Enhanced Vascularization of the Subcutaneous Space using a Vascular Regenerative Biomaterial

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Statement of Purpose:
A major challenge in regenerative medicine is the development of an adequate blood supply for transplant survival. The subcutaneous space has been proposed as a promising site for the transplantation of therapeutic cells such as islets of Langerhans. However, the implantation of islets in the subcutaneous space leads to cell hypoxia that limits the therapeutic effect (insulin secretion). Rather than implanting the islets in the unmodified subcutaneous space, we are investigating the biomaterial induced pre-vascularization of the implantation site prior to cell transplantation.
Materials based on poly-methacrylic acid (poly-MAA), have been shown to enhance the vascularization of the subcutaneous space[1-3] without the need for biological agents such as cells, drugs or growth factors. This study assesses the benefit of using a poly-MAA-based material to pre-vascularize the subcutaneous space.
Methods: MAA-coated polypropylene (PP) meshes of a type similar to that used in a pouch for islet delivery were investigated. The PP meshes were pre-treated by 5mins air plasma treatment, 1min 12M HCl and 5mins plasma treatment, in order to increase PP wettability. Once pre-treated, the meshes were coated with 3 layers of 40% methacrylic-acid-co-isodecyl acrylate (IDA) using a spray coating method. The 40% MAA-co-IDA was synthetized using a free radical polymerization with benzoyl peroxide as an initiator[4]. Mesh surfaces were characterized by SEM and XPS. The 1 cm^2 meshes were implanted in the dorsum of C57BL/6J mice. The meshes were explanted and processed by histochemistry using CD31 (for vessels), smooth muscle actin (vessel maturity) and Masson's trichrome.
Results: A smooth coating that followed the architecture of the mesh was homogeneously deposited by the spray coating technique. Cryo-sectioned meshes (and DAPI staining) showed an ~20µm coating thickness (Figure 1). Vessel density at day 7 was significantly increased in the MAA-coated group compared to the non-coated group (Figure 2).
Conclusions: Simple coating of PP meshes with MAA-based material can be used to pre-vascularize the subcutaneous space before cell transplantation. The next step will involve implanting pancreatic islets in the MAA induced pre-vascularization site and assessing islet survival and function.
References:
1. Martin, DC, *J.Biomed.Mater.Res.A* 93, 484–92 (2009).
2. Fitzpatrick LE, *Biomaterials* 33, 5297–5307 (2012).
3. Butler MJ, *J.Biomed.Mater.Res.A* 82, 265–273 (2007).
4. Wells, LA, *Biomater.Sci.2,* 1768–1778 (2014).

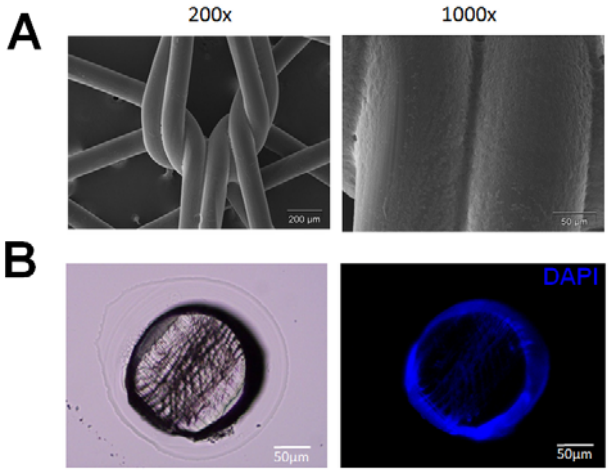

Figure 1. Spray coated mesh characterization. (A) SEM revealed a homogeneous topography that follows the mesh architecture at different magnifications when the mesh is coated with 3 layers of MAA-co-IDA. (B) The coated meshes were embedded in cryo-embedding media, cryo-sectioned and stained with DAPI. The 3-layer coating thickness was 20µm.

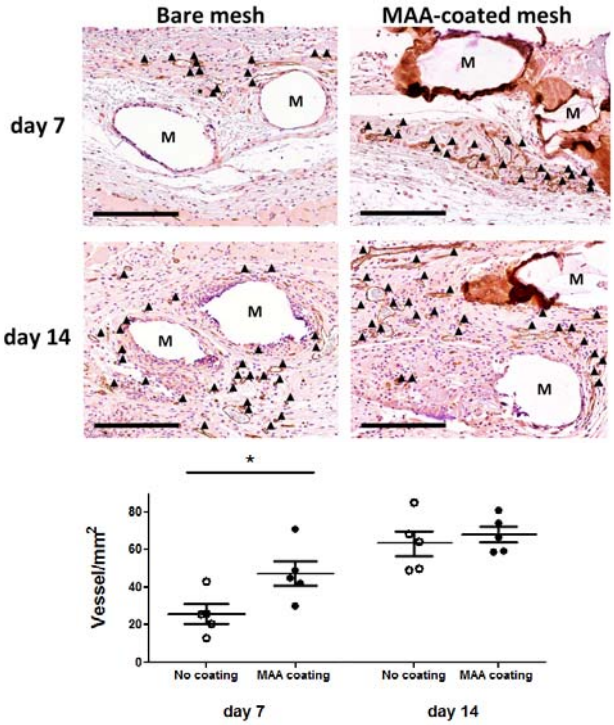

Figure 2. Cross-section of MAA-co-IDA coated or non-coated mesh explants at day 7 and 14. The sections were stained for vessels (CD31 marker) and Masson's trichrome. A two-fold increase in vessel density was seen with the MAA coated mesh at day 7. Arrows indicate the vessels and stars represent mesh filaments. Scale bar: 200µm. M: Mesh. Triangle: vessel.