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Spiral Cuff for Fiber-Diameter Selective VNS

P. Pečlin, J. Rozman

***Abstract*—**In this paper we present the modeling, design, and experimental testing of a nerve cuff multi-electrode system for diameter-selective vagus nerve stimulation.

The multi-electrode system contained ninety-nine platinum electrodes embedded within a self-curling spiral silicone sheet. The electrodes were organized in a matrix having nine parallel groups, each containing eleven electrodes.

Preliminary testing of the nerve cuff was performed in an isolated segment of a swinish left cervical vagus nerve. For selective vagus nerve stimulation, precisely defined current quasitrapezoidal, asymmetric and biphasic stimulating pulses were applied to preselected locations along the left vagus segment via appointed group of three electrodes within the cuff. Selective stimulation was obtained by anodal block. However, these pulses may not be safe for a long-term application because of a frequently used high imbalance between the cathodic and anodic part of the stimulating pulse.

Preliminary results show that the cuff was capable of exciting A and B-fibres, and, that for a certain range of parameters used in stimulating pulses, the contribution of A-fibres to the CAP was slightly reduced and the contribution of B-fibres was slightly larger.

Results also showed that measured CAPs are not greatly influenced by the imbalance between a charge Qc injected in cathodic and Qa in anodic phase of quasitrapezoidal, asymmetric and biphasic pulses.

***Keywords*—**Vagus nerve stimulation, multi-electrode nerve cuff.

I. INTRODUCTION

IN the past few decades, considerable scientific and technological efforts have been devoted to develop electrode systems that interface the human autonomic nerves. Particular attention is paid to vagus nerve stimulation to be used as the method to treat a number of nervous system disorders. In many heart diseases for instance, including hypertension and congestive heart failure, cardiac vagal activity is diminished and unresponsive. Therefore, restoration of cardiac vagal activity using selective vagus nerve stimulation could be an effective clinical target in cardiovascular diseases [1, 2, 3]. Besides, brain stimulation methods that are making significant inroads in psychiatric practice are already used in psychiatry [4, 5]. However, the vagus nerve stimulation used worldwide is in general a non-selective vagus nerve stimulation of the left vagus nerve where the frequent result is the occurrence of undesirable side effects [6, 7]. To alleviate the above-defined problems, different electrode systems that selectively stimulate certain, namely intermediate-diameter B-fibres in a nerve while avoiding stimulation of A-fibres and C-fibres, were developed [8].

In the area of Functional Electrical Stimulation, cuffs have been used as stimulation electrodes as well as electrodes for the recording of the electroneurogram for more than 35 years [9]. While the time was passing, theoretical considerations have stimulated and accompanied the development of cuffs [10, 11].

The aim was to test whether it is possible to reduce an influence of the injected charge onto the CAP elicited during selective vagus nerve stimulation.

One specific aim of the work was to develop and fabricate a single part-multi-electrode cuff which would enable selective vagus nerve stimulation in both, stimulation and recording means.

The last specific aim was testing the developed model and the cuff in a functional swinish left vagus nerve segment at closely simulated physiological conditions.

II. MATERIALS AND METHODS

A. Multi-electrode spiral cuff

It has been demonstrated by several authors that the self-sizing spiral cuff has the ability to conform to the shape of the nerve and to selectively stimulate certain superficial compartments of the nerve [12, 13]. Besides, in the cuff, the mechanical interface and thus the reproducibility of selective stimulation are superior.

The cuff, including arrangement and dimensions of stimulating and recording electrodes, was designed taking into consideration published results of modelling selective stimulation of peripheral nerves [14, 15, 16] and realistic structural topography of the swinish left vagus nerve segments.

To define a relation between structural topography and the physical model, the total number and distribution of fiber diameters in three left vagus nerve segments, were taken into account.

