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cortiQ – Clinical Software for Electrocorticographic Real-Time Functional Mapping of the Eloquent Cortex*

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Abstract— **Planning for epilepsy surgery depends substantially on the localization of brain cortical areas responsible for sensory, motor, or cognitive functions, clinically also known as eloquent cortex. In this paper, we present the novel software package 'cortiQ' that allows clinicians to localize eloquent cortex, thus providing a safe margin for surgical resection with a low incidence of neurological deficits. This software can be easily used in addition to traditional mapping procedures such as the electrical cortical stimulation (ECS) mapping. The software analyses task-related changes in gamma activity recorded from implanted subdural electrocorticography electrodes using extensions to previously published methods. In this manuscript, we describe the system's architecture and workflow required to obtain a map of the eloquent cortex. We validate the system by comparing our mapping results with those acquired using ECS mapping in two subjects. Our results indicate that cortiQ reliably identifies eloquent cortex much faster (several minutes compared to an hour or more) than ECS mapping. Next-neighbour analyses show that there are no false positives and an average of 1.24% false negatives.**

I. Introduction

Epilepsy is a severe neurologic disorder that affects approximately fifty million people in the world. About one third of them is resistant to antiepileptic treatment and therefore suffers from frequent seizures affecting their quality of live [1]. For this group of people, a surgical resection of the seizure focus, i.e., a brain area that shows abnormal electrical activity and is thought to be the source of the seizures, can reduce or even cure epilepsy. To be considered for brain surgery, the seizure focus has to be localized [2]. Furthermore, functional areas close to the seizure focus have to be thoroughly delineated to minimize the possibility of post-surgical functional deficits [3]. This identification of so-called "eloquent cortex" has previously been achieved using several different approaches like electroencephalography (EEG) [2], magnetoencephalography (MEG) [4], functional magnetic resonance imaging (fMRI) [3], positron emission tomography (PET) [5], or electrical cortical stimulation (ECS) [6, 7]. ECS is currently the gold standard procedure to identify eloquent cortex. During invasive pre-surgical monitoring or during the surgery, small currents are applied to electrodes implanted on the patient's brain surface, thus eliciting or inhibiting specific behavioral responses (e.g., hand movements). While ECS mapping is effective, it has considerable time demands and other drawbacks. These issues may limit the detail at which the cortical area can be explored [8]. G. Schalk and his group published a method [9] for mapping brain functional activity by detecting task-related electrical changes, mainly in the gamma band (i.e. between 60 and 170 Hz), using electrocorticographic (ECoG) signals. The test can be executed at the bedside during invasive monitoring, i.e., before the actual resective brain surgery but after the implantation of intracranial electrodes. The method was validated in a multi-center study using research-grade software with excellent results [10]. We are now continuing to improve this method and translating it into a reliable, user-friendly, and widely available software package that is intended to optimize and complement traditional mapping procedures.

In the following sections, we will first introduce the system components of the cortiQ software and describe its characteristics and the workflow of an experiment. Then, we will provide our real-time mapping results obtained from two epileptic patients.

II. System Architecture

A. Hardware

The hardware components of the system included a synchronized array of high resolution multi-channel biosignal amplifiers (g.USBamp, g.tec Guger Technologies OG, Austria) that was connected to the implanted electrodes. A splitter box split the signals coming from the brain into one set that was connected to the cortiQ mapping system and another set that was connected to the clinical monitoring system. The amplifier digitized the signals at a sampling rate of 1200 Hz and transferred them to the computer running cortiQ. This computer had two computer screens connected. One screen displayed instructions for the tasks or visual stimuli to the patient, and also included speakers for auditory stimulation. The second screen displayed the recorded biosignal data and the mapping results to the operator.

B. Software

Before the actual experiment takes place, two steps are required to prepare the system for an individual patient. First

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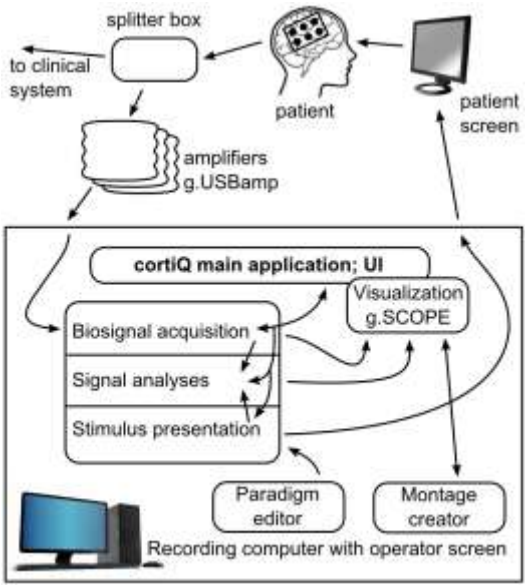

Figure 1. The abstracted hard- and software architecture of the cortiQ system.

an electrode montage, a schematic picture of the implanted electrode alignment has to be created. Second a suitable paradigm has to be selected or created depending clinical needs.

