Contour Fitting High Density Personalized 3 Dimensional Cortical Electrodes

Morris Shayne, M.D.[1)]; Masayuki Hirata, M.D., Ph.D.[1, 2)]; Tetsu Goto, M.D., Ph.D.[1, 2)]; Kojiro Matsushita[1)], Ph.D., Takufumi Yanagisawa, M.D., Ph.D.[1)]; Youichi Saitoh, M.D., Ph.D.[1)]; Haruhiko Kishima, M.D., Ph.D. [1)]; and Toshiki Yoshimine, M.D., Ph.D.[1)]

[1)] Department of Neurosurgery and [2)] Division of Functional Diagnostic Sciences, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

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Correspondence to: Masayuki Hirata, M.D., Ph. D.

Department of Neurosurgery, Osaka University Medical School

2-2 Yamadaoka, Suita, Osaka 565-0871, Japan

Tel.: +81-6-6879-3652; Fax: +81-6-6879-3659

E-mail: mhirata@nsurg.med.osaka-u.ac.jp

1. ABSTRACT

[Purpose] Non-invasive localization of certain brain functions may be mapped down to a level of millimetres. However, the inter-electrode spacing of common clinical subdural electrodes still remains around 10mm. In this paper, we present our progress in the development of next-generation electrodes with the purpose of attaining more precise and higher quality electrocorticographic signals for not only functional brain mapping but also use in brain-machine interface. [Methods] We used platinum plate electrodes with a diameter of 1mm and produced sheet electrodes after the creation of individualized molds using a 3D printer, and a press system that sandwiches the electrodes in-between 2 silicon sheets individualized to fit the surface of a specific brain. [Results] We were able to manufacture arrays with a distance between electrodes of 2.5mm (a density of 16 times that of previous types). We were able to create electrode arrays molded to fit both the surface curvature of the brain and to fit inside the brain sulcus. In addition, rat experiments indicated no signs of long term toxicity. [Discussion] We succeeded in the creation of cortical electrode arrays with high spatial resolution, which are tailor-made to match the brain of an individual. Using automated methods to map sulci and CAD software, we plan to further improve on our methods of manufacturing.

2. INTRODUCTION

Recent developments in the area of brain machine interfaces (BMI) or brain computer interfaces (BCI) have led us to the possibility of a seamless interface between the human brain and surrounding peripheral devices. To achieve this,

neural signals must be attained from the brain and then analysed or decoded to interpret their meaning, where decoding relies heavily on the quality of the measured neural signals.

There are various methods of measuring the neural activity of the brain. One of these includes functional magnetic resonance imaging (fMRI) which examines localized changes in blood flow due to neural activity based on reductions in deoxyhemoglobin. While this method has a high spatial resolution of up to 1 mm[1], it is not suitable for use in the clinical sense of BMI, firstly because of the need for a large MRI unit which is not portable, and also because of the poor temporal resolution partially due to the delay between neuronal activity and corresponding changes in blood flow.

Another method which also has a high spatial resolution is magnetoencephalography (MEG). This tool provides a non-invasive method of measuring neural magnetic field distributions with high temporal resolution in addition to high spatial resolution. While this method can analyze data on a millisecond scale, it is impractical in every-day clinical BMI situations due to the size and non-portability of the unit. A more practical method for measuring neural activity is intracranial electrodes placed strategically. In order to provide higher decoding accuracies and greater information for analysis of more specific and precise functions of the brain, several needle electrode arrays have been developed and used on animals and even in human patients in clinical trials[2], [3]. The most obvious advantage of these types of electrodes is their ability to obtain detailed neural information on a neuronal level. In addition to their susceptibility to electromagnetic noise, one problem with these types of electrodes is micro-motion, which means that a specific electrode may not always be in contact with the same

particular neuron. Micro-motion is said to be the result of microvascular pulsations, changes in intracranial pressure and respiratory motions etc., and may be amplified by differences in the surgical techniques used to implant the electrodes[4]. A more important issue with these types of electrodes is the brain tissue reaction against the implant itself[5]. It has been shown that after these types of electrodes are implanted, reactive tissue begins to form around the electrodes themself, and that such chronic biological reactions may result in reduced decoding results over time. Studies into the relationships between such reactions and electrode designs, coatings, and implantation procedures have also been undertaken[5]. Apart from these problems, perhaps one of the major drawbacks of these electrodes is their invasive nature. An array of needles must be inserted into brain tissue, which in itself carries an increased risk of morbidity.

