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Correlation Between Intra- and Extracranial Background EEG

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***Abstract*— Scalp EEG is the most widely used modality to record the electrical signals of the brain. It is well known that the volume conduction of these brain waves through the brain, cerebrospinal fluid, skull and scalp reduces the spatial resolution and the signal amplitude. So far the volume conduction has primarily been investigated by realistic head models or interictal spike analysis. We have set up a novel and more realistic experiment that made it possible to compare the information in the intra- and extracranial EEG. We found that intracranial EEG channels contained correlated patterns when placed less than 30 mm apart, that intra- and extracranial channels were partly correlated when placed less than 40 mm apart, and that extracranial channels probably were correlated over larger distances. The underlying cortical area that influences the extracranial EEG is found to be up to 45 cm^2. This area is larger than previously reported.**

I. Introduction

The first human electroencephalography (EEG) was measured by Hans Berger more than 80 years ago but humankind is still striving to understand the physiology behind the curves. Especially the differences between the scalp and cortical EEG have long been observed [1–5]. It is well acknowledged that cortical EEG potentials are of higher amplitude and contain more energy in the high frequency bands [6]. This is due to the property of the skull as a spatial averager which only transmits those components common to and synchronous over large areas of the cortex [1].

Existing research trying to explain the cortical substrates of scalp EEG has either focused on *in vitro* measurements [2], describing the volume conduction based on a realistic head model [7], or used the interictal spikes from epilepsy patients to estimate the area of the substrates [8], [9]. The *in vitro* measurements performed by Cooper et al. [2] has often been accepted as the *de facto* standard for synchronized cortical activity necessary for generation of scalp EEG. They reported that an area of 6 cm^2 was most probably necessary. However, *in vitro* measurements are very approximate to volume conduction *in vivo*. The three or four compartment models used in the realistic head simulations have provided estimations of the underlying source regions to be accurate in the range of perhaps 10 or 20 cm^2 [7]. When the distributed sources are broadly localized, the surface Laplacian method used to estimate the dura surface potentials underestimates the true cortical potentials. It tends to filter out very low spatial frequency sources, as well as low spatial frequency potentials due to volume conduction only. Most important though, is that no matter how complicated the geometric model, the volume conductor model will be severely limited by the lack of information on tissue conductivity. Finally, by visual investigation of interictal spikes, the size of the underlying cortical area needed to produce a scalp potential also resulted in 10-20 cm^2 [8]. This area is probably also an underestimation of the cortical area contributing to scalp EEG, since the interictal epileptiform discharges have larger amplitudes than background EEG. As scalp potentials represent summed voltage field potentials generated at the cortical pyramidal cells, larger amplitude as well as higher synchrony between cells will provide greater probability of the potential being recordable on the scalp.

We investigate to what extend cortical source potentials contribute to extracranial normal wake EEG. We found this area of correlation by constructing an *in vivo* setup with aligned electrodes intra- and extracranially. By calculation of the correlation between channels on either side of the skull, we were able to estimate the distance of which channels still have correlates.

II. Materials and Methods

A. Clinical Data

Six patients admitted to the *epilepsy monitoring unit* at Copenhagen University Hospital Rigshospitalet volunteered to participate in the study, see Table 1. They were all undergoing neurosurgery work up for control of medically refractory seizures. Implantation of subdural grid, strip or depth electrodes was conducted in accordance with established standards, and the insertion of the extracranial strip of electrodes was done after agreement on location between neurophysiologists and neurosurgeons. The project

TABLE I. Patient Information

Patient	Sex	Age	Extracranial Electrodes	Intracranial Electrodes	Time Available
#	Male/ Female	Years	C: Contacts	C: Contacts	Hours: Minutes: seconds
1	M	65	2 x 6C strip	1 x 20C grid	00:22:20
2	F	32	2 x 4C strip	1 x 4C strip	00:10:00
3	F	43	1 x 6C strip	1 x 48C grid	00:59:59
4	F	29	1 x 4C strip	1 x 20C grid	00:10:26
5	F	30	1 x 4C strip	1 x 4C strip 2 x 6C strip	00:14:40
6	F	35	1 x 4C strip	1 x 32C grid	00:21:00

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was approved by The Local Committee on Health Research Ethics. The extracranial strip was placed directly on the skull approximately aligned over the cortical electrodes, see Fig. 1. All electrodes were connected to the same recording system (Stellate Systems, Inc., San Carlos, USA). Data were digitized at a rate of 1000 Hz and band pass filtered with cut-off frequencies at 0.3 and 300 Hz. Postoperatively, the patient was CT scanned to precisely determine the location of the electrodes in a three dimensional coordinate system.

For the correlation analysis, at least 10 min of data were selected from artifact free awake EEG. Data were down sampled to 200 Hz for faster computation; a least-squares error minimization FIR-filter with an order of 10 and low pass cut-off at 90 Hz was applied to avoid aliasing followed by data decimation by selecting every 5th sample.

