulic response and remodelling under perfusion. ER-328 owns volumetric-printing physics even when it creates channels, and ER-329 owns organoid/spheroid manufacturing. ER-322 retains GelMA material chemistry; it is not re-owned here when used as a vascular matrix.

2. Channel formation and patency

A channel must remain open after sacrificial-material removal, swelling, handling and connection to tubing or manifolds. Patency should be measured along the full length and across branch points. Nominal CAD diameter is not an adequate descriptor because local constrictions can dominate resistance. [1,2,4]

3. Endothelialisation

Seeding endothelial cells into a lumen does not guarantee a confluent, junction-forming layer. Coverage, orientation, cell-cell junction markers and attachment under flow provide stronger evidence. Where multilayer vessel walls are intended, the location of supporting mural or smooth-muscle cells should also be verified. [2-4]

4. Leakage and barrier function

A perfusable but leaky channel may fail to reproduce vascular transport selectivity. Permeability should be measured with defined tracers and pressure conditions. Leakage through branch junctions, matrix defects or incomplete endothelial coverage should be localised where possible. [3-5]

5. Flow, pressure and hydraulic resistance

Flow rate alone is insufficient because identical flow can require very different pressure if channels narrow or roughen. Pressure-flow curves, calculated resistance and, where relevant, wall shear estimates should be reported. Burst or failure pressure may be needed for mechanically demanding systems. [1,2,4,5]

6. Remodelling under perfusion

Endothelial and supporting cells remodel matrix under flow. The lumen may stabilise, enlarge, narrow or become heterogeneous over time. Longitudinal imaging and repeat hydraulic measurements are therefore more informative than a single endpoint. Remodelling can also change barrier function independently of gross geometry. [2,4,5]

7. Qualification framework

A minimum dataset should include channel dimensions, connectivity, patency, endothelial coverage, permeability, pressure-flow behaviour and time-dependent remodelling. Biological maturation in the surrounding tissue should be interpreted as an additional application outcome, not as a substitute for vascular-function measurements. [1-5]

7.1 Evidence hierarchy and transfer

Vascular-network evidence should connect geometry to hydraulic and biological function. Patency at rest is insufficient: channel dimensions, junctions and surface state must support the intended pressure/flow while the endothelial layer develops barrier function and remodels under shear [1-5].

7.2 Research priorities

Priority studies should report pressure-flow relationships, leakage/permeability, endothelial coverage and stability over repeated perfusion, preferably across a hierarchy of vessel sizes. Quality-assessment reviews identify the lack of common functional benchmarks as a major barrier to comparison [4,5].

7.3 Coupled state variables

Channel geometry, matrix compliance, endothelial state and flow are strongly coupled. A change in diameter alters shear and hydraulic resistance; leakage changes local transport; matrix remodelling can then change diameter again. Static microscopy cannot capture that feedback loop [1-5].

7.4 Decision logic for qualification

Qualification should therefore require a declared hydraulic operating range with structural and barrier endpoints before, during and after perfusion. A channel that is open but leaks excessively, collapses under pressure or loses endothelial coverage has not demonstrated vascular function [2-5].

Table 1. Minimum qualification matrix for perfusable vascular-network biofabrication.

Layer	Measurement	Failure detected
Geometry	diameter map and branch connectivity	local stenosis, collapse or discontinuity
Endothelium	coverage and junction markers	incomplete lining
Barrier	tracer permeability/leakage	nonselective wall or defects
Hydraulics	pressure-flow curve/resistance	narrowing or obstruction
Mechanics	burst/failure where relevant	weak wall or junction
Remodelling	repeat geometry and barrier over time	drift under culture/perfusion

8. Interpretation matrix

Vascular failure analysis should combine geometry, pressure/flow data and barrier measurements. Similar reductions in flow can arise from collapse, thrombosis-like occlusion, swelling, leakage or remodelling, and each mechanism implies a different corrective action [1,2,4,5].

Table 2. Diagnostic interpretation matrix for perfusable vascular-network biofabrication.

Observation	Potential interpretation	Control
Channel is open but tracer leaks rapidly	incomplete endothelial barrier or matrix defect	acellular channel and endothelial coverage map
Flow falls at constant pressure	narrowing, debris or collapse	repeat lumen imaging
Pressure rises with time	remodelling increased resistance	geometry-resistance comparison
Endothelial markers present but barrier poor	coverage/junctions incomplete	junction imaging and permeability
Surrounding tissue matures under perfusion	transport improved, but vascular function not fully proven	retain direct hydraulic/barrier metrics

9. Limitations and evidence gaps

The literature contains many fabrication strategies but limited standardisation of burst pressure, compliance, permeability, patency and long-duration flow testing. Scaling from millimetre channels to microvascular hierarchies and maintaining stable endothelial function remain central evidence gaps [2-5].

10. Conclusions

Perfusable vascular constructs should be judged as fluidic biological systems rather than as hollow geometries. Qualification must demonstrate channel fidelity, endothelial barrier state, pressure-flow behaviour and remodelling together, because failure of any one can invalidate apparent patency [1-5].

References

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Competing interests

The author is Founder, CEO and CTO of 3Dresyns by Resyner Technologies S.L. No comparative product recommendation is made.

Data availability

No new experimental dataset was generated for this review. The analysis is based on the cited literature and the stated engineering scope.