Measurement of Force Development in the Rat's Foot during Electrical Stimulation of the Sciatic Nerve with Polyimide-Based Cuff Electrodes

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Abstract – *In neural rehabilitation cuff electrodes are widely spread for interfacing nerves. Especially for small nerves, a new approach of flexible and light-weighted multichannel cuff electrodes with integrated cables was developed using micromachining technologies. For an evaluation of electrode selectivity, a setup to measure non-invasively the force development after electrical stimulation in the rat's foot was developed. In a first study, the selectivity of small nerve cuffs with twelve electrodes implanted on the sciatic nerve of a rat was investigated. Using one cuff around the nerve, electrical stimulation on different electrode tripoles led to plantarflexion and dorsiflexion of the foot without an* a priori *alignment of the cuff.*

Keywords: Cuff-Electrode, Electrical Stimulation, Peripheral Nerve, Polyimide, Force

1. Introduction

Cuff electrodes became widespread for interfacing peripheral nerves in neural prostheses during the last three decades. The development of multichannel stimulation sites inside the cuffs allows partial excitation of different nerve parts with selective control of different muscles [1]. The force development on the animal's foot was monitored with a non-invasive measurement setup [2]. It allowed repeated measurement on the foot of the cat, the commonly used animal model in the studies of the Mortimer group (CWRU, Cleveland, OH/USA). The knee of the animal was fixed with a clamp and the foot was inserted into a "shoe" that was connected to a measurement device (JR3, Woodland/USA) with three force sensors ($F_{x,y,z}$ < 100 N) and three torque sensors ($M_{x,y,z}$< 8 Nm). Measurement of all directions of movements is necessary in the cat animal model [3]. The maximal measured torque was in the range of 3 Nm in the plantar-/dorsiflexion plane and selective recruitment of different muscles for movement was reported using twelve-polar cuffs [4].

Using smaller animal models, the mass of the JR3 transducer and measurement setup might be too large (and too expensive) for widespread use. A setup with a custom made single axis torque transducer was established at Michigan University (USA) for the mouse animal model [5]. Force development was measured in the plantar-/dorsiflexion plane with a maximum value of 25 Nmm. The development of forces and torques of the commonly used rat animal should be somewhere in between the mouse and the cat. Therefore, a measurement setup for the rat was developed with abilities to monitor the plantar-/dorsiflexion and the medial/lateral rotation plane. Investigations on the rat sciatic nerve that is much smaller than the cat ones should evaluate, if the possibility to selectively control antagonist muscles exists with the recently developed polyimide-based small nerve cuff electrodes.

In this paper, we present our development of a simple and non-invasive force measurement device for the rat animal model and first results from stimulation experiments investigating the selectivity of newly developed polyimide-based cuff electrodes around small nerves.

2. Materials and Methods

First, the measurement setup, the electrodes, and the experimental design of the implantation and stimulation experiments were defined and described.

Torque Measurement Setup

A device was especially designed for the non-invasive measurement of force development of the rat foot during electrical stimulation. A base plate with guides for a mount was build onto which a torque measurement device to monitor the force development was placed (Fig. 1). A further plate made of magnetic stainless steel allowed the fixation of an adjustable clamp via a magnet for the rat's knee.

The torque measurement device was assembled of a „shoe" made of PMMA onto which torque transducers could be mounted on orthogonal axis (Fig. 2). Two flexible bellows couplings (BSK 39 08 40, Baeuerle, St. Georgen/Germany) separate the torques of plantar- / dorsiflexion from those of supination/pronation and lateral rotation.

We chose a strain gauge based torque sensor (DMA/UM-2000, Watzau , Berlin/Germany) with a measurement range up to 2000 Nmm. Bridge amplifier were set up with a sensitivity of 0.4 V/Nmm and 40 V/Nmm, respectively, for output adaptation to standard data acquisition systems.

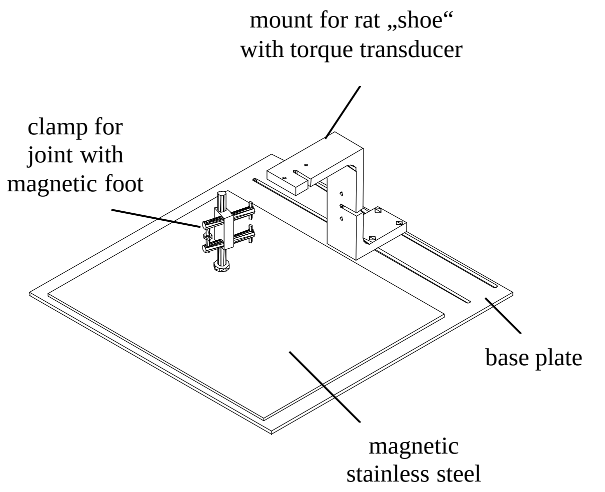

Fig. 1: Base plate with mount for torque measurement device and adjustable clamp.

