Multisite Microelectrodes for Use in Human Deep Brain Stimulation

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Abstract

This study describes a novel multisite recording probe with linear arrangement of recording sites. It is build from a 30cm long, 650µm diameter stainless steel rod featuring 31 microelectrodes on the side of its business end and a conical tip. Recording sites are gold plated and have a complex impedance in saline of few hundred kOhm. It is manufactured by precision mechanics and connected with a low-noise multichannel amplifier to a medical grade recording setup. While mounted to a standard stereotaxic frame its movement in z-direction is controlled with a proven rubber motor.
Preliminary recordings from anesthetized ferret's cortex show its ability to record both Local Field Potentials and Multi Unit Activity of neurons across different layers.

Keywords:
Multsite neuronal recording, steel probe, stereotaxic surgery, animal recording, medical device

1. INTRODUCTION

Parkinson's syndrome represents with an annual incidence of 10 new cases among 100000 inhabitants one of the most abundant neurodegenerative diseases. In an increasing number of cases this disease is symptomatically treated by so called high frequency (130 Hz) functional and permanent stimulation of sensitive brain regions in the basal ganglia [1, 2]. This procedure is principally reversible and adaptable, it only requires the implantation of stimulation electrodes inside the basal ganglia with the maximally achievable precision [3].
Up till now, targeting was performed mainly by image guided pre-operative planning and sometimes by electrophysiological scouting with a single wire microelectrode. With a usual step width of 1000µm along the pre-planned trajectory recordings were taken with this scout electrode. An experienced neurophysiologist is able to localize boundaries of the target region – usually the subthalamic nucleus (STN) - based on the audible signal, thus verifying the stereotaxic and image guided coordinates [4]. New results indicate that this boundary localization might even be performed with an automatized system, based on simple signal processing algorithms [5], but will clearly profit in speed and precision with a higher number of recording positions [8].
In order to support progress in this direction, we developed a novel multi-site microelectrode to improve targeting of the human basal ganglia with a multiplicity of recording microelectrodes. The intended medical use requires the probe to be at least 30cm in length, fitting to standard stereotaxic frames, having a diameter not exceeding the current single site microelectrodes (ø 650µm) and being made of stable and biocompatible materials. Consequently, the use of a precision mechanics and laser based modifications were applied, since no lithographical process is known to cover the whole required length of up to 30cm for sites and contact traces. In fact, the standard material of MST, silicon, wouldn't be stable enough to be used in a human brain in any ways.

2. MATERIALS AND METHODS

2.1. Multisite probe fabrication

A thin stainless steel tube (Figure 1 A) with an outer diameter of 650µm is equipped at its end with a recess which takes up a comb-like plastic microstructure (Figure 1 B), in which 31 insulated wires of 32µm in diameter are fixed. The 31 microwires protruding from the comb and one additional wire (Figure 1 C), connecting the very tip (Figure 1 D), are threaded into the inner lumen of the core. Tube and tip are mechanically, but not electrically connected to each other via

a plastic ring (Figure 1 E). All components are sealed by a thermo-curable epoxy resin. The recess in the steel tube as well as the probe tip is machined by precision wire erosion. The combs as well as the insulating rings are fabricated batch-wise by reaction molding using a microstructured casting mold with twelve cavities, which has been realized by micro die sinking erosion.

After the assembly of the components, subsequent machining by precision turning is performed in which excess of the resin is removed from the probe tip and the electrode sites on the face side of the comb-fixed microwires are opened. Hereafter, the insulation on the very tip is removed by excimer laser ablation. Finally, the very end of the tip is chamfered by mechanical fine grinding and the electrode sites are electroplated with a thin layer of gold (Figure 5). The shape of the tip as well as its chamfering reduce the risk of the damaging of blood vessels as well as effects of tissue traumatization.

All materials used for the fabrication of the probe comply with biocompatibility guidelines and are intended to withstand clinical sterilization procedures.

The 32 channel electrode is integrated in an electrode carrier unit that can be steam sterilized prior to use. The electrode carrier unit protects the electrode during transportation and contains a patented rubber tube drive unit [6]. This carrier unit is loaded to a micro-drive system.

