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What Are the Best Conditions to Study Deep Lung Tissue Non-invasively through Time Domain Diffuse Optics?

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Abstract: We assessed through Monte Carlo simulations and in vivo measurements what are the wavelengths (1150<λ<1250 nm), source-detector distance (about 5 cm) and protocol (forced breathing) to sense deep lung tissue non-invasively with time-resolved diffuse optics. © 2025 The Authors

1 Introduction

In this work, we studied what are the optimal measurement conditions to investigate lungs through time-resolved diffuse optics (TR-DO) in vivo, with enhanced probability to investigate deep layers. This prepares the settings to verify whether TR-DO is a valid option for exploring the diagnosis of pulmonary diseases non-invasively. Currently, such a response can indeed be provided only via computed tomography, chest X-ray and biopsy, that are either expensive or have potential side effects.
The goals of this study are 1) to model the layered structure of the thorax geometrically and optically; 2) to model the changes occurring in lung tissue during breathing from the optical perspective; 3) to define a wavelength window in the 600-1300 nm range where light is most sensitive to these changes, thus conveying the most effective information about lungs health status. To achieve these goals, two different assessments were implemented: Monte Carlo (MC) simulations and in vivo measurements. The results act as a guideline for the design of the experimental setup and protocol to adopt for systematic in vivo measurements.

2 Materials and Methods

2.1 Breathing modeling

Forced breathing was chosen as an expedient to test the effectiveness in reaching lungs with TR-DO. With a simplified approach, we can model breathing as follows. During inhalation, lungs expand and, maintaining the mass fixed, density reduces, thus causing a decrease in absorption and scattering as well. The opposite occurs while exhaling. In other words, we expect the signal intensity to oscillate during breathing, with a positive/negative trend across an inhalation/exhalation cycle, with respect to a baseline. This contrast parameter, if correlated with the breathing rhythm and assuming the superficial layer as constant, could highlight sensitivity to lung changes.

2.2 Thorax modeling

The thorax is a layered structure including, in order of depth, skin, fat, muscle, ribs, pleural membranes and lungs (on the right side, to avoid heart contributions). Also, pulmonary tissue is greatly heterogeneous, due to the presence of alveoli, bronchi and bronchioles. The description of light propagation deep to and within lungs is then challenging. Aware of the marked simplification, we modelled the thorax as a bilayered medium [1], where the superficial layer collectively represents all components but the lung, which is separately represented by the second layer. The thickness of the first layer is 3 cm, based on average values from literature, and source-detector distance is then set to 5 cm to enhance the probability of photons to travel through the second layer.
Given this configuration, MC simulations were run to obtain the corresponding Distributions of Times-Of-Flight (DTOF) in two cases: when the average second layer absorption is higher (μ_{a2} = 0.6 cm^{-1}) and lower (μ_{a2} = 0.07 cm^{-1}) than the superficial layer one (μ_{a1} = 0.12 cm^{-1}).
The absorption spectra over the 600-1300 nm of the first and second layer were retrieved from in vivo measurements on humans at short source-detector distance (2 cm) and on living swine directly in contact with the lung, respectively. The goal is to figure out in which wavelength ranges the contrast is maximum, in function of the optical properties of the two layers.

3 Results and Discussion

Figure 1 depicts the results of the MC simulations. The outcomes of MC simulations are represented taking advantage of the time domain nature of the assessment: instead of integrating photons over the whole DTOF,

summation has been applied limited to time windows (i.e., gates) at increasing delays (400 ps). Variations in absorption (blue), scattering (orange), or both (yellow) were applied between inhalation (IN, first row) and exhalation (OUT, second row), according to the breathing modeling previously explained. Results show not only that contrasts generally grow at increasing delays, but also that when $\mu_{a2}<<\mu_{a1}$ contrasts are larger and driven by absorption. In particular, contrast is higher than 20% for delays longer than 4 ns. This makes the comparison and interpretation of data more readable. The origin of this behavior resides in the fact that gates on the DTOF tail correspond to photons that travelled longer in the tissue, thus maximizing the probability to have explored lungs. This means that the detector should provide DTOFs as clean as possible, especially avoiding artifacts on the tail. Also, the output signal contains more information about lungs tissue when its absorption is lower than the one of the overlying layer. This is because photons likely have travelled more through it, thus experiencing its properties longer.

To understand which is the spectral range where this condition is met, the absorption of the superficial layer and the lung [2] were assessed in vivo, respectively on human and animal lungs. The resulting optimal range ($\mu_{a2}<<\mu_{a1}$) is from 1150 to 1250 nm, around the absorption peak of lipids. This, on one side, brings attention to long wavelengths; on the other, arises additional alert about the performance of the setup: the combination of laser power, detector active area, quantum efficiency and responsivity, and source-detector distance must be enough to grant a satisfying signal-to-noise ratio even at high absorption levels.

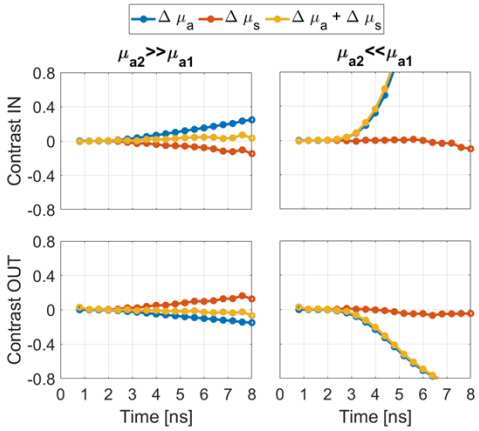

Figure 1: Time-gated results of the MC simulations for variation in optical properties during breathing.

4 Conclusion

Our investigation revealed that a setup operating in time domain, able to collect a DTOF whose duration is at least 4 ns, able to grant enough signal at a source-detector distance of a few centimeters (about 5 cm), and able to emit and collect light at high wavelengths ($1150<\lambda<1250$ nm) could be a good candidate to study pulmonary tissue with TR-DO during a forced breathing task. Data analysis could initially rely on the study of gated contrasts and later explore more sophisticated methods, such as a bilayered model. The final goal is to characterize the lung tissue composition non-invasively for diagnostic purposes.

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