

Cell-Laden Volumetric Bioprinting: Optical Dose, Cell Shadowing, Gelation, Viability and Construct Fidelity

Tomographic projection, nonlinear cure threshold and biological constraints in seconds-scale volumetric fabrication

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Abstract

Volumetric bioprinting forms three-dimensional constructs by delivering many angular light projections into a photosensitive cell-laden volume and solidifying the desired geometry within seconds to tens of seconds. Its speed removes nozzle shear and reduces fabrication time, but it creates a demanding optical-material problem. Cells, proteins and suspended particles can scatter or absorb light; the entire resin volume receives a distributed exposure history; and the printed boundary depends on a nonlinear gelation threshold rather than on a single projected layer. This review focuses on the engineering variables that determine whether a volumetric print is simultaneously geometrically accurate and biologically acceptable. It separates projected optical dose, local accumulated dose, gelation threshold, cell shadowing/scattering, conversion, post-print swelling and viability. A qualification framework is proposed around optical transmission, dose reconstruction, feature fidelity, depth uniformity, cell density and post-print biological function. The central principle is that fast printing does not eliminate dose qualification: it makes three-dimensional dose distribution the primary process variable.

Keywords: volumetric bioprinting; tomographic printing; cell-laden hydrogel; optical dose; scattering; viability; construct fidelity

1. Significance and scope

Volumetric bioprinting was demonstrated for complex living constructs using tomographic visible-light projections, with reported high cell viability and fabrication times of seconds [1]. Later studies have extended the method to heterocellular bone-like constructs and investigated the role of resin composition and laser dose [2].

1.1 Corpus boundary

ER-328 owns cell-laden tomographic/volumetric bioprinting, including three-dimensional optical dose accumulation, cell-induced attenuation/scattering, gel threshold, viability and construct fidelity. It excludes conventional layerwise DLP material optimisation and excludes perfusable vascular-network qualification owned by ER-330 except where a vascular geometry is used only as a volumetric-printing test case. ER-329 owns organoid and spheroid encapsulation, fusion, transport and functional maturation; ER-328 remains limited to volumetric-printing process physics and cell-laden construct fidelity.

2. Tomographic dose accumulation

A volumetric print is generated by the superposition of many angular projections. Each voxel experiences an integrated dose history determined by projection intensity, angle, exposure schedule and optical transport. The desired solid forms where accumulated photochemical response exceeds the material threshold. Dose reconstruction should therefore be three-dimensional rather than inferred from total exposure time alone. [1,2]

3. Cell shadowing, scattering and absorption

Cells and biological macromolecules perturb the optical field. Increasing cell density can change scattering and effective attenuation, while pigments or dense inclusions can add absorption. A resin calibrated without cells may therefore print differently after cell loading. Transmission or scattering measurements at representative cell densities provide an essential transfer control. [1,2]

4. Gelation threshold and material kinetics

Tomographic methods depend on a sufficiently nonlinear relation between accumulated dose and solidification. Oxygen inhibition, inhibitor depletion, photobleaching and diffusion can alter this threshold. The relevant measurand is not merely resin sensitivity but the three-dimensional relationship between local dose, conversion and mechanically persistent gel. [1,3,4]

5. Viability and function

The short fabrication time is favorable, but cells are exposed throughout the volume to light and reactive intermediates. Viability should be assessed immediately and after culture, together with function appropriate to the cell type. A surviving cell population does not prove that projection dose, heat and radical exposure preserved phenotype. [1,2]

6. Construct fidelity

Fidelity should include external dimensions, internal negative features, local overcure and depth uniformity. Swelling after development can mask or exaggerate optical error. Imaging should therefore distinguish the as-cured boundary from the equilibrated hydrated geometry. [1,2]

7. Qualification framework

Minimum reporting includes resin composition, cell type and density, optical transmission, wavelength, projection strategy, reconstructed or calibrated dose, cure threshold, printed feature metrics, swelling, acute viability and later functional assay. This set supports transfer across cell loadings and optical systems. [1-4]

7.1 Evidence hierarchy and transfer

Volumetric-bioprinting evidence must link the reconstructed optical field to the cell-laden resin actually exposed. Cell density, absorption and scattering can change the delivered three-dimensional dose relative to an acellular calibration, while gel threshold and inhibition define whether the reconstructed dose field becomes a faithful solid [1-4].

7.2 Research priorities

Priority studies should measure dose fields or validated proxies across cell densities and construct sizes, then relate them to spatial conversion, viability and post-print function. Reporting only projected energy or nominal reconstruction settings does not establish what individual voxels received [1,2].

7.3 Coupled state variables

The dominant covariance is optical: cell concentration, photoinitiator/absorber content and geometry alter attenuation while the same variables can affect biological tolerance. Increasing dose to recover fidelity can therefore compensate an optical loss at the cost of additional cellular exposure [1-4].

7.4 Decision logic for qualification

Qualification should establish a process window bounded by under-gelation on one side and loss of viability or off-target cure on the other. The window must be demonstrated at the intended construct scale and cell density, not inferred from an acellular small specimen [1-4].

Table 1. Minimum qualification matrix for cell-laden volumetric bioprinting.

Variable	Why it matters	Measurement
Cell density	changes scattering and biological load	cells per volume plus optical transmission
Projection set	defines 3D dose accumulation	angles, intensity and exposure schedule
Resin kinetics	sets nonlinear cure threshold	dose-conversion/gelation calibration
Optical transport	controls depth and blur	transmission/scattering at wavelength
Thermal state	can alter cells and kinetics	bulk temperature during print
Post-print state	swelling changes final geometry	as-cured and equilibrated dimensions

8. Interpretation matrix

Volumetric-printing defects should be mapped back to the reconstructed dose field, resin threshold and cell-dependent optics. A geometric error that grows with cell density points to a different mechanism from an error that follows reconstruction angle or resin conversion [1,2].

Table 2. Diagnostic interpretation matrix for cell-laden volumetric bioprinting.

Observation	Likely mechanism	Discriminating test
Centre undercures at high cell density	cell scattering/attenuation	cell-density transmission series
Fine voids close	dose blur or low threshold margin	3D dose calibration and negative-feature matrix
High immediate viability, later dysfunction	sublethal optical/radical stress	longer functional assay
Outer size correct, internal features wrong	error cancellation/swelling	as-cured tomography plus hydrated geometry
Same resin prints differently across devices	projection optics or irradiance differs	calibrated local dose comparison

9. Limitations and evidence gaps

Tomographic bioprinting has convincing demonstrations but relatively few cross-platform measurements of in-resin dose, cell-dependent optical properties and long-term functional outcomes. Material and reconstruction algorithms also evolve rapidly, limiting direct transfer of numerical exposure windows [1-4].

10. Conclusions

Cell-laden volumetric bioprinting should be qualified as a coupled optical-material-biological process. Fast fabrication is valuable only when the three-dimensional dose field produces the intended gel geometry at the target cell density while preserving viability and subsequent function [1-4].

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.