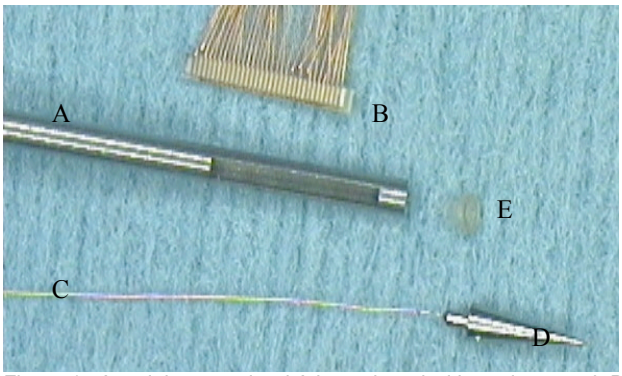

Figure 1: A stainless steel rod A is equipped with a micro-comb B and a conical tip D. The comb holds 31 microwires in a defined position, which are together with the tip-wire C threaded to the contact end of the 30cm rod A. An insulating ring E separates the rod from the tip.

2.2. *In Vivo animal recordings*

The novel steel probe was put to use to record and analyse both multi-unit activity (MUA) and local field potentials (LFP) from area 17 of an isoflurane-anesthetized ferret (Figure 2). Neural activity was recorded using the 32 channel-probe with linearly distributed contacts (spacing: 100µm), spanning all cortical layers. Visual stimulation to the ferret comprised moving gratings, bars, and random dot patterns. Neural responses were analyzed with respect to neuronal synchrony and temporal patterning (to be published elsewhere).

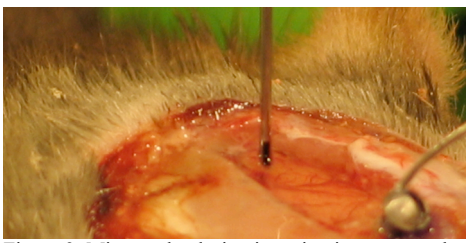

Figure 2: Microprobe during insertion into an anesthtetized ferrets cortex.

3. RESULTS AND DISCUSSIONS

3.1. *Probe infrastructure*

The 32 channel microelectrode was integrated in a micro-drive system containing a patented rubber tube drive (see Figure 3) [6] and a patented xyz-manipulator with telescopic guide tube. The rubber drive allows to record neural signals without motor artifacts while the electrode is moving at slow velocities through the target region. The rubber tube holds the electrode permanently under tension and avoids stick-slip motion and hysteresis effects and therefore guarantees a high reproducibility of the recording position (for details see [6]). The electrode position is software controlled via personal computer software. The electrode position and the recorded data are displayed simultaneously on a graphical user interface.

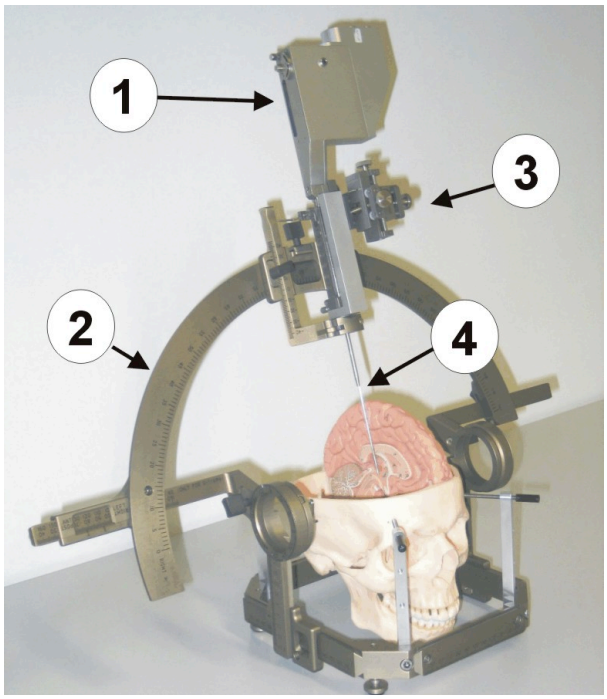

Figure 3: Microdrive (1) with loaded 32 channel microelectrode mounted on a CRW© (Cosman, Roberts and Wells) stereotaxic frame (© by Tyco healthcare, Radionics, USA) (2). The microdrive (Thomas Recording GmbH) is equipped with a 32 channel low noise preamplifier, a rubber tube drive and a xyz-manipulator (3) with telescopic guide tube (4) for exact DBS electrode placement.

The microdrive system and the telescopic guide tube builds an integrated metal shield around the high impedance microelectrode which minimizes electrical noise pickup from the noisy environment of an operating room.

A 32 channel low noise preamplifier is integrated in this microdrive system to further reduce electrical noise pickup (e.g. hum noise) from the electrical environment of an operating room. The preamplifier output is connected to a 32 channel programmable gain main amplifier [7] with integrated patient isolation unit. The signal path of the recording system has a broad bandwidth (0.06Hz…15kHz) so that local field potentials as well as single units can be recorded from each of the 32 recording sites.
Ongoing medical approval procedures prohibit currently the probe's use in human surgeries, instead validation within animal recordings are performed.

