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## **Improved targeting for DBS combining MER- and MRI-derived model structures**

P. Gemmar<sup>1</sup>, Y. Thesen<sup>1</sup>, O. Gronz<sup>1</sup>, F. Hertel<sup>2</sup>

<sup>1</sup> University of Applied Sciences (FH) Trier, Computer Science Dep., Trier, Germany

<sup>2</sup> Centre Hospitalier de Luxembourg, Neurochirurgie, Luxembourg, Luxembourg

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This study describes the investigation and development of advanced methods for improving and aiding target navigation for deep brain stimulation (DBS). Static target information from preoperative magnetic resonance imaging (MRI) is combined with dynamic targeting information from intraoperative microelectrode recordings (MER) for real time target visualization and localization of the stimulation electrodes during DBS surgery.

### **Purpose**

DBS has become an important treatment option for various movement disorders, such as Parkinson's disease (PD) and dystonia, and is increasingly used for the treatment of severe psychiatric diseases. DBS is a sophisticated procedure requiring thorough planning and a high level of accuracy when implanting the stimulation electrodes. An essential task in the stereotactic implant procedure is the navigation of the microelectrodes to the desired target position and the determination of the optimal stimulation site. Target accuracy is affected by potential errors due to brain shift and low imaging resolution as well as mechanical inaccuracies of the stereotactic frame. The preferred surgical targets for the treatment of PD and dystonia are the subthalamic nucleus (STN) and the globus pallidus pars interna (GPI) respectively. Indirect target determination is commonly used based on the well defined location of the anterior and posterior commissures.

In order to improve accuracy and to compensate for potential errors, many groups use up to five test electrodes and intraoperative MER of neural activity for target navigation. With some experience, the MER signals can be distinguished and assigned to the specific neural areas they were recorded from. To determine the optimal stimulation site, the surgeon has to match the manual classification of the MER data with a mental model of the target structure and a model of the intersecting microelectrodes before implanting the final electrode. However, the interpretation of the MERs is subjective and the recordings are often ambiguous. In the case of pallidal DBS for dystonia, the benefit of intraoperative MER is debatable, as the surgery is commonly performed under general anesthesia and reported signal characteristics are

inconclusive. Additionally, the anatomy of the target structures varies from patient to patient. Computer assistance in the form of automatic MER analysis combined with a target model derived from MRI for visual aid can therefore be a great asset in the implant procedure.

## **Methods**

We developed a method for MER classification of signals from subthalamic DBS in Parkinson patients. Feature extraction is based on denoising by soft-thresholding and multi-level decomposition of the MER signals using wavelet transformations. Two features are obtained, one measuring the MER's background activity based on percentiles and standard deviation of the original signal using patient-specific thresholds, and one measuring the variance of the denoised and decomposed signal. The two features are used to train a Takagi-Sugeno type fuzzy classifier, which is capable to label MER intervals as STN and non-STN respectively.

The resulting spatial model of the test electrodes is then matched automatically with a model of the STN derived either from an atlas or manually from the patient's MRI. The matching procedure considers the electrodes as straight lines and calculates their intersections with a multi-plane model of the discrete target volume in an optimized manner. A measure is used to compare the deviations of the model intersections for a set of possible geometric configurations (compensation for the aforementioned potential errors) and for finding the optimal match. This is shown in a 2.5D visualization of the target with intersecting electrodes (figure 1).

In continuation, we considered the classifier structure for recordings from pallidal DBS. We studied MERs from 19 patients exhibiting different forms of dystonia who underwent surgery for pallidal DBS under general anesthesia. As has been reported by others, we found the recordings to be less conclusive in delineating the GPi from the surrounding structures, above all from the external part of the globus pallidus (GPe). The trajectories encountered displayed a broad variety in appearance and showed no obvious patterns that would allow implications regarding the underlying anatomy. We identified several types of signals exhibiting distinct firing characteristics and extracted various features in order to further characterize these signal types. The features were then analyzed using statistical methods and Self-Organizing Maps (SOMs). The information gained was used to generate a fuzzy classifier that is capable of differentiating between non-neuronal and neuronal MERs (figure 2).

## **Results**

The STN classifier was tested with MER data from two hospitals (114 electrode trajectories, 16 patients) and the delivered classifications were congruent with expert decisions and hospital records in 96% of cases. Detection of the substantia nigra based solely on electrophysiological data appears to be difficult, as the characteristic firing patterns found in the literature were significantly less distinct in the data used in this study.