The cuff was manufactured by bonding two 0.05 mm thick silicone sheets together (Medical Grade Silicone Sheeting, Non-Reinforced, 6”x8”x0.002” Matt, SH-20001-002, BioPlexus Corporation, 1547 Los Angeles Avenue #107, Ventura, California 93004. U.S.A.). At room temperature one sheet, stretched and fixed in that position, was covered with a layer of adhesive (RTV Adhesive, Acetoxy, Implant Grade, Part Number 40064, Applied Silicone Corporation, 270 Quail Court, Santa Paula, CA 93060, USA). A second un-stretched sheet was placed on top of the adhesive and the composite was compressed to a thickness of 0.15 mm until the whole curing

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P. P. Author is with the Center for Implantable Technology and Sensors, ITIS d. o. o. Ljubljana, Ljubljana, Republic of Slovenia (phone: +386-41-557-252; (e-mail: polonapeclin@gmail.com).

J. R. Author is with the Center for Implantable Technology and Sensors, ITIS d. o. o. Ljubljana, Ljubljana, Republic of Slovenia (phone: +386-41-415-268; (e-mail: jnzrzmn6@gmail.com).

process was completed. When released, the composite curled into a spiral tube as the stretched sheet contracted to its natural length. As a result, the composite is self-sizing and flexible, spiral tube minimizing mechanical trauma when installed onto the nerve.

Ninety-nine rectangular electrodes with a width of 0.5 mm and length of 2 mm (geometric surface g=1 mm^2, real surface area =~1.4 mm^2, made of 45 μm thick annealed platinum ribbon (99.99 % purity), were then mounted on the third silicone sheet with a thickness of 0.05 mm. They were arranged in nine parallel groups, each containing eleven electrodes, thus forming a matrix of ninety-nine electrodes as shown in an upper part of the Fig. 1.

Afterwards, the electrodes were soldered individually to the high frequency miniature and highly flexible isolated, multi-stranded and enameled finest copper wires (CU-lackdraht DIN 46 435, Φ12x0.04mm, Elektrisola, Reichshof-Eckenhagen, Germany). The multi-stranded wire was used since it has the same average fatigue life as their individual constituent strands but the variance of that life is smaller. To maximize service life it was concluded that wire strands should be manufactured at the smallest diameter possible (without introducing structural flaws).

Afterwards, a spiral tube was opened and the silicone sheet with electrodes was adhered onto an inner side of the tube.

In fabricted cuff shown in a lower part of the Fig. 1, when the martix was spirally rolled up, the longitudinal separation between nine parallel groups of electrodes was 2 mm and the circumferential separation between electrodes was 0.5 mm.

In an upper part of Fig. 2 however, three dimensional model of the cuff is shown. In a lower part of the figure however, a fabricated cuff is presented. The cuff, shown was 42 mm in length and 2.5 mm in i.d. (internal diameter of the first layer).

As the most important in the cuff design, a notion of Sunderland and Bedbrook (1994) [17], that in fascicles extending peripherally along a nerve, fibers extensively interweave so as to converge and diverge into new and different fascicular assemblies, was considered. The idea of Terzis (1990) [18], that the rate at which the confluence of fibres significantly changes would be between 1.5 and 2.5 cm, was also considered.

However, to stimulate a certain group of fibres within a particular compartment of a left swinish vagus nerve segment and to avoid causing an injury associated with charge density at the same time, a well-defined electrical charge should be applied to preselected locations [19]. To keep the electrode-electrolyte interface within capacitive mechanisms, the cathode, as the electrode crucial for reliable stimulation, was dimensioned so as not to exceed the limits for a reversible charge injection [20].

B. Experimental testing of the cuff

An experimental testing of the ninety-nine-electrode cuff was performed in the segment of the left cervical vagus nerve obtained from the male Slovenian Landrace Swine weighing about 150 kilograms.

Animal was killed according to the protocol verified for mature animals, sows or boars (Penetrating Captive Bolt and immediate discharge blood from wound made by severing a major artery).