To avoid issues with a fixed reference electrode that is responsible for most of the correlation, we used bipolar derivations setup for all adjacent electrodes transversally as well as longitudinally. In the correlation analysis we did not compare derivations with electrodes in common to avoid the same problem as a fixed reference that drives the entire correlation. To calculate the Euclidian distance between channels, we defined one channels coordinates as the mean of the two electrodes coordinates.

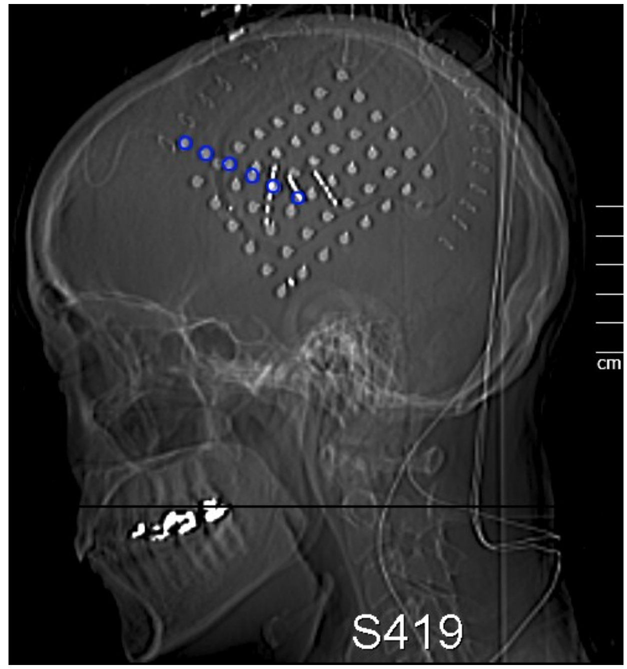

Figure 1. Sagital view of a patient's postoperative CT image. The intracranial electrodes can be seen as light gray dots while the extracranial electrodes are encircled in blue.

B. Pearson Product-Moment Correlation Coefficient

We used the Pearson product-moment correlation coefficient as a measure of dependence between data. This method is well suited to measure the waveform and time coupling between two channels [10]. It is obtained by normalizing the covariance of two variables, x and y, by the product of their sample standard deviations, s_x and s_y, which must be nonzero. If we annotate the sample means of x and y as $\bar{x}$, $\bar{y}$ respectively we find the sample correlation coefficient to be:

$$r_{xy} = \frac{cov(x,y)}{s_x s_y} = \frac{\sum_{i=1}^{n}(x_i-\bar{x})(y_i-\bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i-\bar{x})^2 \sum_{i=1}^{n}(y_i-\bar{y})^2}}, \quad (1)$$

where n is the number of samples. The variables x and y are the time series of two different EEG channels. Note that the correlation coefficient is equal to the normalized cross-correlation at lag 0. For analysis and model fitting we used the absolute value of the correlation coefficient, since we did not mind the sign of the derivations. To find the best model fit, we chose the one with the highest r^2-value following the model:

$$f(n) = (an)^p + b \text{ for } \in \mathbb{Z}.$$

where a is the constant of proportionality and b is a constant term that represent the noise or variance.

III. Results

A. Generic Modeling

A total of 5 195 intra- vs. intracranial EEG (i/iEEG), 955 extra- vs. intracranial (e/i), and 39 extra- vs. extracranial (e/e) comparisons were performed. Fig. 2 illustrates all of the correlations for each of the three situations. For all comparisons there is a clear tendency that the correlation increases with decreasing distance. For i/iEEG comparisons the best fitted line followed the model:

$$f(n) = (an)^{-2} + b.$$

Best e/iEEG comparisons followed the model:

$$f(n) = (an)^{-1} + b,$$

and best e/eEEG comparisons followed the model:

$$f(n) = an + b.$$

Note that the r^2-values are small.

The lines that represent the mean values are calculated based on a moving average filter that simply finds the mean of N succeeding samples and are plotted at the distance of the center sample. In the i/iEEG analysis this line has leveled out at distances above 30 mm, whereas e/iEEG becomes flat after 40 mm. It is impossible to state for the e/eEEG comparisons due to the limited number of correlations. For the i/iEEG correlation it means that any given channel is partly correlated with surrounding channels in a radius of 30 mm. This corresponds to an area of almost 30 cm^2. The radius of 30 mm is in agreement with the work by Bullock et al. [11]. They reported that the coherence between cortical electrodes is in the millimeter domain, i.e. below 28 mm when analyzing their figures. For the e/iEEG correlation we can use the 40 mm to calculate the size of the underlying area an eEEG channel is influenced by. The interesting distance is the tangential, but the distance between the channels is calculated as the Euclidian distance. For the six patients, the radial distance between intra- and extracranial electrodes was in mean 12 mm. By use of the Pythagorean Theorem we find the tangential distance to be 38 mm. This corresponds to an underlying area of 45 cm^2.

