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Interictal ECoG spikes as reflected in MEG

Geertjan Huiskamp, *Member, IEEE* and Zaloa Agirre-Arrizubieta

Abstract—**This study investigates the relationship between the sources of MEG interictal spikes and the distribution of spikes in invasive ECoG in a group of 38 epilepsy patients. An amplitude/surface area measure is defined to quantify ECoG spikes. It is found that all MEG spikes are associated with an ECoG spike that is, according to this measure, among the largest in each patient. For different brain regions considered the inter-hemispheric, tempero-lateral and central regions stand out. However, MEG may only see part of the often complex ECoG spike. In an accompanying simulation study it is shown that MEG as predicted from measured complex ECoG spikes resemble measured MEG and show similar shortcomings with respect to localization.**

I. Introduction

Interictal spikes are short, sharp transients that are observed in the EEG and MEG of epilepsy patients in the period between seizures. They are of paramount importance in the diagnosis of epilepsy, if a first seizure has occurred. In most patients treatment with anti-epileptic drugs will control the seizures. Yet some patients will not respond to drug treatment, and for them epilepsy surgery is an option. In the pre-surgical evaluation of these patients the interictal spikes again play an important role: they are thought to be generated in the region of the brain where the seizure starts as well, the so-called epileptic focus. Localization of the generator of these interictal spikes provides non-invasive information of this focus. If the generator is truly focal it can be adequately modeled by an equivalent current dipole (ECD). Indeed, maps made of EEG/MEG data when these sharp transients occur show dipolar patterns that are perpendicular for the electric and magnetic counterparts. Methods based on the ECD modeling (*e.g.* MUSIC) [1] will localize the position of the assumed dipole generator. This position can be added to other non-invasive information in the planning of the surgical procedure. MEG is shown to be more accurate for this than EEG [2].

However, for some patients non-invasive procedures alone do not provide sufficient information. In these patients invasive data are acquired by placing subdural electrode grids on the cortex (ECoG) in a prolonged (~1 week) monitoring session. During such a registration, some seizures will be captured and analyzed, and an optimal operation strategy is chosen. In addition to the seizures, many interictal spikes will be recorded during this week as well. In this paper we address the question: which of these spikes were detected by MEG non-invasively prior to the implantation ? It is known from other invasive studies that interictal spikes may be complex[3] and cannot be characterized by a single location. Thus the ECD model for intracranial data often is incomplete. So a relevant question is: which part of this complex spike is seen by MEG ?

For answering these questions obviously simultaneous ECoG/MEG data would be perfect [4]. However, considerable risks are involved in such a procedure, at best resulting in short registrations in few patients. This study presents non-simultaneous data in a relatively large group (38) of patients for which both all interictal ECoG spikes during a week of registration and spikes in a 1-2 hour MEG are available. We link MEG to ECoG spikes by co-localization of MEG MUSIC results and ECoG maps that are characterized by an extent and amplitude measure. An attempt is made to simulate MEG from ECoG spikes in order to alleviate shortcomings of the non-simultaneous approach.

Geertjan Huiskamp and Zaloa Agirre Arrizubieta are with the Department of Neurology and Clinical Neurophysiology, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, F02.230 Heidelberglaan 100, 3584 CX Utrecht, the Netherlands,.phone::+31-88-755-8746; e-mail:ghuiskam@ umcutrecht.nl.

II. Material and Methods

A. Patients and imaging

38 patients were studied, all suffering from refractory focal epilepsy and considered candidates for chronic ECoG monitoring. Target areas for implantation included the frontal (36), temporal (32), central (21) parietal (22), occipital (3) and inter-hemispheric (18) regions, either in the left (23) or right (15) hemisphere. For each patient a whole-head high-resolution 3D T1 MRI sequence allowing accurate segmentation of the cortical grey matter and the skin surface was performed**.** During implantation photographs showing grid positions with respect to cortical gyri visible in the trephination were taken. A CT on which electrode positions were visible was matched to the pre-operative MRI.