On the other hand, surface electrodes are less invasive because they do not penetrate the cerebral cortex. These electrodes may be placed at selected locations over the surface of the brain, for example on the scalp, between the dural membrane and skull, or beneath the dural membrane on the brain surface. With respect to the latter, which are referred to as subdural electrodes, we have previously shown the relative importance of anatomical areas for neural decoding, and compared the decoding performances of gyral and intrasulcal electrocorticograms (ECoGs). As a result, movement classes were predicted with 80–90% accuracy, with the intra-sulcal ECoG electrodes on the motor bank side of the central sulcus showing higher performance than the gyral ECoG and intrasulcal ECoG on the sensory bank side even before movement onset[6].

While improvements in neuroimaging have been made over the past few years, with fMRI research being undertaken at resolutions of several millimetres now

possible[1] , with a few exceptions, there have been few instrumental advances made in field of subdural electrodes for clinical use. Presently, the inter-electrode spacing of standard type subdural electrodes used in clinical situations still remains at about 1cm.

In comparison with standard electroencephalographic electrodes, ECoG electrodes provide not only superior spatial resolution, but also deliver signals with higher sensitivities in the higher frequency ranges, making them useful for neural decoding utilizing high gamma band event-related oscillatory changes and phase information[7].

With this in mind, in order to attain neural measurements that are stable over time, that have a higher signal resolution than presently available subdural electrodes, and that are less invasive than needle type electrodes, we aimed to create a high density array of electrodes designed to match the contour of an individual's brain surface.

The surface of the brain, especially the human brain, is curved with bumps and depressions, called gyri and sulci. These structures allow for increased cortical surface areas and neuronal populations as well as greater neural processing performance. It also means that by merely placing electrodes on the immediately accessible gyral surface of the brain, we may be missing out more important information from the sulcal surface. In particular, in the human brain, the cortical surface can be divided functionally into sensory and motor portions at the central sulcus. Although not a simple relationship, inside this central sulcus, the anterior surface towards the frontal lobe controls motor function, while the posterior surface is responsible for sensory function. By inserting electrodes into this sulcus, we may be able to attain a great deal more information on finer motor movements than we

would be able to from merely placing them on the surface of the brain. Indeed it has previously been shown that the placement of electrodes into the central sulcus is superior to placement on the brain surface alone from the perspective of decoding accuracy[6].

Unfortunately, the shape, and depth of the central sulcus is highly individualized and complex, thus making a one-fits-all approach to the design of electrodes, which has been the mainstay until now, almost impossible. In addition, as the spaces between gyri are curved and narrow, even the most flexible of electrode sheets may apply forces on the brain tissue and surrounding blood vessels, resulting in brain contusion and in ischemic infarction or haemorrhaging.

With the above in mind, we developed a method for the creation of individualised, high density electrodes for placement both on the surface of the brain, and perhaps more importantly from the perspective of BMI, inside the central sulcus. These electrodes are designed to match the surface of a specific individual's brain. In this paper, we mainly describe the methods involved in the creation of the electrodes for placement within the central sulcus.

