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Research Article

A testbed for optimizing electrodes embedded in the skull or in artificial skull replacement pieces used after injury

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HIGHLIGHTS

- A preclinical testbed is demonstrated for embedding electrodes in artificial skull.
- Options are explored for increasing electrode surface area using the skull depth.
- Novel electrode designs could also be embedded in the bone directly via burr holes.
- The testbed's high contact density allows one to optimize electrode spacing.
- High density of contacts possible in artificial skull improves movement decoding

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ABSTRACT

Background: Custom-fitted skull replacement pieces are often used after a head injury or surgery to replace damaged bone. Chronic brain recordings are beneficial after injury/surgery for monitoring brain health and seizure development. Embedding electrodes directly in these artificial skull replacement pieces would be a novel, low-risk way to perform chronic brain monitoring in these patients. Similarly, embedding electrodes directly in healthy skull would be a viable minimally-invasive option for many other neuroscience and neurotechnology applications requiring chronic brain recordings.
New method: We demonstrate a preclinical testbed that can be used for refining electrode designs embedded in artificial skull replacement pieces or for embedding directly into the skull itself. Options are explored to increase the surface area of the contacts without increasing recording contact diameter to maximize recording resolution.
Results: Embedding electrodes in real or artificial skull allows one to lower electrode impedance without increasing the recording contact diameter by making use of conductive channels that extend into the skull. The higher density of small contacts embedded in the artificial skull in this testbed enables one to optimize electrode spacing for use in real bone.
Comparison with existing methods: For brain monitoring applications, skull-embedded electrodes fill a gap between electroencephalograms recorded on the scalp surface and the more invasive epidural or subdural electrode sheets.
Conclusions: Embedding electrodes into the skull or in skull replacement pieces may provide a safe, convenient, minimally-invasive alternative for chronic brain monitoring. The manufacturing methods described here will facilitate further testing of skull-embedded electrodes in animal models.

1. Introduction

Cranioplasty with artificial bone replacement material is often used after a traumatic brain injury to replace skull sections that are damaged beyond repair or used after therapeutic bone removal in response to infection, tumors, or cranial swelling (Zanotti et al., 2016). For large repairs, artificial skull replacement pieces are often custom manufactured for each patient using their own computer tomography (CT) scans to ensure each person's replacement piece closely replicates their natural cranial space and forms a smooth transition to the intact skull (Zanotti et al., 2016).

The ability to chronically monitor brain health and watch for epileptic activity development would be quite useful after

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brain trauma or surgery (Ritter et al., 2016; Rao and Parko, 2015). However, continuous brain monitoring via scalp surface electroencephalograms (EEGs) can be cumbersome and impractical outside of the clinical setting and may not be possible if the skin is not healthy enough after injury to safely apply the electrodes. Chronically implanting recording electrodes, such as electrocorticographic (ECoG) arrays, within the cranial cavity would allow for more stable long-term brain monitoring but would also increase the risk of further inflammation, contusions and/or infarcts (Fong et al., 2012). A low-risk alternative that avoids placing invasive electrodes on damaged brain tissue would be to embed electrodes within the artificial skull replacement piece itself. Custom-fabricated skull replacement pieces have been manufactured from a number of non-conductive materials that are well suited to house conductive recording electrodes (e.g. polymethyl methacrylate (PMMA) (Fiaschi, 2016; Chiarini, 2004), polyetheretherketone (PEEK) (Jonkergouw, 2016; Rammos et al., 2015), polypropylene polyester (Kasprzak, 2015; Kasprzak et al., 2012), bioceramic porous hydroxyapetite (Lindner et al., 2016; Stefini, 2013)). Electrodes can be embedded within the artificial skull so that the recording contacts are flush with the inner lumen of the skull to avoid any protrusions into the cranial cavity that might cause pressure and further damage.

Electrodes embedded in one's natural skull could also be useful for many applications. Improvements in real-time neural recording and signal processing technology have spawned the development of a number of 'closed-loop' neural recording applications that could all benefit from a stable permanently-implanted but minimally invasive recording option like embedding electrodes within the skull. For example, chronic brain recordings are being investigated as a means to detect upcoming seizures in time to either warn the person or take measures to counteract the seizure (van Luijtelaar, 2016; Sun and Morrell, 2014; Song and Zhang, 2016). Brain-machine interfacing research has shown that paralyzed individuals can learn to volitionally modulate their sensorimotor field potentials with thoughts of movement, and this modulation can be used to control assistive or therapeutic devices (Wang et al., 2013; Spuler, 2014). For people who are fully paralyzed or 'locked-in', maintained cognitive and sensory responses in their cortical field potentials may be used to drive much needed communication programs (Dijkstra, 2015; Speier et al., 2013). Additionally, researchers are investigating the use of recorded brain activity to continuously update deep brain stimulation settings to more effectively reduce symptoms of Parkinson's disease while minimizing side effects and power consumption (Sun and Morrell, 2014; Little, 2013; Rosin, 2011; Swann, 2016).

