A NOVEL THIN FILM ENDOVASCULAR ELECTRODE ARRAY FOR MINIMALLY INVASIVE NEURAL RECORDING

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ABSTRACT

A thin film endovascular electrode array with 8 electrodes capable of accessing sub-mm diameter blood vessels was designed, fabricated, and tested *in vivo*. Endovascular, surface, and penetrating electrodes were implanted into a sheep brain and concurrent recordings were collected. Recorded data from all three electrode types show a strong correlation, demonstrating the potential use of endovascular electrodes as a minimally invasive alternative to surface or penetrating electrodes with similar recording capabilities.

KEYWORDS

Endovascular electrodes, neural recording, minimally invasive, Parylene C, epilepsy

INTRODUCTION

Neural interfaces, devices which communicate with neural tissue via electrical activity, are integral in advancing knowledge of the nervous system. Non-invasive devices, such as scalp electrodes, record relatively low-resolution neural activity, whereas highly invasive devices, such as depth electrodes, record high-resolution neural activity such as local field potentials (LFPs) and single units. Endovascular (EV) electrodes break this trend by utilizing the blood vessels as a pathway to reach areas adjacent to neural tissue with a minimally invasive procedure, while being capable of recording high-resolution neural activity.

While EV devices have many possible applications, one of the most promising is the mapping of seizure foci in patients with epilepsy. The current mapping procedure requires implantation of multiple surface and/or depth electrodes. This procedure is highly invasive (13-20% prevalence of serious adverse events), recordings are limited to the fixed, implanted electrode position, and some brain regions are inaccessible due to impeding blood vessels or nearby critical brain tissue, resulting in inadequate localization in 60-70% of patients [1,2]. By using minimally invasive EV electrodes, these issues can be bypassed. Commonly used EV devices are either large (>1 mm in diameter), making brain regions without large blood vessels inaccessible, or have very few electrodes (<4), resulting in low spatial coverage [3]. Here, we describe a novel thin film EV multi-electrode array capable of implantation into a sub-mm diameter blood vessel.

MATERIALS AND METHODS

Design and fabrication of the endovascular electrode array

The EV device consists of a thin film, Parylene C-metal-Parylene C (PMP) electrode array, insulated platinum wires (36 µm conductor diameter, 6 µm insulation), a connector, and a commercial guidewire. Electrode arrays were fabricated using a micromachining process described previously [4]. Briefly, 4.4 µm of Parylene C was chemical vapor deposited (CVD) onto a 4" silicon wafer. 15 nm titanium plus 200 nm platinum were deposited via e-beam evaporation and patterned to form electrode sites, traces, and bondpads via a lift-off process. The metal layer was encapsulated with a 4.7 µm Parylene C layer. Electrodes and bondpads were exposed, and the electrode array was cut out using deep reactive ion etching. Devices were released from the silicon carrier wafer manually by wetting with water and lifting the array with tweezers.

The thin film electrode array (Fig. 1) comprises eight electrodes on the distal end, each connected to a single bondpad on the proximal end of the thread-like structure. Electrodes varied in diameter from 100 to 200 µm, with three aggregate electrodes shorting 2-4 200 µm ⌀ electrodes to produce a larger recording site.

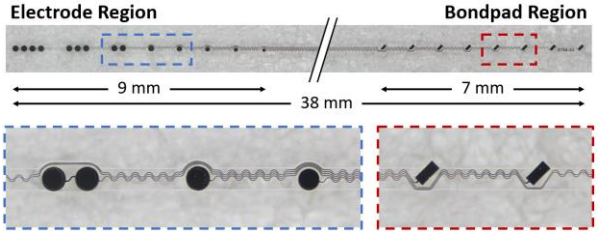

Figure 1: The PMP electrode array, with exposed metal electrodes on the distal (left) side, including a 2x200 µm ⌀ aggregate electrode, and exposed metal bondpads on the proximal (right) side.

After deinsulating the ends, one end of each platinum wire was attached to a single bondpad and the other end to a connector (to interface with recording equipment). The thin film/wire/connector assembly was mounted to a commercial guidewire (assembled diameter <0.4 mm), with the exposed electrodes 10 mm proximal to the distal tip of the guidewire and the connector near the proximal end of the guidewire. A fully assembled device is shown in Fig. 2. Electrode sites were characterized using electrochemical impedance spectroscopy (EIS); a typical result is shown in the Fig. 2 inset.

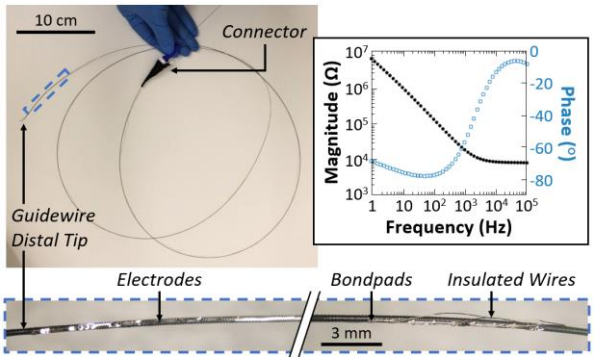

Figure 2: The assembled EV electrode array, with electrodes near the distal tip of the guidewire. The inset graph shows typical EIS data for an electrode with a 1 kHz impedance magnitude of 18 kΩ.

