JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 45 (2015) 83–89

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Research Paper

Biocompatibility evaluation of a thermoplastic rubber for wireless telemetric intracranial pressure sensor coating

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ARTICLE INFO

Article history:
Received 31 October 2014
Received in revised form
21 January 2015
Accepted 26 January 2015
Available online 3 February 2015

Keywords:
Cerebral cortex
Brain implants
Thermoplastic rubber
Reactivity
Toxicity
Biocompatibility

ABSTRACT

This study investigated the biocompatibility of the experimental thermoplastic rubber Arbomatrix™ that will be used as the protective coating on a novel intracranial pressure (ICP) sensor silicon chip. Arbomatrix™ was benchmarked against biocompatible commercial silicone rubber shunt tubing in the brain *via* a rat model with 60-day implant duration. A bare silicon chip was also implanted. The results showed similar cellular distribution in the brain–implant boundary and surrounding tissues. Quantitative analysis of neuron and glia density did not show significant difference between implants. Through histological and immunohistochemical evaluation we conclude that Arbomatrix™ is well tolerated by the brain. Due to its exceptional barrier properties Arbomatrix™ has already been shown to be an excellent protective coating for new ICP monitoring chip.

1. Introduction

There is a great deal of interest in novel technologies for diagnostic and therapeutic procedures for neurological diseases. The response of brain tissue to various sensors/electrodes implanted into the brain has been investigated (Polikov et al., 2005; Winslow et al., 2010). Often the metal sensors and electrodes have protective coatings. Several coating materials have been evaluated both experimentally and clinically and the majority has been discarded (Babb and Kupfer, 1984; Collias and

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http://dx.doi.org/10.1016/j.jmbbm.2015.01.018
1751-6161/

Manuelidis, 1957; Dymond et al., 1970; Stensaas and Stensaas, 1978). Several plastics, aluminum, gold, and platinum have been tested *in vitro* and *in vivo* (Ammar, 1984; Stensaas and Stensaas, 1978). Acute mechanical injuries related to implants and insertion mechanics have also been studied (Welkenhuysen et al., 2011). It should be emphasized that these sensors/electrodes are in direct contact with neurons and are not buffered by cerebrospinal fluid.

We have been developing a wireless intracranial pressure (ICP) sensor on a silicon chip. Attempts to protect the device with a silicone rubber coating failed as water penetrating the coating caused a shift in the electric signal. Preliminary tests with Arbomatrix™, an experimental thermoplastic rubber based on polyisobutylene, have been very promising, due to the exceptional barrier properties of this material. Other advantages include ease of handling: the sensors are coated with Arbomatrix™ dissolved in a solvent, which will then solidify into a transparent rubbery coating without the need of curing. The biocompatibility and biostability of Arbomatrix™ in subcutaneous and intramuscular implantation in a rabbit model has already been demonstrated; its mechanical properties actually improved following explantation, while the benchmark silicone rubber lost some of its strength (Puskas et al., 2005). In order to use this material in the brain, its biocompatibility and biostability needed to be evaluated by implantation in the brain. As a part of our wireless ICP sensor project we histologically evaluated the biocompatibility of bare silicon and Arbomatrix™ after implantation in the cerebral cortex, benchmarked against biocompatible silicone rubber. The data from this study is presented in this manuscript.

