Novel Portable Perfusion System Enhances Tissue Viability for Surgical Applications

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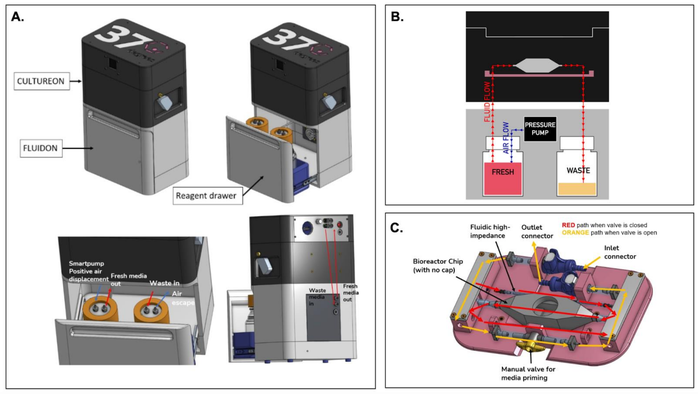
Background

Methods for preserving tissues for transplantation currently revolve around

- cold storage (CS)
- ex-vivo perfusion (EVP).

EVP enhances organ viability compared to CS[1]. Many kidney EVP systems are portable, but there is a need for portable systems for larger organs[2]. Upscaling modular perfusion systems has the potential to improve organ and tissue viability pre-implantation. This study tests the efficacy of the FluidON–an integrated portable system prototype that perfuses tissues in standard incubation conditions with an exchangeable bioreactor.

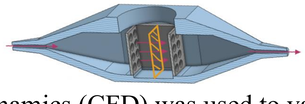
Methods



The flow inside the bioreactor's sample-holding region was designed to perfuse at flow velocities similar to interstitial fluid. It was characterized using the following laminar flow-dependent equations.

For Reynolds number (Re) < 2000 flow is laminar.

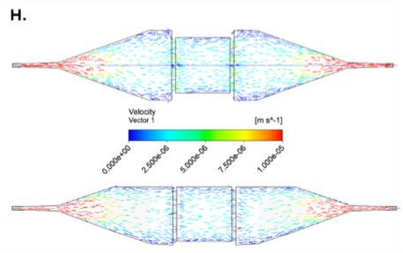
- $v_{avg} = V/A_c$
- $Re = \rho D v_{avg}/\mu$



Computational fluid dynamics (CFD) was used to validate our calculations and visualize the flow velocity profile. The volumetric flow rate (V) was measured by perfusing DMEM for 10 minutes, weighing the perfused fluid, and dividing the mass flow rate by the media density.

Fibrin gels embedded with mMSC/mEC spheroids (fibrin patches) were cultured in the FluidON and static conditions. Flow Cytometry was used to evaluate the fibrin patch viabilities after 24 hours of perfused and static culture. mECs secrete serine proteases that degrade fibrin gel. To test ability for molecular transport between the bulk flow and fibrin patches to clear endogenous cytokines, ImageJ was used to compare the degradation of static and perfused fibrin patches to samples with Aprotinin —a serine protease inhibitor

Results



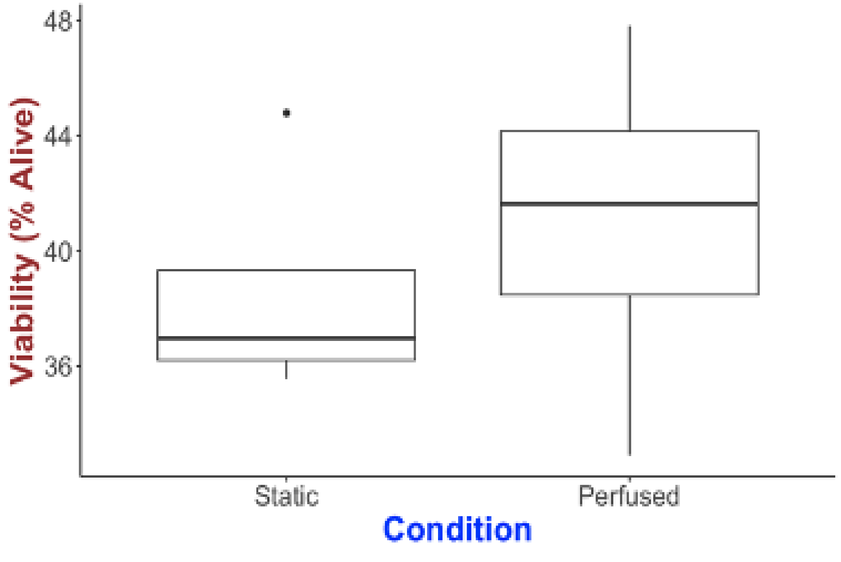
At 1 psi, v_{avg} = 1.69 ± 0.83µm/s which is 2.8 times interstitial flow velocities (0.34-0.6µm/s)[3]. CFD data shows a maximum flow velocity ($v_{max} = 2 \times v_{avg}$) of 3-4 µm/s at 1 psi, as predicted.

Flow Characterization

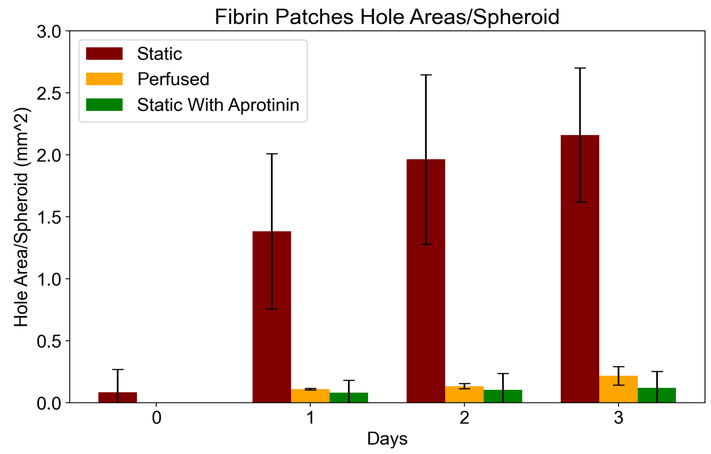
PSI	V (µL/s)	v_{avg}	Re
1	0.40 ± 0.19	1.69 ± 0.83	0.80
2	0.81 ± 0.0083	3.5 ± 0.035	3.30
3	1.1 ± 0.040	4.6 ± 0.17	4.34

After culturing for 24 hours (n=4)

- Perfused fibrin patches were 40.99±6.22% alive
- Static fibrin patches were 38.56±4.22% alive



Perfusion and aprotinin both significantly reduced hole sizes



Conclusion

The FluidOn was able to perfuse model tissue samples with flow velocities at the µm/s scale, but still higher than interstitial flow. The perfused tissue samples were more viable than the static controls, but their difference was not statistically significant (p = 0.55). The CulterON was able to flush serine proteases out of the tissue sample, demonstrating how molecular transport between the sample and bulk flow may allow for clearance of damage-associated molecular patterns. Portable perfusion systems have the potential to impact surgical practices with the ability to culture and maintain patient samples in the lab and/or sustain samples and tissues during transportation.

Sources

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