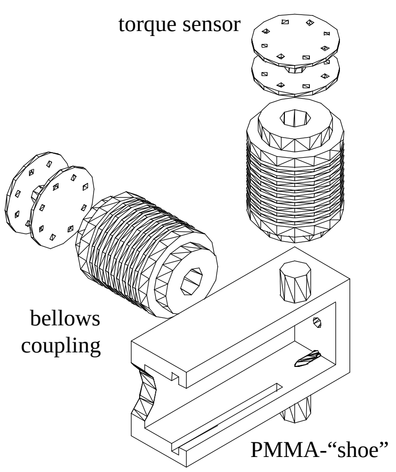

Fig. 2: “Shoe” with couplings and torque sensor to insert the rat’s foot for measurements.

Nerve Cuff Electrodes

Cuff electrodes with 12 dot electrodes that could be arranged to four tripoles were designed and realized (Fig. 3, Table 1). Therefore, a process technology to produce flexible micromachined electrodes with integrated interconnection lines and contact pads was established [6].

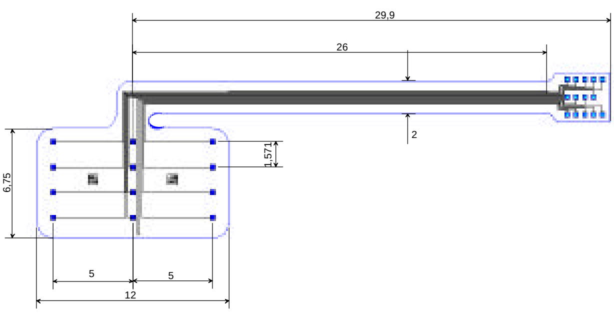

Fig. 3: Design of a 12 channel cuff-electrode. All dimensions are in mm.

Table 1: Cuff electrode specifications

Specification	**Dimension**
thickness of polyimide device	10 µm
cuff diameters	0.7 / 1.0 - 2 mm in steps of 0.2 mm
number of electrodes	12 dots, arranged in 4 tripoles
longitudinal electrode pitch	5 mm
interconnect cable width	2 mm
interconnect length	26.4 mm
cuff length	12 mm
dot electrode area	70685 µm² (diameter 300 µm)

Polyimide (Pyralin PI 2611/DuPont, Bad Homburg, Germany) was chosen as substrate and insulation material for cuff electrodes. The resin like polyimide was spin-coated on silicon wafers. Imidization was performed at 350°C. Then, thin film metallization of platinum was sputter deposited and patterned for electrode areas, interconnection lines, and connection pads. A top layer of polyimide was spin-coated and imidized for insulation and mechanical support. Reactive ion etching (RIE) was applied for opening the electrode and contact areas. RIE was also used to define the outer shapes of the devices. The devices were separated from the silicon wafer and were formed to cuffs. In a temper step, the mechanical stresses in the devices were mainly released. The cuffs stayed stable in the rolled position. For stimulation experiments during acute implantations, each electrode was connected via the integrated connection pads to a plug on a ceramic substrate.

Acute Implantation

Polyimide-based cuff electrodes with 12 stimulation sites that were arranged to four tripoles were used with a diameter of 1.6 mm for acute implantation. Surgical intervention was performed in female Sprague-Dawley rats under pentobarbital anaesthesia (40 mg/kg i.p.) with the aid of a dissecting microscope. The left sciatic nerve was exposed at the midthigh and carefully freed from surrounding tissues from the sciatic notch to the knee. Its diameter was around 1.2 mm. The cuff was opened and placed around the sciatic nerve avoiding compression and stretch. The electrode interconnect ribbon was routed through the muscle plane excision, avoiding tension, placing the ending enlargement on the lateral side of the hind limb. The animal was placed on the stainless steel plate of the torque measurement setup. The left foot was inserted into the “shoe” and gently fixed with adjusting screws to prevent any relative movement inside the “shoe”. The knee was fixed with the adjustable clamp that was placed onto the base plate with the magnet. The animal was fixed with adhesive tape on the base plate to prevent undesired movements due to electrical stimulation. The whole setup was placed over a warm flat streamer controlled by a hot water circulating pump, and the hind paw skin temperature was maintained above 32 °C.

