Cell for electrochemical and electrophysiological measurements in peripheral nerves

Celica za elektrokemijske in elektrofiziološke meritve na perifernih živcih

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Abstract: The aim of the work was to develop the cell to be used in electrochemical and electrophysiological measurements in peripheral nerves, when electrical stimulating pulses are selectively applied to preselected locations along the nerve. The main part of the cell is the silicone spiral cuff system, including spiral matrix of ninety-nine platinum electrodes, arranged in eleven longitudinal spiral electrode configurations of nine electrodes for establishing electrical contact with specific sites on the peripheral nerve. To maximize the fatigue life of lead wires connected to the electrodes, which should sustain frequent bending, a high frequency miniature and highly flexible, multi-stranded and enameled copper wire, was used. The cell is made of Plexiglas and is instrumented with the precision temperature probe, Ag/AgCl reference electrode, 3D micro-manipulator positioning system and custom designed force transducers to measure stretching and radial pressure that could be applied on nerve segment during measurements.

Izvleček: Namen dela je bil razviti celico za izvajanje elektrokemijskih in elektrofizioloških meritev na perifernih živcih v času selektivnega dovajanja stimulacijskih impulzov na predhodno izbrana mesta

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vzdolž živca. Najpomembnejši del celice je spiralna silikonska objemka, ki vključuje spiralno matriko devetindevedesetih elektrod, razporejenih v enajst longitudinalnih skupin po devet elektrod za vzpostavitev stika s posameznimi mesti na perifernem živcu. Za čim daljšo trajnostno dobo žic, povezanih z elektrodami, ki morajo vzdržati pogosto upogibanje, je bila izbrana visokofrekvenčna, drobna in zelo upogljiva ter lakirana bakrena pletenica. Sama celica je izdelana iz pleksi stekla in opremljena s precizijsko temperaturno sondo, referenčno elektrodo Ag/AgCl, z mikromanipulatorjem za 3D pozicioniranje in s posebej izdelanimi senzorji sile za merjenje natega in radialnega tlaka, ki mu bo med meritvami izpostavljen vzorec živca.

Key words: platinum, stimulating electrode, peripheral nerve, electrophysiology, electrochemistry

Ključne besede: platina, stimulacijska elektroda, periferni živec, elektrofiziologija, elektrokemija

Introduction

One of the greatest problems in non-selective vagus nerve stimulation used worldwide as a potentially useful therapy for treating various heart conditions and certain types of intractable epilepsy and major depression is non-selective stimulation of particular superficial regions as well as non-selective stimulation of fibers innervating a targeting organ.[1, 2, 3, 4, 5, 6]

The result is the occurrence of undesirable side effects such as: an intermittent decrease in respiratory flow during sleep, disordered breathing, loud snoring, obstructive sleep aponea, alteration of voice, coughing, pharyngitis, throat pain, hoarseness, frank laryngeal muscle spasm, headache, nausea, vomiting, dyspepsia, dyspnea and paresthesia. To alleviate the above-defined problems, the research was aimed at developing a new model and multielectrode system that selectively and safely stimulates a certain group of fibers in a nerve trunk without excitation of other fibers. For the purpose of performing electrochemical and electrophysiological measurements in functional peripheral nerves an appropriate cell simulating physiological environment needs to be developed.

Materials and methods

The cell was designed taking into consideration the results of histological examination of the left vagus nerve of a pig, the model of selective electrical stimulation of particular superficial regions of the nerve and the model of selective stimulation of nerve fibers with different diameters.[7, 8, 9] The entire cell was machined out from Plexiglas, using CNC milling machine. The cuff however, was designed taking into consideration the model of selective stimulation of particular superficial regions of the nerve and different types of nerve fibers as well as numerical solution of the 3D current density and electrical field distribution in the superficial region of the nerve, generated by a particular group of electrodes.[10]

Accordingly, the cuff was made by bonding two 0.1 mm thick silicone sheets together. One sheet, stretched and fixed in that position, was covered with a layer of adhesive (MED-1511, NuSil, Carpinteria, CA, USA). A second un-stretched sheet was placed on the adhesive and the composite was compressed to a thickness of 0.3 mm until the whole curing process was completed. When released, the composite curled into a spiral tube as the stretched sheet contracted to its natural length.[11, 12, 13] The composite is self-sizing and flexible, minimizing mechanical trauma when installed onto the nerve. Ninety-nine rectangular electrodes with a width of 0.5 mm and length of 2 mm made of 45 μm thick annealed platinum ribbon (99.99 % purity) connected/soldered to the insulated multi-stranded wire, were then mounted on the third silicone sheet with a thickness of 0.05 mm.

As shown in Figure 1, the electrodes having a flat geometric surface of 1 mm^2 were arranged in a matrix of nine parallel groups each containing eleven electrodes with a distance of 0.5 mm between them, while the distance between the groups was 2 mm. Since it is necessary to activate nerve fibers located at a certain distance from the electrode, the electrode should be able to inject enough charge without causing irreversible electrochemical reactions damaging both, the neural tissue and to the electrode itself.[14] Platinum as an electrode material has the advantage of decreasing impedance with increasing frequency. The contact area (0.5 × 2) mm resulted in a relatively low impedance of about 2.5 kΩ measured »in vivo«. However, in case when thick fatty tissue around the nerve is present, significantly higher impedance could be expected.

