

SECOND GENERATION MICROSTIMULATOR

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SUMMARY

The first generation injectable microstimulator was glass encased with an external tantalum capacitor electrode. This second generation device utilizes a hermetically sealed ceramic case, with platinum electrodes. Zener diodes protect the electronics from defibrillation shocks and from electrostatic discharge. The capacitor is sealed inside the case so that it cannot be inadvertently damaged by surgical instruments. This microstimulator referred to as BION[®], is the main component of a 255-channel wireless stimulating system.

BION[®] devices have been implanted in rats for periods of up to 5 months. Results show benign tissue reactions resulting in identical encapsulation around BION[®] and controls. Stimulation threshold levels did not change significantly over time and ranged between 0.81 to 1.35 mA for all the animals at 60 μ sec pulse width. All of the tests performed to date indicate that the BION[®] is safe and effective for long-term human implant.

We have elected to develop BION[®] applications by seeking collaboration with the research community through our BION[®] Technology Partnership.

INTRODUCTION

The BION[®] system is a wireless network of up to 255 single-channel stimulators controlled and powered by an RF link from a central external controller. Each stimulator consists of a ceramic and titanium cylinder capped at each end with anode and cathode, both platinum. The cylinder is 15.6 mm long and 2.5 mm in diameter. Each stimulator produces asymmetric biphasic capacitively-coupled constant-current pulses. Pulse width (0 to 500 μ sec), pulse amplitude (0 to 40 mA) and pulse frequency (0 to 3,472 pps shared among all active BION[®] stimulators) are controlled digitally by the external controller via a 2 MHz AC magnetic link. [1-6]

The second generation BION[®] stimulator includes additional characteristics. a) Bipolar zener diodes were installed around the electronics module to protect the BION[®] from defibrillator shocks and from electrostatic discharge. These diodes can protect against 25,000 volts, 10 μ sec electrostatic discharge and against a 0.3 amp. defibrillator pulse. b) The tantalum capacitor was moved into the package to protect it from accidental damage during handling and implantation. c) The packaging was changed to a 250-micron walled ceramic cylinder hermetically sealed to titanium annular rings, to which platinum electrodes are attached at either end.

MATERIALS AND METHODS

In-vitro Tests

BION[®] stimulators underwent accelerated life and mechanical stress tests. The accelerate test was performed with 31 BION[®] internal electronics activated for 1,000 hours each at an elevated temperature of 125°C while being operated at a maximum energy level (burn-in test). For the mechanical stress tests, the case was subjected to a three-point bend test and a tensile test.

In-vivo Tests

A. Surgical Preparation

Experiments were carried out on 11 rats (4-5 months old, 280 - 300 g females). Animals in the Study Group (n=6) were implanted with four devices: one BION[®] in each thigh, and the two passive controls were implanted sub-fascially on both sides of the thoracic spine area. To insert the implants in the hindlimbs, the sciatic nerve was exposed at the thigh level by separating the fascia and dissecting deeper between the vastus lateralis muscle and the biceps muscle. A 1-2 cm long tunnel was dissected along the mid-thigh exposing the sciatic nerve. The BION[®] was oriented so that the cathode was inserted towards the knee. Implants were not sutured. The fascial layer and the skin layers were then closed. The 2 passive controls, a BION[®] without electronics and a similar sized silicon rod (NuSil Technology, Carpinteria, CA), were implanted in the posterior thoracic area. A mid line skin incision was made midway along the thoracic spine, then about 1 cm off the midline, the underlying muscle fascial layer was separated. A 1-2 cm long tunnel was dissected at 45 degrees outwards on each side so that the 2 controls could be inserted. The fascial layer and skin were then sutured closed. The Control Group consisted of 5 rats implanted with a BION[®] casing (left thigh) and a silicone rod (right thigh) adjacent to the sciatic nerve.