3. METHODS

Common types of electrodes for subdural placement are created by the sandwiching of platinum plate electrodes approximately 1cm in inter-electrode spacing in between 2 silicon sheets. This method has been proven safe in the long term in patients who have had them inserted in the central sulcus for motor cortex stimulation in the treatment of intractable pain[8]. Indeed, at our institution we have patients who have had subdural electrodes implanted for more than 10 years without complications. This method is also attractive not only from the perspective

that direct placement of electrodes on the brain surface allows for a greater signal to signal-to-noise ratio than scalp EEG electrodes, but is also less invasive than needle electrodes inserted directly into brain tissue. For these reasons, we decided to produce platinum plate sheet electrodes with an electrode diameter of 1mm, 1/3rd the diameter of previous standard types, while individualizing the shape of the sheet containing the electrodes using a press mold system. Our method sandwiches the electrodes in-between silicon sheets individualized to fit the surface of an individual patient's brain.

Informed consent was obtained from healthy volunteers and patients, who underwent MRI studies as part of our BMI project, which has been authorised by the medical ethics committee of our institution. First we took a thin-slice MRI series of the subject's brain. In the case of the model demonstrated in this paper, the subject was an intractable epileptic patient.

Next, we converted the patient's DICOM data into the NIFI format using MRIcro (Version: 1.40 build 1, http:/www.mricro.com/). We then imported this data into BrainVISA (BrainVISA 4.0.2, http://brainvisa.info/), where we ran the sulci extraction routine which allowed us to generate a 3D image of the brain surface, and also exudate the majority of the sulci (figure 1).

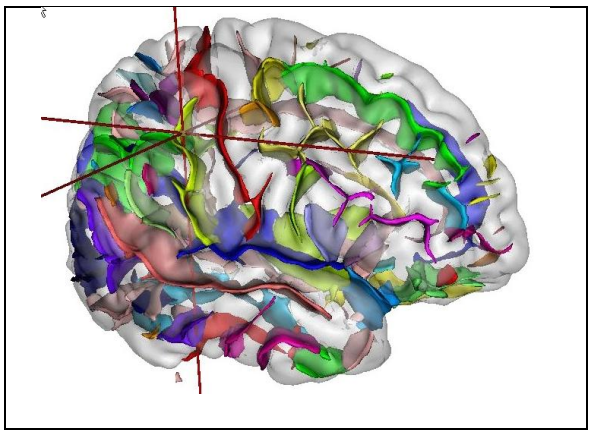


Figure 1. Various sulci shown on a 3-dimensional image of the brain, generated with BrainVISA from patient MRI data

Having generated the shape of the various sulci, we selected those making up the central sulcus. After selecting the related pieces, they were exported in the MESH format. This data was then converted into the STL format using a file format converter (3D Object Converter v4.4 http://web.t-online.hu/karpo/).

The pieces of the central sulcus in the STL format were then imported into two 3D computer aided designing (CAD) software (Mimics v14.12, 3-matic v5.1, Materialise N.V. Leuven Belgium). Using these software, it was possible to combine all the pieces of the central sulcus. After combining the surfaces, and undertaking a variety of smoothing techniques, we are left with a 3-dimentional representation of the central sulcus (figure 2).

The object basically has 2 surfaces, one facing the motor side of the central sulcus and one facing the sensory side. These 2 surfaces were then separated, and the surface facing the primary motor cortex was selected for further processing with 3-matic, because the motor side provides superior decoding accuracy of motor function (figure 3).

