Functional and Morphologic Data Fusion for Epileptogenic Foci Localisation[1]

José Maria Fernandes, António Martins da Silva, João Ramalheira, Pedro M. Gonçalves Pereira and João Paulo Cunha

Resumo - **Uma das tarefas mais dificeis na Epileptologia é a localização da area epileptogénica/focus. Esta tarefa é fundamental para alcançar um bom diagnóstico clínico e um bom tratamento farmacológico. Se necessário, permite melhorar a precisão do procedimento cirúrgico, diminuindo o número de casos resistente, melhorando a qualidade de vida dos doentes.**

Neste trabalho propomos uma solução com o objectivo de melhorar a precisão na localização da origem da actividade epileptogénica tendo em consideração diversos tipos de informação (clínica, EEG de escalpe, SPECT, CT e MRI) através da integração de toda a informação num ambiente multimédia, no contexto clínico da avaliação de candidatos à cirurgia da Epilepsia.

Abstract - **One of the most important and difficult tasks in Epileptology is the localisation of the epileptogenic areas/focus. This is fundamental to achieve good clinical classification and consequent good pharmacological treatment. If needed, it allows adequate surgical procedure consequently decreasing the number of resistant cases and improving patient's quality of life.**

In this work we propose a solution with the objective of improving the accuracy of epileptogenic event origin location taking into account several types of information (clinical, scalp EEG, SPECT, CT and MRI) that are integrated in a multimedia environment available in the clinical context of epilepsy surgery candidates evaluation.

I INTRODUCTION

One of the most important and difficult tasks in Epileptology is the localisation of the epileptogenic areas/focus. This is fundamental to achieve good clinical classification and consequent good pharmacological treatment. If needed, it allows adequate surgical procedure consequently decreasing the number of resistant cases and improving patient's quality of life.

Nevertheless the events origin location, the seizure classification and even the patient selection for determined therapeutic strategy is a rather difficult task gathering information from different origins: clinical; signal (EEG); morphology imaging (CT Scan, MRI) or functional imaging (SPECT, PET) [1, 2]. Based on all of them, clinicians look for answers to the following questions: where is the focus? Is there any functional lesion? Is there any structural lesion? Are they correlated with the focus?

The strategies of non-invasive studies adopted during recent years have determined that some procedures are now well defined. The combination of techniques gives much more information than the traditional sequential association of information [3-8]; some of the techniques are – at the moment – not reliable in specific conditions (for example the use of PET Scan to the study of ictal events); others (such as SPECT in some interictal conditions [9] scalp EEG recording[10]) are considered reliable but are possible to be improved.

The main objective of this work was to support further research on a clinical problem our team has been working for several years: the precise localisation of the epileptogenic area in the brain recurring to non-invasive methods which is the fundamental issue in epileptology, specially in severe epileptic patients. Our approach aimed at improving the accuracy of epileptogenic event origin location taking into account several types of information (clinical, scalp EEG, SPECT, CT and MRI) that are integrated in a 3D frame on a multimedia environment available in the clinical context of epilepsy surgery candidates evaluation [11, 12].

In this work we propose a solution together with a clinical protocol usable in the clinical environment for the integration of the two main computerized approaches available from the literature used in this clinical problem,

- The underlying current sources localisation using several inverse problem solution algorithms from ictal and interictal scalp EEG epochs.
- Functional (SPECT) and morphological (CT/MRI) image co-registration and fusion.

The described approach we are pursuing can be depicted in Figure1.

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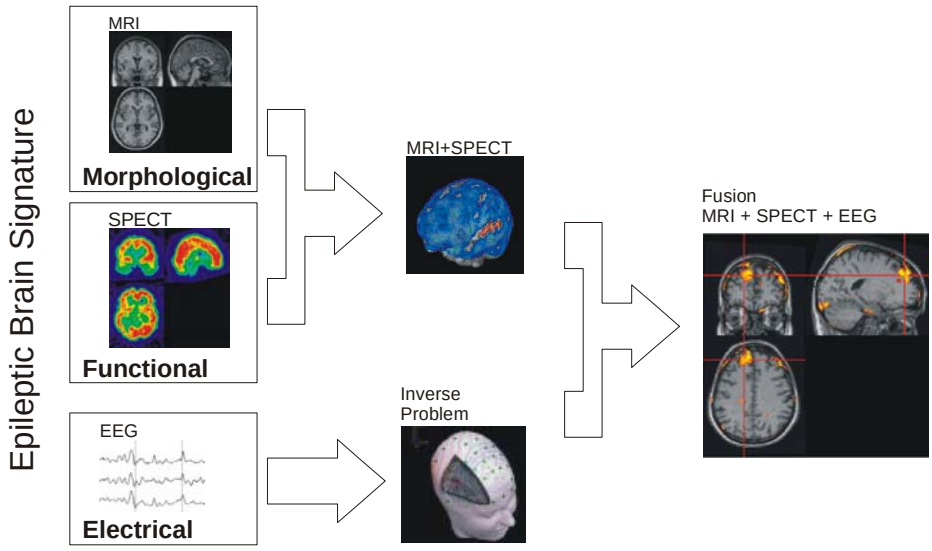

Figure 1 – General approach for the data fusion

II DATA SOURCES & ACQUISITION PROTOCOL

The modalities available were EEG, MRI and SPECT volumes that were acquired from different sources with different characteristics (Table 1).

