

A safe, low-cost and portable instrumentation for bedside time-resolved picosecond near infrared spectroscopy

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ABSTRACT

Continuous wave Near InfraRed Spectroscopy (NIRS) has been used successfully in clinical environments for several years to detect cerebral activation thanks to oxymetry (i.e. absorption of photons by oxy- and deoxy- hemoglobin) measurement. The goal of our group is to build a clinically-adapted time-resolved NIRS setup i.e. a setup that is compact and robust enough to allow bedside measurements and that matches safety requirements with human patients applications. Indeed our group has already shown that time resolution allows spatial resolution and improves sensitivity of cerebral activation detection. The setup is built with four laser diodes (excitation wavelengths: 685, 780, 830 and 870 nm) whose emitted light is injected into four optical fibers; detection of reflected photons is made through an avalanche photodiode and a high resolution timing module used to record Temporal Point Spread Functions (TPSF). Validation of the device was made using cylindrically-chaped phantoms with absorbing and/or scattering inclusions. Results show that recorded TPSF are typical both of scattering and absorbing materials thus demonstrating that our apparatus would detect variation of optical properties (absorption and scattering) deep within a diffusive media just like a cerebral activation represents a rise of absorption in the cortex underneath head surface.

Keywords: Near infrared spectroscopy; time resolution; cerebral activation; phantom.

1. INTRODUCTION

Near infrared spectroscopy (NIRS) is a useful method to monitor brain (i.e. neuronal) activation [1] especially when using fonctionnal Magnetic Resonance Imaging (fMRI, that currently is the gold standard technique for brain activation detection) is at risk: for example, in the case of premature newborns. The NIRS method relies on neuro-vascular coupling meaning that a rise of cerebral blood flow (CBF) is observed in the cerebral region of neuron activation. Oxy- and deoxy- hemoglobin contained in blood absorb light and display two different absorption spectra around an isobestic point at 805 nm. Thus using at least two different excitation wavelengths can provide information on the relative presence of each chromophore within a cortical region of interest thus providing with spatio-temporal information on cerebral response to specific stimuli.

Photons from the red and near infrared spectral bandwidth (approx. [650-950] nm) can reach the cortex that lies underneath skin, meninges and skull because absorption by endogeneous chromophores such as melanin, hemoglobin and water reaches a minimum on this so-called "optical window". However, penetration of such photons down to the cortex is dramatically decreased because of meninges that display a very low reduced scattering coefficient and act as an optical guide.

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Time-resolution, using pulsed excitation light sources and time-resolved detectors, can be used to achieve spatial resolution in order to focus on the depth of interest (cortex) and to get rid of photons back-scattered by superficial layers such as skin and skull that provide no useful information in cerebral activation [2,3].

Several setups have been developed to carry out such time-resolved NIRS studies in laboratories. However most of these cannot be used in a clinical environment mainly because of hazardous lasers, inconvenient dimensions, fragile components and high-cost [4,5].

Several studies showed that continuous wave NIRS is sensitive to newborns' brain oxygenation modulation under olfactory stimulation [6]. We believe time-resolution can improve accuracy of newborns' brain monitoring under sensory stimulation and more specifically olfactory stimulation. Based on our experience of brain oxygenation monitoring under olfactory stimulation [7] and on time-resolved optical instrumentation development [8,9], we designed and developed a compact and robust instrumentation including harmless laser-diodes, single photon detection and counting module in order to be easily transportable into a clinical department. The first step of its technical validation is presented here, using phantoms. Such phantoms aim at mimicking an increase of optical absorption and/or diffusion due to a rise of CBF within deep layers such as cortical regions.

2. MATERIALS AND METHODS

The light source system (Figure 1) is composed of three different parts chosen for their robustness and compactness: 1) a sequencer, 2) four laser diode drivers and 3) four laser diodes coupled on their optical fiber. The sequencer is designed on a Cyclone 3EP2C20 FPGA (Altera) in order to generate the trigger signal of the pulses generator at different times in a user selectable sequence. Each trigger is synchronous with the system Clock which is internally set at 50 MHz or externally applicable from 10 up to 100 MHz. The system Clock can be divided by 2^n with n is user selectable from 0 to 8. The laser diode drivers are fast electrical pulse generators based on bipolar RF transistors. They have a trigger and gating digital input. On the falling edge of the trigger input they generate a fast nanosecond electrical pulse with amplitude adjustable from 2 to 10V. The amplitude is tuned to adjust the light pulse.

The laser diodes (Roithner) (685, 780, 830 and 870 nm central wavelengths) are connected to the laser diode driver with a 50Ω coaxial cable and are directly driven by the fast nanosecond electrical pulse. The dynamic characteristics of the light pulses are measured with a synchroscan streak camera. Full Width at Half Maximum (FWHM) of their Temporal Point Spread Function (TPSF) are respectively: 90, 104, 80 and 52 ps.