Stimulation Experiments

In acute stimulation experiments, monophasic rectangular current pulses (GRASS S88 with voltage to current converter) with a pulse width of 10 µsec. were applied. Compound muscle action potentials (CMAPs) were recorded simultaneously from the tibialis anterior and gastrocnemius medialis muscles with small needle electrodes inserted in each muscle. Additionally, the force development in the foot was measured with the newly developed device. The evoked potentials and the torque were displayed on a storage oscilloscope (Tektronix 2221) at settings appropriate to measure the amplitude from baseline to peak and the latency to the onset. Each of the four tripoles of the cuff with the middle electrode as cathode and outer electrodes short-circuited to be anodes were tested from threshold up to supramaximal excitation.

3. Results

First investigations were performed on four rats using the electrodes and the measurement setup described above. The data presented here are from single measurements being representative for all measurements.

Nerve Cuff Electrodes

Nerve Cuff electrodes with connectors for acute implantation (Fig. 4) were implanted around the sciatic nerve at the midthigh without particular alignment of the stimulation sites to distinct fascicles.

The nerve cuff closed properly after release during implantation covering the whole nerve perimeter, to which it adhered well.

Force Development due to Electrical Stimulation

Increasing the stimulation amplitude on the selected tripole, we obtained CMAPs of graded recruitment curves from gastrocnemius medialis and tibialis anterior muscles. Positive and negative torques were measured indicating dorsiflexion and plantarflexion, respectively.

Stimulation through the tripole that was located near the peroneal fascicle innervating the tibialis anterior muscle produced dorsiflexion at low stimulation amplitudes. At higher stimulation amplitudes the activation of the gastrocnemius muscle, innervated by the tibial fascicle, revailed and led to plantarflexion of the foot (Fig. 6). On the other hand, stimulation applied through tripoles near the tibial fascicle produced plantarflexion with increasing degree of force from low to high stimulus intensity (Fig. 7). On the other two animals, the same results were obtained without an *a priori* alignment of the nerve cuff electrode. At least one tripole was able to excite the peroneal fascicle to obtain dorsiflexion at low stimulation amplitudes.

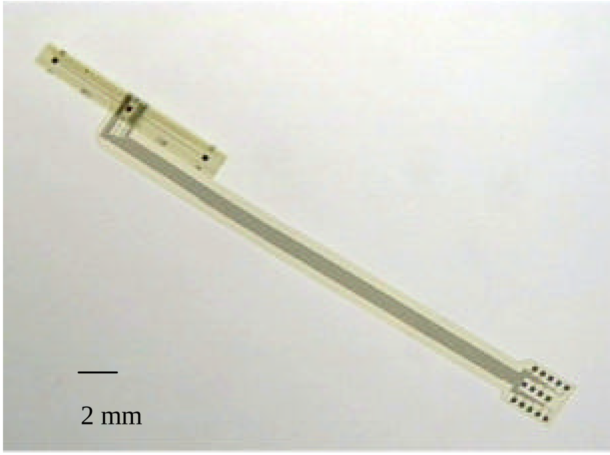

Fig. 4: Polyimide-based cuff-electrode with 12 stimulation sites.

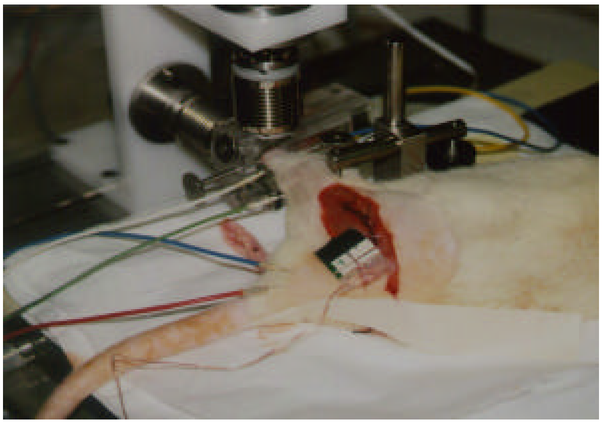

Fig. 5: Polyimide-based cuff implanted on the sciatic nerve of the rat. Needle electrodes to record CMAPs and rat's foot in torque measurement setup.