1) Montage Creator

The Montage Creator allows for easy definition of the location of the electrodes. To facilitate this process, the software includes all standard electrode grids of all major manufacturers. For better orientation arbitrary background images of the brain can be used. Individual electrodes can be deactivated in case they are physically removed from the grid by the surgeon, or are not needed for other reasons. Electrodes selected as the amplifier's ground and reference channels have to be marked as such. After that the program automatically creates the channel assignment table, which is a detailed list and graphical representation that shows where every electrode channel has to be connected on the amplifier. This feature should help to minimize connection errors.

2) Paradigm Editor

The paradigm editor supports efficient editing of the tasks the patient should accomplish. Important parameters of these tasks, such as number of repetitions, type of stimulus, etc., can be changed by the operator. Specifically, stimuli can contain images, audio files, text and even tactile stimulation. Tasks can further be subdivided to allow for example the presentation of rapidly progressing image sequences. The editor also allows for the definition of the mapping contrast, e.g., brain activity during stimulation vs. that during rest.

3) Main Application

The main application is intended to provide the operator with a very clear and structured way of conducting the experiment with only the fewest needs for input. The system presents itself with a small startup screen that allows for selecting the montage of the patient stored previously during preparation. Here a preview and the display of the patient ID helps to assure correct selection. Immediately before the start of the experiment, the channel assignment list can be checked again to assure correct hardware connections. After this is done, raw data monitoring begins. In this phase, the operator can check the channels for data quality issues where they are supported by aids that highlight channels with abnormal peak-to-peak amplitude or noise power. Individual channels can be enlarged and power spectrums can be displayed. The operator has the possibility to exclude noisy channels from signal processing and to re-assign ground and reference electrodes.

After signal inspection is finished, the paradigm for the experiment can be selected, and the operator can start the mapping procedure. During operation, the results of the mapping are displayed on the operator screen for each individual task using the selected electrode montage. The screen also shows raw ECoG. After mapping is complete, the results can be cleared, refined using an additional mapping session, or finalized. Once finalized, the system generates a detailed report with one mouse click that contains all the information relevant for the experiment. This includes the used montage, used electrode grids, channel numbering, channel assignment, paradigm settings, data quality issues during recording, and of course the result maps as figures as well as in the form of value tables.

III. System Validation

For system validation, two epilepsy patients of the Florida Hospital for Children (Orlando, FL, USA) participated in cortiQ brain mapping experiments. They underwent surgery to place 64 (patient 1) and 118 (patient 2) subdural platinum electrode grids over different clinically critical brain regions several days prior to resection of a seizure focus. The eloquent cortex of the patients was identified using ECS. For patient 2, only 85 electrodes were stimulated because the others were located quite far away from the epileptic center. The patients gave informed consent through a protocol approved by the Institutional Review Board of the Florida Hospital.

A. Experimental Procedure

After the preparation of the electrode montage scheme and the paradigm for every patient the experiment data were collected with the g.USBamp amplifiers at the bedside of the patients. As ground and reference grid electrodes have been used. The processing of the data and the stimulus presentation entirely was accomplished by the cortiQ software.

The patients went through a paradigm with the following four tasks: open/close the left hand (task 1), repetitively stick out and retract the tongue (task 2), feel touch that was applied to the palm and inner side of the fingers of the left hand (task 3), and listen to a story (task 4). After an initial delay of 10 seconds, where no data were considered for analysis, the paradigm started with a 15 second resting period in which the instruction for the patient presented on the display was 'relax'. After that, starting with task 1, the patients were visually instructed about what to do in the tasks. Each task lasted 15 seconds with 15 seconds rest in between, respectively. The tasks were repeated three times. As described above, the brain signals were transferred to the computer running cortiQ, were analyzed there in real-time to

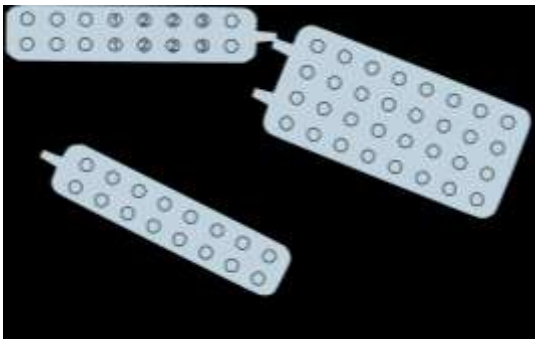

Figure 2. Result of the ECS mapping for patient 1.

gradually build the result in form of topographical brain maps that revealed the task-related differences in activity under certain electrode positions.

