See the Brain at Work – Intraoperative Laser Doppler Functional Brain Imaging

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ABSTRACT

During open brain surgery we acquire perfusion images non-invasively using laser Doppler imaging. The regions of brain activity show a distinct signal in response to stimulation providing intraoperative functional brain maps of remarkably strong contrast.

Keywords: Laser Doppler imaging, brain maps, functional imaging, intraoperative diagnostics, neurosurgery, tumor, regressor analysis

1. INTRODUCTION

The surgical removal of a lesion adjacent to motor, sensory, language or visuospatial areas requires their identification in order that these functionally-important regions of brain are preserved. Neurosurgy has gained immensely in precision over recent years thanks to the availability of methods for visualising the brain and its functioning (fMRI [1], optical intrinsic signal and near infrared spectroscopy amongst others [2]) and to the integration of fMRI into 3-D models for application during surgery together with cortical stimulation [3]. Nevertheless there remains need for a rapid, high resolution, non-invasive method applicable in theatre that allows visualization of areas of cortical activation across the exposed brain, i.e. a wide field of view. To this end we have designed and constructed a Laser Doppler imaging system to visualize blood perfusion, cerebral blood volume and blood velocity intraoperatively. Visualizing blood flow is an indirect but standard method for observing brain function, the link between neuronal activity and blood flow being recognized for many years although the spatiotemporal details are still subject to active research.

2. METHOD AND RESULTS

The Laser Doppler Imager (LDI) [4], is integrated beneath a surgical microscope (Zeiss Pico). The imaging system uses a fast CMOS camera as detector and has been designed to image the area of interest (currently 4 x 3.5 cm at 20cm distance and 140x120 pixels) with white light, producing a conventional optical image, simultaneously with the 808nm laser which generates the LDI image at 1.48Hz. The wavelength chosen allows the imaging of total blood flow; the absorption of oxy- and deoxy-hemoglobin being essentially equal at this wavelength [5].

Here we present perfusion images of high spatiotemporal resolution taken during open brain surgery with an awake patient performing specific tasks. These functional images have been post-processed using a wavelet-based statistical framework that performs a robust fit of the various regressors. It has thus been possible to identify and map the periodic image contributions from breathing, pulse and vasomotion, and then to extract the information pertaining purely to the
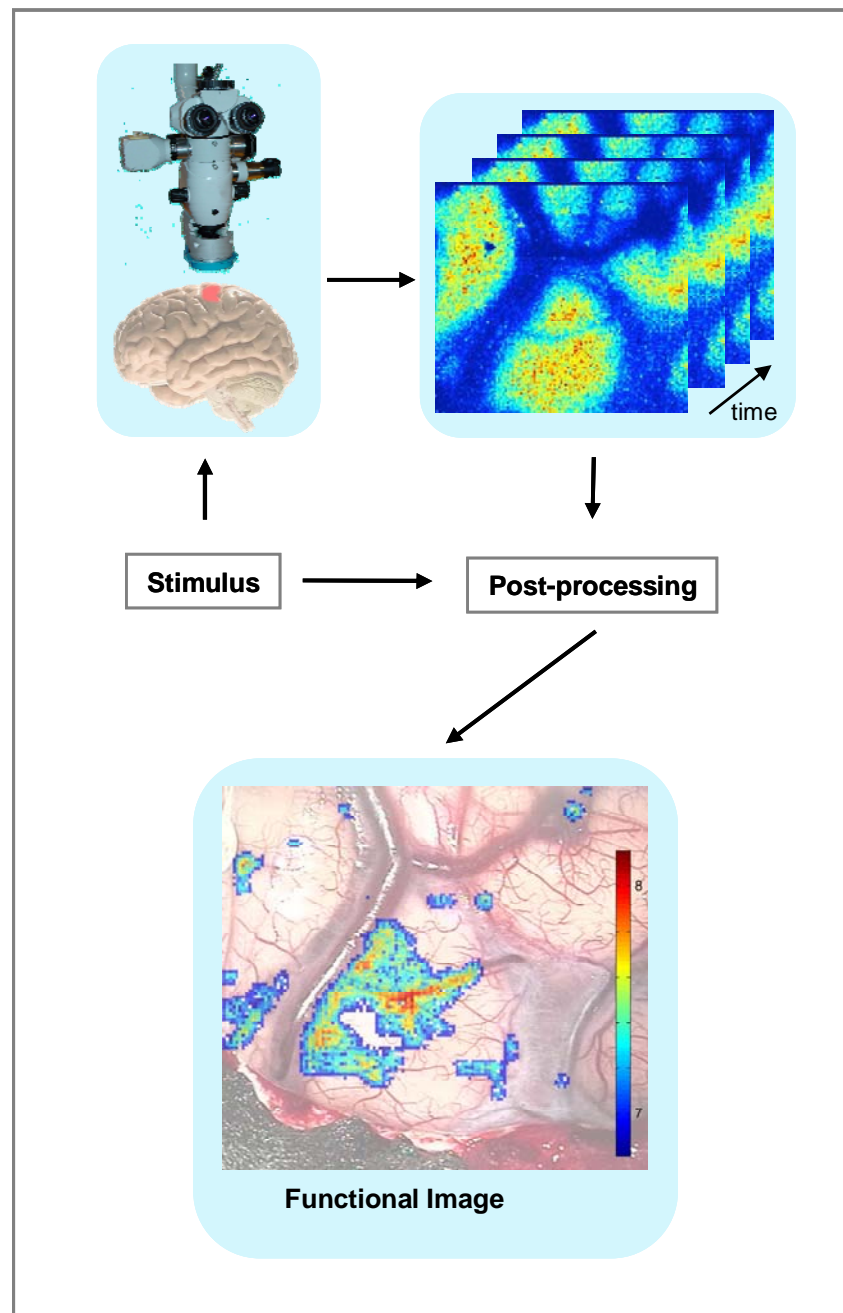
Fig. 1. Schematic of LDI functional brain image formation. The surgical microscope with the LDI is focussed on the area of brain open ready for surgical intervention and the informed patient is requested to perform the predetermined tasks. During the brain stimulation a series of LDI perfusion images is taken; these images are synchronised with the predetermined task protocol and subjected to post processing. The linear model and wavelet-based statistical test are applied and the functional image is generated in 1-2 mins.

