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Non-invasive In-vivo sensing of metabolites with a novel Optoacoustic Spectroscope in the SWIR

M.Mehdi Seyedebrahimi*[a,b], Miguel A. pleitez [a,b] , Pouyan Mohajerani[a,b], Vasilis Ntziachristos [a,b]
[a] Chair for Biological Imaging, Technische Universitaet Muenchen, Ismaningerstr. 22, 81675, Munich, Germany; [b] Institute for Biological and Medical Imaging, Helmholtz Zentrum Muenchen, Ingolstaedter Landstr. 1, 85764, Neuherberg, Germany

ABSTRACT

In this work we developed a novel near-infrared two-path optoacoustic spectrometer (NiR-TAOS) that could sense OA intensity changes due to metabolite concentration changes in-vivo. The main aim of dividing the optical path in two is 1) perform real time correction of the laser emission profile of the laser source at different wavelengths and, 2) perform pulse to pulse correction to remove laser beam fluctuation and instability to increase signal to noise ratio. Signal to noise ratio improvement was significant not only at spectral peaks, but also at all other wavelengths. The system can be used for broad applications in biomedical measurements such as various metabolites in the SWIR.

Keywords: Non-invasive In-vivo sensing of metabolites, Optoacoustic, sensitivity and specificity improvement, near-infrared two-path OAS

Among all in vivo non-invasive sensing methods, optical techniques are particularly attractive because of characteristics such as fast response, reagent free and non-ionizing radiation. However, purely optical approaches developed so far suffer from low specificity [1, 2] as they are adversely affected by the strong tissue scattering of photons [3]. Optoacoustic spectroscopy (OAS) offers a promising alternative to purely optical methods for non-invasive sensing. OAS potentially offers higher specificity than optical methods, since acoustic scattering is 2-3 orders of magnitude weaker than light scattering [3]. Furthermore, earlier OA studies showed that metabolites, such as glucose, can be detected in-vivo [4].

In this work we developed a novel near-infrared two-path OAS (NiR-TAOS) that could sense OA intensity changes due to metabolite concentration changes in-vivo (Fig. 1a). The main aim of dividing the optical path in two is to simultaneously measure two optoacoustic signals, one for sample measurements and the other for serving as an optoacoustic reference in order to 1) perform real time correction of the laser emission profile of the laser source at different wavelengths and, 2) perform pulse to pulse correction to remove laser beam fluctuation and instability. Scans can be performed at different spectral range, but at a first implementation we were particularly interested in the spectral range between 1350 nm to 2000 nm with 10 nm step size. Averages of fifty measurements at each wavelength are typically recorded simultaneously at the two measurement paths. The OA intensity (I_{OA}) is measured by transforming OA raw signal (RS), using Hilbert transformation, and integrating the area of interest under the envelope curve, as also previously suggested [5]. Moreover, the spectrometer performs pulse to pulse correction by normalizing OA intensity at each measurement in the sample path (SP) to the corresponding OA intensity in the reference path (RP). The final corrected OA signal, i.e. the average of 50 normalized measurements at each wavelength is computed with Eq.1:

$$I_{OA} = Mean\left(\frac{[I_{SA}]_{1X50}}{[I_{RA}]_{1X50}}\right) \quad (1)$$

where I_{OA} is the corrected signal, $[I_{SA}]_{1X50}$ is the vector of 50 measured OA intensities at each wavelength in the SP, and $[I_{RA}]_{1X50}$ is the vector of 50 measured intensities at each wavelength in the RP.

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Fig. 1b shows OA measurements of distilled water at 1940 nm, before and after the pulse to pulse correction. It can be seen that the variation of OA intensity decreases significantly, which leads to higher signal to noise ratio (SNR). Fig. 1c shows SNR of water signal in the wavelength range 1350–2000 nm, before and after pulse to pulse correction. It can be seen that SNR improvement is significant not only at water spectra peaks at 1450 and 1940 nm but also at all other wavelengths.

In conclusion, we have developed a highly performing spectrometer for biomolecular measurements in the short wavelength. The system is now ready for broad applications in biomedical measurements and will significantly improve our understanding of sensitivity and specificity of detecting various metabolites in the SWIR.

