TITLE PAGE

Citation Format:

G. Maffeis, N. Serra, A. Bossi, E. Avanzi, R. Cubeddu, A. Dalla Mora, L. Di Sieno, A. Pifferi, and P. Taroni "Large source-detector distance time-resolved measurements to probe adult lungs non-invasively", Proc. SPIE 13314, Optical Tomography and Spectroscopy of Tissue XVI, 133140Q (20 March 2025).

Copyright notice:

DOI abstract link:

https://doi.org/10.1117/12.3042953

Large source-detector distance time-resolved measurements to probe adult lungs non-invasively

G. Maffeis*[a], N. Serra[a], A. Bossi[a], E. Avanzi[a], R. Cubeddu[a], A. Dalla Mora[a], L. Di Sieno[a], A. Pifferi[a] and P. Taroni[a]
[a]Department of Physics, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133, Milano, Italy;

ABSTRACT

Time-resolved measurements over a broad spectral range and at multiple source-detector distances show that gated contrasts vary synchronously with breathing. This result hints at the potential of time domain diffuse optics to probe lungs non-invasively.

Keywords: *In vivo* lung probing, time-resolved diffuse optics, large source-detector distance.

1. INTRODUCTION

Nowadays, the origin and the onset of lung diseases are mainly investigated through Computed Tomography (CT), Chest X-Ray (CXR) and Biopsy (B). However, these techniques cannot provide any physiological insight (CT, CXR) or they cannot be performed on a routine basis given their expensiveness (CT) and invasiveness (CT, CXR, B).

This work delves into the design of a strategy to probe adult human lungs *in vivo* through Time Domain Diffuse Optical Spectroscopy (TD-DOS) [1], based on its capability to characterize non-invasively biological tissues down to a depth of a few centimeters, especially when a large source-detector distance is used. This is particularly important in the case of the lungs, given the stratified structure of the chest, where they occupy the deepest position after skin, lipids, pectoral muscle, ribs and pleural membranes.

Simulations and measurements on phantoms were conducted to test different scenarios in terms of wavelength and geometry to sense the optical properties of the lungs. Then, a breathing protocol was employed on healthy subjects to ascertain whether re-emitted pulses have effectively propagated through pulmonary tissue. More experimental setups were used to cover a broad spectral range (600–1300 nm) and test different source-detector distances. In this work, we will focus on large source-detector distance measurements performed *in vivo*.

These initial results lay the groundwork for further research on how to best exploit the potential of TD-DOS to probe the lungs non-invasively.

2. MATERIALS AND METHODS

Experimental setup

In the following, we will focus on a setup involving an actively mode-locked Titanium Sapphire laser tuned at 1080 nm, able to offer an average power of up to 100 mW [2], to be properly expanded and attenuated to comply with safety limits. Such power grants the possibility to perform measurements at large source-detector distances. A 1.3 mm-side Silicon Photomultiplier detector is placed at 5.5 cm from the source, directly in contact with the subject's skin. A time correlated single photon counting board is employed to reconstruct the output pulses.

Measurement protocol

In vivo measurements (after written informed consent) are performed in reflectance mode on the chest of 8 healthy adult volunteers in lying position. In particular, the probe is positioned orthogonally to ribs, on the upper right side of the chest, between the nipple and the sternum, to minimize possible effects of the heartbeat. The subject is asked to perform a thoracic (not diaphragmatic) breathing at a fixed cadence, inhaling or exhaling as fast as possible to reduce transients, and holding breath at each phase for 10 seconds, to sample the tissue at exam in stable conditions. The procedure is repeated 5 times and it is preceded and followed by 20 seconds of baseline acquisition (i.e., standard breathing).

