EVENT ABSTRACT

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In vitro and in vivo assessment of magnetically actuated biomaterials for tendon regeneration

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Introduction: Tendon regeneration can be undermined by the formation of fibrous adhesions (scar tissue) between the healing tendon and the surrounding tissues. Scarring is associated with the recruitment of inflammatory cells such as macrophages and mast cells[1]. To tackle this issue we advocate the implementation of postoperative rehabilitation programmes to control inflammation levels and scarring, ensuring this way better clinical outcomes. In this study we propose the insertion of a magnetic responsive biomaterial between the healing tendon and the surrounding tissues. We hypothesise this material in combination with a magnetic field will modulate inflammation and reduce fibrous adhesion. Here we present the results from the first stage of our study, where magnetic biomaterials were tested subcutaneously to evaluate the inflammatory response and the ability of this material to control the presence of fibrous tissue.

Methods and Materials: Starch poly-caprolactone (SPCL) membranes were obtained by a solvent casting method and magnetic SPCL by a solvent casting method followed by doping iron oxide particles (Micromod) at a concentration of 1.8 (magSPCL-1.8) or 3.6 (magSPCL-3.6) w/w (%). Magnetic saturation values of casted membranes were characterised by vibrating sample magnetometer (VSM). Human adipose derived stem cells (hASCs) were seeded at a density of 10.000 cells/cm2 and cultured in α-MEM medium (plus 1% antibiotic, 10% serum) under static or magnetic conditions (Nanotherics 2Hz, 350 mT) for 1, 3 and 7 days. At these time points cell metabolic activity and proliferation was assessed under in vitro conditions by the alamarBlue®, and Quant-iT™ PicoGreen® assays, respectively. The presence of reactive oxygen species (ROS) was estimated through the DCFDA assay. For the in vivo experiments, male Wistar rats were subcutaneously implanted with SPCL and magSCPL and divided in two groups: unstimulated and magnetic stimulated (2 hours/day, 75Hz). This study was conducted for 9 weeks with intermediate time points at week 1 and 4. After sacrifice of the animals, the explants were histological analysed by hematoxilin and eosin to enumerate the presence of mast cells and measure the thickness of the fibrotic capsule surrounding the implants.

Results: VSM analysis demonstrated that magnetic SPCL exhibited satisfactory magnetic saturation values (above 0.049 emu/g)[2]. Proliferation remained unchanged in magSPCL-1.8 compared to SPCL, either under static as magnetic conditions. Results from the Quant-iT™ PicoGreen® assay shows that cell proliferation in magSPCL-3.6 was significantly lower when compared with SPCL ($p<0.05$). With regard to ROS production, the DCFDA assay demonstrated that magnetically stimulated magSPCL had fewer molecules than SPCL ($p<0.05$). Under in vivo conditions, magSPCL-1.8 membranes from non-stimulated rats presented higher number of mast cells 4 weeks post-implantation when compared with week 1 ($p<0.05$) and prevented thickening of the fibrotic capsule when combined with magnetic stimulation at every time points ($p<0.05$).

Conclusions: The performance of magnetically actuated magSPCL-1.8 was the most satisfactory under in vitro and in vivo conditions. Due to the promising nature of this formulation, future work will be carried out to test magSPCL-1.8 in injured tendon models. Magnetic responsive biomaterials are a promising field of investigation in tissue engineering and regenerative medicine and our findings underpins its biomedical potential in tendon healing.

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