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Customizable cap implants for neurophysiological experimentation

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HIGHLIGHTS

- Implanted three rhesus macaque primates with novel, customizable PEEK cap implants.
- Each implant was acrylic-free.
- Reduced surgical invasiveness while increasing strength and utilizable surface area.
- Head fixation and chronic recordings were successfully performed.

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ABSTRACT

Background: Several primate neurophysiology laboratories have adopted acrylic-free, custom-fit cranial implants. These implants are often comprised of titanium or plastic polymers, such as polyether ether ketone (PEEK). Titanium is favored for its mechanical strength and osseointegrative properties whereas PEEK is notable for its lightweight, machinability, and MRI compatibility. Recent titanium/PEEK implants have proven to be effective in minimizing infection and implant failure, thereby prolonging experiments and optimizing the scientific contribution of a single primate.
New method: We created novel, customizable PEEK 'cap' implants that contour to the primate's skull. The implants were created using MRI and/or CT data, SolidWorks software and CNC-machining.
Results: Three rhesus macaques were implanted with a PEEK cap implant. Head fixation and chronic recordings were successfully performed. Improvements in design and surgical technique solved issues of granulation tissue formation and headpost screw breakage.
Comparison with existing methods: Primate cranial implants have traditionally been fastened to the skull using acrylic and anchor screws. This technique is prone to skin recession, infection, and implant failure. More recent methods have used imaging data to create custom-fit titanium/PEEK implants with radially extending feet or vertical columns. Compared to our design, these implants are more surgically invasive over time, have less force distribution, and/or do not optimize the utilizable surface area of the skull.
Conclusions: Our PEEK cap implants served as an effective and affordable means to perform electrophysiological experimentation while reducing surgical invasiveness, providing increased strength, and optimizing useful surface area.

1. Introduction

Cranial implants are essential for non-human primate neurophysiological experimentation and their continual refinement enhances the well-being and potential scientific contribution of each primate. The rapid development of pre-fabricated cranial implants in recent years has motivated researchers to improve traditional techniques and materials and create safer, more effective, and more sustainable alternatives. These improvements are made

Abbreviations: PEEK, polyether ether ketone.

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to two fundamental properties: implant design and implant material. Both factors are critical determinants of cranial bone, skin, and muscle health, which ultimately affects the comfort of the research animal as well as the longevity of the implant. Therefore, clear demonstration of improvements to animal welfare and experimental outcomes are important for justifying the substantial investment in time and money necessary to adopt a new technique (Adams et al., 2007).

Traditionally, cranial implants such as a headpost or recording chamber have been attached to the skull using anchor screws embedded in a cap of acrylic or dental cement (Lisberger and Westbrook, 1985; Mitz et al., 2009; Mueller et al., 2014; Pfingst et al., 1989). Acrylic does not bond directly to the skull but instead serves to hold the cranial implant to the anchor screws (Mulliken et al., 2015; Overton et al., 2017). Using acrylic in this way is fast, familiar, inexpensive, and well documented. In fact, Adams et al. (2011), found that 33/36 US primate visual laboratories that responded to their questionnaire had used the method of embedding both a chamber and headpost into a single acrylic cap. Though this material and technique are common, they are associated with adverse effects to bone, skin, and muscle health.

Acrylic undergoes an exothermic reaction when applied to the skull, releasing heat that may cause bone necrosis (Dunne and Orr, 2002; Eriksson and Albrektsson, 1983; Ormianer et al., 2000). Furthermore, because acrylic does not bind to the underlying bone directly, granulation tissue may form between the acrylic cap and skull, thus increasing the chance of the implant dislodging from the skull (Adams et al., 2011; Betelak et al., 2001; Mulliken et al., 2015). This risk is further enhanced by acrylic's cytotoxity and lack of biocompatibility (Dahl et al., 1994; Treon et al., 1949). Acrylic is also difficult to mold intra-surgically; the outer surface of the acrylic cap may be left coarse with sharp edges at the skin border. These factors prevent skin healing, harbor infection, and make the cap difficult to clean (Adams et al., 2007; Adams et al., 2011). Lastly, after the acrylic cap has set, its surface cannot be utilized for experimental purposes (e.g. electrode pedestal or headpost attachment) unless an additional surgery is performed to cut the acrylic and access the skull. Taken together, acrylic can be biologically harmful and often compromises both the lifespan and stability of implants.

