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Multidistance Optical Characterization of the Female Breast by Time-Resolved Diffuse Spectroscopy

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ABSTRACT

Two systems for time-resolved diffuse spectroscopy were used for the optical characterization of the female breast in 4 volunteers. A first system was a compact laser diode instrument operated at 660 and 785 nm, while the second one was a broadband laboratory set-up based on mode-locked lasers tunable in the 610-1000 nm range. Measurements were obtained both in transmittance and in reflectance geometry at 5 inter-fiber distances ranging from 1 to 4 cm at different locations on the breast. Distinct spectral features both in absorption and in scattering were observed among the 4 volunteers, and for each subject between reflectance and transmittance measurements. These differences are correlated with the abundance of the glandular tissue and blood absorption. Upon increasing the inter-fiber distance in reflectance, deeper tissue structures were investigated, generally resulting in higher water contribution.

Keywords: absorption, scattering, in vivo spectroscopy, photon migration

1. INTRODUCTION

The strong interest for development of optical mammography and tomography, as a clinical modality for breast cancer detection and diagnosis, has fostered a number of studies on in-vivo breast spectroscopy. In-vivo measurements have been performed in order to determine the range of absorption (μ_a) and reduced scattering (μ_s') coefficients for healthy tissue, which is strongly influenced by factors such as age and hormonal cycle. The measurement techniques employed are usually based on spatial-resolved approaches, frequency-modulated light sources or time-resolved diffuse spectroscopy. In general, the breast structure of young women is characterized by dense, glandular and thus water-rich tissue. The post-menopausal breast, in contrast, presents a reduction in the glandular volume, and the relative amount of adipose tissue increases.

The aim of this work was to investigate and quantify the effects of tissue heterogeneity in breast, when applying an inverse homogeneous model to deduce the optical properties. Measurements were performed at different locations on the breast of 4 volunteers, both in transmittance and in reflectance geometry using different inter-fiber distances.

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2. MATERIALS AND METHODS

Two systems were employed. The first one is a portable instrument constructed at the Lund Medical Laser Centre, Lund, Sweden, that was used for measurements at short inter-fiber distances on various locations on the breast. It is based on two pulsed diode lasers and an electronic board for time-correlated single-photon counting. The two lasers emitted at 660 and 785 nm, respectively, with a pulse length < 70 ps, a maximum power < 2 mW, and a repetition rate of 80 MHz. Light was injected into and collected from the tissue by means of two 1 m long, 600 μm core step index fibers. The emitted signal was first detected by a microchannel plate photomultiplier and than processed by a PC board for time-correlated single-photon counting. The FWHM of the overall instrumental transfer function (ITF) was < 100 ps. A second system is a broad band spectroscopy laboratory set-up constructed at the Politecnico di Milano, Italy, which was used to perform spectral measurements on the breast at different inter-fiber distances. The system is based on mode-locked tunable lasers and an electronics for time-correlated single-photon counting. A dye (DCM) laser together with a Ti:Sapphire laser covered the 610-1000 nm spectral range. Light coupled from the two lasers was redirected into the launching fiber by an optical switch and attenuated by a variable filter. A 4 mm diameter fiber bundle collected the light re-emitted from the tissue and conveyed photons to a cooled microchannel plate photomultiplier with a S1 surface. A PC board for time-correlated single-photon counting was used for signal processing. A small fraction of the laser power was split-off, directly coupled to the photomultiplier, and used as a reference pulse for continuous recording of the ITF. All laser tuning and optimization, as well as signal attenuation and acquisition were PC controlled.

2.1. Evaluation of time -resolved data

For both systems, μ_a and μ_s' were obtained by fitting the solution of the diffusion equation for a semi-infinite homogenous medium [1]. The fit was performed with a Levenberg-Marquardt [3] algorithm using a program developed at the Politecnico di Milano. We used the extrapolated boundary condition and, according to Furutsu and Yamada [2], the diffusion coefficient D [i.e. $D = 1/(3\mu_s')$] was independent from the absorption properties of the medium. The theoretical curve was convoluted with the ITF and normalized to the area of the experimental curve. The fitting range included all points with a number of counts higher than 80% of the peak value on the rising edge of the curve and 1% on the tail.

