Nanostructured Mesoporous Silicon / Polymer Composites as Ophthalmological Platforms: An In Vivo Assessment

Jeffery Coffer,[1] Dongmei Fan,[1] Keryn Williams,[2] Kirsty Marshall,[2] Sonja Klebe,[2] Nicolas Voelcker,[2] Armando Loni,[3] and Leigh Canham[3]

Texas Christian University,[1] Flinders University,[2] PSi Medica Ltd, (now with Intrinsiq Materials Ltd.)[3]

Statement of Purpose: Semiconducting mesoporous silicon (pSi) is currently receiving extensive evaluation as a biomaterial, both as a sensing platform and therapeutic vehicle. For the latter, the fabrication of composite materials containing both this resorbable porous crystalline solid along with established biopolymers such as polycaprolactone (PCL) has recently shown merit in applications such as tissue engineering scaffolds.[1] However, a much broader range of applications in areas such as drug delivery is envisioned, and in this study we extend our assessment of this combination to the eye, with an *in vivo* evaluation of biocompatibility using a rat model. Microfibers of PCL containing totally encapsulated PSi particles in two different concentrations (6 and 20%) were fabricated as non woven fabrics; given the dependence of Si particle dissolution kinetics on porous Si surface chemistry, two different types of porous Si particles were evaluated, as prepared and surface oxidized. These silicon fabric samples were implanted beneath the conjunctiva of rat eyes and followed for 8 weeks. Importantly, we found that the implanted composite containing the nanostructured mesoporous Si and the polymer did not cause visible infection or inflammation, and did not erode the ocular surface.

Methods: Composite fibers comprised of encapsulated mesoporous Si (67% porosity) and polycaprolactone were prepared by electrospinning technique that utilizes a fixed amount of Si by mass and a 20 wt% solution of PCL (60,000 mol. wt.) in chloroform placed in a 5 ml glass syringe, connected to a 21 gauge stainless steel needle, with an applied potential of 20 kV used. To ideally slow down pSi dissolution kinetics, the as prepared (hydride-terminated) porous Si was oxidized by a thermal anneal at 600^{o}C in oxygen for 60 min for individual fiber samples at Si concentrations of both 6 and 20%.

All samples were sterilised by overnight immersion in 70% EtOH and rinsed in sterile ophthalmic BSS before implantation. Pieces of each fabric (~2 x 2 mm^2) were sutured under the superior, temporal and inferior conjunctiva of the right eye of each rat, and monitored at the operating microscope weekly. Three rats were implanted with each of the four composite materials. After 8 weeks, rats were euthanised, and the enucleated eyes fixed in buffered formalin at room temperature, dehydrated, embedded in paraffin wax, sectioned at 8 micron on a microtome, and stained with H&E for end-point histology.

Results: Use of the electrospinning method described above produces composite fibers with an average width in the 5-8 micron range (Fig 1). The presence of silicon in the fiber is readily detected at the wider portions by energy dispersive x-ray analysis (not shown).

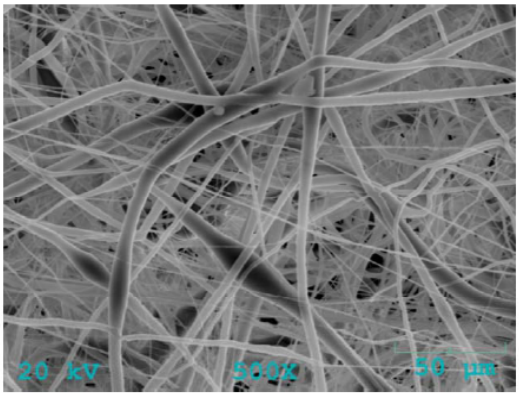

Figure 1. Scanning Electron Micrograph of PCL microfibers containing encapsulated pSi particles (6 wt. %).

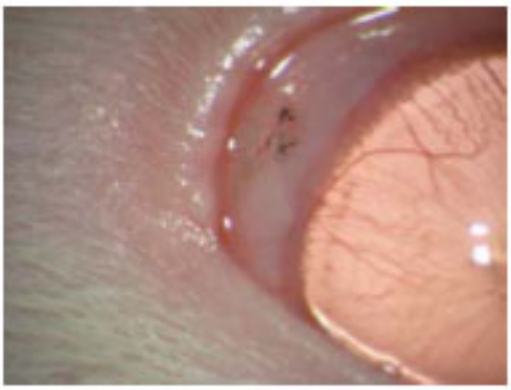

Figure 2. Temporal view of Rat 1 at Week 8 (containing a fabric of 6 wt.% of surface oxidized pSi particles in PCL).

Little inflammation or evidence of vascularization was observed around any implant. More tissue reaction was seen around the sutures used to hold the implant in place. Histologically, a thin fibrous capsule was observed around the implant, with some histiocyte infiltration but little neovascularization. The surrounding tissue appeared normal. Composite fibers containing the surface-oxidized porous Si particles appeared to perform better, as the capsule was thinner. There was no significant difference in the response between the 6% and 20% porous silicon.

Conclusions: The composite materials were well tolerated following implantation into the rat subconjunctival space. After 8 weeks, histology indicated a minimal foreign-body reaction.

References: 1. Whitehead, M.; Fan, D.; Mukherjee , P.; Akkaraju, G.; Canham, L.T.; and Coffer, J.L. Tissue Engineering A, 2008, 14(1): 195-206.