3.2. *Linear probes in vivo*

Probes with different site spacings were manufactured, but in animal experiments the ones shown in Figure 4 were used.

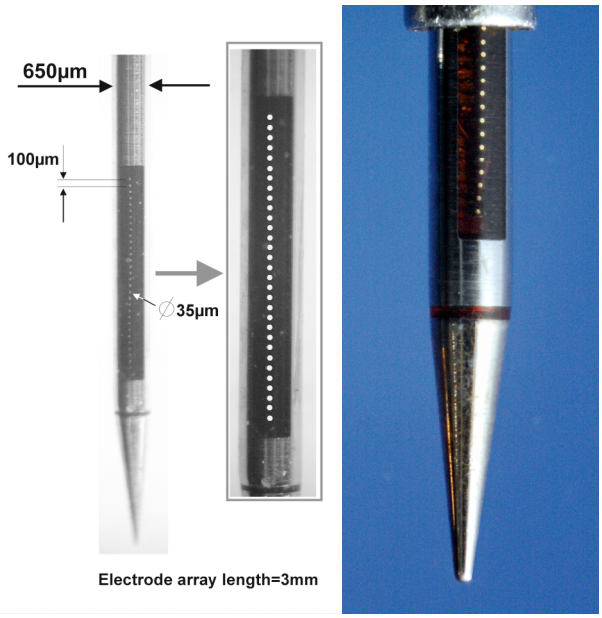

Figure 4: Working end of the linear array probe Note the tight spacing of sites over a distance of several Millimeters.

Even though the diameter of the probe is due to its intended use in humans not very suitable for small animals, their site spacing is with 100µm small enough to record several cortical layers at once. Recording site diameter of 35µm (Figure 5) translates in a complex impedance in the range of a few hundred kOhm in saline.

Peri-stimulus time histograms of the recorded MUA showed consistent on- and off-responses across all cortical layers. As revealed by autocorrelograms, multiunit-oscillations (see Figure 6) at gamma-frequencies were readily evoked with all types of stimuli used, predominantly within the pyramidal cell layers. For a wide variety of stimuli, the induced oscillatory response showed a frequency-adaptation during the first second of the stimulus period. This variation in time and the primary frequency content of the oscillatory response was consistent across all layers of the primary visual cortex, with highest power-values for the pyramidal cell layers (layer 5/6 > layer 2/3 > layer 4 > layer 1/2).

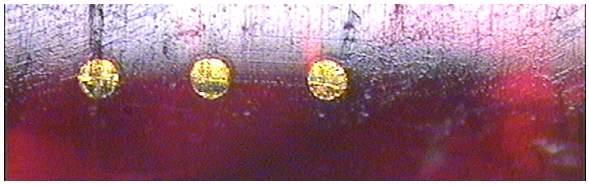

Figure 5: Light microscope photo of three gold plated electrode contacts with a complex impedance in the range of 250kOhm.

The animal results suggest the usefulness of the described multi-channel probe for recording neuronal activity from widely spaced contacts.

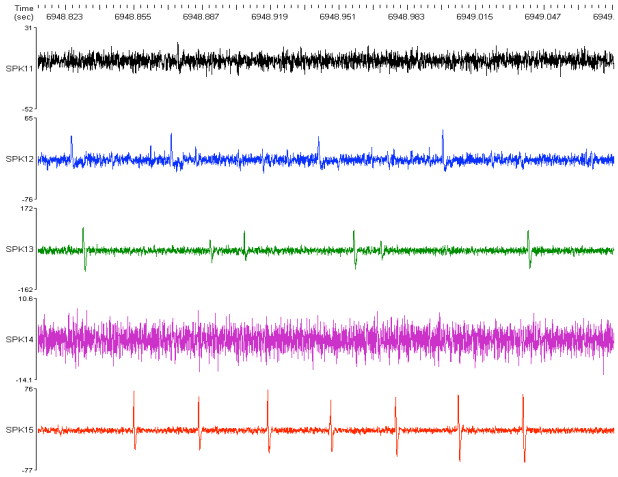

Figure 6: Synchronous five channel recordings of multi-unit activity (high-pass filtered above 300Hz-6kHz) from the ferret's cortex.

We therefore conclude, that this novel, unbreakable, long multisite recording probe and its accompanying infrastructure will not only improve electrophysiologic targeting during brain pacemaker implantation, but in addition lead to revolutionary new insights into the functional structure of the human brain.
We even suggest to further develop this type of human use probe as a carrier for future lab-on-chip development, thus rendering the brain accessible for minimally invasive analytical devices in situ.

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