2.2 Tissue composition and structure

To evaluate the percentage composition of tissues, the absorption spectra were best fitted with a linear combination of the spectra of the main tissue constituents [*i.e.* lipid, water, oxyhemoglobin (HbO_2) and de-oxyhemoglobin (Hb)].

$$\mu_a(\lambda) = \Sigma_i \, c_i \, \varepsilon_i(\lambda) \qquad (1)$$

Where λ is the wavelength, c_i is the concentration (free parameter in the fitting procedure) and $\varepsilon_i(\lambda)$ is the specific absorption of the *i*-th constituent. To this purpose, the spectra of water [4], Hb and HbO_2 [5] were obtained from the literature, while the authors have measured the absorption spectra of lipid (lard) previously [6]. The knowledge of the absorption properties of the two forms of hemoglobin allowed us also to evaluate the total hemoglobin content $tHb = [Hb] + [HbO_2]$ and the hemoglobin oxygen saturation $SO_2 = [HbO_2]/\{[Hb] + [Hb\,O_2]\}$

We calculated the Hb, HbO_2, SO_2 , water and lipid content for all volunteers at different inter-fiber distances and for the transmittance geometry as well.

The dependence of the scattering coefficient on the wavelength can be described by a power law derived – empirically – from Mie theory [7,8], where the exponent (i.e. the slope of the spectrum in a log scale) is related to the mean effective size of scattering centers, while the amplitude is affected by the density of scattering centers. Thus, a higher exponent of the power law that corresponds to smaller effective scattering centers characterizes the steepest spectrum.

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2.3 Measurement protocol

Four healthy volunteers (26, 28, 39, and 50 years old) were enrolled for the *in-vivo* measurements. The subjects were sitting in an upright position, and the measurement probes were placed on the breast with minimal pressure. Using the diode laser system, measurements were recorded on the right breast of each subject, at five positions: the four quadrants and on the areola complex at $\rho = 1.0$ and 1.5 cm. With the spectroscopy system measurements were performed in reflectance geometry with $\rho = 1.5$, 2, 3, 4 cm and in transmittance geometry at mild breast compression, on the upper outer quadrant.

3. RESULTS AND DISCUSSION

An example of reflectance (R) at $\rho = 1.5$ and 4 cm, together with transmittance (T) measurements are presented in Fig. 1 for the 26 years old volunteer. Absorption spectra (Fig. 1a) show an increase in water content either for a high inter-fiber distance or for transmittance. Correspondingly, the scattering spectra (Fig. 1b) in transmittance are generally higher and steepest as compared to the reference data.

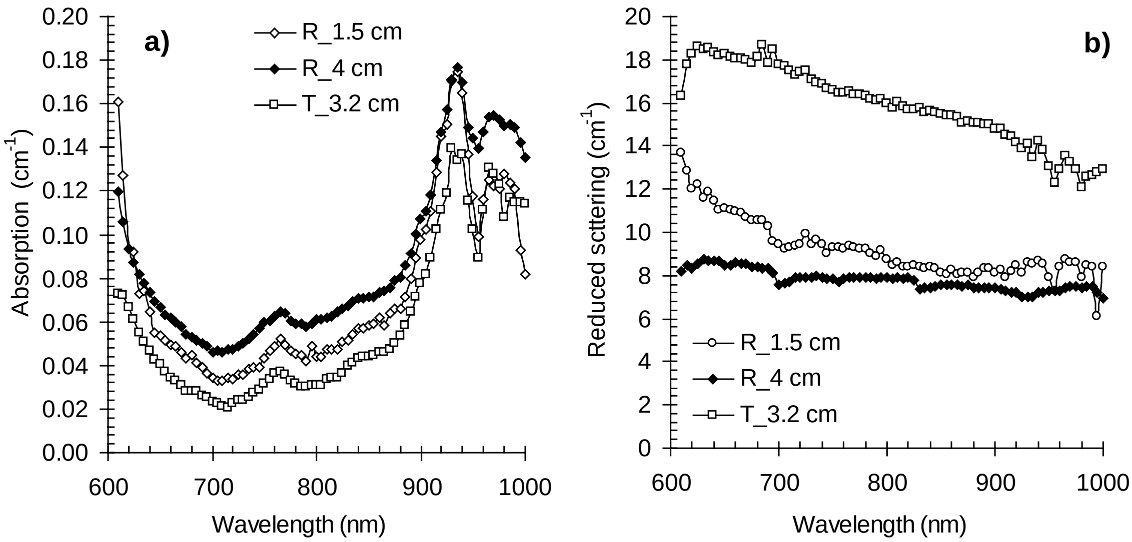

Fig. 1 absorption (a) and scattering (b) spectra for a 26 yrs volunteer

This behavior is consistent with expected differences in probed volumes for the 3 measurement geometries. In-fact, at low interfiber distances, reflectance is more sensible to the subcutaneous lipid layer, while longer distances or transmittance probe more deeply the core glandular tissue. Generally, similar results were obtained on the other volunteers, yet with a great inter-subject variability.

Figure 2(a) compares the absorption spectra obtained by the spectroscopy system, on the 4 volunteers at $\rho = 2$cm. The corresponding scattering spectra are reported in Figure 2(b).

