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Arteriosclerosis, Thrombosis, and Vascular Biology

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Abstract 550: Magnetic Nanoparticle-mediated Targeting Of Endothelium To Address Restenosis In A Bioprinted *In Vitro* Model Of Pulmonary Arteries

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Originally published 30 Nov 2022 | https://doi.org/10.1161/atvb.42.suppl_1.550 | Arteriosclerosis, Thrombosis, and Vascular Biology. 2022;42:A550

Abstract

Vascular restenosis is a major complication in recanalized arteries. Nanoparticles (NPs) have shown great promise as delivery systems in advancing strategies to treat such vascular anomalies. By enabling precise targeting, NPs can overcome the challenges of low drug efficacy and off-target effects. Here we present a biomimetic *in vitro* platform comprised of 3D bioprinting, nanomaterials, and perfusion technologies, to study the use of NP targeting to address endothelial overgrowth. We bioprinted 3D vascular channels at high fidelity, using gelatin methacrylate as bioink, with artery-like stiffness. Human endothelial cells (ECs) were used to endothelialize the printed channels. GFP-labelled superparamagnetic iron oxide NPs (SPIONs), loaded with the *Rapamune* anti-proliferative drug, were perfused through the bifurcated artery model at physiological rate. Computational modeling predicted greatest level of alterations in wall shear stress in the conduit's junction with the artery, identifying this region prone to restenosis. A neodymium disc magnet was embedded in the printed tissue to attract the therapeutic SPIONs to the region of high risk. *In vitro* dynamic culture was conducted for 2 wks. We assessed cell viability, proliferation, and function using AlamarBlue and immunohistochemistry. Results showed

significant targeted effect of NP delivery in reducing EC overgrowth. This platform enables design of precise targeting of therapeutics to treat a variety of cardiovascular diseases at a high spatial and temporal control.

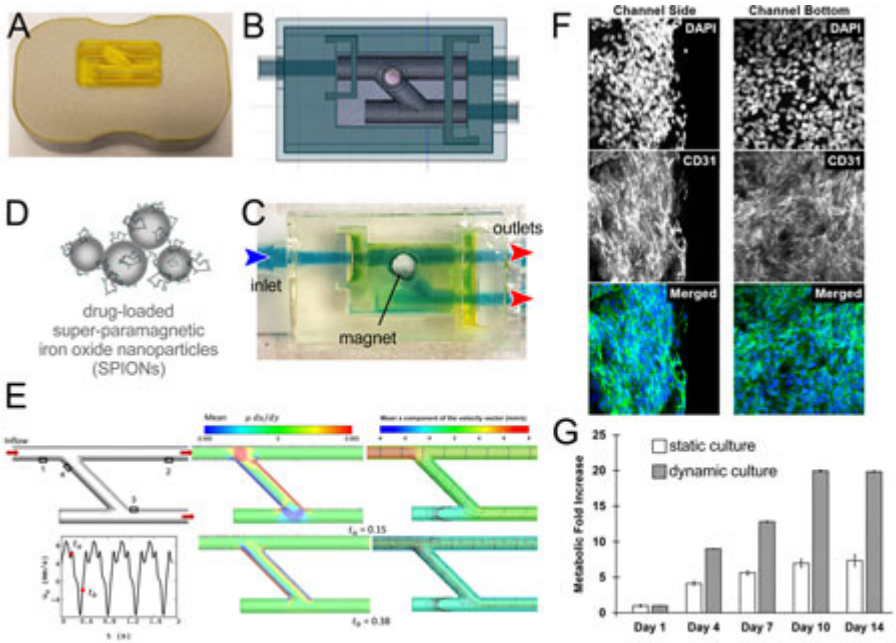

Figure 1. A 3D model of anastomosed arteries is bioprinted (**A**), housed in a customized perfusion chamber (**B-C**), and perfused with media containing drug-loaded SPIONs (**D**). **E**: CFD modeling assessed flow hemodynamics in 3D artery model. **F-G**: Vascular constructs are seeded with endothelial cells and cultured under flow. The effect of magnetic targeting of therapeutic SPIONs on EC function was evaluated by IHC (**F**) and AlamarBlue (**G**) assays.

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Footnotes

Author Disclosures: For author disclosure information, please visit the AHA Vascular Discovery: From Genes to Medicine 2022 Scientific Sessions Online Program Planner and search for the abstract title.

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