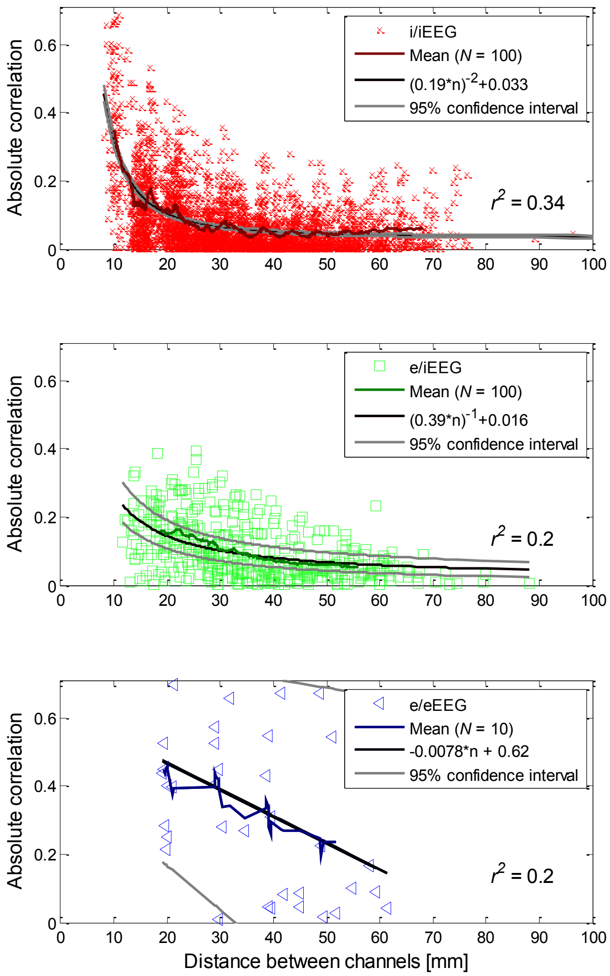

Figure 2. Generic modeling of i/iEEG, e/iEEG and e/eEEG. All comparing samples are used for obtaining the best fitted regression line.

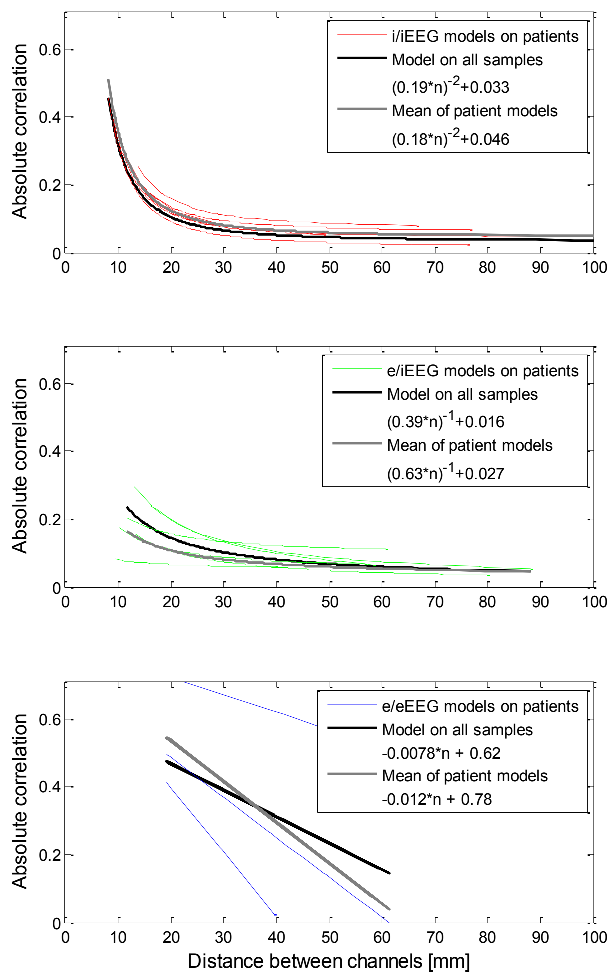

Figure 3. Patient-specific modeling of i/iEEG, e/iEEG and e/eEEG. Especially the i/iEEG comparisons show high similarity. For e/iEEG and e/eEEG all regression lines also have a negative slope, giving credibitily to the model.