The neural tissue was treated in accordance with the approval provided by the ethics committee at the Veterinary Administration of the Republic of Slovenia, Ministry of Agriculture, Forestry and Food (VARS), (Telephone: +386 1 300 1300, URL: http://www.vurs.gov.si).

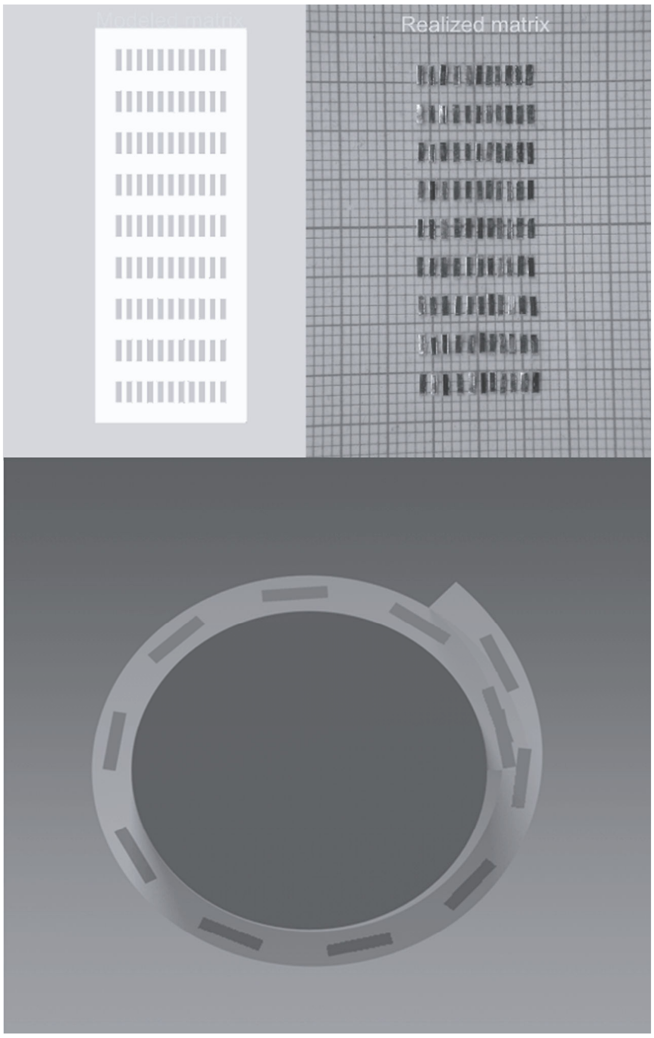

Fig. 1 (upper) Matrix of ninety-nine electrodes, (lower) Cross-section through the cuff

Vagus nerve segment was insulated using a technique of neuro-surgery and shortened to about 8 cm. Afterwards, a segment was placed into the mechanically opened cuff. Finally, the composition was placed into the especially designed experimental chamber shown at the right in Fig. 3, which was heated to temperature of 37°C to keep the excitation threshold at physiological level. Generally, the left vagus nerve segment was prepared for the experiment within 15 to 20 minutes after the stabbing.

The stimulating pulse used in the test was current, biphasic, charge balanced and asymmetric pulse composed of a precisely determined quasi-trapezoidal cathodic phase with a square leading edge with intensity ic=4 mA, a plateau with width tc=120 μs and exponentially decaying phase texp=100 μs, followed by a wide rectangular anodic phase ta=490 μs of a magnitude ia=0.8 mA.

