CyberBrain
A Preliminary Experience on Non Human Primate

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Abstract: The study of abnormal electrical activity of the brain, such as epilepsy, is attracting more and more interest for its wide impact on the population. Intracranial EEG recording (electrocorticogaphy; EcoG) and direct cortical stimulation (DCS) are, nowadays, the most accurate and reliable techniques to map cortical function and to identify the boundaries of an epileptic focus. In this work we present the preliminary testing of intra-operative ECoG and DCS performed in a non-human primate using a new custom-made fully-implantable wireless 16-channels device (Patent Number: WO2012143850), called ECOGW-16E. This fully-integrated device, housed in a compact hermetically sealed Polyetheretherketone (PEEK) enclosure, exploits the newly available Medical Implant Communication Service band (MICS: 402-405 MHz). ECOGW-16E is wirelessly rechargeable using a special designed cage for recharge, developed in accordance with guidelines for accommodation of animals by Council of Europe.

1 INTRODUCTION

Multichannel electrophysiological measurements of neural activity are a fundamental method in neural research and in medical applications. Nowadays Intracranial EEG recording (electrocorticography, EcoG) and direct cortical stimulation (DCS) are the gold standard techniques to map the cortical functions and to identify the epileptogenic foci (Spena et al., 2010; Borchers et al., 2012) but provide also an exquisite tool to assess the function and interactions of neuronal ensembles. For example, observing the activity in a great number of simultaneously measured channels is necessary for understanding the functions of the visual cortex, where the signals from many millions of neurons represent the first stages of creating our visual perceptions. Electrode arrays are essential tools to localize the source of epileptic seizures and later remove these parts from the brain during a surgical intervention (Crone et al., 1998): the higher the spatial resolution of the array, the less healthy tissue needs to be removed from the brain. Finally in a not so distant future, integrated devices provided with appropriate algorithms, can deliver performant closed-loop stimulation modulating brain function. Closed-loop stimulation can be used to abort seizures or to provide countless potential intervention opportunities to counteract brain disorders such as pain, tremor and Parkinsons disease (Warren and Durand, 1998; Moro et al., 2002; Johnson et al., 2013). Todays electrode arrays are mostly connected via cables through the skull which always brings the risk of infections, limiting the observation window to short-term only. There is therefore a strong need to develop wireless systems able to extend substantially the monitoring window, up to a chronic use. Our group developed a highly innovative wireless externally-rechargeable multi-channel EcoG device. Preliminary results of experimental tests on a monkey will be presented here.

2 MATERIALS & METHODS

2.1 Surgical Process

One male macaque monkey was used in this study (Macaca fascicularis, 6.95 kg). Experimental protocol was approved by the regional committee (Cometh Grenoble) and registered to the national committee under the number 12/136_ Clinatec-NTM-01 and complied with the EU directive 22th September 2010 (2010/63/EU) on the care and use of laboratory animals. MRI was performed prior to surgical explo-

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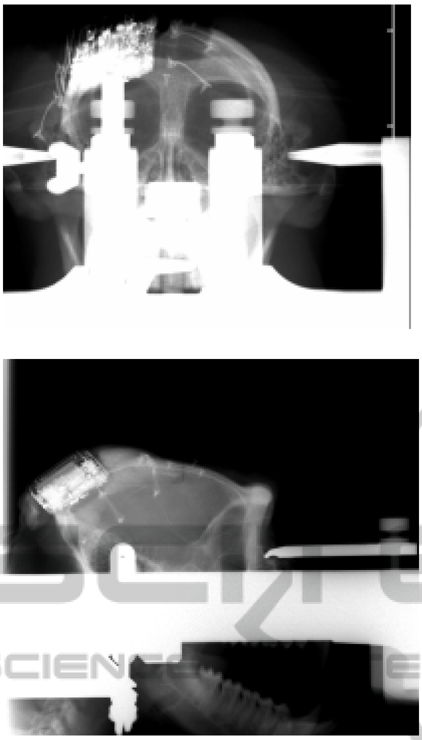

Figure 1: Post-op radiographic image of the device.