To maximize the fatigue life of lead wires shown in Figure 2, high frequency miniature and highly flexible insulated, multi-stranded and enamelled copper wire (CU-LACKDRAHT DIN 46 435, NENN Φ (12 × 0.04) mm, ELEKTRISOLA, Dr. Gerd Schildbach

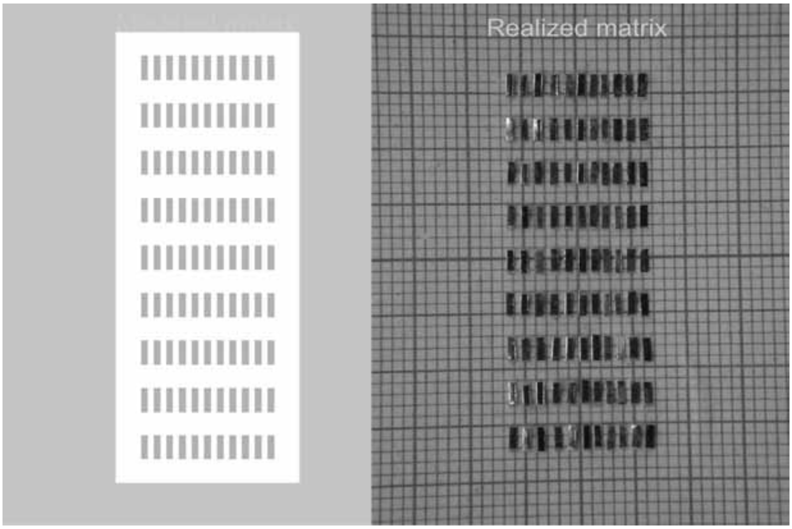

Figure 1. Modeled and realized matrix of 99 platinum electrodes

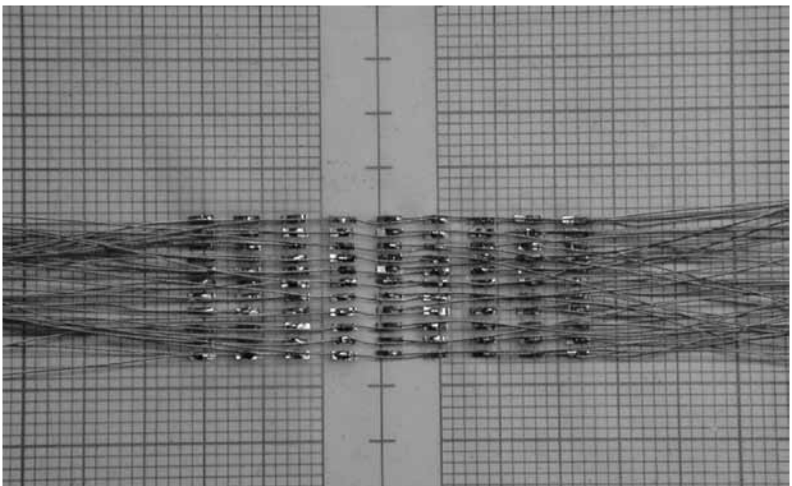

Figure 2. Multi-stranded copper wires, soldered on platinum electrodes within the matrix

GmbH & Co. KG, Hüttenwiese 2-4, D-51580 Reichshof-Eckenhagen, Germany, Tel: +49(0)2265 12 0, Fax: +49 (0)2265 9436, e-mail: sales@elektrisola.de), was used.[15] In the wire drawing process, the finest copper wire with diameter of 0.04 mm is drawn through a series of dies. Before enameling process, the bare wire is annealed in annealing oven to achieve necessary softness of the copper. 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. However, to maximize service life it was suggested that wire strands should be manufactured at the smallest diameter possible (without introducing structural flaws).

Stretching force that could be applied to the nerve could be adjusted in fine increments, using especially designed micrometer mechanism. Stretching force is transmitted via the surgical suture, attached serially to the nerve to the custom designed miniature force transducer, which is an integrating part of the experimental cell.

To measure a length of the neural segment stretching, a voltage divider realized by using precision linear potentiometer attached to sliding elements of a mechanical micrometer stretching system, was used (Spectrol, 20 kΩ).

Radial pressure applied onto the nerve when the cuff is installed, could be adjusted at different values in fine increments. For this purpose, especially designed precise mechanism containing a miniature custom designed force transducer, which was an integrating part of the experimental cell, was used. Namely, the cuff will be subjected to a procedure of defining the pressure which appears when the cuff is installed on the nerve trunk with a diameter of 3 mm. The radial pressure in the cuff should be below the pressure of 2.66 kPa (20 mm Hg) which could induce an interference with intra-neural blood flow.

