

TITLE PAGE

Citation Format:

Nicola Serra, Giulia Maffeis, Vamshi Damagatla, Rinaldo Cubeddu, Antonio Pifferi, and Paola Taroni "Initial non-invasive in vivo assessment of breast density with time resolved diffuse reflectance", Proc. SPIE 13935, Diffuse Optical Spectroscopy and Imaging X, 139350B (18 December 2025); <https://doi.org/10.1117/12.3098358>. European Conference on Biomedical Optics 2025 (ECBO), 22-26 June 2025.

Abstract link:

<https://www.spiedigitallibrary.org/conference-proceedings-of-spie/13935/139350B/Initial-non-invasive-in-vivo-assessment-of-breast-density-with/10.1117/12.3098358.short>

Initial Non-Invasive In Vivo Assessment of Breast Density with Time Resolved Diffuse Reflectance

Nicola Serra^{1,*}, Giulia Maffei¹, Vamshi Damagatla¹, Rinaldo Cubeddu¹, Antonio Pifferi^{1,2} and Paola Taroni^{1,2}

¹Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133, Milano, Italy

²Istituto di Fotonica e Nanotecnologie, Consiglio Nazionale delle Ricerche, Piazza Leonardo da Vinci 32, 20133, Milano, Italy

*nicola.serra@polimi.it

Abstract: Breast composition of 11 volunteers is measured using reflectance, broadband time-domain diffuse optical spectroscopy to optimize measurement protocols for breast density estimation, aiming to develop a non-invasive optical device for breast cancer risk assessment.

© 2025 The Authors

1. Introduction

Breast cancer is one of the leading causes of death in women and early diagnosis significantly boosts survival rates [1]. Risk assessment enables close monitoring of high-risk subjects while facilitating the development of targeted prevention strategies. An important independent risk factor is breast density, the amount of fibro-glandular stroma compared to adipose tissue, which is typically assessed through x-ray mammography during screening programs for breast cancer. Women under 50 years of age are typically excluded from these programs, due to their lower risk, to the lower sensitivity of the technique in dense breasts, common in young women, and to the ionizing nature of the radiation.

Time-resolved diffuse optical spectroscopy (TD-DOS) enables the non-invasive, quantitative characterization of breast tissue composition and provides information on the microscopical structure, enabling the estimate of breast density. This tissue characterization is effective in both cancer detection and risk assessment, but the clinical implementation of TD-DOS for large scale screening remains a challenge.

In an upcoming clinical study, we plan to use broadband TD-DOS to identify a minimal set of wavelengths and measurement configurations that provide a reliable estimate of breast density. Our objective is the design and development of a small, cost-effective and non-invasive optical device for the routine assessment of breast density. In this preliminary laboratory study, we optimized a new setup for broadband acquisitions over a continuous spectrum and tested it in vivo with a simple patient- and operator-friendly measurement configuration in reflectance geometry, that avoids the discomfort of breast compression and reduces the complexity of the setup. Results are tested against time domain transmittance outcomes, that were shown to effectively correlate with mammographic density in previous studies on a larger cohort of subjects [2]. We also investigated tissue heterogeneity through measurements on both breasts, in different positions and for different source-detector distances.

2. Materials and methods

Light generated from a picosecond pulsed supercontinuum laser is dispersed by a prism for wavelength selection in the range 600-1100 nm in steps of 10 nm and injected into and collected from the tissue through optical fibers. An electronic board for time-correlated single photon counting allows one to reconstruct the temporal shape of the output pulse. The diffusion equation (DE) is used to model photon propagation through the tissue. When fitting the experimental data to the DE, the Lambert-Beer's law and an empirical power law from Mie theory are replaced, respectively, to the absorption and reduced scattering coefficients, allowing the direct estimate of constituent concentrations (water, lipids, collagen), blood parameters (oxy- and deoxy-hemoglobin, from which total hemoglobin *tHb* and oxygen saturation are computed), and the scattering parameters (amplitude *a* and power *b*) [3]. Measurements are performed on 11 healthy women of average age 39 ± 14 years. Due to the young age of the subjects, mammographic information was not available. The measurement protocol includes transmittance and reflectance acquisitions, with the subject either sitting or lying supine, on 3 different positions (outer, lower and inner quadrants) on both breasts and at two source-detector distances ($\rho = 2$ cm and $\rho = 3$ cm). The positioning of injection and detection fibers in the sitting measurements and of the optical probe in the supine measurement is illustrated in Fig. 1.

This study was approved by the ethics committee of Politecnico di Milano and written informed consent was signed by all participants.