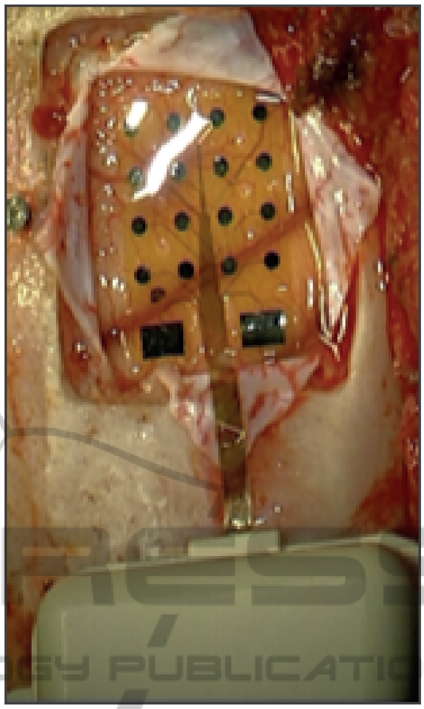

Figure 2: Device placement over the sensorimotor cortex: the central sulcus is visible under the grid

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ration to define surgical management. The animal was anesthetized using a loading dose Xylazine 5 mg/kg, and Ketamine hydrochloride 20 mg/kg, IM and then a maintenance dose of 1.25 mg/kg, 5mg/kg Xylazine /Ketamine respectively. Heart rate, blood pressure, respiratory depth, and body temperature were constantly monitored by veterinary staff. Surgical procedures took place in standard aseptic conditions. When deep anesthesia was achieved, the animal was secured to a stereotaxic frame, and a craniotomy was performed over the left motor cortex (M1), in Brodmann area 4. The dura mater was cut in a Y fashion and the leafs were retracted and sutured on the sides in order to expose the central sulcus and the surfaces of the primary motor(M1) and sensory (S1) cortex. Radiographic images (Fig.1) during surgery were acquired to guide device placement. The device was positioned orthogonally and the grid was centered above the hand knob of the left motor cortex (Fig.2).

2.2 ECOGW-16E

The device, called ECOG-16W (Cristiani et al., 2012) (total length 58.3 mm), specifically designed for monkeys, consits of two parts (Fig.3): the grid (Fig.4), consisting of a single sheet of flexible polyimide support that integrates 16 platinum electrodes (Neuronexus, Ann Arbor, MI, USA) and the body, casing in PEEK, includes a microcontroller handling local processing and the transceiver module for implantable medical applications within MICS band with a 800/400/200 kbps raw data rate. In addition, it includes a triaxial accelerometer, a stimulus generator, a sensor of temperature/load current and a Li-Ion battery(3,6V 150mA/h ISO 13485). PEEK case was chosen for its high and well documented biocompatibilty in prosthesis in different field of medicine (Rivard et al., 2002). Finally, we have adopted a charging apparatus to provide an induction charger (250mW, 70mA @ 3.7V) for a wireless rechargeable battery. The interface consumes 58mA(16CH @ 500SPS + TX_RF), 30mA(16CH @ 500SPS) and 7mA in standby. The device was positioned orthogonally and the grid was centered above the hand knob of the left motor cortex (Fig.2) providing also coverage of the central sulcus and part of S1.

ECOGIW-16E is wirelessly rechargeable using a special designed cage for recharge (Fig. 5).

Wired systems expose the cables to the risk of damage induced by the monkey , which pulls them away. To perform behavioral experiments, the monkey needs to seat in a special chair that does not allow the arms of the animal to reach the cables. Our cable free system opens therefore a new window of opportunities to observe the neural activities in unrestrained animals. Using the smart wireless recharge cage it is

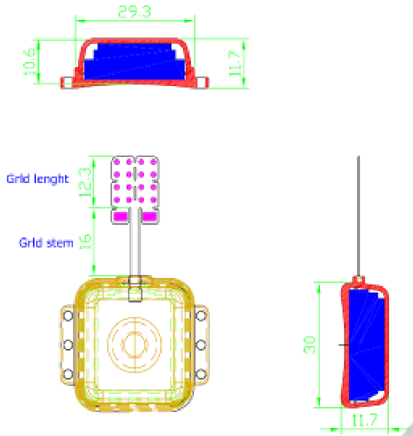

Figure 3: The scheme of the ECOG-16E.

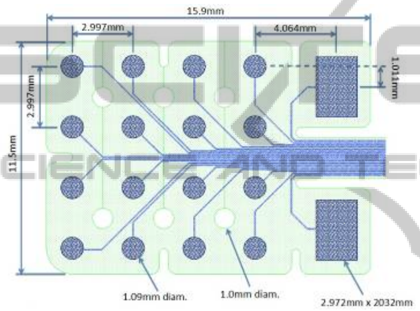

Figure 4: The grid by NeuroNexus.

