Archives of Oral Biology 81 (2017) 81–89

Contents lists available at ScienceDirect

Archives of Oral Biology

journal homepage: www.elsevier.com/locate/archoralbio

Research paper

Magnetic implants in the tongue for assistive technologies: Tests of migration; oromotor function; and tissue response in miniature pigs

Alan J. Sokoloff[a,*], Zhongtao Yang[b], Saman Sargolzaei[b], Karen Strait[c], Andrey Krasnopeyev[c], Kirk A. Easley[d], Sylvie Mimche[a], Maysam Ghovanloo[b]

[a] Department of Physiology, Emory University School of Medicine, 615 Michael St., Atlanta, GA 30322, United States
[b] School of Electrical and Computer Engineering, Georgia Institute of Technology, 85 Fifth Street NW, Atlanta, GA 30308, United States
[c] Division of Animal Resources, Emory University School of Medicine, 615 Michael St., Atlanta, GA 30322, United States
[d] Department of Biostatistics and Bioinformatics, Emory Rollins School of Public Health, Atlanta, GA 30322, United States

ARTICLE INFO

Keywords:
Tongue
Tongue drive system
Magnet
Spinal cord injury

ABSTRACT

Objective: Uncertain biological consequences of titanium-magnet (Ti-mag) tongue implants constrain application of the Tongue Drive System (TDS), a brain-tongue-computer interface for individuals with severe physical impairment. Here we describe oromotor function and tongue tissue response following Ti-Mag implantation and explantation in the miniature pig, an animal model with a tongue similar in size to humans.

Design: A 1.8 × 6.2 mm Ti-mag tracer was implanted into the anterior tongue in five Yucatan minipigs. X-rays were taken immediately and > six days after implantation to evaluate tracer migration. In three minipigs, the tracer was explanted > 16 days after implantation. Twenty-five days post-explantation, tongue tissue was harvested and processed for histological and immunohistochemical (IHC) markers of healing. In two minipigs tissue markers of healing were evaluated post-mortem following > 12 days implantation. Drink cycle rate (DCR) was characterized to determine the impact of procedures on oromotor function.

Results: Neither implantation (N = 5) nor explantation (N = 3) changed DCR. X-rays revealed minimal tracer migration (N = 4, 0–4 mm). By histology and IHC a robust capsule was present two weeks post-implantation with limited fibrosis. Explantation produced localized fibrosis and limited muscle remodeling.

Conclusions: These findings suggest the safety of Ti-mag anterior tongue implants for assistive technologies in humans.

1. Introduction

Some 12,000 individuals in the United States suffer spinal cord injury (SCI) each year; of these, individuals with incomplete (39.5%) and complete (16.9%) tetraplegia have limited options for and high costs of assistive devices (Figures, 2011). Despite advances in neuroprostheses and brain-computer interfaces, individuals with severe SCI and other neurological diseases which lead to tetraplegia, such as amyotrophic lateral sclerosis and brainstem stroke, have limited options for control of their environments. Currently such control relies upon interaction via a voluntary motor system unaffected by the SCI, typically muscles of the neck, eyes, or face. However, these systems provide limited signal diversity and bandwidth for computer access, are difficult to decode from unintended activities, and cannot be used over extended periods because of inducing fatigue.

Volitional control of the tongue is spared, even in individuals with high-level SCI (i.e., C4 and above); for those individuals the tongue would appear to be the natural interface between cognition and computer because of its many degrees of freedom and facility for acquiring novel movements. Heretofore, the unique inherent abilities of the tongue as an interface have not been fully exploited due to limitations in translating voluntary tongue movements in a precise, reproducible, unobtrusive, practical, and safe manner. These limitations arise from the inaccessibility of the tongue inside the oral cavity and the requirement that interfaces do not impair preservative functions of the tongue in respiration, oral transport, and swallowing, as well as speech.