response to the given stimulus. The processes necessary for obtaining the final perfusion or concentration image are depicted in Figure 1.

A male patient (44 years) with an anaplastic astrocytoma (WHO °III) close to the dominant (left sided) dorsal inferior frontal gyrus was investigated. Before surgery a functional MRI (1,5 Tesla Siemens Magnetom Vision) was performed so as to identify the hand, foot and tongue motor centers, and integrated in the neuronavigation 3D data set. The patient's head was immobilized ensuring a rigid mechanical connection to the operating table and positioned to minimize brain shift. The craniotomy was performed under local anesthesia so that the patient was fully awake during surgery. Once exposed, the area of brain was mapped for motor and language function at 5mm intervals by standard cortical electrostimulation. The areas proven to be active after at least three nonconsecutive trials were labeled.

After identification of the motor hand map, the patient was asked to perform a finger tapping task to generate the activation for the LDI imaging. The finger tapping protocol was designed such that an initial rest baseline could be obtained with the patients eyes closed and quiet in the operating theatre. Once this achieved, each set of finger-tapping was initiated and terminated by a visual cue. The rest periods between sets were of varying lengths to eliminate any low frequency interference. Breathing and heart rates were also noted for inclusion in the calculation.

The time-series of perfusion images was then analyzed using the wavelet-based regression technique [6]. A general linear model comprising various regressors was used to map the time-course of each pixel [7,8]. Within this model, the activity-related regressor is modelled as the stimulus function convolved with a hemodynamic response function for the local cerebral blood flow inspired by fMRI studies and using a time to peak of 3s and a post stimulus undershoot [9,10]. Additional regressors include; baseline, linear drift, low-pass DCT basis (up to 0.01Hz) and periodic components at 0.1Hz (vasomotion) and 0.36Hz (respiration). The framework makes use of the spatial wavelet transform to efficiently exploit the spatial correlation present in the data. In Fig. 2 (a), the statistical map for the task-related regressor for a confidence level of 0.01% (corrected for multiple comparisons) is superposed on the conventional optical image. In (b), the average time-course of the most-activated region is extracted after removal of the non-stimulus related regressors. The activation related signal change is of a magnitude of 10-20% with respect to the baseline. The stimulus (blue) and blood-flow regressors (black) are also shown. Finally, in (c), we show the full area of the craniotomy and the corresponding MRI Mercator representation with fMRI activations (white) for a finger tapping task. The region correlates well with that detected by LDI [11].