B. MEG and ECoG processing

A 151-channel whole-head axial gradiometer MEG (CTF, Port Coquitlam, BC) was recorded. Data sets of 10 to 15 minutes were recorded, until 60-90 minutes of MEG data had been obtained. Head position with respect to the MEG helmet was measured. Head-shape information was acquired for MRI co-registration. Two clinical neurophysiologists independently reviewed interictal spikes in MEG datasets. Only interictal spikes from sets for which there was sufficient agreement (inter-observer $\kappa > 0.4$) [5] were used for source modeling. Spatiotemporal clustering of consensus spikes was performed [6] and spikes from each cluster were averaged. The averaged clusters were modeled in CURRYV3.0 using a realistic skull model as extracted from MRI. The interval from the beginning of the rising slope of the spike to the spike maximum was used [7] for a rotating dipoles MUSIC analysis. Points on the cortical surface with an average which the resulting MUSIC metric exceeded 2/3 of the overall

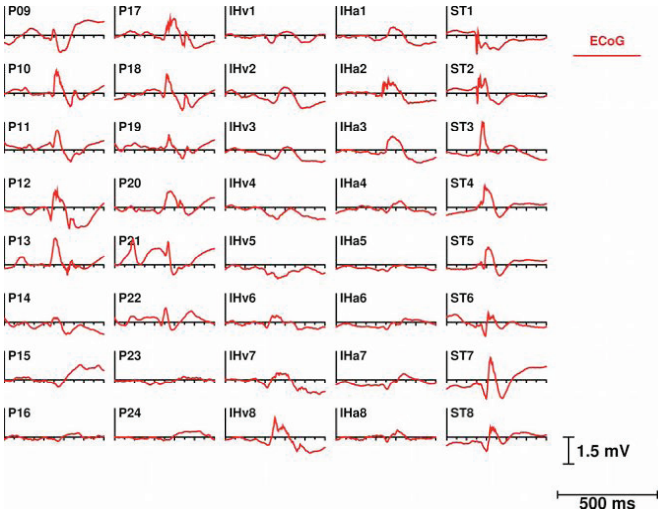

Fig. 1. Measured ECoG for one patient for a selection of grid electrodes in the parietal (P), inter-hemispheric (IH) and temporal-mesial (ST) region. Note that earliest activity is in the ST area, around 150 ms, followed by activity in the parietal and inter-hemispheric region.

maximum were displayed on a cortical rendering from MRI. ECoG was performed with subdural grid electrodes (Ad-Tech, Racine, WI) with up to 80-120 electrodes per patient. Electrodes were embedded in silicone with a distance of 1 cm and a 3 mm contact surface. An extra-cranial reference on the contra-lateral mastoid was used. ECoG was continuously recorded 24 hours a day for an average of 7 days. For each patient one hour of representative samples including all the different interictal ECoG spikes observed during the recording period were collected. The different spike types were identified and averaged. For each averaged ECoG spike, the following combined amplitude *and* synchronous surface-area measure was calculated. First, for each patient, 2 seconds of representative background activity was selected and its root mean square value (*RMS_bg*) was computed. Then for each averaged spike an interval of 200 milliseconds was chosen centered on the time of the maximum. The rms value (*RMS_spike*) for that interval was determined for each electrode. Also for each electrode a baseline interval of 100 milliseconds before the start of the spike was chosen and its rms value (*RMS_base*) was computed. Electrodes for which *RMS_spike* exceeded the criteria of twice the overall *RMS_bg* and twice the *RMS_base* for that electrode were marked and the *RMS_spike* values were integrated to form a single value (*RMS_int*). The *RMS_int* value was used to rank each interictal ECoG spike. Only spikes where at least one of the electrodes met the background criteria were ranked from large to small and used for subsequent association with MEG results.