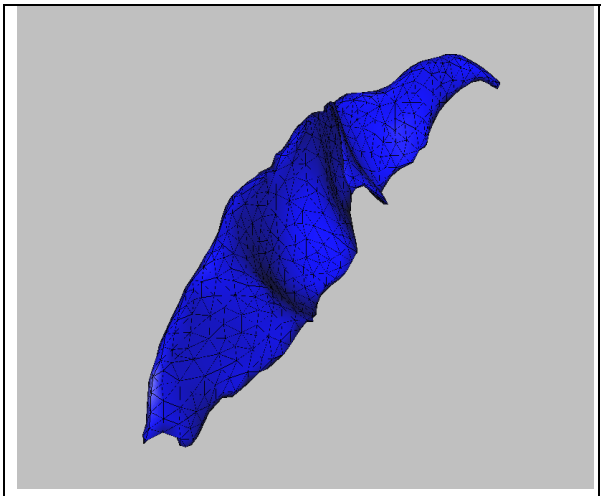
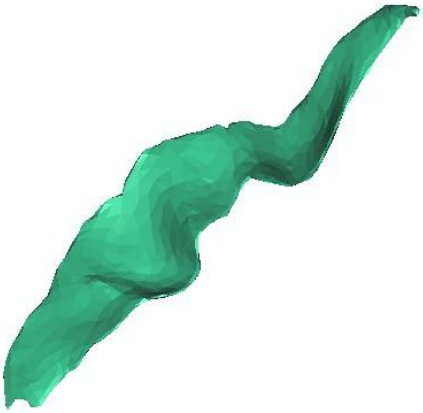
	

Figure 2. Sulcus data is removed and converted into the STL format for further processing.	Figure 3. The surface on the motor side of the central sulcus is then removed for further processing.

Next, sides were extended downward from the surfaces, after which a base was then added to generate CAD data for a mold of the central sulcus surface facing the primary motor cortex (M1). Then an inverse of this mold was produced, so that we now had both male and female molds of the primary motor cortex surface inside the central sulcus. Holes were placed in the four corners of the base of the molds to allow for fine configuration of the male and female molds and adjustment of the final thickness of the electrode sheet. This data was then exported in the STL format (figures 4 & 5).

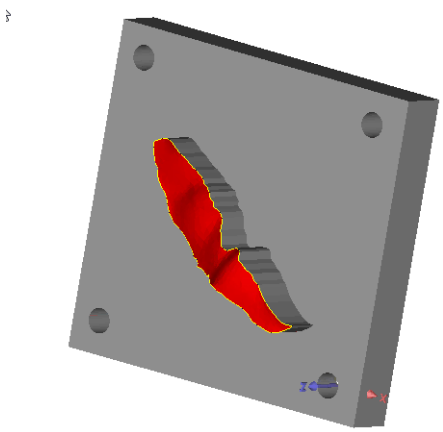


Figure 4. A mold created from the surface facing the motor side of the central sulcus using 3-matic.

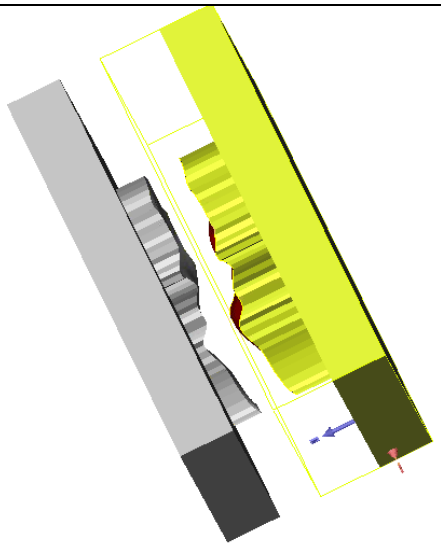


Figure 5. An inverse mold was also created using 3-matic.

Next, using this data, we used a 3D printer (Polyjet 3D printer, Objet Geometries Ltd., Israel) to create the actual molds. Dimensions of the mold base were 130mm x 138mm with a thickness of 20mm, and 10mm holes in each corner to insert rods to allow controlled compression and adjustment of the thickness of the silicon sheets. The contour mold portion representing the central sulcus was 95mm at maximum length and measured between 6mm and 24mm in depth depending on the location along the maximum length axis. The distance of the central sulcal mold surface from the mold base varied from 1mm to 12mm for the sensory bank facing mold, and from 11 to 22 mm for the motor bank facing mold. We marked the desired positions of the electrodes on the mold surface, with the surface facing the motor bank of the central sulcus having 35 electrodes while the surface facing the sensory bank had 15, since the primary motor cortex provides greater information on motor

function(figure 6)[6], [9]. We also placed a higher emphasis on the hand-knob area in the form of higher electrode densities.