The Tongue Drive System (TDS) was specifically designed with these considerations in mind. A key innovation of the TDS is the translation of voluntary tongue movements to user-defined commands

Abbreviations: HE, hematoxylin and eosin; PS, picrosirius red; SCI, spinal cord injury; TDS, tongue drive system; Ti-Mag, titanium-encased magnet; DCD, drink cycle duration; DCR, drink cycle rate

* Corresponding author at: Department of Physiology, Emory University School of Medicine, 615 Michael St., Rm. 605, Atlanta, GA 30322, United States.
E-mail address: asokolo@emory.edu (A.J. Sokoloff).

http://dx.doi.org/10.1016/j.archoralbio.2017.04.034
Received 22 September 2016; Accepted 30 April 2017

via real-time detection of the position of a small titanium-encased permanent-type magnet affixed to the anterior tongue in the form of a dumbbell-shaped tongue stud (Huo & Ghovanloo, 2010; Kim et al., 2012; Laumann et al., 2015). The TDS consists of an array of four 3-axial magnetic field sensors, mounted near the user's cheeks on a headset to track the position of a tiny magnetic tracer, the size of a lentil (3.18 mm length, 1.6 mm thickness). Any tongue movement results in changes in the magnetic field inside and around the user's mouth. The electronics on the headset wirelessly transmit the measured magnetic field variations from the sensor array to a nearby PC or smartphone, which runs a sensor signal processing (SSP) algorithm that removes the earth's magnetic field (EMF) components from the incoming signals, followed by a magnetic signal classification method that can currently indicate 7 distinct positions of the magnetic tracer within the 3-D oral space in real-time. These tongue gestures are then translated to specific user-defined commands in real time, and used to access the PC/smartphone or control target devices, such as a wheelchair (Huo & Ghovanloo, 2010; Kim et al., 2012).

The effectiveness of the TDS has been demonstrated in both SCI and healthy individuals in pilot studies with magnets attached by temporary adhesion to dorsal tongue epithelium or by tongue piercing (Huo & Ghovanloo, 2010; Kim et al., 2012). However, these approaches are either impractical or undesired for long term use due to lingual and dental complications, the requirement of persistent hygienic maintenance and psychosocial resistance, particularly by older patients, to tongue piercing. An optimal solution is to implant a biocompatible titanium-encased magnetic tracer (Ti-Mag) in the tongue body obviating the need for maintenance (as with tongue piercing), while minimizing the risk of swallowing the magnetic tracer and damage to teeth and gums.

Features unique to tongue biology may impact the safety and reactivity of implantation of a free-standing device in the anterior tongue. Complex changes in tongue stress-strain patterns during oromotor behaviors (e.g., (Felton et al., 2008) as well as routine tonic and forceful tongue muscle activation in preservative behaviors (i.e., respiration, swallowing) may impact the formation of a sequestering implant capsule. Additionally, the rich capillarization of tongue muscles (Granberg, Lindell, Eriksson, Pedrosa-Domellof, & Stal, 2010) and presence of large ventral lingual arteries raises the possibility of embolization if a small device is not appropriately integrated into surrounding tissue.

Previously we demonstrated encapsulation and limited migration of a 0.5 mm stainless steel sphere injected into the anterior tongue of the rat (Mimche et al., 2016) suggesting the general safety of unanchored tongue implants. Here we test encapsulation, migration, and drink behavior of 1.8 × 6.2 mm cylindrical implantable Ti-mag that is injectable through a hypodermic needle into the anterior tongue of the mini-pig, a mammal with tongue similar in size to humans. Fig. 1 shows a close up view of the Ti-mag implant used in this study. We also test the consequences of device explantation on mini-pig drink behavior, and tongue anatomy. Our preliminary study indicates limited impact of Ti-Mag implantation and explantation on tongue function.

