IN VIVO RESPONSE TO TISSUE ENGINEERED ELECTROSPUN SCAFFOLDS WITH DRUG DELIVERY AND ENHANCED POROSITY

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ABSTRACT

The desired healing response to electrospun scaffolds in tissue engineering is often limited by poor ingrowth due to insufficient porosity, thrombogenicity, lack of vascularisation and/or excessive inflammation[1]. This study aimed at increasing structural porosity and incorporating/delivering anti-thrombotic/angiogenic (heparin) and anti-inflammatory (dexamethasone) agents.

Porosity enhancement techniques were explored using two different approaches i) electrospinning polyurethane (PU) with concomitant electrospraying of soluble microparticles, which were subsequently removed to increase scaffold interconnectivity and ii) electrospinning polyesterurethane (PEU) at low collecting temperatures. Dexamethasone was incorporated by simple admixture, however, heparin required chemical modification to achieve solution solubility. Release rates were determined *in vitro*, followed by thrombogenicity (thromboelastography) and cytotoxicity (cell viability) assessments of modified/unmodified heparin prior to incorporation and after elution. Finally, *in vivo* responses were evaluated in a subcutaneous model (24 rats) for up to 12 weeks.

Porosity was increased from 79 to 90% ($P<0.001$) and 50 to 83% ($P<0.001$) for the PU and PEU scaffolds respectively. Both drugs showed an initial burst delivery in the first week (dexamethasone 36%, heparin 50%) followed by a linear release over a 12-week period (78%, 60%). Heparin, after modification, retained its anti-thrombotic properties and showed no difference in cytotoxicity ($P>0.1$). High porosity PU scaffolds achieved full tissue ingrowth while conventional scaffolds allowed <42% ingrowth after 12 weeks. The localised delivery of heparin resulted in additional blood vessel formation after 12 weeks ($P<0.01$). Dexamethasone did not significantly reduce inflammatory response ($P>0.3$).

Combined electrospinning/spraying produced highly porous scaffolds that have the potential to enhance healing. Dexamethasone or heparin can be incorporated and eluted from low temperature spun structures at controllable rates. Moreover, localised delivery of heparin further improves vascularisation. This study alligns with requirements for developing tissue regenerative vascular grafts where anti-thrombogenicity and increased vascularisation are desired.

Acknowledgement: Helen Ilsley for histological preparations and our sponsors: National Research Foundation (NRF), Medical Research Council (MRC IUCHRU) of South Africa and Ab Medica (Italy).

References:

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