C. Association analysis

Specific anatomical regions, reflecting the practice of epilepsy surgery, were defined. The temporal lobe was divided into a lateral and a mesial region. The frontal lobe was divided into a fronto-orbital region and the inferior, medial and superior frontal gyri. The inter-hemispheric was region ranged from the frontal to the occipital lobe. The central region consisted of the gyri lining the central sulcus. The parietal region consisted of the superior and inferior lobules and the parietal parts of the supra-marginal and angular gyri. The occipital region contained the convexity and posterior part of the occipital lobe. For each patient each MEG MUSIC result and each ranked ECoG spike were allocated independently to these predefined anatomical regions. Then, the association between ECoG and MEG was made by checking if anatomical regions corresponded. Thus for the whole group of patients, the percentage of ECoG spikes that had a MEG associate, the ranking of these spikes and the regions in which there was correspondence were tabulated. For ECoG spikes for which here was a MEG association it was checked whether it was "focal" (covering a single, congruent region) or "complex".

TABLE I
ECoG SPIKES WITH MEG ASSOCIATE FOR DIFFERENT ANATOMICAL REGIONS

region	#ECoG spikes	#associated with MEG	#association in region
Fronto-orbital	10	10 - (100)	4 - (40)
Inter-hemispheric	45	40 - (89)	32 - (80)
Central	42	32 - (76)	25 - (78)
Temporal-lateral	79	58 - (73)	52 - (90)
Frontal-superior	54	39 - (72)	23 - (53)
Temporal-mesial	51	14 - (28)	0 - (0)

Only regions where values were significant are shown. Between brackets:%. Note that complex spikes involve multiple regions

D. Simulation of MEG from ECoG

For one, representative, complex ECoG spike in one patient a distributed double layer model defined on the cortical surface was fitted to the data. The cortical surface was restricted to hemisphere that was covered by grids. The volume conductor model used was based on a single closed shell enveloping this surface, accounting for the insulating effect of the silicone grid embedding. The cortical conductivity value used was 0.33 $S \cdot m^{-1}$. A minimum norm estimate was computed, where the weight of regularization was determined by considering the L-curve, with the purpose of fitting prominent aspects, not details, of the ECoG data.
For the double layer cortical model a transfer function to the MEG gradiometer configuration was computed. A single compartment defined by the inner skull surface (conductivity 0.33 $S \cdot m^{-1}$) was used. MEG data were then simulated based on the regularized minimum norm solution, and compared to the measured data. Finally, MUSIC localization was performed on the simulated MEG data, and results were compared to those for the real MEG data of the same patient.

III. RESULTS

In total 51 different MEG clusters were found. When localized using MUSIC each cluster could be associated to at least one ECoG spike. Moreover, there was always an association with ECoG spikes having a high *RMS_int* value

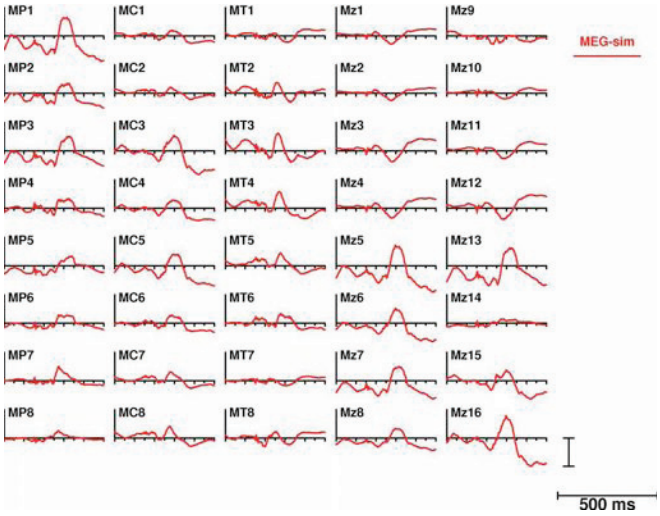

Fig. 2. Simulated MEG for distributed source fitted to ECoG data of Fig.1 for a selection of MEG sensors in the left parietal, central, temporal and midline area. Vertical scale 2 pT, horizontal 500 ms. Note the lack of a clear reflection of the mesial-temporal activity around 150 ms