2. Materials and methods

2.1. Animal subjects and husbandry

Six adult male Yucatan mini-pigs (*Sus scrofa*, 18–25 kg, Sinclair BioResources, Columbus, Missouri) were used in this study. All experiments were conducted in accordance with the Emory University Institutional Animal Care and Use Committee and the Eighth Edition of the Guide for the Care and Use of Laboratory Animals. Mini-pigs were housed singly to facilitate investigation of drink behavior by subject, fed daily, given access to water *ad libitum* via automatic dispenser system and weighed weekly. Mini-pigs were trained to drink dilute apple juice (AJ, 2/3 apple juice, 1/3 water) from a 32 ounce dog water bottle and conventional stainless-steel roller-ball nipple (i.e., with two roller balls to impede fluid flow, Lixit, Napa, California), a behavior learned in 1–3 sessions. Subsequently, tests of drinking during consumption of ~400 cc AJ were conducted several times per week.

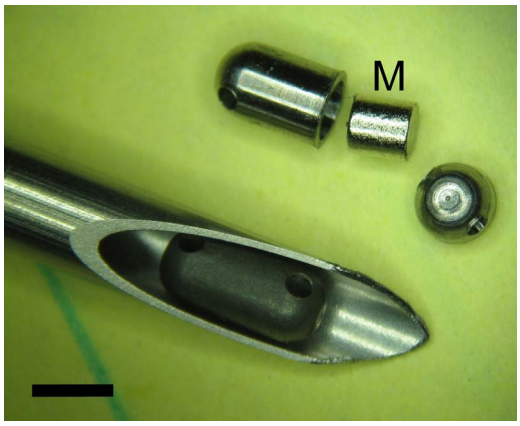

Fig. 1. Titanium-encased magnet (Ti-mag) used in this study. The magnet (M) and unassembled Ti-casing are shown. The assembled Ti-mag, with two bore holes, is shown in a 12 gauge needle. Calibration bar = 2 mm.

2.2. Experimental procedures

2.2.1. Implantation and X-ray

Following at least seven days of acclimatization, mini-pigs (P1-P6) were anesthetized with ketamine (35 mg/kg, IM), atropine (0.4 mg/kg, IM) and acepromazine (0.8 mg/kg, IM) or with xylazine (1 mg/kg, IM) and ketamine (35 mg/kg, IM) and maintained on ~2% isoflurane. The tongue was washed with povidone-iodine antiseptic solution, the tongue tip was held by gauze or foerster clamp, and a sterile Ti-Mag tracer was injected into the superficial anterior tongue at or near midline by sterile injection assembly (syringe, 12-gauge hypodermic needle, metal plunger; Fig. 1; Fig. 2). Additionally, two sterile stainless steel pellets (0.9 mm) were injected anterior and posterior to the Ti-Mag for X-ray reference (sterile syringe/16-gauge injection assembly). Bleeding, when present, was minimal and resolved by pressure. While anesthetized, lateral and dorso-ventral X-rays of the oral cavity were taken (minXray, Illinois, model, HF100AP, 46 kVp. 0.712 mAs) to enable localization of implant relative to reference pellets and structures of the oral cavity. Meloxicam (0.4 mg/kg) was given IM.

2.2.2. X-ray and explantation

Seventeen or eighteen days following implantation, mini-pigs were anesthetized as above and lateral and dorso-ventral X-rays were taken to evaluate tracer migration and assist in explantation. These X-rays revealed the tracer implant to be present in only three mini-pigs (P1, P3, P4), indicating extrusion of the implant in the other mini-pigs (P2, P5, P6). In the three mini-pigs with implant, the tongue was washed with povidone-iodine antiseptic solution, the tongue tip held by gauze or a foerster clamp, and the anterior tongue protruded from the oral cavity by application of gentle tension at the tongue tip. Tracer location was identified by palpation or by dorso-ventral X-ray following insertion of a reference sterile 25 gauge needle. A small incision was made through the dorsal epithelium dorsal to the tracer with a sterile scalpel. Tongue tissue was gently spread with a sterile forceps to expose the Ti-mag tracer, which was removed (Fig. 2). The incision was closed with sterile 4-0 polydioxanone (PDS) suture and animals were given meloxicam (0.4 mg/kg, IM).

2.2.3. Re-implantation and X-ray

X-rays revealed extrusion of the tracer in P2, P5 and P6, likely soon after implantation, possibly facilitated by action of the animal or much