# Advances in neuro diagnostics based on microwave technology, transcranial magnetic stimulation and EEG source localization

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#### 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.

## 1. 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.

#### 2. 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  $\mu$ s) 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.

## 3. EEG source localisation

Surgical therapy has become an important therapeutic alternative for some patients with medically intractable epilepsy. Correct and anatomically precise localization of the epileptic focus is mandatory for the decision if resection of brain tissue is possible. Electroencephalography (EEG) is a vital non-invasive diagnostic tool used at epilepsy surgery centers. To find the brain sources, which are usually modeled as current dipoles, that are responsible for the measured potentials at the EEG electrodes 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 EEGbased 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 associated differential equations are the guasi-static Maxwell equations, which reduce to a Poisson equation. The sources are electrolytic currents, usually modeled as point dipoles, which are activated during epilepsy. The goal of this project 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. From a segmentation of the MRI a patient specific head model is generated, see an example in Figure 1. Due to geometrical complexity of the human head and the fact that the tissue conductivity is highly inhomogeneous and even anisotropic, an adaptive FEM solver is a natural choice for discretization of the forward problem. In an iterative process the location of the source is found by using a genetic particle swarm optimization algorithm. The approach has been validated with promising results for realistic models in the Virtual Family, see figure 2, and validation on real patient data is ongoing.