Light of each diode is injected through collimation and focalization lenses (Thorlabs) into a $50 \mu\text{m}$ -core diameter optical fiber (Sedi) with an 80% efficiency. The mean output power at a repetition rate of 20 MHz is 100 to 200 μW . Each pulse energy is therefore about 10 pJ. The four optical fibers are gathered into a single bundle whose tip can be put in gentle contact with the tissue to explore. The optical fibers, emission and reception, can be ended with a prism reflecting light at 90 degrees, allowing to gently press the fiber and fix it on the skin of a neonate through a head-band. Back-scattered light is collected into an $800 \mu\text{m}$ -core diameter optical fiber and then detected by a single photon avalanche photodiode (id1000-MMF50, id Quantique), with a time resolution (FWHM) lower than 60 ps. A high resolution timing module (HRM-Time, SensL) with a time resolution as low as 27 ps is used to record TPSFs of detected photons. The whole system is controlled by a dedicated software written under Labview.

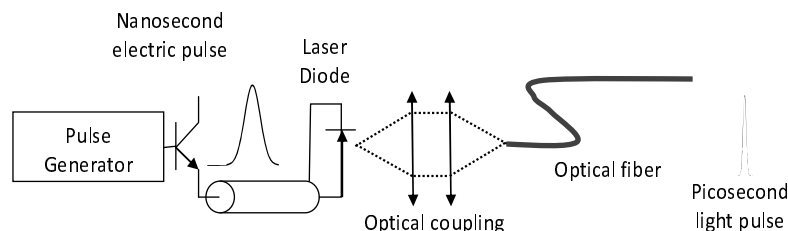


Fig.1. Scheme of the optical picosecond pulse generator.

Two 4 cm-diameter cylinders made of resin polyester (Carl Roth) including TiO_2 (Sigma) and black ink (Conte) achieving reduced scattering (μ_s') and absorption (μ_a) coefficients of 0.6 and 0.008 mm^{-1} respectively are used to test our instrument's ability to detect deep absorbing and scattering inclusions. One cylinder is homogeneous and the second one contains 3 inclusions (so called "inhomogeneous"). These inclusions are 8-mm diameter cylinders, centered at a 10 mm-depth within the cylinder. Three inclusions are used (see Figure 2): a more absorbing one (10 times more absorbing than the surrounding material), a more scattering one (5 times more scattering) and a more scattering and more absorbing one (twice as absorbing and scattering). The excitation bundle is set 29 mm (54 deg) away from the collection fiber. For the experiments described below, the 3 inclusions are successively placed in the centered angular position between excitation and collection fibers (27 deg from each).

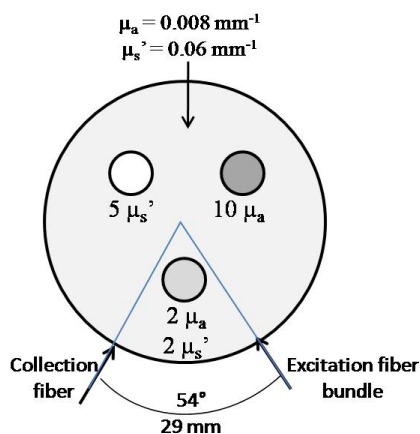


Fig.2. Schematic of the inhomogeneous cylinder including more absorbing and/or scattering inclusions. Here is represented the excitation and collection fibers angular position to acquire TPSF of the more absorbing and more scattering inclusion.

3. RESULTS AND DISCUSSION

Figure 3 shows the TPSF for the 680 nm excitation laser diode. The average FWHM of the four excitation wavelengths is about 250 ps. Also in Figure 3 are shown the TPSFs measured on the homogeneous cylinder as well as on the inhomogeneous one containing three inclusions, each of these inclusions being successively placed between the excitation and collection fibers.

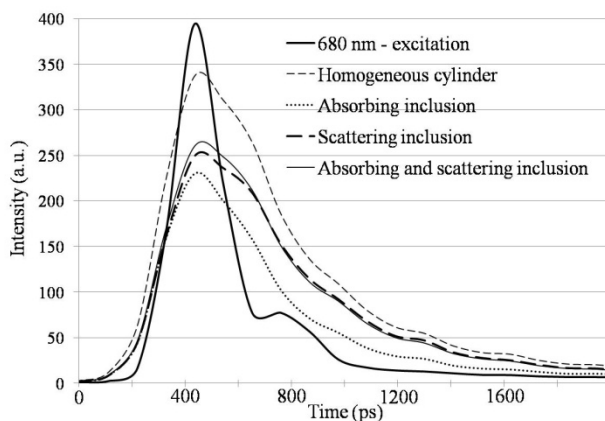


Fig. 3. Excitation laser TPSF and TPSF measured on the homogenous cylinder at each of the three positions on the inhomogeneous one: absorbing inclusion, the scattering one and the scattering and absorbing one. 680 nm-excitation wavelength.

