Potential Neural Interface Material Printed via Projection Micro-StereoLithography (PμSL)

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Statement of Purpose: Neural interface devices bridge the peripheral nervous system (PNS) and an external device, allowing for electrical signals to control prosthetic devices as well as augment nerve regeneration. Although many neural interfaces have been explored and implemented, a major limitation of these materials lies in the mismatch in material's elastic modulus and the modulus of the PNS (~0.45 MPa).[1] The mechanically incompatibility of high moduli materials (ie. silicon and polyimide) has lead to limited device lifetime and the need to develop a more compatible peripheral nerve interfaces (PNI).[2] Our research focuses on the development and application of projection micro-stereolithography for the fabrication of flexible conducting polymeric materials which will overcome the limitations of the current state of the art neural interfaces.

Methods: Projection micro-StereoLithography (PμSL): PμSL apparatus and technique was used as described previously.[3] Substrate Fabrication: A solution of phenylbis(2,4,6-trimethylbenzoyl)-phophine oxide (BAPO) (0.03g) was dissolved in 300μl of chloroform and added to methacryloxypropyl terminated polydimethylsiloxane (PDMS) (1g) and vortexed briefly. A 1x1" silicon chip was placed on the printing stage of the PμSL apparatus where the PDMS/BAPO solution (150μL) was added and allowed to self-level (2 min) prior to exposure to light from the projector. The substrate and polymer was exposed (60 sec) and developed in toluene followed by a water rinse. The structure was further cured (5 min) under a UV source (λ= 365nm.) Prior to implantation, substrates were sterilized through ethylene oxide treatment.
Substrate Implantation: The model used was the rat hind-limb peroneal nerve in 8 month old Sprague-Dawley male breeder rats. Rats were anesthetized (intramuscularly injection) and their left thigh shaved to gain access to the peroneal nerve proximal to the knee. The substrate was implanted in between the cut ends of the nerve and the ends of the nerves sutured with 11-0 nylon.

Results: Substrates with an average pore size of 221±1 μm and a pitch of 527±1 μm (Figure 1A) were produced using PμSL. Mechanical properties of the porous material were assessed to confirm that the crosslinked PDMS substrates would more closely match the modulus of the nerve. The modulus was determined to be 10.7±0.4 MPa at 37°C. Biocompatability and neuronal growth was assessed *in vivo* in the peroneal nerve of rats. An H&E stained cross section of a substrate 3 weeks post implantation (Figure 1B) shows nerve ingrowth through the pores of the implant as well as a minimal immune response. In addition, multi-walled carbon nanotubes (MWCNTs) at various weight percent's have been patterned using the same PμSL technique in order to make the PDMS conductive (Figure 2). The addition of MWCNT required no modifications to the solution itself, but did require an increase in exposure time from 60 sec to 120 sec.

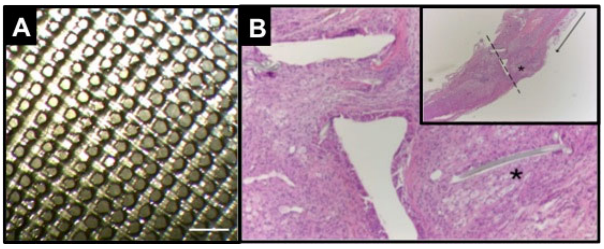

Figure 1. (A) Optical image of porous PDMS PμSL printed sheet, and (B) and H&E histology after 21 days in the rat peroneal nerve, where the inset is a low magnification image of the nerve-implantation site (nerve fibers (+), nylon suture (*), plane of implant (- -) and proximal to distal (↙)).

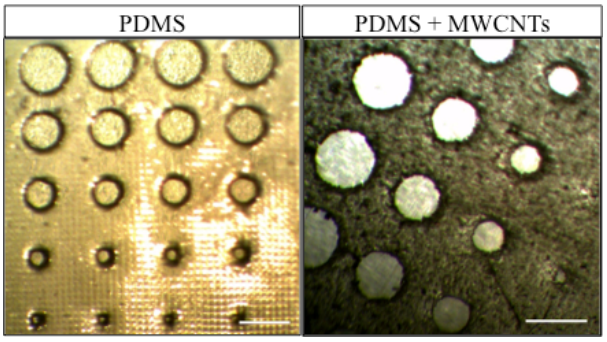

Figure 2. Printed substrates by PμSL of PDMS (left) and PDMS loaded MWCNTs (10wt%)(right). Scale bar = 1mm

Conclusions: Projection micro-StereoLithography was used to rapidly and inexpensively produce patterned PDMS substrates with well-controlled pore sizes and geometries. PDMS shows promise as a suitable interface material because of the desired biocompatibility and mechanocompatibilty to peripheral nerve tissue. Ongoing research is being conducted to examine the short and long term electrical communication between nerves and the interfaces *in vivo*. In addition, the inclusion of bioactive factors to augment nerve regeneration is being explored.

References: (1)Rydevik, BL *et al* (1990) J Orthop Res **8**:694 (2)Normann, RA (2007) Nat Clin Pract Neurol **3**:444 (3)Cicotte, KN *et al* (2012). MRS Proceedings **1418**