B. Patient-Specific Modeling

Based on the results in the generic modeling, data from each patient were fitted with the model that had the best fit for each of the three comparisons. Fig. 3 shows how the i/iEEG models were similar decreasing correlation across patients (red lines). For e/iEEG and e/eEEG all comparisons (i.e. the green and blue lines) also showed a decreasing correlation with increasing distance although the variances between the models were higher. The black lines correspond to the model on all samples in Fig. 2, and the grey lines are calculated based on the mean of the parameters a and b in the model fittings for each patient.

IV. Discussion

A. Background EEG for Analysis

Our approach of assessing cortical substrates in extracranial EEG based on analysis of background EEG activity is very different from previously published methods. Others based their comparisons on either visual interictal spike analysis [4] or a realistic head model [7]. The first approach is very confined to the high frequencies in spikes and does not take into account how the spikes usually contain high power and thus have a higher probability of propagation through the skull despite a small synchronous cortical area. This aspect suggest a smaller area than if background EEG was used. The approach of realistic head modeling can show interesting properties of volume conduction, but has serious limitations in estimating correct and general conductivities of the brain, cerebrospinal fluid, skull and scalp. Our approach of using awake background EEG also has its limitations and advantages. As opposed to realistic head modeling we will not be able to circumvent the breach effect where cortical brainwaves pass through the craniotomy to the scalp without the moderation by the skull [12]. Another possible technical confound is the Silastic membrane and metal electrode disks of the subdural grid or strip. Both might exhibit an attenuating and blurring effect on the extracranial voltage field, although Tao et al. [8] reported no appreciable amplitude asymmetry in EEG from the two temporal areas where only one was affected by a subdural grid. How much the breach effect and subdural grid/strip influence the correlation will be a subject for further research.

As a non-stationary signal, the EEG will exhibit different power spectra throughout the at least 10 min of recording. As the correlation coefficient does not assume stationarity this is actually an advantage. It means that we have a broad view of the activity of the brain, and that the underlying cortical area values we estimate are based on common observations. On the other hand, this paper does not distinguish between conductivities at different frequency bands. This will also be subject for further research.

B. Generic vs. Patient-Specific Modeling

We used two different approaches for modeling of the correlation data, both having advantages and downsides. The generic modeling has the advantage of using a lot of sample points to model the data; unfortunately each patient does not contribute with an equal amount of samples. E.g. does patient 3 have a total of 410 different e/iEEG comparisons, while patient 5 only has 39. This means that patient 3 contributes more to the generic model than patient 5. On the other hand, the mean of the patient-specific modeling might put too much emphasis on patients whose model was weak with a large confidence interval due to few sample points. The weak model of patient 5 contributes here equally to the very strong model of patient 3. In Fig. 3 we could compare the model on all samples (generic) and the mean of patient models (patient-specific). It is not possible to conclude which is better.

C. Models for Regression Lines

The models for the different comparisons all had a constant term and a slope in different powers. For the i/iEEG and e/iEEG the power of the slope was negative meaning that this term will approach zero when distance goes to infinity. The constant term is thus the "noise" in the measurement that will exist no matter how far the distance between channels. We assume that the different powers of the slope can be interpreted through Coulomb's law from which it follows that the magnitude of the electric field, E, created by a single point charge, q, at a certain distance, r, is given by:

$$E = \frac{q}{4\pi\varepsilon_0 r^2},$$

where ε_0 is an electric constant that describes the properties of the electric field in relation to its sources. The theorem states that the electric field from a single point charge radiated outward in three-dimensional space is inversely proportional to the square of the distance. Due to Ohm's law, the potential from a given point charge will follow the same relationship as seen in our i/iEEG comparisons.

For the e/iEEG relationship, the geometry is different. An electrical emission will always travel the route with the smallest resistivity. Electrical currents will primarily travel radially through the skull, and tangentially along the scalp or brain due to higher conductivities. This means that the skull will entail a constant attenuation of the correlation independent of distance between channels. The scalp will then primarily be responsible for carrying the electric field. As the spread only occurs in two dimensions, the electric field will be inversely proportion to the distance as our findings also indicated.

The e/eEEG comparisons should theoretically follow the same decline as the e/iEEG comparisons, but it had too large a confidence interval for us to comment on the actual decline.

V. Conclusion

We succeeded in estimating the underlying cortical area correlated with extracranial EEG based on background brain activity from six patients. Using a realistic analysis setup we obtained an estimate of the true area that contributes to an extracranial recording. It was found to be correlated with an underlying cortical area of approximately 45 cm^2. Even though the intracranial channels located directly underneath an extracranial channel are more correlated than those placed on the brink of the field of view, they are still not that similar with correlation coefficients approximately at 0.2.

The 45 cm^2 field of view is larger than previous reported correlates between intra- and extracranial channels that are based on interictal spikes [8] or realistic head modeling [7]. It should be noted though that the scopes are different. For intracranial recordings we found the correlation area to be within a radius of 30 mm corresponding to an area of approximately 28 cm^2. This is in concordance with previous reports [11].

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