Figure 4 exhibits differences between the TPSF acquired at each of the three positions of the inhomogeneous cylinder (excitation and collection fibers are set respectively on each side of the 1) absorbing 2) scattering and 3) scattering and absorbing inclusion) and the TPSF acquired on the homogeneous cylinder.

As expected, the homogenous cylinder TPSF is more intense than the three other TPSFs acquired through absorbing and/or scattering inclusions. TPSF differences aim at getting rid of the background optical coefficient and thus at accessing features that are typical of more absorbing and/or more scattering inclusions. We precisely observe on the TPSFs that were recorded, but also on simulated data, that the TPSF difference corresponding to the more absorbing inclusion displays the widest FWHM while the two other TPSFs display approximately the same width.

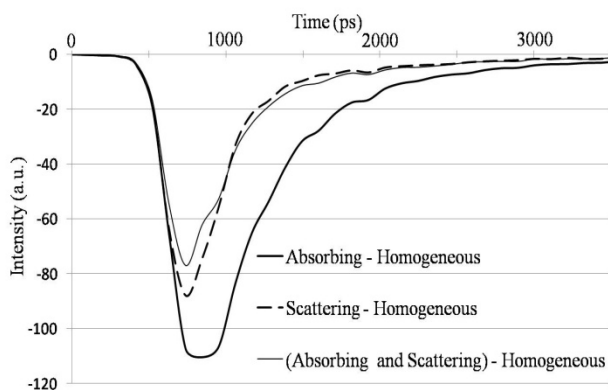


Fig. 4. TPSF differences between data acquired on the inhomogeneous and the homogeneous cylinders with successively the more absorbing, the more scattering and the more scattering and absorbing inclusion set in between excitation and detection fibers.

4. CONCLUSION

TPSFs recorded on phantoms made of materials in concentration such as matching biological tissues optical properties proved that our instrument is sensitive to absorbing and scattering inclusions included deep within biological tissues. Such inclusions aim at mimicking increased CFB i.e. higher concentrations of hemoglobin.

Typical TPSFs recorded through biological tissues are usually a few nanoseconds long, meaning that temporal profile of each of our four excitation laser diodes (250 ps-FWHM) is adapted to detection of physiological event that would locally and temporally modify scattering and/or absorbing properties.

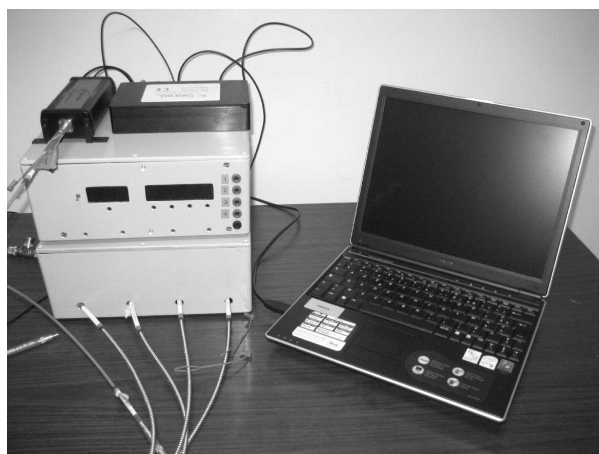


Fig. 5. Picture of the time-resolved NIRS compact set-up we developed.

The use of laser diodes implies our excitation module to be at most in the laser safety class III which is mandatory to obtain an authorization to carry a clinical trial out with our optical setup. French national safety recommendations on eye exposition to pulsed near infrared laser light for 10 s (in case of accidental exposition of eyes to excitation light) mentions that continuous power should be in the milliwatt range; currently our laser diodes output power is a few hundreds of microwatts. Therefore our apparatus should be authorized for clinical experimentation without any kind of safety fear.

Also robust and rather cheap materials that can be easily transportable were used to build the apparatus. As shown in Figure 5, compactness of our set-up (approx. 30 x 30 x 30 cm³, miniaturization still in progress and use of OEM components will reduce the size by a factor of 2) will allow us to freely go from one bedside to the other.

It has been demonstrated that the use of time resolved techniques allows retrieving depth-related information with a single measurement at a given position but also amplifies the differences between rest and activation period, improving the ability of NIRS methods for brain function studies. So we expect to be able to successfully use the described setup in a clinical department in a very near future.

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