Advances in Neuro Diagnostic based on Microwave Technology, Transcranial Magnetic Stimulation and EEG source localization

Advances in Neuro Diagnostic based on Microwave Technology, Transcranial Magnetic Stimulation and EEG Source Localization

Mikael Persson[#], Tomas McKelvey[#], Andreas Fhager[#], Hoi-Shun Lui[#], Yazdan Shirvany[#], Artur Chodoroski[#], Qaiser Mahmood[#], Fredrik Edelvik[*], Magnus Thordstein[^], Anders Hedström[^], Mikael Elam[^]

[#] *Chalmers University of Technology, SE412-96, Gothenburg, Sweden*
[1]Mikael.Persson@chalemrs.se

[*]*Fraunhofer-Chalmers Research Centre for Industrial Mathematic, SE412-88, Gothenburg, Sweden*

[^]*The Sahlgrenska Academy, Gothenburg University ,SE413-95, Gothenburg, Sweden*

Abstract **— Advances in neuro diagnostics based on microwave antenna system in terms of a helmet including a set of broad band patch antennas is presented. It is shown that classification algorithms can be used to detect internal bleeding in stroke patients. Transcranial magnetic stimulation has traditionally been used for brain mapping and treatment of depression. In this paper we discuss the use of the method for neuro diagnostics with the help of integrated image guidance. Surgical therapy has become an important therapeutic alternative for some patients with medically intractable epilepsy. Electroencephalography and the associated model based diagnostics as a non-invasive diagnostic tool is also discussed.**

Index Terms **— Microwave Technology, Transcranial Magnetic Stimulation (TMS), EEG source localization.**

I. MICROWAVE BASED STROKE DIAGNOSTICS

The diagnostic of stroke patients suffer from a number of serious limitations. The most severe problem is that the diagnosis often takes too long time to establish. In 80% of the patients the stroke are caused by a clot, which can be treated with clot-resolving medication if given in time. Unfortunately most patients will not receive their diagnosis in time to save the brain from damage due to delays in the chain of care. This is because it needs to be established that the stroke is not caused by hemorrhage. It has been suggested that microwave based systems can solve some of these outstanding problems. For this purpose we have developed a microwave helmet and performed an initial clinical study on 20 stroke patients. Using classification algorithms we have obtained encouraging results, but more patients have to be measured before any definitive conclusions can. The stroke detection helmet is built by 10 patch antennas that have been mounted in a helmet and the multistatic scattering matrix is measures at a large number of frequencies. The measured scattering coefficients are then used as input for the classifier algorithm. This measurement strategy is similar to what is commonly used in microwave tomography experiments.

The multistatic matrix is measured using each antenna both as transmitter as well as receiver. A two port network analyzer is used as the transmitting and receiving unit. To fully control the experiment a multiplexer module is used to automatically connect and disconnect the different combinations of antenna pairs to the network analyzer. A particular problem with the helmet is that it is rigid whereas the size and shape of different patients varies. To fit the antenna to individual patients the solution is to mount flexible plastic bags inside the helmet that can be filled with water. The purpose of the water bags is to fill up the space between the antennas and the skull but also to provide impedance matching between the antenna and the skull. If the antennas were just left with an air gap between the antenna and the skull the differences in intrinsic impedances between skin and air would cause a strong reflection at the surface of the skin, thereby preventing a large portion of the signal to penetrate into the skull. Only the signal penetrating will be useful in stroke detection and a weak signal into the skull means a weak signal out and consequently also a low signal to noise ratio.

We are currently investing data driven approaches to develop detection and classification algorithms where the scattering measurements are treated as multidimensional signal samples. Based on labeled data we construct the classifier by extracting features from the high dimensional data and then project them to lower dimensions suitable for discrimination between the classes. Subspace based techniques both in classical euclidean spaces as well as in higher dimensional linear spaces has been successful in medical applications detecting bleeding stroke.

