

Photocurable Organoid and Spheroid Manufacturing: Encapsulation, Nutrient Transport, Fusion and Functional Maturation

Engineering aggregates as living building blocks without confusing placement, survival and tissue function

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Abstract

Organoids and multicellular spheroids are living building blocks whose behaviour cannot be reduced to single-cell viability. They contain pre-established cell-cell contacts, internal diffusion gradients and self-organising programs that can be altered by printing, encapsulation and photocuring. This review examines photocurable manufacturing strategies in which organoids or spheroids are positioned within hydrogels, printed as dense assemblies or embedded in supporting matrices. It separates four distinct engineering outcomes: geometric placement, aggregate survival, fusion/remodelling and functional maturation. Hydrogel stiffness, degradability, mesh size and light dose can support handling while simultaneously restricting expansion or fusion. Nutrient transport becomes increasingly important as aggregate size and packing density rise. A qualification framework is proposed that measures aggregate size distribution, spacing, viability by depth, hydrogel transport, fusion kinetics and organoid-specific functional markers. The central objective is to prevent a construct from being called organoid-printed merely because organoids were deposited: the manufacturing process must preserve or enable the intended higher-order biological function.

Keywords: organoid bioprinting; spheroid; photocurable hydrogel; encapsulation; fusion; mass transport; maturation

1. Significance and scope

Organoid bioprinting combines additive placement with intrinsic self-assembly and has emerged as a route toward complex multicellular tissues [1]. Photocurable matrices can immobilise aggregates rapidly, but the network that provides geometric control also defines the mechanical and transport environment experienced by the organoid.

1.1 Corpus boundary

ER-329 owns photocurable manufacturing with organoids and spheroids as multicellular building blocks, including aggregate identity, encapsulation, transport, fusion and functional maturation. ER-330 owns general vascular-network fabrication and perfusion; vascularisation is considered here only insofar as it constrains organoid/spheroid maturation. ER-328 owns cell-laden volumetric bioprinting and optical-dose fidelity, whereas ER-329 is limited to organoid and spheroid manufacturing and maturation.

2. Aggregate identity and size distribution

Organoids and spheroids should be characterised by origin, cell composition, age, size and distribution. Aggregate diameter directly affects diffusion distance and internal viability. Printing studies should therefore report more than aggregate count or nominal cell number. [1]

3. Encapsulation and mechanical confinement

A photocurable matrix can stabilise aggregate position but also mechanically confine growth. Stiffer or slowly degradable networks may prevent fusion or budding even when cells remain viable. The relevant comparison includes matrix modulus, stress relaxation and degradation, not only polymer concentration. [1,4]

4. Nutrient and oxygen transport

Dense aggregate packing increases oxygen and nutrient demand while the hydrogel imposes an additional transport path. Viability should be assessed spatially, including aggregate cores. Perfusion, channel proximity or vascular co-culture may become necessary as construct dimensions increase. [1,2]

5. Fusion and remodelling

Spheroid fusion is time-dependent and requires cell migration and matrix remodelling. Photocrosslink density can either preserve deliberate spacing or obstruct fusion. Time-resolved imaging should distinguish simple adjacency from true tissue fusion and boundary disappearance. [1,2]

6. Functional maturation

Organoid-specific function can include contraction, secretion, electrophysiology, barrier activity or lineage markers. These endpoints should be measured after printing because survival alone does not demonstrate retained organoid identity. The matrix should be considered part of the maturation environment. [1,4]

7. Qualification framework

Minimum reporting includes aggregate origin and size distribution, loading density, matrix composition and mechanics, dose, transport context, depth-resolved viability, fusion metric and organoid-specific function. This separates manufacturing success from biological maturation. [1-4]

7.1 Evidence hierarchy and transfer

Organoid and spheroid printing evidence must preserve aggregate identity as a process variable. Diameter distribution, cell composition, developmental state and handling history influence transport and fusion before the bioink is considered, so equivalent hydrogel conditions do not make two aggregate populations equivalent [1-4].