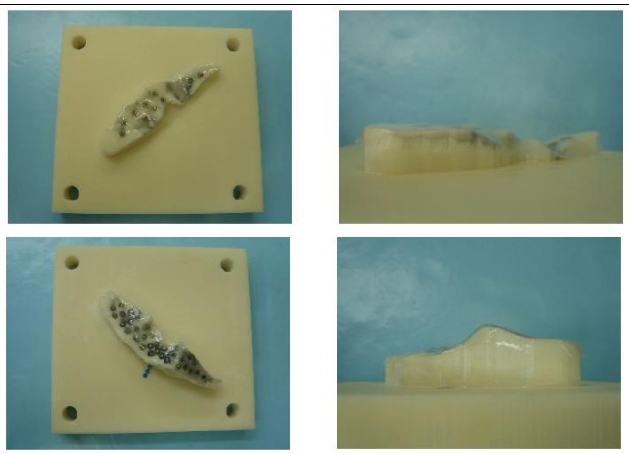
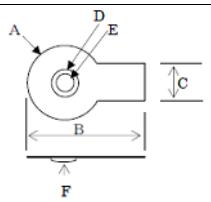


Figure 6. Male and Female Molds Created with a 3D Printer.

A silicon sheet (SILASTIC MDX4-4210) was then heated to 76° C for 5 seconds and placed on the mold using a variety of techniques. A heat gun was also used to improve contact with the mold surface and to remove air bubbles. The sheet was then allowed to cool naturally to room temperate and left for 3 days to harden. The silicon sheet was then carefully removed from the molds. The same process was repeated to produce 3 sheets (one for contacting the primary motor cortex surface (M1 sheet), one for contacting the primary sensory cortex surface (S1 sheet), and one for placement in between these 2 sheets (middle sheet) to isolate the 2 sets of electrodes. Next, holes were punched out for the electrodes at predetermined locations in the sheet facing M1 placing relative importance in the form of a higher electrode density on the hand knob area. Platinum electrodes (diameter 1mm, thickness 0.02mm (figure 7)) were in-set into these locations and temporarily fixed

before flexible stainless leads (⌀0.05mm polyurethane coated, impedance ≤ 80Ω) were attached individually to each of the electrodes (impedance: electrodes ≤ 10Ω, lead ends (platinum) ≤ 10Ω) (figure 8). After completion of attachments, the lead wires were bundled together and passed through a silicon tube. To fix the electrodes, wires, and silicon tube, a silicon adhesive was added and the second silicon sheet placed on top and compressed in the molds. The process was repeated for the electrodes facing the primary sensory cortex surface, the end result being 2 sets of electrodes sandwiched between 3 silicon sheets, with the leads all protruding from a single location near the middle of the sheet electrode at the surface of the brain (figure 9).



		Specification(mm)
A	Diameter	2.1 ± 0.1
B	Length	3.8 ± 0.15
C	Width	1.2 ± 0.15
D	Embossment Outer Diam.	1.2 ± 0.15
E	Embossment Inner Diam.	0.8 ± 0.15
F	Embossment Hight	0.1 ± 0.05

Figure 7. Electrode Dimensions

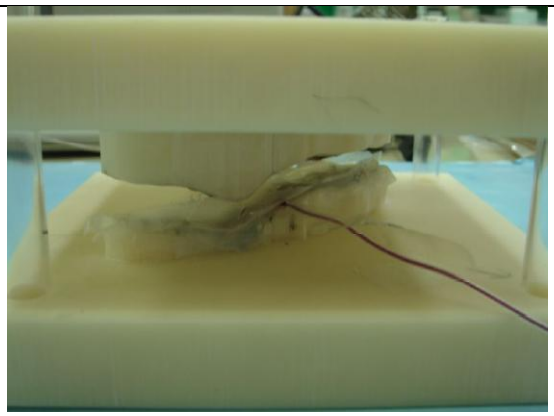


Figure 8. Silicon Sheet Compression. A silicon sheet is created on the mold, and holes were made for electrode embedding. Flexible stainless leads were then individually connected. A second silicon sheet is adhered to the back of sheet implanted with the

	electrodes.
	