IV. RESULTS

In this section, we want to present the results of the validation experiments for the cortiQ software by comparing the outcome of ECS with the results of the software. For the comparison, we simply counted the sites that were assigned to a particular function/area in the ECS procedure and checked whether the significant result values of the cortiQ software indeed were at the same locations. Figure 2 shows the ECS results and Figure 3 shows the results from the cortiQ software for the four executed tasks by patient 1. Table 1 shows the error rates for tasks 1 to 3 (left hand movement, left hand sensation, and tongue/mouth movement) for the patients. As there were no checks for auditory brain regions using ECS, task 4 was excluded from the comparison.

TABLE I. EXACT LOCATION ANALYSES

	Task 1		**Task 2**		**Task 3**	
	FN	***FP***	***FN***	***FP***	***FN***	***FP***
P1	33.3%	0.0%	no ECS test		0.0%	4.48%
P2	no ECS test		75.0%	6.14%	0.0%	1.72%

During the analyses, false positives identified by cortiQ tended to be adjacent to the locations identified by ECS. So we loosened the correctness criterion in the way that we also allowed next neighbors of the ECS positions to count as correctly identified locations [10]. The results of these analyses are shown in Table 2.

TABLE II. NEXT-NEIGHBOUR ANALYSES

	Task 1		**Task 2**		**Task 3**	
	FN	***FP***	***FN***	***FP***	***FN***	***FP***
P1	0.0%	0.0%	no ECS test		0.0%	1.61%
P2	no ECS test		0.0%	0.88%	0.0%	0.0%

As can be seen, the error rates reduced significantly with this next-neighbor comparison. There are no more false negatives and the average of false positive identifications was reduced to 1.24%.

V. DISCUSSION

In this paper, we demonstrated a clinical hardware and software system for cortical functional mapping of the eloquent cortex to be used prior to resective surgeries in epilepsy patients. Based on extensions of methods described in previous studies [9, 10], the results of the next-neighbor evaluation of cortiQ mapping findings are almost identical to those determined by the well-established ECS procedure. Thus, the system has the potential to be used in neurosurgery stations in hospitals as it is designed to be easy to use for a straightforward workflow.

While we are very encouraged by these results, several important questions remain to be investigated before cortiQ mapping may be used as primary results guiding invasive brain surgery. First and foremost, the relationship of cortiQ mapping and post-operative deficit still needs to be established. Thus, at present, we can confidently recommend the use of cortiQ as a procedure that is complementing and/or optimizing existing mapping techniques.

Clearly, ECS is a well-established approach which has been applied regularly in the past decades. However, it has some disadvantages compared to our system. Current spread can distort results because of the need of bipolar stimulation. Another aspect is that there are no clearly defined standards for ECS mapping. Using the cortiQ software causes no distortions by artificially induced signals to the brain, because only task-related brain activity changes are measured. Typically a paradigm consisting of four tasks lasts about 6 minutes, so the procedure is also considerably faster than ECS procedures which can last an hour or more.

We conclude that the cortiQ software is a well-suited and easy to use functional mapping system, which can be used to cross-check, guide or verify eloquent cortex identified with the ECS procedure.

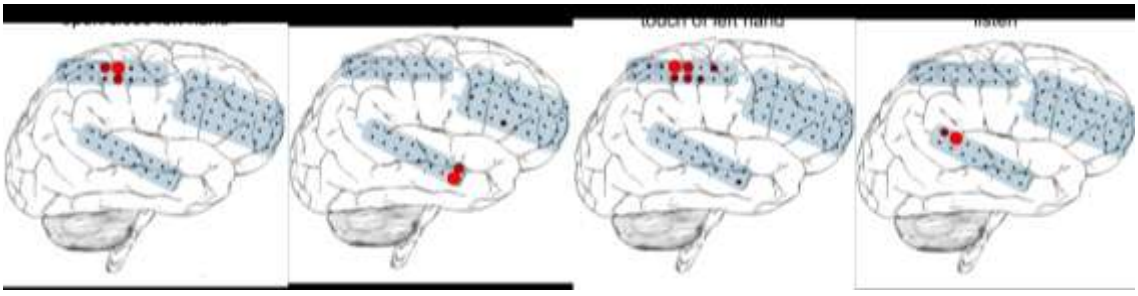

Figure 3. Mapping results from the cortiQ software for tasks 1 to 4 of patient 1.

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