B. Stimulation

After surgery, animals were allowed to recover for 2 weeks. Animals in the Study Group were placed into rodent restrainers (Harvard Apparatus, Holliston, MA) and then in groups of three into the transmitting coil that sends data and power to the BION[®] stimulators. In all but one animal, the BION[®] implanted in the left leg was set as inactive and the stimulation settings were programmed to zero. Stimulation settings (Pulse Width, Pulse Amplitude) required to produce threshold twitches of the muscles were determined for each active BION[®]. The Current amplitude used during daily stimulation was set in order to produce a strong visible twitch (usually twice the threshold). Three animals were stimulated with a stimulation pattern of 25-s OFF period and 5-s ON period at 20 Hz. The other three animals were stimulated with a stimulation pattern of 5-s OFF period and 5-s ON period at 20 Hz. In all the animals, stimulus trains were applied starting at two 20-min sessions a day and finishing with three 1-h sessions a day, four to five days a week, for a period of up to five months [7].

C. Measurements

In order to verify the implant location X-rays were taken after the 2-week recovery period and again before the explantation. To take x-rays, animals were anesthetized with isoflurane gas, 1.5 - 2.5 % via facemask. Thresholds to produce a palpable muscle were measured twice a month for every implanted BION[®]. The daily stimulation was video recorded.

D. Tissue Processing

Animals were euthanized using pentobarbital S (100 mg/kg, i.p.). Passive implants and their surrounding tissues were dissected from the mid thoracic spine area. Each rear leg containing a BION[®] was also dissected. All the samples were preserved in 10% neutral buffered formalin and sent to a commercial lab (Pathology Research Laboratory, Berkeley, CA).

Implants were removed and each muscle sample containing fibrous tissue capsule was divided in three segments including anterior, middle and posterior levels. The corresponding segment of Sciatic nerve at the various regions was also included. The sections were sent to HistoTec Laboratory (Hayward, CA) for tissue processing and hematoxylin and eosin slide preparations. Selected slides were further stained with Siever-Munger and Cresyl Echt Violet stains to evaluate the nerve fibers.

RESULTS

In-vitro Tests

All 31 units successfully passed the 1,000-hour burn-in test. When comparing the device parameters before and after the burn-in, only the 10 microamps recharge current was altered. The average 10 microamps recharge current increased by about 4 microamps and the maximum increase in recharge

current was 6.7 microamps. The changes in the 0, 100, and 500 microamps recharge current were negligible.

The mechanical tests showed that the ceramic case can sustain approximately 40 lbs of force in a three-point bend test while the glass BION[®] fails at around 5 lbs. The ceramic-metal brazed case pulls apart at 40 pounds of applied tension, which is equivalent to over 10,000 psi of internal pressure.

In-vivo Tests

All BION[®] devices stimulated and produced muscle contractions in the legs during the total duration of the study. The twitches were well tolerated by the animals, which usually slept during the stimulation period. During the study period, thresholds were measured for each implanted device, including the inactive BION[®] devices. These thresholds did not change significantly over the study period and rather decreased when compared to those values measured right after the implantation (Figure 1). Figure 2 shows the cumulative charge density applied to each animal. No device migration was found.