Data type	Source	Type
MRI Source I	GE Signa System with Advantage Windows OS (UNIX) – 1.5T	3D Volume 512x192 1.6mm
MRI Source II	Picker machine using a UNIX based OS – 1 T	3D Volume 256x256 1.3mm
SPECT Source	SophyCamera DST	3D Volume 128x128x128
EEG Source	ONYX digital Video-EEG [13]	Biosignal 21-64 Channels 512Hz

Table 1 - Data sources

The 3D imaging data sources (MRI and SPECT) were acquired as 3D data volumes. For this modalities a image pre-processing was necessary, which consisted in converting the data to DICOM and Analyze formats and readjusting the volume acording to morphological references – the commissures [14, 15] - following well established procedures from the literature

The choice of the DICOM [16] and Analyze [17] as data formats for the MRI and SPECT information are mainly due to the fact that they are common used formats. DICOM is a standard from ACR/NEMA and Analyze is a popular format in this area which ensures the availability of a wide number of applications both for imaging processing/visualisation and for neurophysiology specific applications.

The MRI protocol is described in detail in [18, 19]. The SPECT protocol followed closely the procedure proposed by Chiron et al. [20-22].

III DATA FUSION

The fusion of different modalities poses several technical problems, namely due to the different natures of the sources and morphologic constraints of the 3D space of interest.

The electric activity information is related with the estimation of the brain sources that generate the EEG measurements on the scalp. Usually the set of techniques and application are classified and inverse problem techniques [23-25]. It was not our objective to focus in this problem, as there are several applications/methods available to obtain acceptable solutions (as there is no unique and optimal one).

The solutions of these problem are in the form of electric dipoles or areas suspected of being the electrical sources. Dipoles consist of vectors located at a specific brain position, which are the estimated brain source that produces the activity measured in EEG collected from the scalp. Our work was restricted to inverse problem techniques that retrieve dipole sources [26-28]. For this purpose we use a commercial software package called “Advanced Source Analysis (ASA)” [29]. For high accuracy of these methods is mandatory the determination of the realistic electrod positions. We used an approach proposed by J C de Munck et al. [30]. For this purpose it enables both the use of realistic electrode position in inverse problem techniques [24, 29, 31], ensuring better solutions within the realistic brain morphology [10, 32] and a mapping between dipole referencial and the MRI volume.

A Brain Atlas and reference systems

For performing any kind of coregistration of 3D volumes it is needed to establish some common reference to all modalities. In this work context, we adopted the *Montreal Neurological Institute* (MNI) average brain[15]. This is based on an average of a large number of acquisitions in several 3D modalities of normal subject mapped into the Talairach space - a stereotaxy brain atlas [14, 15].

Based on this reference system, we can adjust different modalities (MRI, SPECT, PET, for instance) to the same 3D referential.

B Coregistration using the MNI approach: Data Normalisation

The coregistration process we followed implies the normalization of the data volumes of the different modalities into the same reference system. The normalisation process consists of, by means of volume transformations, try to minimise the differences between the volume data and the respective modality template. The minimisation may involve techniques from simple linear minimisation to mutual information based methods. Using a proper software tool we obtain the necessary volume transformation for each type of data (MRI, SPECT and dipole 3D Mask) [33-35].

The dipole 3D Mask of the dipole related information is initially coregistrated with the MRI of the patient. It is normalized through the application of normalization transformations used for that MRI, converting it into the MNI space. After the normalization process is complete, the coregistration enables a precise alignment between any modality in the MNI space (MRI/SPECT/PET and the EEG related dipoles, as a 3D dipole mask) of the same patient

C SPECT subtraction: an useful tool

In some publications, SPECT subtraction appears to be a highly successful and recommended procedure in the context of the localization of the activity areas during epileptic seizures [36-38]. The SPECT subtraction consists in subtracting SPECT 3D data volumes acquired during seizures (ictal SPECT) and on their absence (inter ictal SPECT, or, in other words, SPECT acquired between seizures). Through this subtraction it is possible to identify areas with more / less activity during seizures against the “normal” brain activity. These areas correspond to areas related with the epiloptogenic areas of the brain.

On the technical side, this subtraction implies some careful steps, mainly due to some problems directly related with the SPECT technique:

- the SPECT perfusion is not constant. The range of SPECT values may vary between different exams (specially the higher ones).
- The position of the patient may differ between exams. Which means that different exams have different spatial orientations.

The first problem is attenuated by assuming that it is possible that maximum perfusion values in exams can be matched. Assuming that, they can be used as a reference to rescale the data volumes to a common value scale. After this rescaling, it is possible to subtract both SPECT volumes and obtain a data volume with the difference values voxel by voxel. To solve the second problem, we use the normalization, to map this voxel matrix exams into the same MNI referential system.

