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Time-Resolved multi-wavelength, dual-channel system for diffuse optical spectroscopy: performance assessment

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ABSTRACT

In this paper we present the *ex-vivo* characterization of a full-custom made multi-wavelength, two channel Time-Resolved Spectroscopy (TRS) module developed with the aim of being integrated in to a multi-modal spectroscopic device. This module overcomes all the main drawbacks of systems based on time-domain techniques such as high complexity and bulkiness while guaranteeing performances comparable to expensive state-of-the-art available devices. Each sub-component of the module has been tailored and optimized to meet all the above-mentioned requirements. In order to assess and translate the performances of these tools for effective clinical use, we characterized the system following the guidelines of common standardization protocols. By following MEDPHOT guidelines, the linearity and accuracy in retrieving absolute values of absorption and scattering coefficients were determined by means of measurements on homogeneous phantoms. Finally, by means of a mechanically switchable solid inhomogeneous phantom (developed under the nEUROPT project) we simulated the clinical problem of detecting and localizing an absorption perturbation in a homogeneous background with broad applications such as detection of cancer lesions, thyroid, etc.

Keywords: Time-Domain Diffuse Optics, Time-Resolved Spectroscopy

1. INTRODUCTION

The non-invasive nature of Diffuse Optics combined with the fact that Near-InfraRed light (NIR) can reach deep tissues buried around 1-3 cm from the outer skin layer, makes it an ideal choice for non-invasive clinical monitoring.
In particular, among DO techniques, Time Resolved Spectroscopy (TRS)[1] allows us to extract independently the absolute values of absorption and scattering coefficients from the Distribution of Time-Of-Flight (DTOF) of the detected photons. Since the depth information is encoded in the photon arrival times, the probing depth is independent of source-detector separation. Moreover, multi-wavelengths TRS allows us to accurately measure the absolute concentrations of blood volume, blood oxygenation and also the concentrations of additional constituents, such as water, lipids and collagen.
Diffuse Correlation Spectroscopy (DCS)[2], on the other hand, monitors non-invasively the blood flow by quantifying the temporal fluctuations of NIR light fields due to dynamic scattering from moving red blood cells.
In this framework, the Horizon 2020 LUCA (Laser and Ultrasound Co-Analyser for thyroid nodules) project, proposes a low cost, non-invasive device based on a multimodal approach combining diffuse optical techniques such as DCS and TRS, along with Ultrasounds (US) with the aim to fully characterize and highlight the presence of microvascular altered tissues distinguishing them from the surrounding healthy muscles (i.e. thyroid nodules) by exploiting all the information that these techniques provide.

This work will mainly focus on the characterization of the performances of the TRS system under widely accepted guidelines of MEDPHOT[3] and nEUROPt[4] in order to validate its performances for clinical usability.

2. INSTRUMENT DESCRIPTION AND CHARACTERIZATION

The TRS system[5], while guaranteeing compact dimensions and cost effectiveness, maintains performance comparable to state-of-the-art systems. The system hosts eight custom-made picosecond pulsed laser sources based on commercially available compact and low-cost edge-emitting diode lasers, operating in gain switching mode. These selected lasers provide

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an average output power higher than 1 mW, at 40 MHz repetition rate to the sample, while maintaining a pulse width exceeding 150 ps over the entire available range of wavelengths from 635 to 1040 nm. The LUCA system features an US probe that embeds DCS and TRS. In particular, TRS houses an injection point along with two detection points consisting of wide-area Silicon Photomultipliers (SiPM), at different source-detector separations enabling a better discrimination between different layers of the tissue under investigation. The signal is then processed by two time-measurement units based on a custom-made Time-to-Digital Converter (TDC) in order to reconstruct accurately the DTOF curves.
At first, the performance validation of the TRS system was carried out on solid phantoms in order to assess: i) linearity and accuracy in retrieving the homogeneous absorption and reduced scattering coefficients of the medium (MEDPHOT protocol) and finally the ii) capability in detecting and localizing absorption changes within a homogeneous medium (nEUROPt protocol). Results are shown only for one channel of the system at source-detector distance of 2.56 cm.

2.1 Linearity and accuracy

Linearity and accuracy determine whether the device is able to linearly follow changes in the optical properties of the medium and how far these values are from the nominal ones, respectively. We performed tests on a set of 32 homogeneous phantoms with nominal values of absorption coefficient μ_a ranging from 0 to 0.49 cm^{-1} (0.07 cm^{-1} steps) and reduced scattering coefficient μ_s' from 5 to 20 cm^{-1} (5 cm^{-1} steps). We performed a fitting procedure between the DTOF acquired in reflectance mode and the analytical model for a semi-infinite homogeneous medium convoluted with the Instrument Response Function of the system that accounts for all the non-idealities of the device. For all the wavelengths we observed a good linearity and an accuracy of about 6% (14%) for absorption (scattering) values corresponding to biological tissues. Figure **1** shows linearity in μ_a at 670 nm for phantoms corresponding to μ_s'=10cm^{-1}.