2. Materials and methods

2.1. Evaluated materials

Sensor material (silicon chip, used for making microelectronic sensors), *Beads* (Arbomatrix™, a block copolymer of polyisobutylene and polystyrene with a branched polyisobutylene core, used for sensor packaging and coating) (Puskas and Chen, 2004; Puskas et al., 2005; Teck Lim et al., 2013), and *Control* (shunting tubing end, silicone rubber, Medtronic #41101, Goleta, CA) were used for implantation (Fig. 2A–C). The *Beads* were cut from compression molded sheets of Arbomatrix™. The specimen sizes are given in the figure caption. The *Beads* were analyzed quantitatively before and after implantation by using Size Exclusion Chromatography (SEC) for possible degradation after implantation. SEC measurements were conducted at The University of Akron. The SEC system consists of an HPLC pump (Waters 515 HPLC Pump), a Waters 2487 Dual Absorbance UV Detector (UV), a Wyatt OPTILAB DSP Interferometric Refractometer (RI), a Wyatt DAWN EOS multiangle light scattering (LS) detector, a Wyatt ViscoStar viscometer, a Wyatt QELS quasi-elastic LS instrument (QELS), a Waters 717plus autosampler, and 6 Styragel VR columns (HR6, HR5, HR4, HR3, HR1, and H0.5). The columns were thermostated at 35 °C and THF, continuously distilled from CaH_2, was used as the mobile phase at a flow rate of 1 ml/min. The results were analyzed by using the ASTRA software (Wyatt Technology).

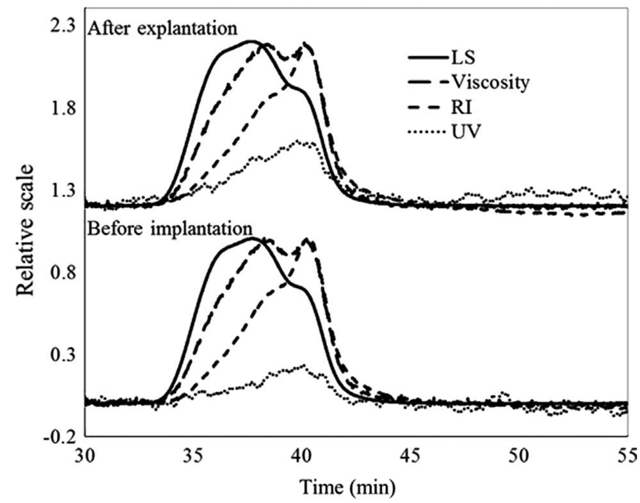

Fig. 1 – Size Exclusion Chromatography (SEC) traces of *Beads* before and after implantation. The molecular weight and molecular weight distribution of beads before and after implantation are shown and no degradation was observed in the implanted materials.

2.2. Animal surgery

Animal experiments were carried out in accordance with the Cleveland Clinic Animal Research Committee's rules for the care and use of laboratory animals (IACUC protocol # 2011-0646). Fifteen adult healthy male Sprague Dawley rats (Harlan, Indianapolis, IN) weighing 380–450 g were randomly divided into three groups for implantation: *Sensor*, *Bead*, and *Control*. Rats were housed in individual cages and maintained on a 12-h light-dark cycle with food and water available as required. All efforts were made to minimize the number of animals used and minimize suffering.

Animals were anesthetized with ketamine (80 mg/kg, intraperitoneal) and xylazine (5 mg/kg) and placed in the Kopf stereotaxic frame (David Kopf Instruments, Tujunga, CA). After the implants had been sterilized *via* ethylene oxide (EtO), they were inserted into the frontoparietal cortex through burr holes in the skull at the coordinate of AP: −2.0 mm; ML: 2.0 mm from bregma, and DV: under cortex (Paxinos and Watson, 2007). Routing post-operative cares include pain relieve with buprenorphine, neurological status evaluation, and monitoring for abnormal behavioral.

2.3. Sacrifice and sample collection for histological study

Sixty days post-implantation, rats were deeply anesthetized with pentobarbital (100 mg/kg, intraperitoneal) in combination with inhaled isoflurane and underwent trans-cardiac perfusion with 0.9% saline followed by 4% paraformaldehyde (PFA) in 0.1 M Phosphate Buffered Saline (PBS). Bulk brain tissues with the implants were carefully removed without damaging the brain–implant boundary. Brains were post-fixed overnight and cryoprotected in graded sucrose solution for 24 h. After photographic evaluation of implant location, brains were blocked and frozen in optimal cutting temperature gel (OCT, Sakura Finetek, Torrance, CA) and stored at