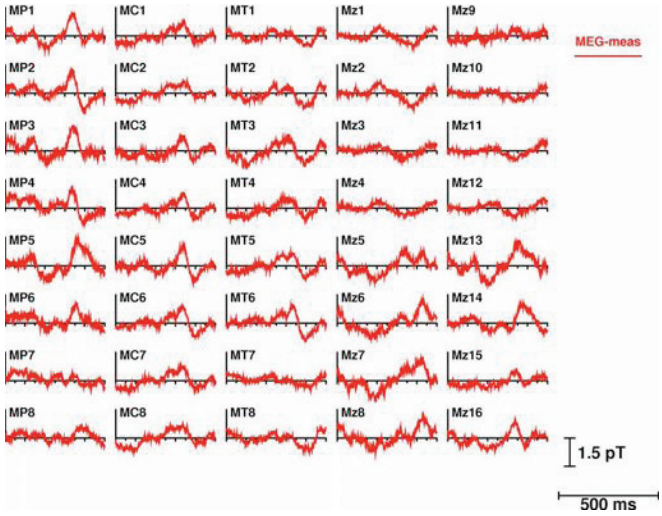

Fig. 3. Fragment of measured MEG recorded prior to the implantation. Vertical scale 1.5 pT, horizontal 500 ms. Note the correspondence with the MEG simulated from the ECoG as shown in Fig.2.

ranked 1st, 2nd or 3rd. There were no MEG results in the area covered by grid-electrodes that did *not* have an ECoG associate. Conversely, of 221 ECoG spike types found 97 (44%) did not have a MEG associate. Of the 124 ECoG spikes that had a MEG associate, 36 (29%) were "complex", covering more than one congruent region. Results specified for different anatomical regions are given in Table 1. An example of a complex ECoG spike is shown in Fig.1, in a selection of grid electrodes covering the sub-temporal/temporal-mesial (ST), parietal (P) and inter-hemispheric region (IH). The earliest sharp activity is in the ST1 electrode (near the hippocampus) around 150 ms, followed by parietal and inter-hemispheric activity. A selection of MEG signals, simulated on basis of a source estimation of the ECoG in Fig.1, is shown in Fig.2.Note that here the early activity around 150 ms is not reflected. In Fig. 3 for the same selection of channels, measured MEG for this patient is shown. MUSIC results for the simulated and measured data of Figs.2 and 3 are given in Figs.4 and 5. The MUSIC metric is color coded, with maximum value in red. Shown is a right view on the left inter-hemispheric area. The white dots indicate grid electrode positions.

IV. Discussion

The first major result of this study is that for all spikes seen by MEG an ECoG spike could be found .in the area of the MUSIC localization, and these ECoG spikes could always be characterized as "large": *RMS_int* values were ranked either 1st, 2nd or 3rd. Conversely, 44% of ECoG spikes could not associated to a MEG results. Regional differences exist for the sensitivity of MEG (Table 1): for inter-hemispheric, central and lateral-temporal areas MEG seems more sensitive (for a further discussion of this table see [8]). A possible explanation for this is that in these areas relatively large, synchronous and parallel tangential patches can exist, whereas other areas are more curved, deep or have a more radial overall orientation. A second important result is that ECoG spikes can be complex, and that MEG can in many cases sees only part of them. All of the mesial temporal ECoG spikes that showed an association with MEG (Table 1, 14 out of 51) did so because they were part of a complex that involved temporal-lateral or other areas. This is illustrated by the example given, where MEG is simulated from such a complex ECoG spike (Figs. 2-5). Although real simultaneous data would be the most convincing here, these simulations show that (1) waveforms simulated from ECoG resemble actual measured waveforms and (2) MUSIC based on the simulated MEG localizes the same region as the measured data does. In the case presented this is in the inter-hemispheric area, where the overall results of this study suggest that MEG is especially sensitive. And indeed, MEG misses the mesial temporal component, for which overall results suggest low sensitivity.