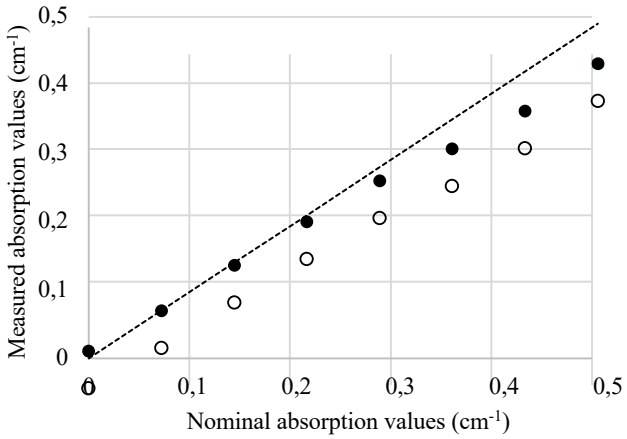

Figure 1 Measured absorption coefficients against nominal values at 670 nm (dots). The dashed line shows ideal values.

2.2 Detection of localized absorption changes

In order to detect localized absorption changes as required in the detection of absorption perturbations, we applied the guidelines of the nEUROPt protocol. We calculated the contrast as a function of the position (in step of 2 mm) of a movable rod hosted in a homogenous solid phantom[6]. The rod in particular is made of the same material of the homogeneous host phantom in which a small black PVC cylinder (5 mm diameter, corresponding to a $\Delta\mu_a$=0.17 cm^{-1}) is included in order to mimic realistic absorption changes. The detector and the source fibres are attached to the top (lateral) surface and symmetrically arranged perpendicularly to the axis of the rod at a source-detector interfibre distance of 2.56 cm. The contrast for lateral and depth scans is calculated for 8 different time gates of 280 ps each starting from the IRF barycentre (time 0 ns) up to 2.52 ns. It is shown in Figure 2 a) and b) respectively. Gating different regions of the DTOF allows us to distinguish the information obtained from early and late photons and thereby allowing us to retrieve information about deeper layer buried in the tissue (by separating the contributions from the superficial tissue). As expected, in the lateral scan the contrast for late gates reaches the maximum value when the inclusion is directly below the source-detector pair.

On the other hand, in the depth scan the maximum is reached when the cross-section between the inclusion and the probing volume is maximum.

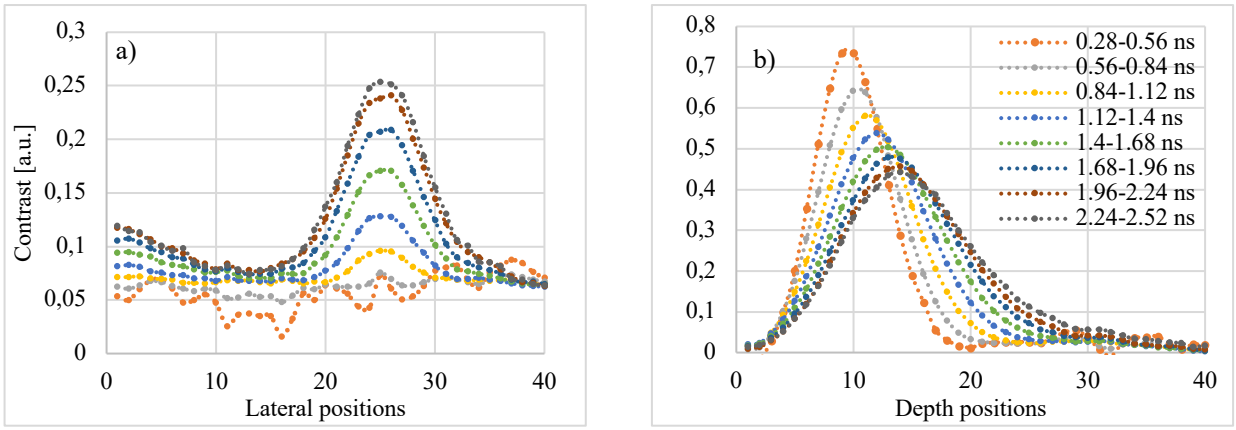

Figure 2 Contrast as a function of the position obtained during a) lateral and b) horizontal scan for different time gates.

3. CONCLUSIONS

In this paper we validated on phantoms the performance of a compact, low-cost and fully custom made TRS system, which will become part of a multimodal device for thyroid nodules screening. The standard characterization on phantoms showed a good behavior in terms of linearity and capability of detecting deep localized absorption at all the wavelengths and at absorption and scattering coefficients values corresponding to biological tissues.
Future developments will involve the validation of the entire LUCA device on real-settings integrating the instrument in the clinical monitoring work-flow.

4. ACKNOWLEDGMENTS

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