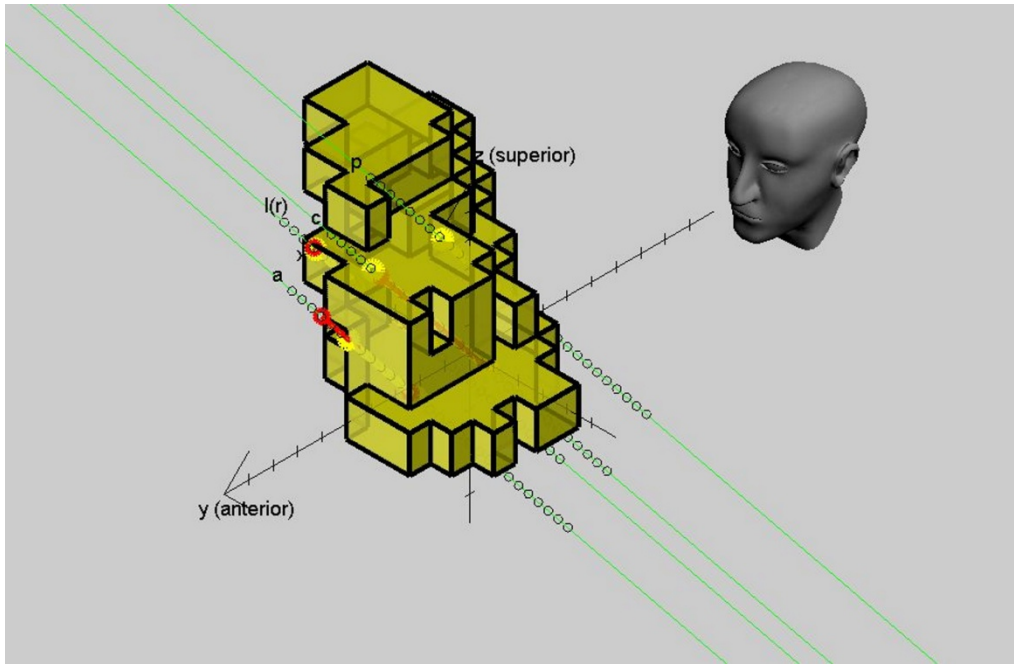
The fusion of the MER classifications with a model of the STN segmented in T2-MRI was tested with data from 6 patients. The system showed stable results when at least 4 electrodes with labeled STN intervals were available.

Previous reports of MERs from pallidal DBS for dystonia being less conclusive and more variable were confirmed. Of initially 16 features considered for detecting neuronal recordings, the most promising three were selected and a fuzzy classifier was automatically generated. The system was then presented with testing data (691 MERs), which it successfully divided into the expected classes in nearly all of the cases.

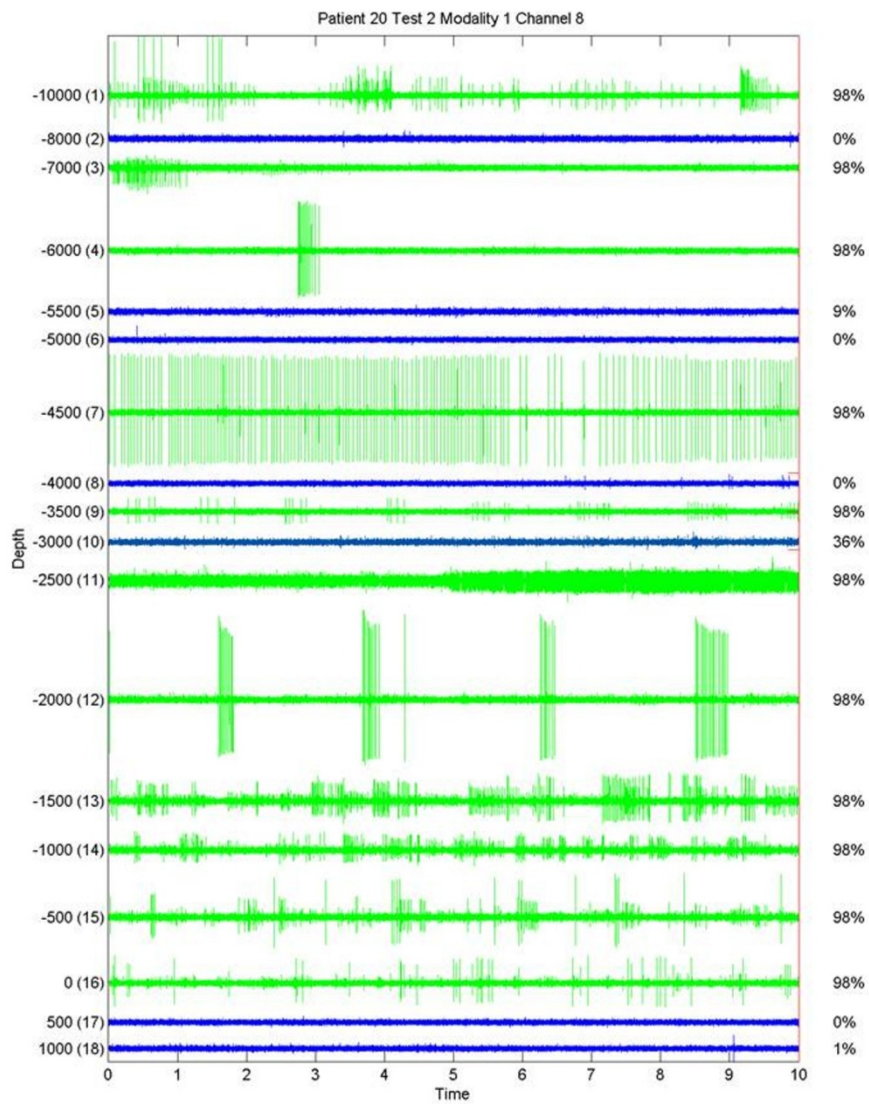
## **Conclusion**

Automatic detection of MERs from the STN of Parkinsonian patients undergoing subthalamic DBS using our technique is possible with high certainty. Matching the MER results with a patient-specific model of the STN and visualizing the most probable orientation of the electrodes relative to this model provides a comprehensive view of the actual situation.

Although a straight-forward classification of MERs from pallidal DBS for dystonia appears to be difficult, it is possible to differentiate neuronal from non-neuronal signals. Using this information, we expect it to be manageable to match a model of the globus pallidus with electrode models in a way similar to the matching procedure described for subthalamic DBS. Additionally, as the globus pallidus is considerably larger than the STN, an automatic segmentation of the structure from the patient's MRI seems feasible.



**Fig.1.** Spatial model of electrodes intersecting target area



**Fig. 2.** Automatic classification (neuronal vs. non-neuronal) of MERs from pallidal DBS