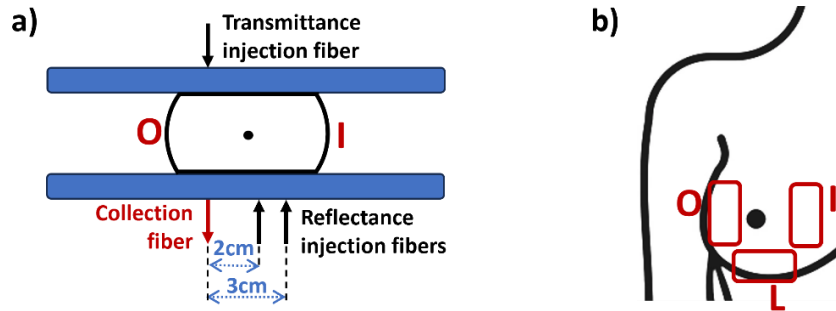


Fig. 1 Fibers and probe positioning for acquisitions on the right breast for the a) sitting subject and b) supine subject (O = outer, L = lower, I = inner).

3. Results and discussion

The scatterplots in Fig. 2 show the correlation between reflectance results at $\rho = 3$ cm and transmittance results, for all optical parameters and for the different measurement configurations. Scattering amplitude a is excluded from the representation for the sake of compactness. Correlation coefficients are high and significant for water, lipids, collagen and b . Linear correlation is weaker for tHb , but still statistically significant. Results for oxygen saturation and scattering amplitude a show poor correlation, but these parameters typically do not convey information about breast density. The good correlation between reflectance and transmittance results is used as an initial validation of the new reflectance protocol, since in previous studies tissue parameters from transmittance measurement proved to correlate with mammographic information [2], which was not available in this work.

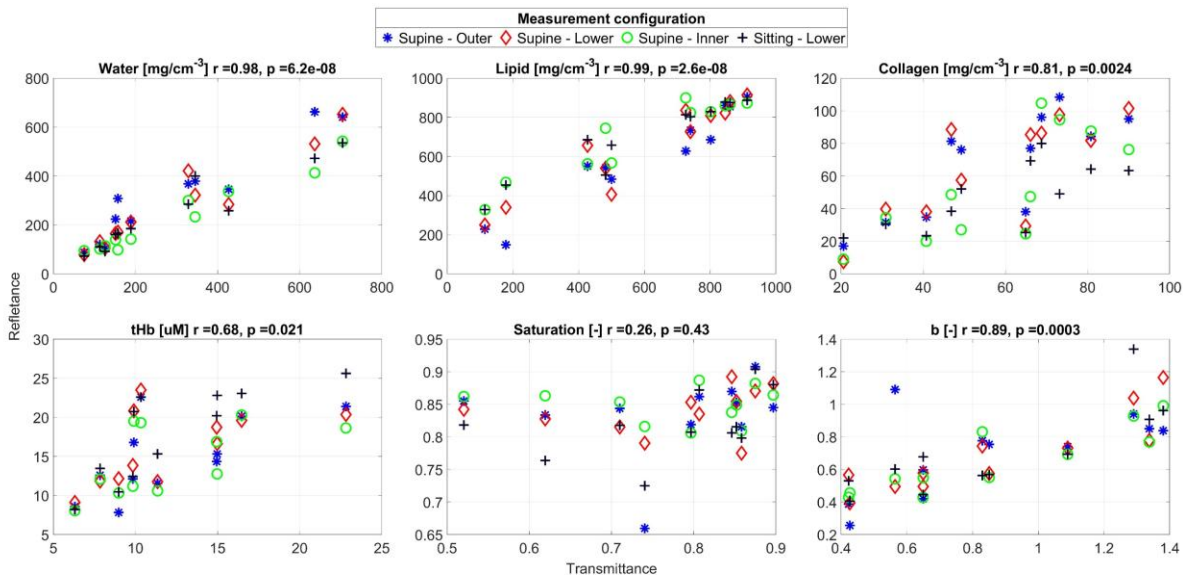


Fig. 2 Reflectance vs transmittance results for tissue parameters of interest. Results are averaged over both breasts, at $\rho = 3$ cm and presented for the different reflectance measurements for the supine subject (outer quadrant in blue, lower in red, inner in green) and the sitting subject (black). The correlation coefficient r and p -values are reported.

Fig. 3 presents results on tissue parameters for the different measurement configurations used in the study averaged over the 11 subjects and both breasts. The high standard deviations are due to the strong inter-subject variability in tissue composition, also apparent from Fig. 2. Nevertheless, a trend can be observed moving from the outer, to the inner, to the lower quadrant, with a progressive increase in lipid and decrease in water and collagen. This trend is more marked for $\rho = 3$ cm and the difference in tissue composition between outer and inner quadrants is statistically significant when assessed with the Wilcoxon paired signed-rank test (water $p = 0.005$, lipid $p = 0.010$, collagen $p = 0.019$). This pattern reflects the breast anatomy, as the mammary gland, composed of fibro-glandular stroma, rich in water and collagen, is located towards the outer quadrant. The difference between the inferior and the other quadrants is not always significant, since this probing position is likely to include contributions from outer and

inner quadrants. Scattering and blood parameters do not have a clear trend, except for a significant difference in tHb and a between inner and lower quadrants ($p = 0.005$ for both). Results at $\rho = 3$ cm suggest higher density tissue (i.e. higher water and collagen content and lower lipid) than $\rho = 2$ cm. The difference is confirmed by the Wilcoxon test (water $p = 0.01$, lipid $p = 0.02$, collagen $p = 0.01$). This is coherent with a better probing of deep tissue for the highest source-detector distance, since fibro-glandular stroma is expected to be concentrated deeply in the breast, overlaid by predominantly adipose tissue. Scattering power b is significantly lower at $\rho = 3$ cm ($p = 0.001$). Results from the right and left breasts are well correlated, suggesting that measurements on a single breast might be enough for the assessment of breast density. However, asymmetries in breast composition have been previously suggested as an independent risk factor, hence it is worth investigating both breasts [4].