In vivo evaluation of the endovascular electrode array

EV, surface, and depth electrodes were implanted concurrently in a sheep brain. Experiments were reviewed and approved by the

Institutional Animal Care and Use Committee (IACUC) of the Lundquist Institute for Biomedical Innovation.

The animal was anesthetized and placed in a supine position. Femoral arterial access was established percutaneously and a catheter was positioned in the common carotid artery for arterial and venous angiograms of the cerebral vasculature. Internal jugular (IJ) venous access was established by exposing the IJ vein and placing an introducer sheath into the vein. A coaxial system of EV catheters was advanced into the cerebral venous system. Once the inner most catheter reached the superior sagittal sinus (SSS), the EV electrode array was advanced to the tip of the inner most catheter, then the catheter was withdrawn 20-30 mm to expose the electrode array.

After placement of the EV device, the animal was turned to a prone position. The skin and muscle above the target brain region were opened using a scalpel, a small craniotomy was performed above the SSS using a craniotome drill, and the dura was incised. A 1x6 subdural strip electrode for electrocorticography (ECoG, Ad-Tech) recording was placed under the dura, and a depth electrode with six macro-electrodes and ten micro-electrodes for stereoelectroencephalography (SEEG, Ad-Tech) recording was inserted adjacent to the EV electrodes using standard surgical techniques. Fig. 3 illustrates the location of all implanted electrodes.

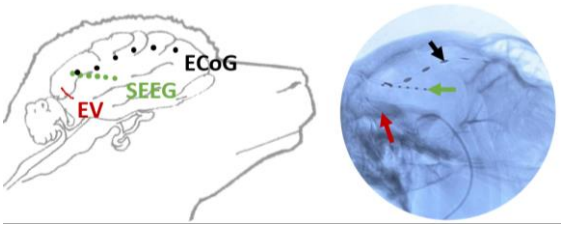

Figure 3: Locations of concurrently implanted EV (red), SEEG (green), and ECoG (black) electrodes on (left) a diagram of the sheep head and brain and (right) an intraoperative angiogram.

All electrodes were connected to a LabLynx recording system (NeuraLynx). Electrical recordings were collected simultaneously from all electrodes while the animal was under anesthesia with 3.5% isoflurane. Later, isoflurane was decreased to 1.5%, and more recordings were collected to verify electrode functionality with more brain activity.

RESULTS AND DISCUSSION

The novel EV device was successfully fabricated and implanted into the superior sagittal sinus of a sheep, with ECoG and SEEG electrodes implanted nearby. All connected EV electrodes (n = 7) remained functional after implantation and were able to record burst-suppression, a typical pattern induced by the administration of anesthetic medicines. Signal features (amplitude, resolution, bursts) in concurrent recordings from all electrode types were highly correlated (representative recordings in Fig. 4), as quantified by high Pearson correlation coefficient values. Upon lightening anesthesia (Fig. 4, right), burst activities became more frequent. This result is consistent with recordings from surface (ECoG) electrodes in a rat brain from Stenroos et al. [5] and validates that the recorded signal is from spontaneous brain activity.

Minor differences in signal amplitudes and high-frequency electrical activity are due to differences in electrode size and proximity to target tissue. ECoG and SEEG electrodes are in direct contact with neural tissue, increasing the signal-to-noise ratio (SNR) and signal amplitude. EV electrodes record signals across the blood vessel wall, introducing some signal damping and decreasing the SNR. Macro-electrodes (ECoG and SEEG) have surface areas on the order of 5-13 mm^2 which record lower frequency neural activity (such as LFPs) due to spatial averaging of all signals near the electrode surface, resulting in minimal high-frequency activity. Micro-electrodes (SEEG and EV) have a smaller surface area on the order of 0.01-0.1 mm^2 and can record both low and high frequency signals (LFPs and single units) due to less spatial averaging. This results in more low amplitude fluctuations in the recorded signal representing activity from smaller groups of neurons.

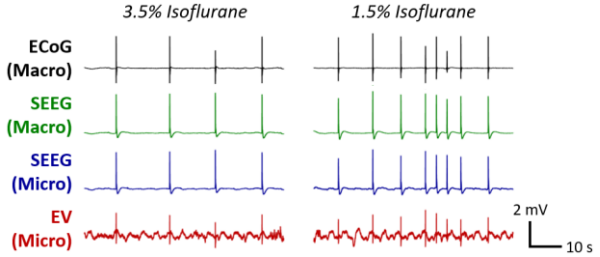

Figure 4: Simultaneous recordings from ECoG, SEEG, and EV electrodes with (left) 3.5% isoflurane and (right) 1.5% isoflurane.

CONCLUSIONS

This work presents the design and fabrication of the first thin film EV electrode array with multiple electrodes and sub-mm diameter, allowing access to small, branched blood vessels in a large animal model. The functionality of the EV device was tested in a sheep model concurrently with surface (ECoG) and depth (SEEG) probes. Highly correlated neural recordings from the three electrode types support the use of EV devices as a minimally invasive alternative to ECoG or SEEG devices for the recording of neural signals in many applications, including seizure mapping.

Future studies will be conducted to evaluate the functionality of the novel EV device in an awake, freely moving animal to achieve more realistic and clinically relevant recordings. In addition, the EV device will be tested in an animal model of epilepsy to assess its efficacy in seizure localization.

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