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Ring and peg electrodes for minimally-Invasive and long-term sub-scalp EEG recordings

Y.B. Benovitski[a,1,*], A. Lai[b,1], C.C. McGowan[a], O. Burns[a], V. Maxim[a], D.A.X. Nayagam[a,c], R. Millard[a], G.D. Rathbone[a], M.A. le Chevoir[f], R.A. Williams[c], D.B. Grayden[e,g], C.N. May[d], M. Murphy[b], W.J. D'Souza[b], M.J. Cook[b], C.E. Williams[a]

[a] The Bionics Institute, East Melbourne, Victoria, Australia
[b] Department of Medicine, St. Vincent's Hospital, The University of Melbourne, Melbourne, Victoria, Australia
[c] Department of Anatomical Pathology, The University of Melbourne, St Vincent's Hospital, Melbourne, Australia
[d] The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Melbourne, Victoria, Australia
[e] Department of Electrical and Electronic Engineering, The University of Melbourne, Melbourne, Victoria, Australia
[f] Faculty of Veterinary and Agricultural Science, The University of Melbourne, Melbourne, Victoria, Australia
[g] Centre for Neural Engineering, The University of Melbourne, Melbourne, Victoria, Australia

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ABSTRACT

Objective: Minimally-invasive approaches are needed for long-term reliable Electroencephalography (EEG) recordings to assist with epilepsy diagnosis, investigation and more naturalistic monitoring. This study compared three methods for long-term implantation of sub-scalp EEG electrodes.
Methods: Three types of electrodes (disk, ring, and peg) were fabricated from biocompatible materials and implanted under the scalp in five ambulatory ewes for 3 months. Disk electrodes were inserted into sub-pericranial pockets. Ring electrodes were tunneled under the scalp. Peg electrodes were inserted into the skull, close to the dura. EEG was continuously monitored wirelessly. High resolution CT imaging, histopathology, and impedance measurements were used to assess the status of the electrodes at the end of the study.
Results: EEG amplitude was larger in the peg compared with the disk and ring electrodes ($p < 0.05$). Similarly, chewing artifacts were lower in the peg electrodes ($p < 0.05$). Electrode impedance increased after long-term implantation particularly for those within the bone ($p < 0.01$). Micro-CT scans indicated that all electrodes stayed within the sub-scalp layers. All pegs remained within the burr holes as implanted with no evidence of extrusion. Eight of 10 disks partially eroded into the bone by 1.0 mm from the surface of the skull. The ring arrays remained within the sub-scalp layers close to implantation site. Histology revealed that the electrodes were encapsulated in a thin fibrous tissue adjacent to the pericranium. Overlying this was a loose connective layer and scalp. Erosion into the bone occurred under the rim of the sub-pericranial disk electrodes.
Conclusions: The results indicate that the peg electrodes provided high quality EEG, mechanical stability, and lower chewing artifact. Whereas, ring electrode arrays tunneled under the scalp enable minimal surgical techniques to be used for implantation and removal.

1. Introduction

Around 50 million people worldwide have epilepsy and 30–40% of these patients are drug resistant (Kwan and Sander, 2004). One study estimated that 92,000 people were misdiagnosed with epilepsy in England and Wales in 2002 and were inappropriately prescribed anti-epileptic drugs (Juarez-Garcia et al., 2006). The side effects of anti-epileptic drugs include cardiovascular complications (Vyas et al., 2015), cognitive and behavioral deficits (Ortinski and Meador, 2004), and other adverse reactions (Bainbridge and Oh, 2013). These diagnostic and therapeutic issues put patients at significant risk and cause a substantial burden on the healthcare system (Juarez-Garcia et al., 2006).

The most common diagnostic instruments for epilepsy involve the

Abbreviations: EEG, electroencephalography; Micro-CT, micro-computed tomography; FFT, fast fourier transform; aEEG, amplitude-integrated electroencephalography; H & E, haematoxylin and eosin

* Corresponding author at: Bionics Institute, 384-388 Albert St, East Melbourne VIC 3002, Australia.
E-mail address: ybenovitski@bionicsinstitute.org (Y.B. Benovitski).

[1] Equal contributors.

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analysis of EEG signals recorded from scalp electrodes. These are useful for short-term recordings but are not currently suitable for long-term monitoring indications. Moreover, blackouts are often misdiagnosed as having an epileptic cause (Benbadis, 2009; Petkar et al., 2006; Smith, 2001) because these events are often infrequent (weeks to months apart) and can be situational, so it is difficult to capture them with in-patient EEG monitoring.

Earlier studies indicate a need for a long-term implantable device to continuously monitor epileptiform events to aid clinical management of epilepsy patients (for review see Freestone et al., 2015). A recent long-term clinical trial of a seizure advisory system with electrodes implanted under the skull showed that entries in patient diaries often do not correspond with recorded epileptiform events (Cook et al., 2013). This study used epidural electrodes that require craniotomy. Other surgical approaches, used for acute epileptogenic zone identification, involve subdural and depth electrodes (for review see Sperling, 1997). However, these are highly invasive and are not suitable for long-term monitoring of epilepsy in a wider patient population, especially in ambulatory setting, so a less invasive approach is required. Sub-scalp electrodes may provide an optimal solution for minimally-invasive, long-term epilepsy monitoring.

