Using Bioprinting to Achieve Enhanced Persistence, Consistency in Cell Loading across Scaffolds, and Long-Term Sustained Release of Cells from Scaffolds

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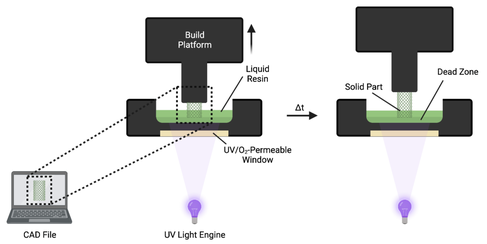
INTRODUCTION

Glioblastoma (GBM) is a highly invasive, incurable brain cancer with a median survival term of 15 months. Many cancer cells remain in the brain even after surgical removal of the main tumor mass. We can turn NSCs into targeted drug carriers, allowing them to go on and rid of GBM cells that remain in the brain after tumor removal.

We hypothesized that by using the bio-printing strategy, we will achieve enhanced persistence, consistency in cell loading across scaffolds, and long-term sustained release of cells from the scaffold. This will be done by designing scaffolds using Continuous Liquid Interface Production (CLIP), a photochemical process that converts liquid plastic resin into solid parts using UV light. Improving the long-term survival of therapeutic NSCs using CLIP scaffolds as protective barriers will lead to more effective treatment of GBM and increased life expectancy for GBM patients.



A schematic of the continuous liquid interface production (CLIP) process.

METHODS

The overall goal of this project is to make new designs and find their impact on scaffolds' degradation rate.

- Printing resin was prepared and printed using the formulation and printing parameters listed in the tables
- The printed scaffolds were blotted dry w/ a kimwipe and their initial "wet" weights were measured
- The printed scaffolds were suspended in a solution of 0.5 mg/mL collagenase and their "swollen" weights were measured at different time points
- The "dried" weights of these scaffolds were measured 7 days after measuring their swollen weights
- % swelling was calculated (swollen weight at time point/ initial "wet" weight)
- % degradation was calculated ([initial dry weight - dry weight at time point]/initial dry weight)

Substance	Weight % and Effect
PEGDA	14%, offers structural integrity and rigidity to the scaffolds
GelMA	10%, provides cell adhesion sites to promote cell survival
LAP	0.5%, a water soluble photoinitiator which catalyzes the polymerization of PEGDA and GelMA
ED	1.5%, UV absorber that improves resolution
Citric acid	5%, delays the physical gelation of GelMA

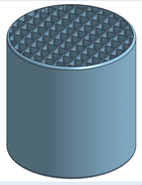
Printing Parameters	
Speed (mm/hr)	48
Light (mW/cm2)	10
Base delay (s)	10
Base exposure (s)	3
Slice thickness (μm)	1

Tables of resin formulation ingredients and printer settings used during 3D-printing process.

RESULTS

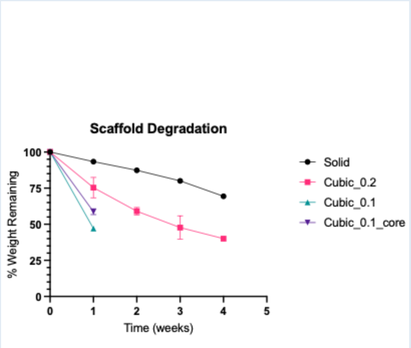
Solid cylinder
- r = 0.6 mm, h = 0.6 mm
- Volume: 169.47576 mm³
- Surface area: 167.66237 mm²

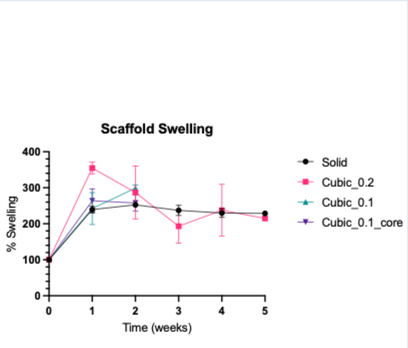
Cylinder w/ cubic planar lattice
- 0.12 mm struts
- r = 0.6 mm, h = 0.6 mm
- Volume: 68.87597 mm³
- Surface area: 1039.09443 mm²

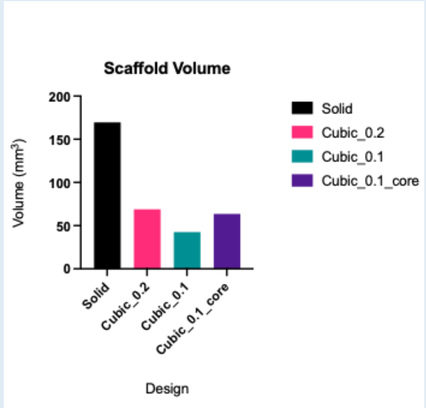


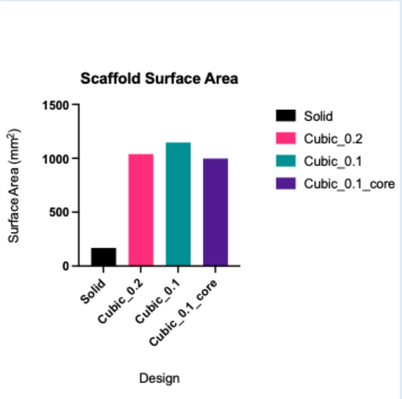
Cylinder w/ cubic planar lattice
- 0.06 mm struts
- r = 0.6 mm, h = 0.6 mm
- Volume: 42.54655 mm³
- Surface area: 1146.47971 mm²

Cylinder w/ cubic planar lattice
- 0.06 mm struts
- 0.66 mm thick hollow, rectangular, prismatic core
- r = 0.6 mm, h = 0.6 mm
- Volume: 63.5372 mm³
- Surface area: 997.97346 mm²





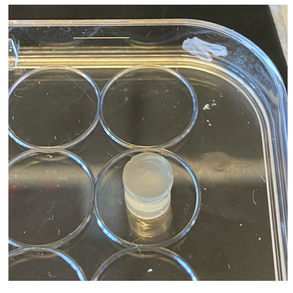




CONCLUSION

We used scaffolds created with CLIP to control the release of embedded cells over time. The design and consequently the volume and surface area of these scaffolds were varied and the trend is as follows: as surface area increases, scaffold degradation increases. There is no discernible trend in scaffold swelling as the volume or surface area is changed.

Improving the long-term survival of therapeutic NSCs using CLIP scaffolds as protective barriers will lead to finer treatment of GBM and increased life expectancy for GBM patients. In the future, we hope to develop more designs and different formulations to maximize persistence.



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