*giulia.maffeis@polimi.it

Optical Tomography and Spectroscopy of Tissue XVI, edited by Sergio Fantini, Paola Taroni, Proc. of SPIE Vol. 13314, 133140Q · © 2025 SPIE
1605-7422 · doi: 10.1117/12.3042953

Data analysis

Data are analyzed taking advantage of the strength of time domain measurements: different time gates on the reflected signal (R) have experienced different depths of the tissue. In particular, the later the gate, the deeper the probed tissue. Two possible initial methods of analysis derive gated contrasts (C) using Eq. 1, and the variation in absorption ($\Delta\mu_a$) with respect to a reference gate, using Eq. 2.

$$C(\tau,t) = \frac{I(\tau,t) - I_0(\tau,t)}{I_0(\tau,t)} \qquad (1)$$

$$\Delta\mu_a(\tau,t) = -\frac{1}{v\tau_L} \ln\left[1 + \frac{I(\tau_L,t)}{I_0(\tau_L,t)} - \frac{I(\tau_E,t)}{I_0(\tau_E,t)}\right] \qquad (2)$$

τ refers to the microtime of the pulse (of the order of some nanoseconds), t the macrotime of the task (of the order of tens of seconds), $I(\tau,t) = \int_{\tau}^{\tau+\Delta\tau} R(\tau')d\tau'$ denotes the intensity in a gate of width $\Delta\tau$ (i.e., 1 ns), $I_0(\tau,t)$ the corresponding intensity averaging R on inhaling and exhaling acquisitions of the current repetition, τ_L is a late gate (e.g., the third, on the trailing edge of the pulse), τ_E an early gate (e.g., the first, including the rising edge of the pulse), v is the speed of light.

3. RESULTS AND DISCUSSION

TD-DOS systems employ picosecond pulsed lasers, that most of times maximize only one between extension of the spectral range or power, for technological constraints. We conducted measurements under various conditions, such as different wavelengths and source-detector distances, using multiple setups. These experiments generally show a correlation with breathing, although not always consistent. These tests are crucial for determining the optimal experimental settings for probing the lung. However, we now focus on an example that emphasizes source-detector distance and then briefly describe results for broad spectral range measurements.

Figure 1 reports the results of Eq. 1 and 2, acquisition by acquisition during the task, with reference to gate 1 and 3. We observe a variation in contrast synchronous with the breathing rhythm. This can be considered a piece of evidence that photons have effectively propagated through the lung. Also, contrasts are higher for the later gate, which is associated with photons that have travelled in the lung longer. Contrast is positive during inhalation and negative during exhalation. While inhaling, the density of lungs decreases because of their expansion, so photons' travel through pulmonary tissue is shorter, thus inducing a higher output intensity and consequent lower absorption value. The opposite occurs during exhalation. Finally, variations in absorption are indeed consistent with the corresponding contrasts: the higher the signal, the lower the absorption.

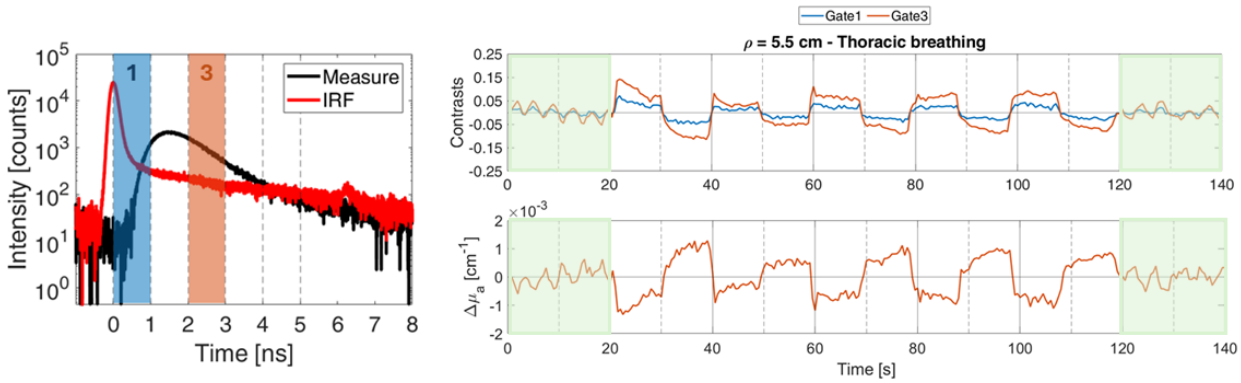

Figure 1. Left, example of Instrument Response Function (IRF) and measurement pulses at 1080 nm, highlighting the first (blue) and third (red) time gates. Right, example case of the time evolution of the gated contrasts (top) and variation in absorption (bottom)during the breathing task. Solid vertical lines denote the beginning of inhalation phase, dotted ones of exhalation, green shade represents baseline.