7.2 Research priorities

Priority studies should stratify outcomes by aggregate size and maturation state, measure diffusion-limited regions, and distinguish true tissue fusion from simple hydrogel confinement. Functional readouts after printing are more informative than early viability alone [1,2,4].

7.3 Coupled state variables

Aggregate size, spacing, matrix stiffness and degradation are coupled with oxygen/nutrient transport and fusion. Larger aggregates can increase tissue density while also increasing diffusion distance; a stiffer photocured matrix can preserve geometry while delaying coalescence or morphogenesis [1-4].

7.4 Decision logic for qualification

Qualification should therefore declare the starting aggregate distribution, encapsulation state and culture interval, then demonstrate both structural integration and organ-relevant function. A construct that remains viable but fails to fuse or mature is not a successful organoid-manufacturing outcome [1-4].

Table 1. Minimum qualification matrix for photocurable organoid and spheroid manufacturing.

Domain	Minimum measurement	Purpose
Aggregate state	diameter distribution and composition	defines living building block
Placement	spacing and positional error	tests manufacturing control
Matrix	modulus, relaxation/degradation	defines confinement/remodelling
Transport	construct thickness and perfusion/diffusion context	defines nutrient limitation
Viability	spatial/core-sensitive assay	detects hidden aggregate death
Function	organoid-specific endpoint	tests maturation beyond survival

8. Interpretation matrix

Interpretation requires separating aggregate-intrinsic heterogeneity from matrix and process effects. Matched aggregate batches across different cure conditions, and matched cure conditions across size classes, provide the most direct discrimination [1,4].

Table 2. Diagnostic interpretation matrix for organoid and spheroid manufacturing.

Observation	Possible cause	Control
Aggregates survive but do not fuse	matrix too stiff/nondegradable or spacing too large	mechanics/degradation and spacing series
Core necrosis increases after printing	transport path or aggregate growth	size-resolved oxygen/viability mapping
External construct shape stable	does not prove organoid maturation	functional organoid assay
Fusion occurs with large shrinkage	cell compaction/remodelling changes geometry	time-resolved geometry and matrix mechanics
Different organoid lots behave differently	developmental state differs	age/composition-matched controls

9. Limitations and evidence gaps

Organoid/spheroid biofabrication is heterogeneous in cell sources, aggregate size, maturation stage, matrices and functional assays. Long-term comparisons of fusion, perfusion, innervation and organ-specific function remain limited, and early viability is often a weak surrogate for maturation [1-4].

10. Conclusions

Photocurable organoid and spheroid manufacturing should be qualified around the multicellular building block, not only the hydrogel. Aggregate identity, transport, fusion and functional maturation must remain connected to the encapsulation and cure history used to assemble the final construct [1-4].

References

1. Huang MS, Christakopoulos F, Roth JG, Heilshorn S. Organoid bioprinting: from cells to functional tissues. *Nature Reviews Bioengineering*. 2025;3(2):126-142. doi:10.1038/s44222-024-00268-0.
2. Skylar-Scott MA, Uzel SGM, Nam LL, Ahrens JH, Truby RL, Damaraju S, Lewis JA. Biomanufacturing of organ-specific tissues with high cellular density and embedded vascular channels. *Science Advances*. 2019;5(9):eaaw2459. doi:10.1126/sciadv.aaw2459.
3. Lim KS, Galarraga JH, Cui X, Lindberg GCJ, Burdick JA, Woodfield TBF. Fundamentals and Applications of Photo-Cross-Linking in Bioprinting. *Chemical Reviews*. 2020;120(19):10637-10669. doi:10.1021/acs.chemrev.9b00812.
4. Keshavarz Afshar A, Mirshafiei M, Saberi A, Yazdian F, Rashedi H, Rahdar A, Baino F. From light to life: Photocrosslinkable bioinks and their role in 3D bioprinting for shaping future regenerative medicine. *Bioprinting*. 2026;57:e00487. doi:10.1016/j.bprint.2026.e00487.

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.