II. ADVANCES IN TRANSCRANIAL MAGNETIC STIMULATION

Since its introduction into modern medicine in 1985, transcranial magnetic stimulation (TMS) is increasingly used as a means of investigating various aspects of central nervous functioning in humans. A recent development of the technique is that of navigated stimulation using dedicated equipment. One such equipment; Eximia, Nexstim Ltd, Helsinki, Finland, has been used by us. Briefly, the patient sits in a comfortable chair and his/her structural MR images are uploaded to the system. In a three dimensional freely moveable image, the visualised depth can be chosen to optimise the search for stimulation points. A tracking system with infrared light is used to inform the system of the location of fixed points on the head also defined on the MR image.

Reflecting balls on spectacle frames secured to the head during this process, allows the patient to move freely in the chair. The position of the magnetic coil (figure of eight with winding diameter 50 mm, biphasic pulse of 280 μs) is also detected by affixed reflecting balls. Thus, chosen cortical areas can be stimulated while observing the movements of the coil on a screen. The calculated electrical field strength (V/m) is continuously updated and indicated. On a separate screen, the surface electromyogrammes (sampling frequency 3000 Hz, band pass filter 10-500 Hz) is displayed, both free running and as responses from stimulations. All data is saved and can be retrieved and edited after the stimulus session allowing appropriate quality control of the responses.

Due to the increased precision compared to standard TMS, the navigated technique provides possibilities for improvements of pre operative investigations before neurosurgery. The locations of areas for activation of various muscles can be defined based on the patient's own MRI, thus taking into consideration individual variation and pathological changes. The results can be exported to the neuronavigation equipment used during surgery. They can also be used as the basis of the technique where the intracerebral tracts are delineated; diffusion tensor imaging or tractography. This also helps in planning the optimal surgical approach.

Using a specially developed amplifier, the TMS induced activity can be analysed by EEG. This allows for the evaluation of what has been named effective cortical connectivity, believed to be essential for so called higher brain functions. With this technique, the sensitivity and prognostic capacity of neurophysiologic methods are likely to increase which may lead to earlier and more accurate diagnosis and prognosis concerning e.g. dementia and brain trauma patients.

When TMS stimuli are given repetitively, the activity level of the part of cortex that is stimulated and those areas to which this is coupled, may change. This has been used to both increase and decrease the activity to promote function. The potential for this new therapeutic principle is large and promising reports have been presented concerning effects on e.g. motor function after stroke, central pain and mental depression.

III. EEG SOURCE LOCALIZATION

Epilepsy is one of the most common neurological diseases and about 0.5 to 1% of the population suffers from it. Surgical therapy has become an important therapeutic alternative for patients with medically intractable epilepsy. Correct and anatomically precise localization of the epileptic focus is mandatory to decide if resection of brain tissue is possible.

The most important non-invasive diagnosis tool used at epilepsy surgery centers is electroencephalography (EEG). To find the brain sources, which are usually modeled as current dipoles, that are responsible for the measured potentials at the EEG electrodes on the scalp is an inverse problem. Inverse problems are in general more difficult to solve than direct problems mainly due to ill-posedness and non-linearity. Methods for solving the inverse problem in EEG-based source localization are based on solutions of the corresponding forward problem, i.e. simulation of the potentials on the scalp for a given source. The sources are electrolytic currents, usually modeled as point dipoles, which are activated during epilepsy.

A major limitation in EEG-based source reconstruction has been the poor spatial accuracy, which is attributed to low resolution of previous EEG systems and to the use of simplified spherical head models for solving the inverse problem. EEG-based source localization is an active field of research [1], but partly due to the mentioned shortcomings the computational techniques are not yet part of the standard presurgical diagnostic workup.

Realistic models of the human head are generated from a segmentation of the patient's MRI. The geometrical complexity and the fact that the tissue conductivity is highly inhomogeneous and even anisotropic makes finite element methods (FEM) well suited. The critical issue is how to handle the computational complexity of FEM with regard to the inverse problem. As has been shown in recent publications by Wolters et al.[2] this can be accomplished through the use of algebraic multigrid preconditioners, parallel computing, and not the least the concept of reciprocity which makes it possible to solve the forward problem for each electrode position rather than for each possible dipole position.