The distributed double layer source on which the simulations are based should only be interpreted as an effective source for describing major aspects of the ECoG signal. Since is based on a fairly accurate individual cortical rendering and measured (either by photography or CT) grid electrode positions, it can be considered to contain both radial and tangential components which allow the simulation of MEG waveforms that are qualitatively accurate. Quantitatively, modeling errors, especially the distance between ECoG electrodes and the assumed cortical generators, may dominate the results. This may be apparent from the difference in the vertical scale (2 pT vs. 1.5 pT) in Figs. 2 and 3 – although actually this result isn't too bad: the non-singular nature of the double layer source [9] (as opposed to the point dipole) probably accounts for that.

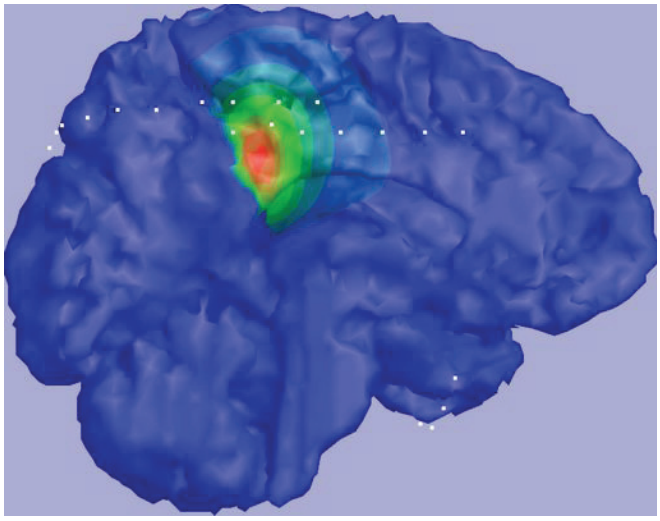

Fig.4, MUSIC result for simulated MEG of Fig. 2. MUSIC metric values range from minimal (blue) to maximal (red). Right view of the left inter-hemispheric region. White dots indicate visible ECoG electrode positions. MEG localization is in the central inter-hemispheric area, near electrodes IHv7 and IHv8.

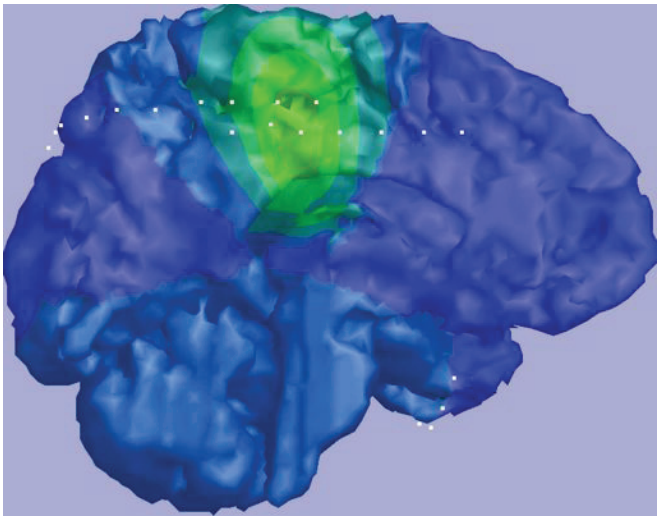

Fig.5, MUSIC result for measured MEG of Fig. 3. MUSIC metric values range from minimal (blue) to maximal (red). Right view of the left inter-hemispheric region. White dots indicate visible ECoG electrode positions. MEG localization is in the central inter-hemispheric area, near electrodes IHv6 and IHv7.

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