The main objective of the current study was to assess the feasibility of three types of sub-scalp electrodes for long-term implantation. These were developed to suit three different sub-scalp surgical approaches: peg electrodes inserted into burr holes in the cranium, disk electrodes slid into pockets created under the pericranium, and ring electrodes tunneled under the scalp via a small guide cannula. Electrodes have been previously placed in burr holes (Barnett et al., 1990; Holthausen et al., 1994; Williams et al., 1990) but not tunneled under the scalp such as the ring and disk. Compared to earlier versions, electrodes fabricated for this study are fixed in size. This approach allows the implant to be pre-assembled, reducing surgical complexity and improving reliability.

The aim of this project was to compare long-term signal quality of the EEG, surgical feasibility, and stability of these three types of electrodes in sheep. Sheep were used in this study because their skull thickness (6 vs. 6.3 mm; Laure et al., 2012) and dimensions are comparable to humans.

2. Material and methods

2.1. Subjects

This research was approved by the Florey Institute of Neuroscience and Mental Health Animal Ethics Committee, AEC Number 14-108-FINMH, that adheres to the Australian Code for the Care and Use of Animals for Scientific Purposes.

Five healthy Merino ewes, 1.5-2 years old (sheep S1 to S5) were used for this study. Sheep were individually housed in 12 h light/dark cycle and given free access to water and fed oaten chaff once a day. Food and water intake and the well-being of the animals were monitored daily.

2.2. Implant

Three types of electrodes, peg, disk, and ring, were fabricated at the Bionics Institute from biocompatible silicone and stainless steel (Fig. 1). They were designed for sub-scalp placement procedures and removability. The surface areas of the three types of electrodes were similar at about $\sim 32\ mm^2$, which resulted in comparable saline impedance. Peg electrodes had a progressive taper to prevent bone encapsulation and promote ease of removal.

They were connected to a fully-implantable transmitter (PhysioTel model D70-EEE, 455 kHz, input voltage range ± 2.5 mV, and channel bandwidth 1–100 Hz from Data Sciences International, DSI, New Brighton, MN, USA) used to transmit EEG signals to a DSI external data logger. All DSI equipment was factory calibrated. Pairs of peg and disk electrodes were individually attached and the two ring electrodes were connected as an array (Fig. 2). Implants were assembled in a clean room, tested for impedance, and cold sterilized prior to implantation. Implants had fixed dimensions and came in one piece so no additional assembly was required during implantation.

The first animal was implanted with an earlier version that did not have the two ring electrodes thus the total number of electrodes was 28.

2.3. Implant surgery

Electrodes and transmitter were implanted under general anesthesia using standard sterile surgery techniques. Anesthesia was induced with intravenous sodium thiopental (15 mg/kg) and ongoing intubation was maintained with 1.5–2.0% isoflurane/O2. Sheep were treated with intramuscular antibiotics (900 mg, procaine penicillin, Troy Laboratories, NSW) at surgery and 2 days post-operatively. Analgesia was maintained with intramuscular flunixin meglumine (1 mg/kg; Troy Laboratories) at surgery and 4 h post-surgery. Reflexes were tested to ensure adequate anesthetic and vital signs were recorded throughout the procedure. Sheep were placed in a stereotaxic frame and electrodes were implanted via a midline incision. The soft tissue was separated from the skull on the right side using hemostats to form a skin “flap”. The anatomical targets are illustrated in Figs. 2 and 3.

For the disk electrodes, a periosteal elevator was used to create a sub-pericranial pocket for each disk. The first disk was positioned 1.5 cm from midline and the second disk 2 cm posteriorly to the first.

For the ring electrode, a small, custom-made guide cannula was tunneled under the scalp through to the open flap. The cannula tip was removed and the ring electrode array was inserted into the cannula so it could be positioned under the scalp and the cannula was removed.

For the peg electrode, a periosteal elevator was used to clear the location of the burr hole. A 3.1 mm diameter round cutting burr was used to drill to the lower table until the dura was just visible. The wall of the burr hole was widened using a handheld 4.5 mm diameter reamer for the silicone overmolding to fit. Depth and size of burr hole were checked for fit using silicone dummy electrodes. Each electrode was inserted into the hole and rotated so that the leads had the right amount of tension and minimum slackness. The first peg was positioned 7 mm from the midline suture and 16 mm anterior from bregma and the second peg 6 mm posterior to bregma/occipital suture.

Leads were tunneled under the skin so that the telemetry device could be placed into the pocket in the neck. Following implantation of the electrodes, the skin was brought together and sutured.

2.4. EEG recordings

EEG recordings were made over 10 weeks for all five animals and all 28 implanted electrodes. This allowed assessment of signal quality and stability over time. Sheep were videotaped to document movements. Recordings were made simultaneously from three electrode pairs at a sampling rate of 500 Hz. The rostral electrodes were likely covering the parietal cortex and the caudal ones the occipital cortex. These regions are involved in cognitive association.

2.5. EEG signal processing

Recordings were imported into proprietary EEG software (Persyst, San Diego, CA, USA) for amplitude-integrated electroencephalography (aEEG), and fast Fourier transform (FFT) spectrogram analysis. The aEEG relies on the specifications of the original cerebral function monitor (Maynard et al., 1969). Time course measurements were binned as follows: 0.4–0.9, 0.9–3, 3–5 and 10–35 weeks.

Using the filters and the spectrogram function in Persyst, high amplitude slow wave long duration epochs (below 15 Hz and over 15–20 min), short duration high amplitude slow wave (below 15 Hz and over 1–2 min without chewing or any other artifacts), chewing