Micropuncture Vascularization of Intraoperative Bioprinted Scaffolds

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Purpose

- Tissue loss is a major cause of worldwide morbidity and mortality, and plastic surgeons are tasked with its correction.
- Intraoperative bioprinting (IOB) represents the next generation of reconstructive surgery.
- Although promising, translation and scalability are limited by poor recipient vascularization.
- Recently, we described a microsurgical approach which rapidly vascularizes an adjacently placed scaffold.[1]
- In micropuncture (MP), the recipient blood vessel wall is precisely disrupted to provide an immediate route for cell extravasation.
- We **hypothesized** that MP integration with IOB would improve scaffold vascularization.

Methods

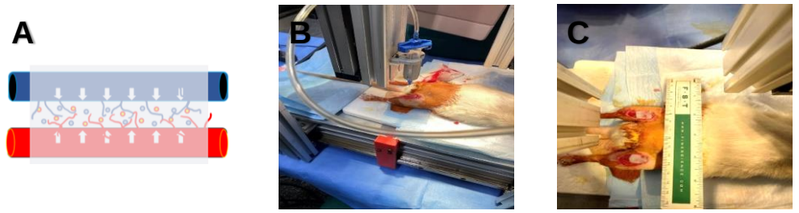

Figure 1. Micropuncture schematic and actual intraoperative bioprinting.

- MP **(Fig. 1A)** was tested in the rat femoral artery and vein (n=5) with control animals receiving no MPs (n=5).
- Immediately after, an extrusion bioprinter was brought into the operative field **(Fig. 1B)** and deposited a collagen-based scaffold directly over the femoral vessels **(Fig. 1C)**.
- At Day 10 animals underwent *in situ* fluorescence angiography.
- Samples were analyzed using whole mount angiography and histology.
- Vessel metrics were analyzed using artificial intelligence.
- Endothelial (EC; CD31) and nucleated cells (DAPI) were quantified.

Results

- Increases in EC and nucleated cell counts was seen in MP scaffolds **(Fig. 2**).
- Vascular density was increased 2-fold in MP scaffolds **(Fig. 3)**.
- Capillary network expansion was attributed to increased branch numbers within MP scaffolds resulting in more vascular loop formation (**Fig. 4**).
- Increases in tube length and diameter were also seen in MP scaffolds (**Fig. 4**).

Endothelial Cell Quantification

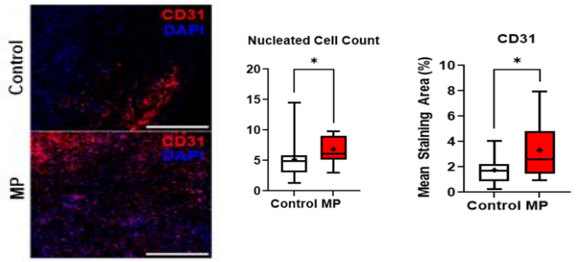

Figure 2. Endothelial (CD31) and nucleated cell (DAPI) staining at Day 10 (*p <0.05).

Vascular Quantification

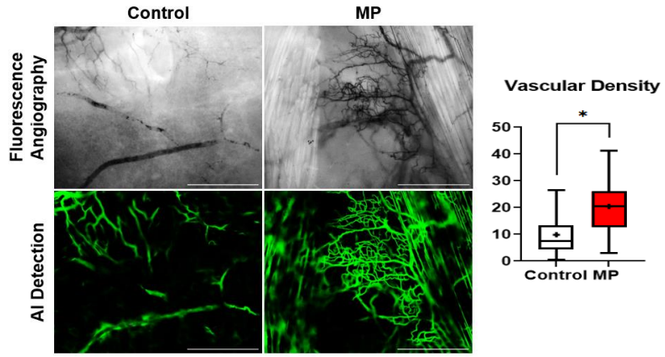

Figure 3. Whole mount angiograms showing vascular density at Day 10 (*p <0.05).

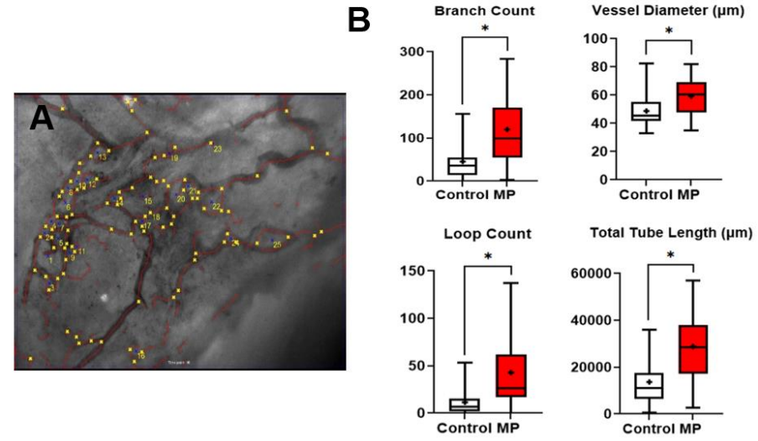

Figure 4. Artificial intelligence detection and quantification.

A) Detection image with the “blue x” representing loop formation and total tube length shown by “red lines”.

B) Vascular metrics including branches, loops, diameters, and total tube length.

Conclusions

- Here we demonstrate the simple integration of microsurgery with IOB as a platform approach for engineered tissue vascularization.
- MP appears to be suitable with collagen-based bioinks and creates a pro-angiogenic microenvironment.
- Ongoing work will determine the feasibility of also introducing cells into the bioprinted scaffold with the long-term goal of building in-situ flaps for tissue reconstruction.

References

1. Hancock, P., Koduru, S., Sun, M. and Ravnic, D., 2021. Induction of scaffold angiogenesis by recipient vasculature precision micropuncture. *Microvascular Research*, 134, p.104121.