Figure 9. Completed Electrode. Two layers of electrodes are embedded into the silicon sheets. One layer to face the motor bank, and one layer to face the sensory bank, with a silicon sheet in between to isolate the two electrode arrays.	

Using the same 3D printer methods we also created a model of the subject's brain to confirm that the manufactured electrodes fit properly into the central sulcus.

5. RESULTS

Electrodes

We were able to manufacture an array of electrodes with an inter-electrode distance between electrodes of 2.5mm (a density of 16 times that of previous standard types), and we were able to create electrode arrays molded to fit both the surface curvature of the brain and to fit inside the central sulcus (total of 50 plate electrodes (35 facing the motor bank and 15 facing the sensory bank)). The length

of the central sulcus electrode shown is around 95 mm with a maximum depth of close to 24 mm. The thickness varied between 0.81 ~ 0.96 mm at sample locations (figures 10 & 11). Using a 3D model of the same subject's brain, also created with the 3D printer, we confirmed that the electrodes fitted into the central sulcus (figure 12).

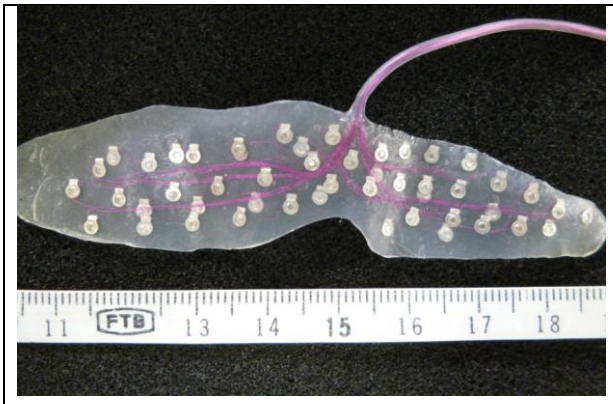


Figure 10. Electrodes for the central sulcus

The length of the central sulcus electrode shown is around 9cm with a maximum depth of close to 2cm.

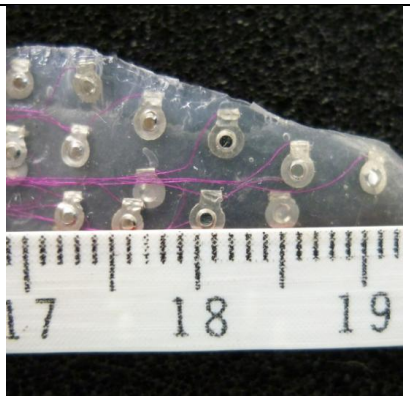


Figure 11. Inter-electrode Distance

Electrodes with distances of approximately 2.5mm between electrodes (a density of 16 times that of previous types)

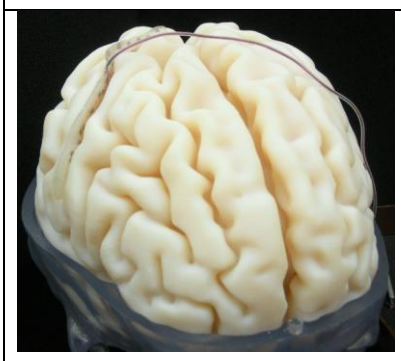


Figure 12. Inserted Electrodes

Using the 3D model of the same subject, also created the 3D printer, we confirmed that the electrode fitted into the central sulcus. Note, in order that the electrodes may be seen in this image, they are not fully inserted to their maximum depth.	

We also used similar processes to created electrodes that match the contour of the brain gyral surface. Unlike the central sulcus electrodes which have 2 layers of electrodes, these electrodes are single layered, and may also be placed over the top of the sulci electrodes to cover a predetermined surface of the brain (figure 13 & 14).