The goal of this effort is to develop an innovative software tool for EEG-based source localization that given the patient's MRI and a recording from a high resolution EEG system accurately and fast can demarcate the epileptogenic tissue on a virtual 3D representation of the patient's brain. Here, we present a novel approach for source localization that combines an adaptive FEM solver with a particle swarm optimization (PSO) algorithm.

A. Forward Problem

The characteristic frequencies of the signals in the kHz range make it possible to use the quasi-static approximation of Maxwell's equations and the potential $\mathbf{\Phi}$ is the solution of the following Poisson's equation:

$$\nabla \cdot (\sigma \nabla \mathbf{\Phi}) = \nabla \cdot \mathbf{j}^s \text{ in } \Omega, \tag{1}$$

subject to the conditions

$$\hat{\mathbf{n}} \cdot (\sigma \nabla \mathbf{\Phi}) = 0 \text{ on } \partial\Omega, \tag{2a}$$

$$\mathbf{\Phi}(x_{ref}) = 0. \tag{2b}$$

The source current $\mathbf{j}^s$ is modeled by a mathematical dipole at position $\mathbf{x_0} \in \Omega$ with the moment $\mathbf{M} \in R^3$,

$$\mathbf{j}^s(\mathbf{x}) = M\delta(\mathbf{x} - \mathbf{x_0}) \quad . \tag{3}$$

The source has a singularity at x_0 and is therefore difficult to model with standard finite elements. A subtraction method

[3] is used to circumvent this problem, where the total potential is split into two parts,

$$\mathbf{\Phi} = \mathbf{\Phi}^{\infty} + \mathbf{\Phi}^{corr} \,. \tag{4}$$

The first part, $\mathbf{\Phi}^{\infty}$, is the solution to (1) in an unbounded domain with constant conductivity σ^{∞}, and an equation for $\mathbf{\Phi}^{corr}$ is derived by inserting (4) in (1),

$$-\nabla \cdot \left(\sigma \nabla \mathbf{\Phi}^{corr}\right) = \nabla \cdot \left(\left(\sigma - \sigma^{\infty}\right) \nabla \mathbf{\Phi}^{\infty}\right) \text{ in } \Omega \,, \tag{5}$$

subject to the conditions

$$\hat{\mathbf{n}} \cdot \left(\sigma \nabla \mathbf{\Phi}^{corr}\right) = -\hat{\mathbf{n}} \cdot \left(\sigma \nabla \mathbf{\Phi}^{\infty}\right) \text{ on } \partial\Omega \,, \tag{6a}$$

$$\mathbf{\Phi}\left(\mathbf{x}_{\mathbf{ref}}\right) = 0 \,. \tag{6b}$$

This approach to the problem ensures that the RHS of (5) is non-singular in the case where σ is constant in a small ball around x_0 [2]. The discretization of (5) is performed by piecewise linear FEM with basis functions φ_i centered at the mesh points ζ_i of an adaptive octree grid. After applying variational and FEM techniques to (5) and (6) we arrive at the system of linear equations

$$\mathbf{Ku} = \mathbf{j} \,, \tag{7}$$

where $\mathbf{u}$ contains the nodal degrees of freedom. More details are found in [4], where also a modified subtraction approach with more compact support is presented. The system of linear equations (7), can be efficiently solved iteratively by a conjugate gradient (CG) solver preconditioned by an algebraic multigrid (AMG) method.

B. Inverse Problem

The following minimization problem for localization of the electrical activity inside the brain can be derived:

$$J = \min_{x \in \Omega_{gray}, M \in R^3} \left\| \mathbf{u}^{\mathbf{meas}} - G(\mathbf{x})\mathbf{M} \right\| , \tag{8}$$