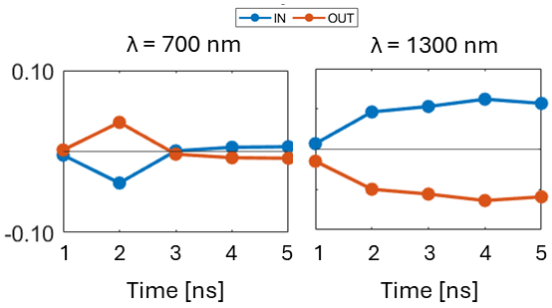

Figure 2. Example of broad spectral range measurements at 700 nm and 1300 nm. Dots correspond to gated contrasts along pulse microtime during inhalation (blue) and exhalation (orange).

Figure 2 depicts the results for broadband measurements along the pulse microtime. As already mentioned, gated contrasts should increase with delay, which is observable for 1300 nm and not for 700 nm. Also, at 1300 nm the amplitude and the sign of the signal comparing inhalation and exhalation phases is more compliant with expectations. This could hint at a better sensitivity of higher wavelengths to deeper chest layers, while the measurements at shorter wavelengths, like 700 nm, might be affected by confounding effects, like blood circulation in superficial layers.

4. CONCLUSION

Measurements performed on different subjects, in various experimental conditions (wavelength, source-detector separation, position on the chest) always show a correlation between the detected signal and the breathing task. However, very diverse situations are observed. Criticalities might arise from the complex anatomy of the thorax and the alveolar nature of lung tissue, that make the description of photon propagation difficult. Therefore, simulations, measurements on phantoms and assessments on more subjects over a broad range of wavelengths (600 – 1300 nm) and at multiple source-detector distances (3 – 7 cm) with different breathing protocols are being performed to achieve a full interpretation and help identify the best conditions to probe the lung transcutaneously in an efficient manner.

ACKNOWLEDGEMENTS

This work was partly funded by the National Plan for NRRP Complementary Investments (PNC, established with the decree-law 6 May 2021, n. 59, converted by law n. 101 of 2021) in the call for the funding of research initiatives for technologies and innovative trajectories in the health and care sectors (Directorial Decree n. 931 of 06-06-2022) - project n. PNC0000003 - AdvaNced Technologies for Human-centrEd Medicine (project acronym: ANTHEM), by the European Union's NextGenerationEU Programme with the I-PHOQS Infrastructure [IR0000016, ID D2B8D520, CUP B53C22001750006] "Integrated infrastructure initiative in Photonic and Quantum Sciences and by the European Union's NextGenerationEU Programme with PNRR - M4C2, investment 1.1 - "PRIN 2022 fund" - ALPHA [ID 2022HHZWRS , CUP D53D23013540006].

REFERENCES

[1] A. Pifferi, M. Miniati, A. Farina, S. Konugolu Venkata Sekar, P. Lanka, A. Dalla Mora, G. Maffeis, and P. Taroni, *Initial Non-Invasive in Vivo Sensing of the Lung Using Time Domain Diffuse Optics*, Sci. Rep. **14**, 6343 (2024), doi: 10.1038/s41598-024-56862-0.

[2] A. Bossi, S. K. V. Sekar, M. Lacerenza, V. Gandolfi, S. Šušnjar, P. Lanka, C. D'Andrea, R. Vanna, G. Valentini, A. Farina, and A. Pifferi, *Time Domain Diffuse Raman Spectroscopy Using Single Pixel Detection*, Biomed. Opt. Express **14**, 5749 (2023), doi: 10.1364/BOE.502022.