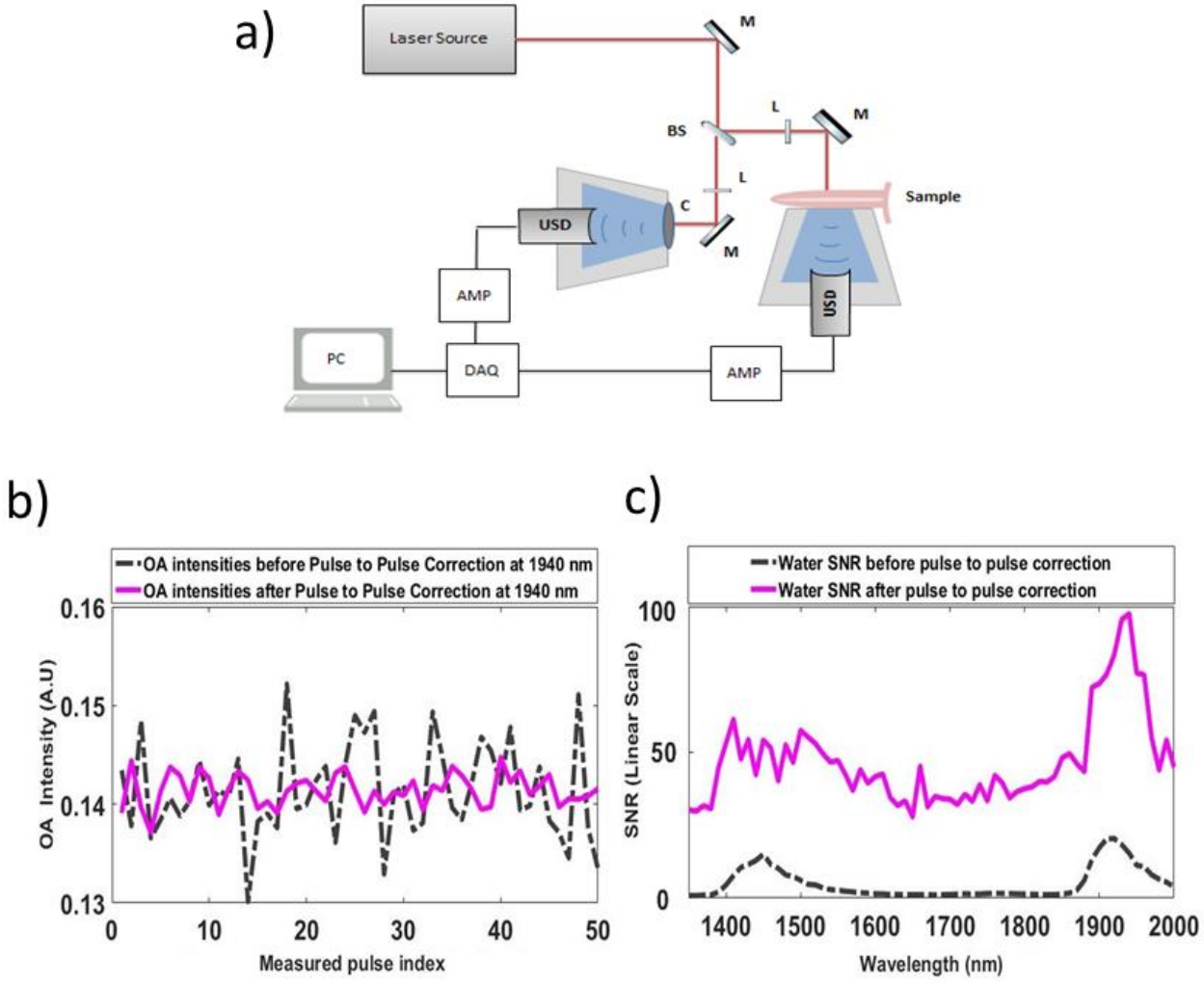

Figure 1. a) Schematic representation of NiR-TAOS and SNR improvement. HWP – Half wave plate; PL – Polarizer, USD– ultrasound transducer; BS – beam splitter; AMP – Amplifier; PC – personal computer; DAQ – data acquisition card; L – lenses, M – Mirrors, b) pulse to pulse correction of water signal at 1940 nm, c) SNR improvement of water spectra at 1350 nm -2000 nm.

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