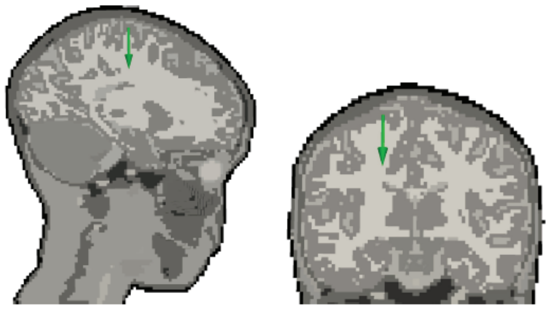
where $\mathbf{u}^{\mathbf{meas}}$ is a vector of the measured potentials and $G(\mathbf{x})$ is a gain matrix that maps the FEM right-hand side vector onto the non-reference electrodes. As shown in (8) source localization is linear in $\mathbf{M}$ but non-linear in x. We can therefore solve the minimization problem in two steps. First an optimal x is found using a PSO algorithm and then the corresponding $\mathbf{M}$ is determined by minimizing the least square error. Two different PSO algorithms have been implemented. The algorithm described in [5], which is usually denoted as standard PSO (SPSO) and a new modified PSO (MSPO) algorithm. In MPSO we have made several problem specific modifications of the standard algorithm such as adaptive swarm size, adaptive neighborhood size, and used the swarm gravity center as well as concepts from evolutionary programming. More details will be found in the forthcoming paper [6].

C. Results

The head model for the test case is the 11 year old girl from the Virtual Population [7] with a voxel resolution of 2 mm resulting in roughly 400.000 DOFS. The conductivities of the 22 different tissues in the model were taken from a database. The 81 EEG electrodes were placed on the head surface according to the 10/10 EEG electrode system. For generating the EEG data two dipole sources were placed inside the brain. Source 1 intended to resemble the spike pulse, while source 2 corresponded to lower-amplitude background activity. The spike dipole is placed at the right motor cortex and the background dipole at the occipital lobe with orientations orthogonal to the gray matter surface, see Figure 1. Simulation results for the different methods after 300 iterations are shown in Table 1.

Table 1: Averaged results for 10 runs, where 'LE' is the localization and 'OE' the orientation error, and 'RE' the relative error.

Method	LE(mean±std[mm])	OE([deg])	RE
SPSO	1.5±0.9	3.25	0.0236
MPSO	0.2±0.25	1.9	0.0103



(a) Side view (b) Top view

Figure 1: Position of the source located in the motor cortex area.

D. Conclusions

We have presented a novel technique for EEG-based source localization based on a combination of adaptive FEM and particle swarm optimization. The results show that the modified PSO method is superior to the standard method and additional tests have shown that the method is relatively insensitive to noisy data. It is therefore a promising method for source localization that we will investigate more in future work and apply it to real patient data.

REFERENCES

[1] H. Hallez, B. Vanrumste, R. Grech, J. Muscat, W. De Clercq, A. Vergult, Y. D'Asseler, K. P. Camilleri, S. G. Fabri, S. Van Huffel, and I. Lemahieu. Review on solving the forward problem in EEG source analysis. *Neuroengineering and Rehabilitation*, 46(4), 2007.

[2] C. H. Wolters, H. Köstler, C. Härdtlein J. Möller, L. Grasedyck, and W. Hackbusch. Numerical mathematics of the subraction method for the construction of a current dipole in EEG source reconstruction using finite element head models. *SIAM J. Scientific Computing*, 30(1):24–45, 2007.

[3] S. van den Broeh, H. Zhou, and M. Peters. Computation of neuromagnetic fields using finite-element method and Biot-Savart law. *Medical and Biological Engineering and Computing,* 34(1):21–26, 1996.

[4] F. Edelvik, B. Andersson, S. Jakobsson, S. Larsson, M. Persson, and Y. Shirvany. An improved method for dipole modeling in EEG-based source localization. *In World Congress on Medical Physics and Biomedical Engineering, volume 25/9 of IFMBE Proceedings*, pages 146–149. Springer Berlin Heidelberg, 2009.

[5] R. C. Eberhart and Y. Shi. Comparing inertia weights and constriction factors in particle swarm optimization. *In Evolutionary Computation, 2000. Proceedings of the 2000 Congress on*, volume 1, pages 84 –88 vol.1, 2000.

[6] Y. Shirvany, F. Edelvik, S. Jakobsson, A. Hedström, and M. Persson. Application of particle swarm optimization in epileptic spike EEG source localization. *Manuscript in preparation*, 2011.

[7] www.itis.ethz.ch/services/human-and-animalmodels/human-models