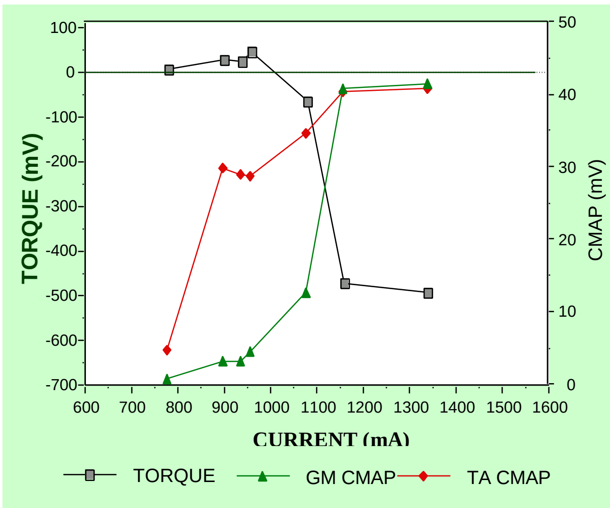

Fig. 6: Muscle excitation (CMAPs) and torque development with increasing stimulation amplitude: dorsiflexion (pos. torque) at low amplitudes, plantarflexion (neg. torque) at higher amplitudes. A Cuff was placed around sciatic nerve, tripole active at 0°. (Torque: 100 mV = 2.5 Nmm; GM: gastrocnemic muscle; TA: tibialis anterior)

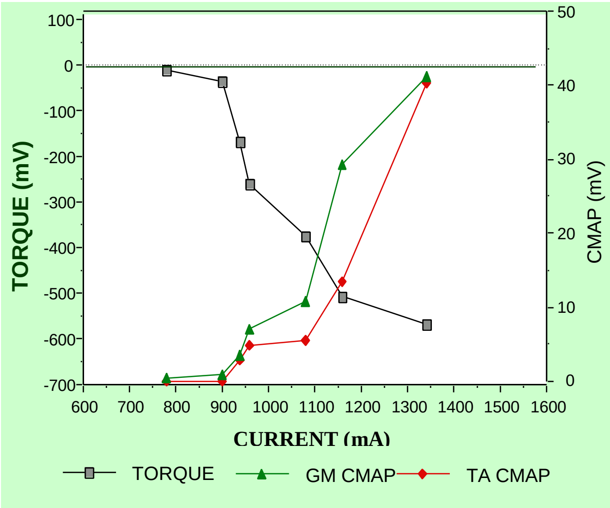

Fig. 7: Muscle excitation (CMAPs) and torque development with increasing stimulation amplitude: plantarflexion (neg. torque) during the complete stimulatoin range. A Cuff was placed around sciatic nerve, tripole active at 180°. (Torque: 100 mV = 2.5 Nmm; GM: gastrocnemic muscle; TA: tibialis anterior)

4. Discussion

We set up a measurement device to monitor the force development of the rat's foot with a torque transducer. The setup proved to be stable and delivered reproducible data in the first experiments in the animal operation theatre. Polyimide-based nerve cuffs with three ring electrodes were tested in chronic experiments on the sciatic nerve of rats previously [7]. Therefore, the implantation of the slightly modified cuffs with twelve electrodes caused no problems during implantation. Excitation thresholds of the tibialis anterior and gastrocnemic muscle were below 800 µA at a pulse width of 10 µs with tripolar stimulation. CMAPs increased gradually with increasing stimulation amplitudes. Due to the large muscle mass of the gastrocnemic muscle (GM) in comparison to the tibialis anterior (TA) muscle, there is a large imbalance in torque development during stimulation. Even if the levels of the CMAPs are much lower in the TA (Fig. 6) than those of the GM, the GM revailed at higher stimulation amplitudes and changed dorsiflexion to plantarflexion. On another stimulation tripole, CMAPs of GM were slightly higher than CMAPs of TA and led to a clear plantarflexion from low stimulation amplitudes on (Fig. 7). The co-contraction of both muscles during stimulation is a point for further investigations. The application of steering currents or prepulses will be examined in future experiments to obtain higher selectivity and hopefully single muscle responses on different tripoles in distinct stimulus amplitude ranges.

Using only single pulses during stimulation experiments with long interpulse intervals in between we did not induce fatigue of the stimulated muscles. The torque development remained stable and was reproducible over the experimentation time indicating (also) no muscle fatigue and a stable fit of the rat's "shoe".

5. Conclusions

At the end of the first set of experimentation we conclude that polyimide-based nerve cuffs seemed to be suitable for selective control of different muscles stimulating even small nerves. In chronic implantations, these nerve cuffs were mechanically harmless for the nerve and allowed stimulation within a wide margin of safety [7]. Future studies should be addressed to multipolar cuffs for selective stimulation and on measurements to analyze changes of excitation thresholds and force over time after chronic electrode implantation.

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