	
Figure 13. Single layer sub-dural electrodes for placement on the brain surface.	Figure 14. Inter-sulcal and Gyral surface electrodes Both central sulcus electrodes and

	surface electrodes shown positioned in a model of the subject's brain.

Biocompatibility

In order to test the safety of the electrodes before implantation into patients, we have undertaken toxicity tests. In these tests, 3D-high density electrodes and control materials (φ20 mm) were implanted sub-cutaniously into male rats and then removed after 26 weeks to examine the effects of the subject material on the histology of the implanted rats. The study is carried out in accordance with related regulations and protocols for the protection of animals. The electrodes and a control material were symmetrically implanted subcutaneously at the dorsal end of the spinal column while under intraperitonial anaesthesia, with the electrodes implanted on the left side and the control implanted on the right side of the scapula. While this study is not complete, mid-term results 13 weeks into the study are as follows. One out of 12 rats showed slight swelling at the sites of implantation four days after sub-cutaneous placement. In this subject, swelling on the electrode implanted side continued for 41 days, while swelling on the control implanted side was also observed for 19 days. No superficial abnormalities were observed in any of the subjects after 42 days.

After implantation, no abnormalities were observed in weight gains. Final histological testing will be carried out at the end of the 26 week period.

6. DISCUSSION

We succeeded in the creation of cortical electrode arrays with high spatial resolution, which are tailor-made to match the brain surface of a particular individual. By using automated methods to map sulci and by utilizing CAD software and 3D printers.

In this paper, we explained our methods for manufacturing electrodes for placement within an individual's central sulcus. We have yet to insert these electrodes into a human subject's central sulcus, but we plan to begin clinical trials in the near future on Amyotrophic lateral sclerosis (ALS) patients as part of our BMI project. Concurrently, we are now developing a fully-implantable Wireless System for Human Brain-Machine Interfaces using our Brain Surface Electrodes W-HERBS system. On the other hand, tests on our electrodes in monkeys have shown high spatial resolution and signal-to-noise ratios were maintained even 1 year after placement[10]. In addition, at the 3 month stage of a 6 month test on the electrodes, electrode materials are shown to be stable and to have no toxicity over this time period.

There are still various problems that have to be overcome. While the risk of damage to blood vessels and brain tissue is obviously less with surface electrodes in comparison to needle electrodes, one problem that can be envisioned is the problem of micro vascularity within the central sulcus. Care has to be taken not to damage or compress arteries and veins during placement of the electrodes within this tight space. Overlaying enhanced MRI images back onto the STL data of central sulcus model may aid in this pursuit.

Despite the above mentioned minor hurdles, we believe that this approach to placing individualized electrodes within the central sulcus will not only lead to higher decoding accuracies of motor function, but it may also allow for the analysis

of finer motor functions, that have been until now, difficult to obtain. Furthermore, in the case of our central sulcus electrodes, not only is primary motor cortex information attained, information from the sensory bank may also be obtained.

It goes without saying, the same manufacturing processes used here may be utilised to produce electrodes for other sulci, and thus the same methods may be applicable for use in the analysis of other functions, such as language etc.

Of course, despite being far less invasive than needle electrodes, use of subdural electrodes is still an invasive procedure, and thus they will be limited to patients who may benefit most from them, such as severely paralysed patients suffering from ALS, PMD, and those in locked-in states, where patients lose their ability to move limbs, respiratory movement, and communication etc., while still maintaining a clear level of consciousness. Decoding signals directly from the brain, may allow peripheral devices to provide methods of communication, and motion, thus much improving the quality and possibly the length of the life of such patients.

There is still a lot of work to be done with the neural decoding of data from electrodes, but we believe that the use of more refined data, originating from locations closer to the areas thought to play large roles in functions of interest will be a major step towards achieving a practical BMI.

Acknowledgments

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manufacturing of the models and casts using the 3D printer.

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