In spite of the many potential advantages of embedded electrodes into artificial skull replacement pieces or directly in intact bone, work on chronic skull-embedded electrodes in primates or humans has been relatively limited (Kennedy, 2004). The appropriate number and distribution of electrodes still need to be optimized for each specific neurotechnology application. Additionally, unlike subdural or epidural ECoG electrodes that should be thin and flat, skull embedded electrodes can have more elaborate conductive surface structures including conductive channels that extent up into the skull to increase the surface area for charge transfer while maintaining a small contact diameter and high spatial resolution along the inner lumen of the skull. Exploring this electrode design space will require a testbed that allows for comparisons between different individual electrode geometries and comparisons of different spatial distributions of electrodes.

This paper describes how to make and attach a custom-fitted skull replacement piece with embedded electrode arrays in a large animal model. Methods described here can be used as a preclinical testbed to facilitate further development of skull-embedded electrode technology for future use in human. The arrays described are also suitable for use in basic science research in animal models.

We also show how to manufacture a number of different prototype electrode contact designs that make use of the skull's depth dimension to increase each recording contact's surface area while maintaining a constant footprint and spatial resolution along the inner lumen of the skull. Finally, we demonstrate how an artificial skull piece with a high density of electrodes can be used to compare different electrode density options for a desired application simply by comparing different subsets of the available channels. Electrodes embedded in natural bone have to be far enough apart to maintain the health and integrity of the skull. Therefore, the higher density of electrodes that can be installed in this artificial-skull testbed allows one to test out different subsets of contacts to compare different spacing option before deciding on a distribution of electrodes to embed in natural bone.

2. Materials and methods

2.1. Design manufacturing

As part of other ongoing studies, two Rhesus macaques were chronically implanted with custom acrylic skull replacement sections containing an integrated 8 × 8 grid of electrodes designed to record epidural field potentials at the inner lumen of the skull. These skull replacement electrode arrays (SREAs) were custom manufactured to match the curvature of each animal's skull using CT scans to determine precise bone geometry. One animal was sequentially implanted with two different SREAs (designs I and V) and a second animal was sequentially implanted with three different SREAs (designs II, III, and IV). With each new version, the embedded electrodes themselves were modified to alter the surface area and impedance of the recording contacts while still maintaining a similar spatial resolution over the cortical anatomy. Fig. 1A shows the cortical anatomy spanned by the 8 × 8 electrode grids in all five SREA designs.

To make custom-fitted SREAs for each animal, three dimensional (3D) computer models of the skull and brain were first generated from the computer tomography (CT) and magnetic resonance imaging (MRI) data respectively (Fig. 1B & C). The software package 'monkey Cicerone' (Miocinovic et al., 2007; Miocinovic, 2007) was used for visualizing the co-registered 3D macaque skull and brain images so that we could customize our SREAs to fit over the premotor and primary motor cortices associated with upper limb function. However, upon inspection of the skull model, we found that the skull model itself contained pronounced ridges and valleys reflecting the underlying anatomical landmarks. Therefore, the MRIs were not essential in this non-human primate model as the CT alone turned out to be sufficient to identify the desired skull section on which to base our SREAs for placement over the desired upper limb cortical locations. Co-registered MRIs may still be useful in other large animal models where the internal skull surface does not reflect the brain surface anatomy as clearly.

The skull replacement portion of the SREA could potentially be manufactured from the computer model directly via rapid prototyping if one is lucky enough to have a local rapid prototyping service that works with biocompatible non-conductive plastics. If that is the case, Solidworks or other 3D software can be used to trim down the computer model of the skull to the desired final SREA shape and to configure holes in the skull replacement piece for insertion of the electrodes once the replacement piece is made (see hypothetical example in Fig. 1D).

Most researchers, however, typically only have access to rapid prototyping services that use non-biocompatible plastics. Therefore, in this paper, we describe the 'indirect' manufacturing method