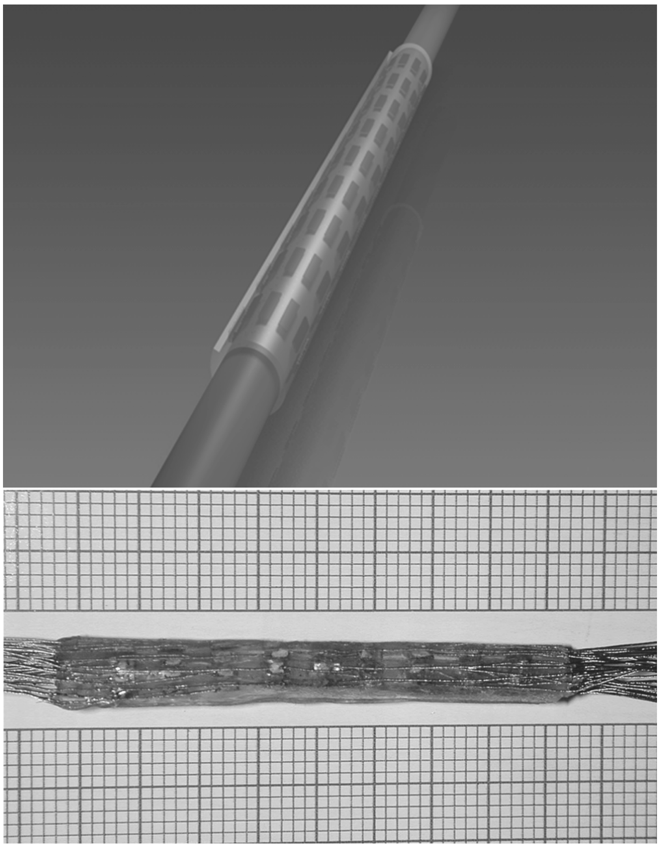

Fig. 2 (upper) 3D model of the cuff, (lower) fabricated cuff

Fig. 3 (upper left) Experimental conditions, (lower left) insulation of the left vagus nerve segment, (right) installation of the left vagus nerve segment into the cuff

To put a certain group of three stimulating electrodes within the stimulating section of the cuff in function, corresponding switches at the especially designed switching module were alternately turned into a particular position.

To stimulate a certain group fibers within a particular compartment of a segment however, aforementioned stimuli at frequency of 1 Hz were applied via an appointed stimulating group of three electrodes to preselected location.

III. RESULTS

Results showed that stimulating pulses, having preset certain degree of imbalance between a charge Qc injected in cathodic phase and charge Qa injected in anodic phase, elicited a slight change in a positive waveform deflection of CAP under a cathodic phase as well as slight change in a negative waveform deflection of CAP under an anodic phase. Accordingly, it could be concluded that measured CAPs are not greatly influenced by the imbalance between a charge Qc injected in cathodic and Qa in anodic phase of quasitrapezoidal, asymmetric and biphasic pulses.

It was also shown that the contact area 0.5x12.00 mm resulted in a relatively low impedance of about 2.5 kΩ measured “in vivo”.

From electrochemical point of view, however, electrochemical reactions that occurred at the cathode due to a charge Qc, injected within a time tc via an ic, were reversed in part or in full, by the charge Qa, injected via a rectangular charge balancing anodic phase ia within a time ta.

IV. DISCUSSION

An aim of the work was to contribute to the development of multi-electrode spiral cuffs to be used for efficient and safe fiber- diameter selective stimulation of autonomous peripheral nerves and for selective recording of compound action potentials at the same time. Namely, the CAP recorded selectively from fibres of the vagus nerve could be effectively used for the closed-loop control of implantable stimulators selectively activating different neural pathways.

Besides, such a preference towards nerve-fibre type is advantageous in applications where organ-specific stimulation is required and the side-effect profile related to the propagation of the APs of the A-fibres towards the CNS needs to be minimized [21, 22, 23, 24].

We believe that this design has strong potential for applications in neuro-prosthetic technology in the future. Namely, it would be very desirable to control different internal organs such as cardio-vascular system in patients with heart failure or atrial fibrillation by only one implanted system, e.g. on the lef cervical vagus nerve.

Directions that our further work would be the following: further development of the cuff for a given applications and accomplishment of electrochemical measurements under realistic conditions. It could be expected that a direction to enhance electrode efficiency will lead to an overall more efficient and effective device.

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