The interpretation of the SPECT subtraction depends on the clinicical purpose. If we want to find the areas of higher activity during seizures (hiperdebits), we should subtract an interictal SPECT to an ictal SPECT.

IV DATA FUSION IN EPILEPSY: A COMPLETE CASE

The result of this work may be synthetised in this complete case, were the final protocol was applied and illustrated

As described previously, after the acquisition of the data (SPECT, MRI) some scaling and orientation procedures must be performed, in order to be able to proceed with the normalization process. We will skip details on this phase.

From the acquired EEG we proceed with the inverse problem analysis as described previously. Assuming that we have a dipole at as a position in the MRI of the patient, we can generate a 3D mask volume (as a image or as a region of interest – ROI) to be coregistratable over the MNI space.

In the normalization process, we map all modalities into the MNI referential space. This process is applied to the MRI, SPECT and dipole masks.

The subtraction of both ictal and inter ictal SPECTs is performed after the SPECT spatial normalization. In this process, a rescaling of the SPECT range values was performed.

The coregistration of the SPECT subtraction, MRI and dipole enables to localize in the brain the zones of hipo and hiper debits In this case we are only interested in the difference between ictal and inter ictal SPECT (positive difference)

The fusion results can be depicted in Figure 2. In Figure 2 (a) the coregistration is performed over the complete skull and brain, while in Figure 2 (b), the coregistration is constrained by a brain segmentation, eliminating all the noise outside the brain area. In both, it is visible a activation area in SPECT subtraction (bright area) and the dipole (darker are near the crosshair – in detail in Figure 2 (b)).

V CONCLUSIONS AND FUTURE WORK

We aimed at a specific technical research objective centered on data fusion of several information used in epilepsy surgery candidates evaluation. As a general conclusion we may say that we achieved the technical objectives but we need the clinical validation process to be performed in order to assert the contribution of this work against the current clinical practice.

It is our belief that this line of research may enhance more the sensitivity and specificity of the overall integrated information in comparison to side-by-side evaluation for localising the seizure focus in severe epilepsies. Further clinical validation needs to be performed to confirm this issue.

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AFFILIATIONS

José Maria Fernandes and João Paulo Cunha work the Departamento de Electrónica de Telecomunicações at Universidade de Aveiro, Portugal.

A. Martins da Silva and João Ramalheira work at Serviço de Neurofisiologia of Hospital Geral de Santo António, Porto, Portugal.

Pedro M. Gonçalves Pereira works at Serviço de Neuroradiologia of Hospital Egas Moniz, Lisboa, Portugal.

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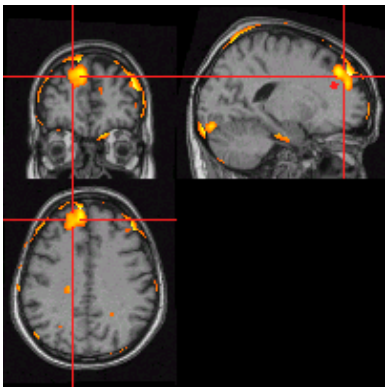
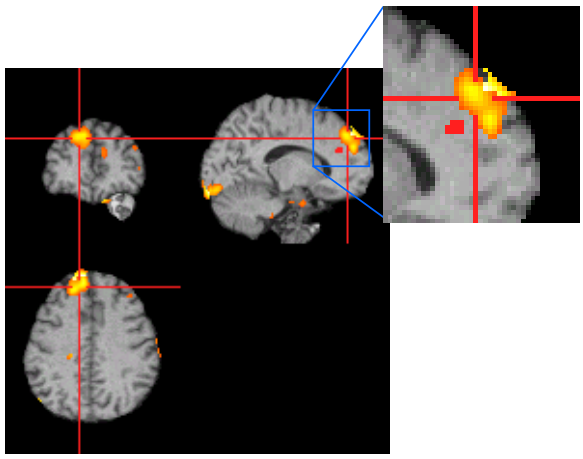
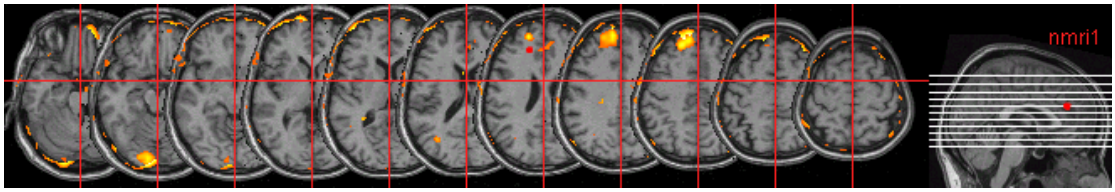


(a) Axial, coronal and sagital with SPECT subtraction and dipole mark



b) Segmented brain: axial, coronal and Sagital with SPECT subtraction and dipole mark (the darker area near the crosshair)



(c) Axial slices with SPECT subtraction and dipole mark

Figure 2 – Coregistration of SPECT subtraction (with a threshold applied to localize better hiper debit). The dipole, in (a) and (b), is localized near the intersection of the crosshairs (darker area). The areas outside the brain are due to different noise conditions in the ictal and inter ictal SPECT.

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