To circumvent the issues associated with acrylic, many groups have adopted alternative materials including stainless steel, titanium or plastic polymers such as polyether ether ketone (PEEK) for headposts and recording chambers. Titanium has gained popularity for these implant designs because of its mechanical strength, biocompatible coatings, customizability, and osseointegrative properties (Adams et al., 2007, Adams et al., 2011; McAndrew et al., 2012; Overton et al., 2017). Osseointegration refers to the process in which bone grows around the implant, increasing its durability and longevity (Buser et al., 1991; De Rezende and Johansson., 1993; Pfingst et al., 1989). Titanium is preferred over other metal alloys, such as stainless steel because of its lighter weight and lower elastic modulus, which is the ability to resist permanent deformation when a force is applied. If a material with an elastic modulus higher than bone is directly attached to the skull, the force shielding problem may occur. This refers to when a material absorbs and prevents the transmission of force delivered to a bone (Huiskes et al., 1992; Sagomonyants et al., 2008). Without force being continually transmitted to the skull, regular bone growth cannot occur and the bone under the cranial implant may degrade (Huiskes et al., 1992). Titanium has a lower elastic modulus than other metals, but its value may still be 6–20 times larger than cortical bone (Rho et al., 1993; Sagomonyants et al., 2008). This difference is large enough to cause force shielding. Another concern associated with titanium is its tendency to introduce MRI distortions (Mulliken et al., 2015; Chen et al., 2017). Titanium creates shadows and distortions in the images, making subsequent brain navigation or electrode implantation inaccurate and potentially unachievable. There are also concerns regarding ion release from titanium, which may cause osteolysis (Niki et al., 2001). In contrast to titanium, PEEK has an elastic modulus closer to bone, is entirely MRI compatible, and does not corrode or release metal ions (Hunter et al., 1995; McAndrew et al., 2012). PEEK is also biocompatible, lightweight, and easily machined (Katzer et al., 2002; Sagomonyants et al., 2008).

The use of these strong acrylic alternatives has led to the development of implant footprint designs that cover smaller portions of the cranium, such as the K-headpost design (Adams et al., 2007; Adams et al., 2011; Chen et al., 2017; Lanz et al., 2013;). Ideally, after implantation the skin covers the legs while the protruding portion remains exposed and accessible. In older iterations, the legs were bent intra-surgically to conform to the shape of the skull. This process is laborious and frequently prone to error, resulting in an imperfect fit and a gap that is typically sealed with acrylic (McAndrew et al., 2012). To avoid intra-surgical bending, a mold of the skull may be taken ahead of time and subsequently used to create a model skull to bend the legs of the implant around (Betelak et al., 2001). Unfortunately, this process requires an additional surgery to expose the skull (Chen et al., 2017). As an improvement, researchers have recently used computed tomography (CT) or magnetic resonance imaging (MRI) techniques to non-invasively pre-form the feet of the implant to the skull, eliminating the need for manual bending (Chen et al., 2017; McAndrew et al., 2012; Mulliken et al., 2015). Together, these improvements have greatly enhanced implant stability and bone health when compared to acrylic caps. However, the main disadvantage of using 'legged' implants is the tendency for skin recession (McAndrew et al., 2012; Pfingst et al., 1989). Skin recession occurs because of the lack of bonding between the skin and the implant as well as the tension pulling the skin outward (Mulliken et al., 2015). As the skin recedes, the skull is gradually exposed, resulting in an open wound in which bacteria can be introduced, thus increasing the risk of infection. In these cases, the open area and exposed legs are typically covered with acrylic, incurring the adverse bone and skin effects previously mentioned, albeit at some delay.

To prevent skin recession, Mulliken et al. (2015) have developed form-fitted column implants that house the screw holes on the inside of the implant. As a result, the skin surrounding the column is directly bonded to the skull and does not recede. Though effective at preventing skin recession, Chen et al. (2017) have noted that concentrating the screws to one area of the skull reduces force distribution and increases the risk of the implant breaking from the skull. Furthermore, implants that sit higher off the skull, like the headpost shown in Mulliken et al. (2015), will experience more torque during head fixation. This is because the length of the lever arm (i.e. headpost), is directly proportional to torque when a force is applied perpendicular to the axis of rotation. This, combined with the fact that the headpost regularly receives substantial force, makes it a likely candidate for implant failure (e.g. breakage, dislodging from skull, failure to restrain head).

In the current study, we extend the tradition of cranial implant development in primate neurophysiology to improve the stability of implants and the health and longevity of research subjects. Using the workflow described here, we create customizable, skull-formed PEEK cap implants that facilitate better surgical pre-planning and simplify surgical procedures, while attempting to increase implant strength, reduce surgical invasiveness, and optimize the useable surface area of the skull.