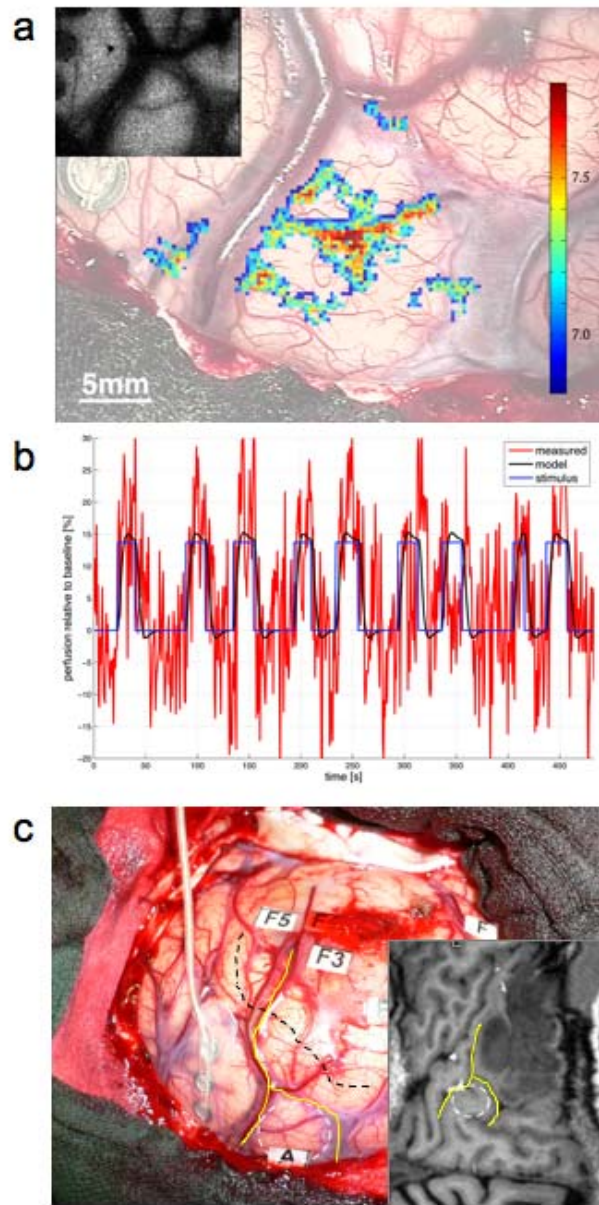
Fig. 2. The conventional optical image forms a reference background for the statistical parametric map of the main response to the activation (a), the colorbar shows t-values (Student's test) for the map and the inset shows a single LDI perfusion image. The average time course of the activated region (t-value above 7.5) after subtracting unrelated regressors, also the model for task-related signal and the stimulus function are shown (b). The site of operation (c), showing the region identified by electrostimulation as being responsible for finger tapping (encircled area 'A') which corresponds to the MRI hand knob, the right inset is a Mercator flat map MRI surface reconstruction with fMRI activation regions (in white) obtained during finger tapping; the tumor (T) has compressed the hand-knob area such that the fMRI signal obtained during finger tapping has been split. The arrows indicate the central sulcus. The left inset represents an enlarged image corresponding to figure 2a.

3. CONCLUSION

This case is representative of observations made during a series of surgical interventions and demonstrates a prospective method for surgical application and for brain research. The technique has proven to be fast (frame rate of 1.48Hz), of high spatial resolution (~290μm) and temporal response and to be readily integrated within standard surgical procedures. It is non-invasive (class 1 laser equipment) and, compared with electrostimulation, may considerably shorten the time required for mapping the exposed brain, eliminate the risk of inducing seizure and allow the brain to be mapped with more complex paradigms. It could be applied repeatedly and rapidly in theatre generating superposable maps of different activations for injection into a surgical microscope ocular, thus alleviating certain difficulties associated with brain-shift.

 This represents a step towards the neurosurgeon's dream of visualizing the functional areas he strives to preserve in the surgical microscope, easily, on-line and with high spatiotemporal resolution. The imaging performance achieved so far represents the current best compromise between spatial resolution and frame rate but by no means defines its upper limit. Optimization of the signal handling and processing will improve the spatiotemporal resolution markedly.

The observations were carried out with the approval of the ethics committee of the University Clinics of Frankfurt am Main with the patient's written informed consent.

4. ACKNOWLEDGMENTS

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