To maintain a constant temperature of 37 °C, a water bath circulator (Boehringer, Labor Manheim GmbH für Labortechnik, Perfectherm PFV, 20–65 °C, 220 V, 1000 W, Fixed Temperatures: (25/30/37/56) °C, Waterbath (36 × 14 × 13) cm, Capacity: 6,5 L), which controls a temperature within the range of ±0.003 °C, is used. For precise measurement and recording of a temperature just below the site where the cuff is mounted onto the nerve, the micro-BetaCHIP temperature probe (Part Number: 10K3MCD1), which is actually the smallest semi-conductive packaged thermistor device, was used. Namely, the probe is produced for applications where space is limited. The probes are extremely small (Diameter 0.457 mm, Nominal Length 3.18 mm) and fragile.

Results and discussion

In Figure 3, a fabricated ninety-nine electrode spiral cuff, actually installed into the cell, is presented. It could be seen that the nominal length of the cuff is 44 mm, external diameter is 5 mm and internal diameter is 2.5 mm.

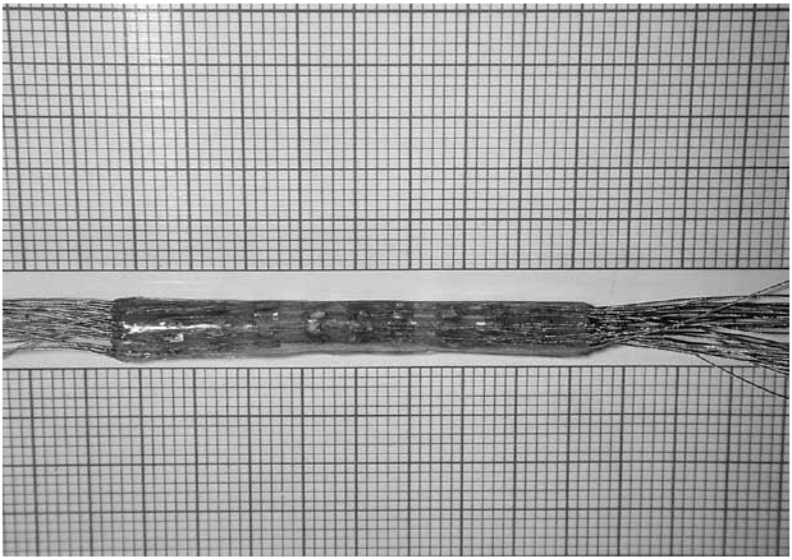

Figure 3. Fabricated ninety-nine-electrode spiral cuff

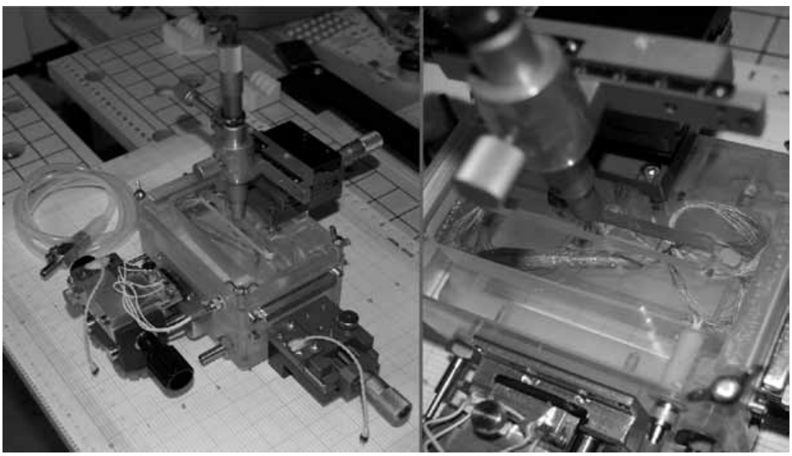

Figure 4. Completed cell for electrochemical and electrophysiological measurements in peripheral nerves

In Figure 4 however, a completed cell enabling electrochemical and basic electrophysiological measurements that could be performed in functional peripheral nerve segment under simulated physiological environment, is presented. In the lower left part of the figure, the micrometer mechanisms enabling precise measurements of stretching of the nerve and radial pressure are shown. In the upper right part of the figure however, a 3D micro-manipulator positioning system, enabling for the intra-neural micro-electrode used in the method of voltage clamp measurements to be positioned into the neural cell.

Our work contributed to the development of models and multi-electrode spiral cuffs to be used for efficient and safe selective stimulation of autonomous peripheral nerves and for selective recording of compound action potentials at the same time.

One weakness of a multi-electrode cuff manufacture however, is a technically demanding and a time consuming process. The technical solutions described in our study could be used in various animal and human basic studies concerning neurophysiology of internal organs, and their relation to bodily changes and diseases.

Conclusions

The cell enables for the electrophysiological technique of compound action potential measurement to be used in testing the proposed model under realistic conditions, using insulated functional left vagus nerve of a pig. Besides, the electrochemical technique of cyclic voltammetry could be used to delineate a safe operational potential window of platinum stimulating electrodes also under realistic conditions, using functional left vagus nerve of a pig. This design has strong potential for applications in neuro-prosthetic technology in the future. For instance, it would be very desirable to control different internal organs for instance cardio-vascular system in patients with heart failure or atrial fibrillation by only one implanted system, e.g. on the vagus nerve.

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