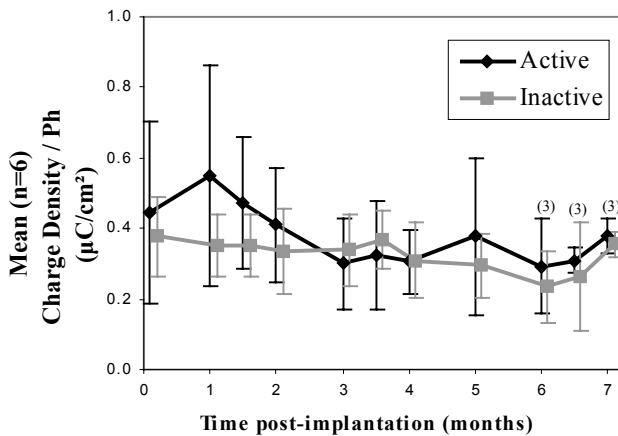


Figure 1. Threshold level mean for active and inactive BION[®] stimulators

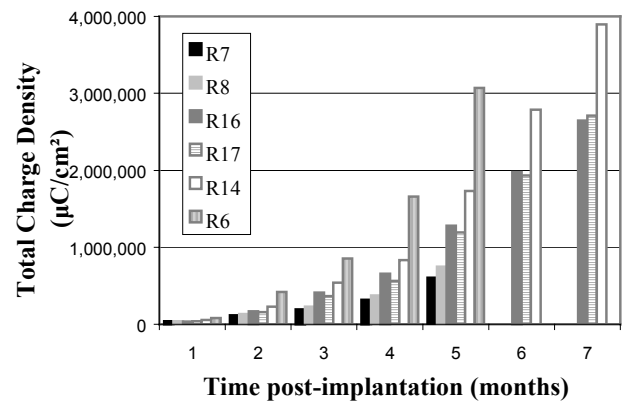


Figure 2. Cumulative charge density applied to each individual

All sections of the leg muscles implanted with BION[®] or silicone rods had similar fibrous tissue reaction (encapsulation). The round capsules consisted of compact laminated layers of fibro-collagenous tissue varying from 50 to 100 microns in thickness. There were varying degrees of mononuclear cell infiltration, primarily small macrophages and lymphocytes, within the capsular walls. Polymorphonuclear cells (neutrophils) were rare. Sciatic nerves and/or nerve branches were evident in each of the sections. Microscopically, all nerve bundles and muscle fibers were within normal limits. The two special stains confirmed cellular integrity of the nerve sections (figure 3).

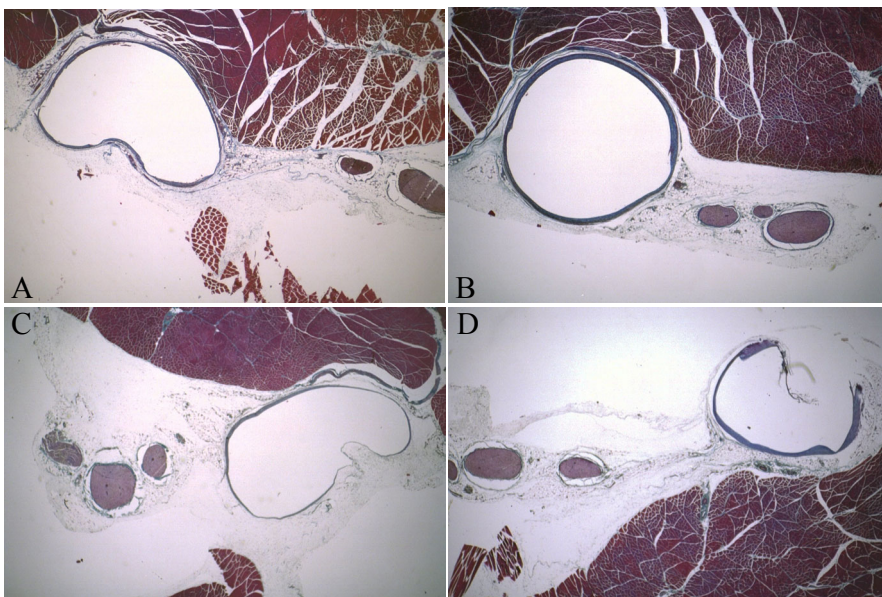


Figure 3. Photomicrographs of the implantation site of (A) an active BION[®]; (B) inactive BION[®]; (C) casing; and, (D) silicone rod. Sciatic nerve bundles, capsule and muscle tissue are shown.

DISCUSSION

All of the tests performed to date indicate that the BION[®] is safe and effective for long-term human implant. BION[®] technology could enable many FES applications. We considered developing applications in house vs. the alternative of developing an infrastructure that would enable collaborators to develop applications with our support. In coordination with Advanced Bionics – the licensor of this technology, we opted to do the latter. Our decision was primarily based on our desire to make BION[®] technology as widely available as possible. This infrastructure is the BION[®] Technology Partnership or BionTech[™].

Through BionTech[™] we offer technical and regulatory support, an arena for communication and exchange of information through our web site: www.biontech.org and of course, BION[®] devices available for a nominal price.

Also, to support this project we have been developing a control system containing external hardware and fitting software both designed for many purposes. The external controller is easily wearable; it can control up to eight BION[®] devices and can be attached to a wide range of coils. The fitting software is also designed for general purpose and for ease of use in a clinical setting.

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