A Time-Domain NIR Brain Imager Applied in Functional Stimulation Experiments

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Abstract: We present our prototype of a 3-wavelength time-domain brain imager. The instrument was tested on inhomogeneous phantoms. Various functional stimulation experiments on adults demonstrate its ability to combine lateral resolution with depth selectivity.

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1. Introduction

Optical imaging methods are being developed as valuable complement to other imaging modalities like MR or CT since they can be applied repetitively at the bedside. Moreover, optical methods can be used in combined measurements with MRI or electrophysiological methods (electro- and magnetoencephalography) and can thus be employed for studying neurovascular coupling. Although the spatial resolution of optical methods is intrinsically low due to the strong scattering in tissue, diffuse optical imaging devices have been developed to better localize lesions or activated areas. Such devices are based on cw light, frequency domain or time-domain [1, 2] methods. Recording distributions of times of flight (DTOFs) of diffusely reflected photons offers the opportunity to achieve depth localization of absorption changes [3, 4]. In particular, cortical and extracerebral responses to functional stimulation can be discriminated.

In this contribution a time-domain instrument for optical topography of the head will be presented. Its application in functional stimulation experiments is focused on the demonstration of the ability of the method to separate between cortical (deep) and systemic (superficial) responses to stimulation.

2. Instrumentation

Near-infrared picosecond pulses are generated by diode lasers (PDL-800, PicoQuant, Germany) at wavelengths of 687nm, 803nm, and 826nm with repetition rates of 40 MHz. The laser light at the 3 wavelengths is coupled into individual multimode glass fibers of 50 µm diameter. The three fibers are combined in a common connector and connected to the 200 µm input fiber of a 1x9 multimode fiber switch (switching time < 2 ms; Piezosystem Jena, Germany). The nine 200 µm output fibers are arranged on an optode holder pad together with four detection fiber bundles (diameter 4 mm, NA 0.54, length 1.5 m; Loptek Glasfasertechnik, Germany). The 16 relevant source-detector pairs (separation 3 cm) form a 4x4 grid (see Fig. 1). Other arrangements can easily be implemented.

The four independent detection channels consist of home-built detection modules connected to the channels of a multi-board TCSPC (time-correlated single photon counting) system (SPC-134, Becker&Hickl, Germany). The detection modules contain photomultiplier tubes R7400U-02 (Hamamatsu Photonics, Japan), high voltage power supplies, preamplifiers as well as relay optics and a mechanical shutter [5]. The instrument response function (IRF) is the convolution of the laser pulses, the temporal dispersion in the fiber bundle, and the transit-time spread in the photomultiplier. The FWHM of the IRF is typically between 500 ps and 900 ps.

Time-resolved diffuse reflectance is recorded in the "continuous flow mode" of the SPC-134. The trigger pulses for data acquisition as well as for fiber switching are obtained from a programmable counter/timer board. In the present setup, single photon pulses are collected simultaneously in all 4 detection channels while one of the 9 source fibers is active. After the collection of a set of 4 DTOFs the next source fiber is switched on. Cycling through all 9 source fibers is performed within 1 s or less.

3. Data analysis

First, the measured DTOFs were corrected for the differential nonlinearity of the relation between time-channel number and time. After background subtraction, the total number N_{tot} of counts was derived together with mean time of flight $<t>$ and variance $V=<t^2>-<t>^2$. These quantities, as a function of time during the experiment, were related to their baseline values, i.e. the homogenous case (phantom) or the rest condition during functional stimulation. The resulting time series of the ratio (for N_{tot}) or the difference (for $<t>$ and V) values were associated with the pixels in the 4x4 image according to the corresponding source-detector combinations.

4. Phantom experiments and simulations

Phantom experiments were carried out to study the performance of the instrument and to characterize its lateral and depth resolution. An example is illustrated in Fig. 1. The imager was tested with a semi-infinite medium with an immersed inclusion. The optodes were held in a black plate. The source-detector separations were 3 cm, i.e. the edges of the square pad had a length of 8.5 cm. Each "pixel" was thus 2.1 cm wide. The plate was immersed in a turbid fluid consisting of dilute milk with black ink added. The reduced scattering coefficient was 10 cm^{-1}, the absorption coefficient 0.1 cm^{-1}. To model an activated area in the brain, a black disk (diameter 2 cm, thickness 2 mm) was positioned 10 mm underneath the interface between the black plate and the fluid. The disk was centered between a source and a detector (a), under a source (b), under a detector (c) or in the maximum distance from sources and detectors inside the grid (d). After each time series recorded with the inclusion, the disk was removed keeping the optodes unchanged, and data for the homogenous case were acquired.

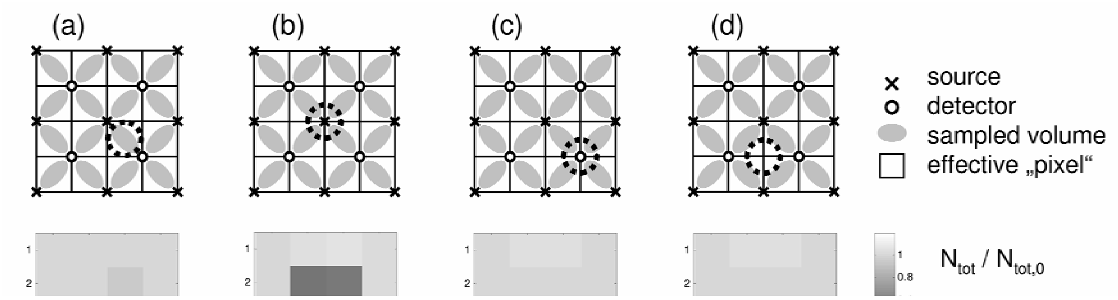

Fig. 1. Measurement on a semi-infinite phantom with an inclusion at various positions (see text). Upper row: Arrangement of sources and detectors in the imager pad and position of inclusion (marked by dashed circles) Rows 2-4: Maps of changes in total photon count, mean time of flight and variance of DTOFs. The gray scales are the same within each row.