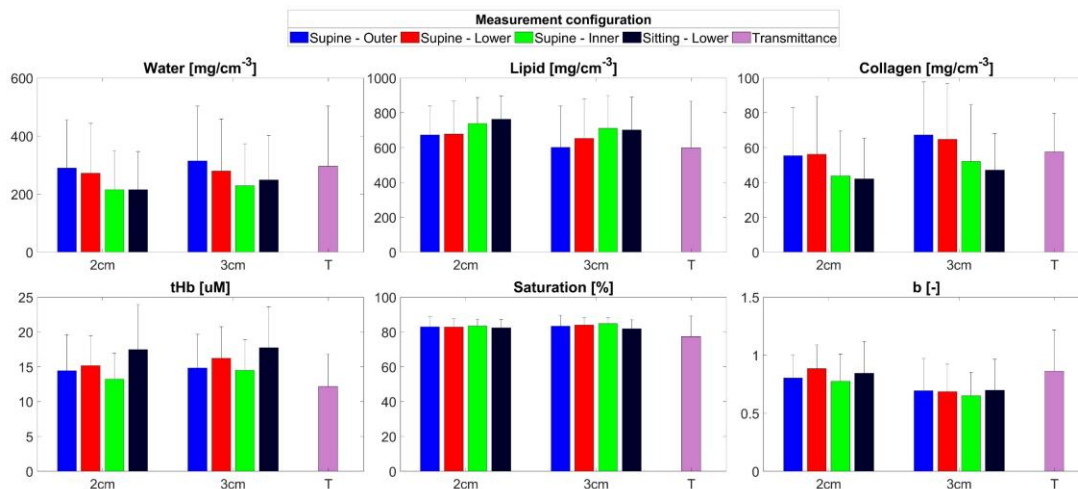


Fig. 3 Tissue parameters averaged over the study population and both breasts, measured in reflectance geometry on supine subjects (outer quadrant in blue, lower in red, inner in green), on sitting subjects (in black), at 2 cm and 3 cm source-detector distance, and in transmittance geometry (violet). Vertical lines indicate standard deviations.

4. Conclusions

In this study, a portable, broadband time-resolved diffuse optical spectroscopy system is employed to measure breast composition *in vivo* on 11 healthy subjects. We test a new reflectance measurement protocol and analyze the effects of tissue heterogeneity on the retrieved tissue parameters. Optical findings with the new reflectance configuration are in good agreement with breast anatomy and with transmittance results, which were validated against mammographic breast density in previous studies. This new measurement protocol (reflectance, $\rho = 3$ cm, outer and inner quadrants) is simpler than previous ones, does not require a compression stage and causes less discomfort to the patient, easing its integration in the clinical workflow. In the next clinical trial, a broader cohort with available mammograms will be enrolled, allowing us to investigate the down-scaling of the experimental setup to the minimal requirements for an effective estimate of breast density.

5. Acknowledgments

The authors acknowledge funding from the European Union's Horizon 2020 research and innovation programme as part of the PHAST-ETN project under the Marie Skłodowska-Curie grant agreement No. 860185 and from the European Union's NextGeneration EU programme "Integrated infrastructure initiative in Photonic and Quantum Sciences" - I-PHOQS (IR0000016, ID D2B8D520, CUP B53C22001750006).

6. References

- [1] R. Siegel, E. Ward, O. Brawley, and A. Jemal, "Cancer statistics, 2011," *CA Cancer J Clin*, vol. 61, no. 4, pp. 212–236, Jul. 2011, doi: 10.3322/caac.20121.
- [2] P. Taroni *et al.*, "Noninvasive assessment of breast cancer risk using time-resolved diffuse optical spectroscopy," *J Biomed Opt*, vol. 15, no. 6, p. 060501, 2010, doi: 10.1117/1.3506043.
- [3] C. D'Andrea *et al.*, "Time-resolved spectrally constrained method for the quantification of chromophore concentrations and scattering parameters in diffusing media," *Opt Express*, vol. 14, no. 5, p. 1888, 2006, doi: 10.1364/OE.14.001888.
- [4] B. Zheng, J. H. Sumkin, M. L. Zuley, X. Wang, A. H. Klym, and D. Gur, "Bilateral mammographic density asymmetry and breast cancer risk: A preliminary assessment," *Eur J Radiol*, vol. 81, no. 11, pp. 3222–3228, Nov. 2012, doi: 10.1016/j.ejrad.2012.04.018.