Figure 5: The recharge cage.

also possible to recharge the implanted device during the physiological rest period.

3 DATA ANALYSIS AND RESULTS

In this study we used a commercial software for ECoG recording (Micromed, Treviso; Italy) and we tested software specifically developed for our hardware (Aethra Communication company; Ancona, Italy) for DCS and impedance measurement. The procedure and post-operatory course was uneventful. The monkey recovered immediately and was able to

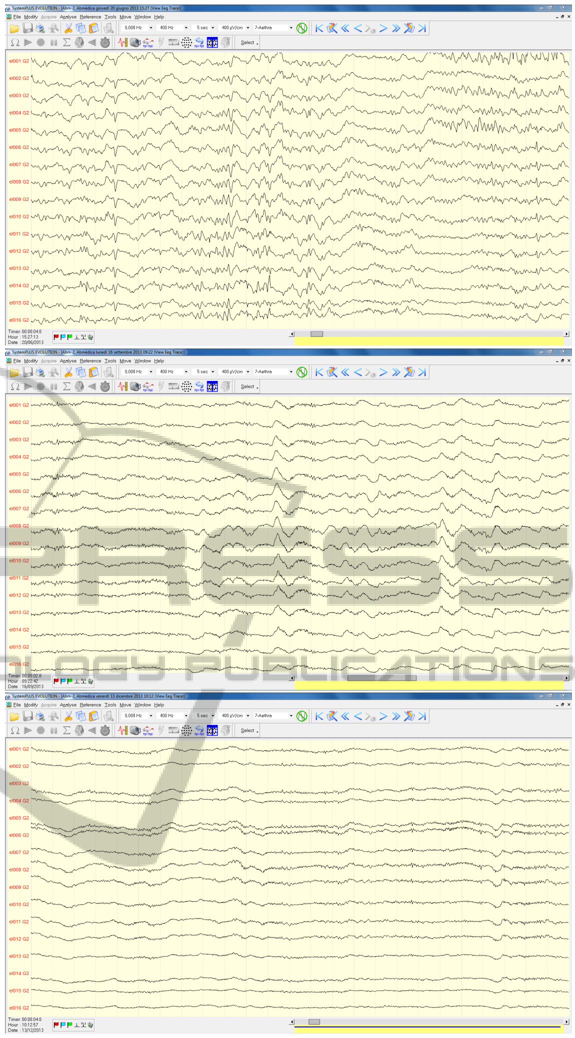

Figure 6: Tipical Ecog traces: after the implant (top), after three months (middle) and after six months (bottom).

resume all the normal motor activities within a few hours. The ECoG signals of sixteen electrodes was recorded with a 512 Hz sampling rate and a software-imposed band-pass filter from 0.008-400 Hz. We first removed all frequencies below 0.5 Hz from the ECoG signals using a high-pass filter. EcoG signal recording was performed every day for 6 months and remained excellent for all the time (Fig.6). In the figure 6 three screenshots are shown: after few hours since the implant, after three months and after six months. It is possible to notice the high fidelity of the signal with no visible distortion and noise.

We measured, every day, the values of impedance at different frequencies (from 16Hz to 2048Hz) in all channel (Fig.7); in our experiment, impedance is measured at different frequencies; as you can see in figure 7, the values of the impedance for each elec-

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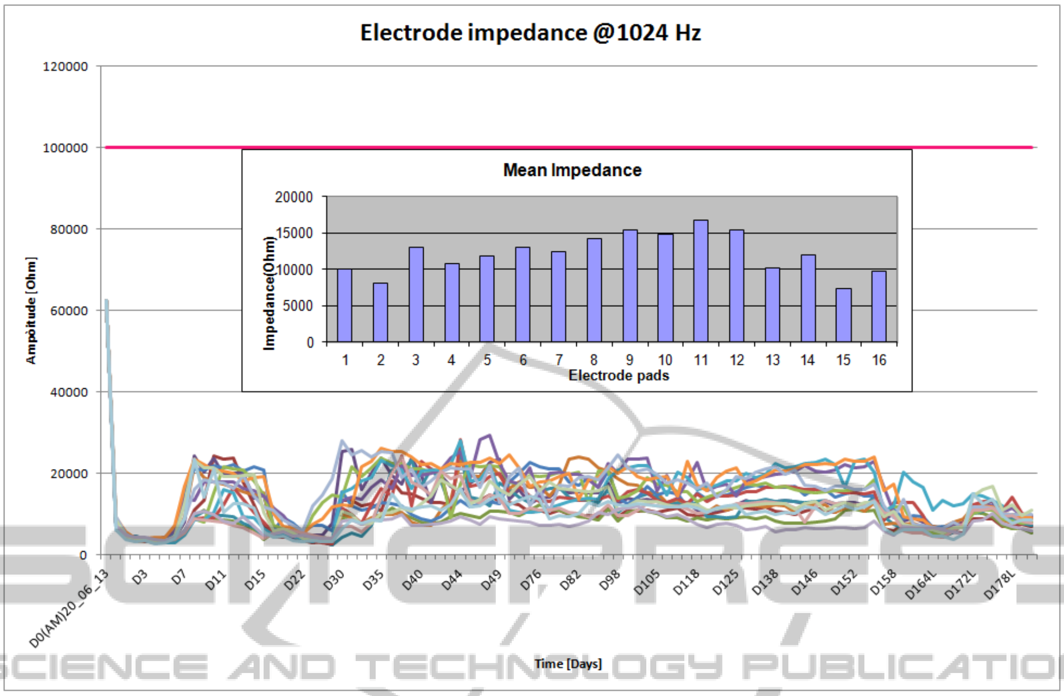

Figure 7: Impedance values over time

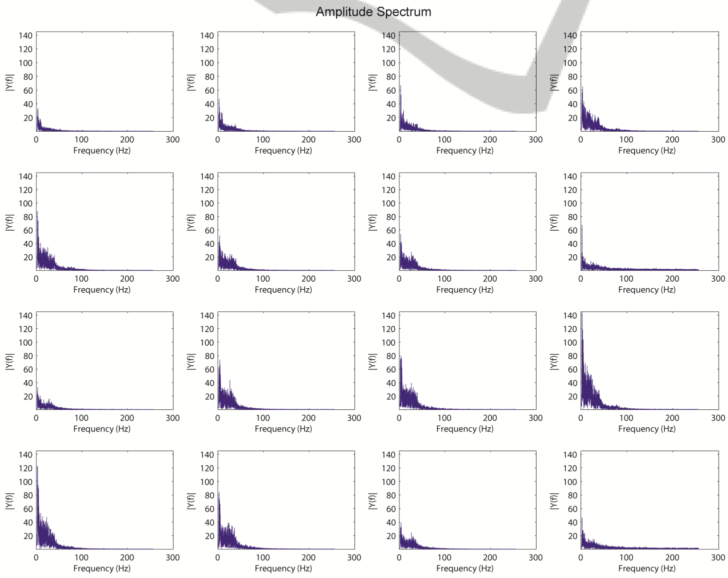

Figure 8: Impedance values over time.

trode is got @1kHz; in the inset the mean value for each electrode is also reported. For all the days the device has been implanted, impedance values has remained under the horizontal pink line (@100 KHz), representing the maximum limit of the impadance. Our device has impedance values consistent to the ones found in literature (Kellis et al., 2011). We computer, also, the Fast Fourier Transform (FFT) of the ECoG traces. The frequency spectrum shows the characteristic decrease in amplitude at higher frequencies and also that there are all the characteristic frequency components of an ECoG signal (Fig.8). Cortical stimulation was performed with a protocol planning to stimulate the primate every seven days. We performed bipolar stimulation by pulses of rectangular shapes with anodal monophasic current pulses

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of 0.5 ms duration. The stimulation technique consists of a train of 5 pulses delivered at 1 Hz, which is equivalent to an interstimulus interval of 100 ms. Stimulus intensity was gradually increased in increments of 0.5 mA, starting at 1 mA, up to a maximum of 3 mA. We testing all the contact with a reference electrode positioned in the left of grid. During cortical stimulation of the expected motor cortex, movements of distinct portions of the right arm were observed with a stimulation intensity of 2 mA.

4 CONCLUSIONS

The implantable wireless device, here presented, allow us to perform chronic EcoG recording and DCS. research and clinical applications of this novel technology include brain mapping, seizure foci localization and BCI. Wireless technology for transmitting EcoG signal provides several advantages: risk and limitation related to the presence of subcutaneous connecting cables (Behrens et al., 1997) are removed and the recording time can be substantially prolonged. This fully-integrated system can also be used as a closed loop system providing electrical stimulation “on-demand” to abort promptly detected seizure activity in drug-resistant epilepsy patients.

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