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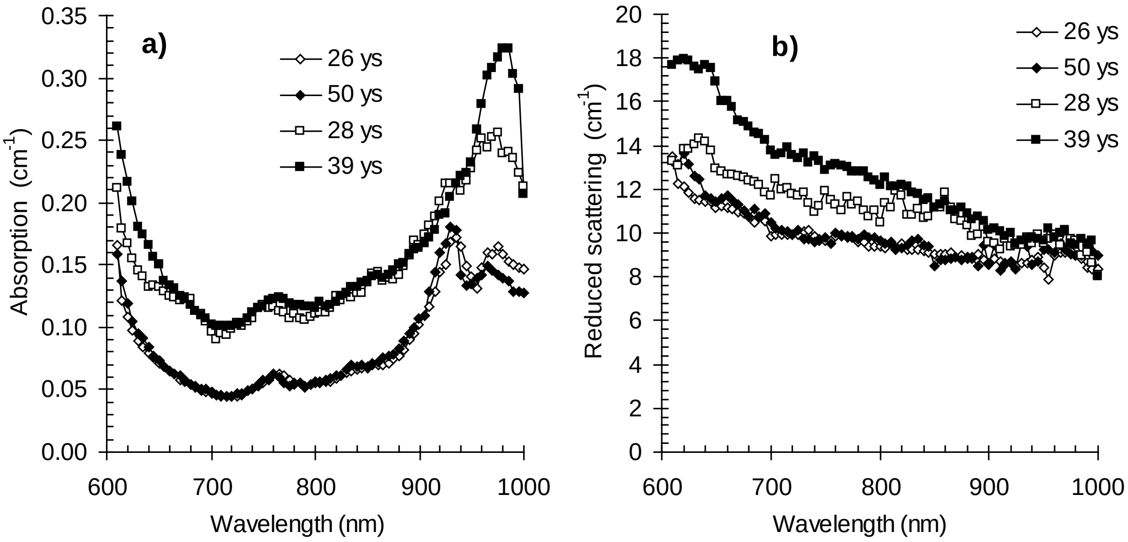

Fig. 2 absorption (a) and scattering (b) spectra for all volunteers at 2 cm interfiber distance.

Results clearly show marked variations of the breast spectral features among volunteers. The absorption spectra for the 28 and 39 y volunteers are similar, as well as the spectra, for the 26 and 50 y volunteers. The absorption coefficients for the first couple are higher than for other two within the whole wavelength range. The absorption peak of water at 970 nm is much more obvious for the 28 and 39 y volunteers, at the same time the peak of lipids at 930 nm is hardly noticeable, also due to the strong water absorption, while in the other case it is quite significant. These differences may be ascribed to a different breast pattern leading to glandular or adipose tissue prevalence. For a glandular rich breast the water content is high, while the prevalent adipose tissue imply more lipids. As we see, from Fig.2(b) the scattering properties vary less among the subjects, though we can notice different slopes and also different absolute values. The curves for the 26 years old and 50 years old volunteers are flatter and overall the scattering coefficient values are lower than for the other 2 volunteers. This corresponds to the adipose structure of the breast for these volunteers that produces a slowing descendent spectrum.

Table 1 reports the estimated tissue composition and Mie-equivalent parameters for measurements at $\rho = 2$ cm derived from the absorption and scattering spectra, respectively. It is confirmed that the 28 and 39 y volunteers have higher water and a lower lipid content as compared to the 26 and 50 y group. In addition, the formers present a higher *b* value corresponding to a steepest scattering spectrum. This can be explained assuming that "glandular" breast is characterized by small scattering centers, being rich of fibrous structures, in contrast to "adipose" tissues.

Table 1 – Tissue composition and Mie-equivalent values derived from the absorption and scattering spectra at $\rho = 1$ cm.

age	lipids	water	tHb	SO_2	a	b
26	55%	22%	16 µM	75%	8.3	0.56
28	42%	29%	17 µM	76%	9.3	0.75
39	33%	44%	28 µM	71%	9.5	1.14
50	57%	19%	18 µM	75%	8.3	0.61

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The results for 26, 28 and 39 years old volunteer, using the "Diode laser system" for different inter-fiber distances are shown in Fig.3 (a,b,c,d). For all volunteers the absorption coefficient is higher at ρ = 1 cm than at ρ = 1.5 cm for both wavelengths. It seems that at short inter-fiber distances we can mostly probe only the skin and very superficial layers, without reaching glandular and adipose tissue structures. Is clear that there is a very strong variation among subjects, depending on the breast composition in agreement with the results of the spectroscopy system.

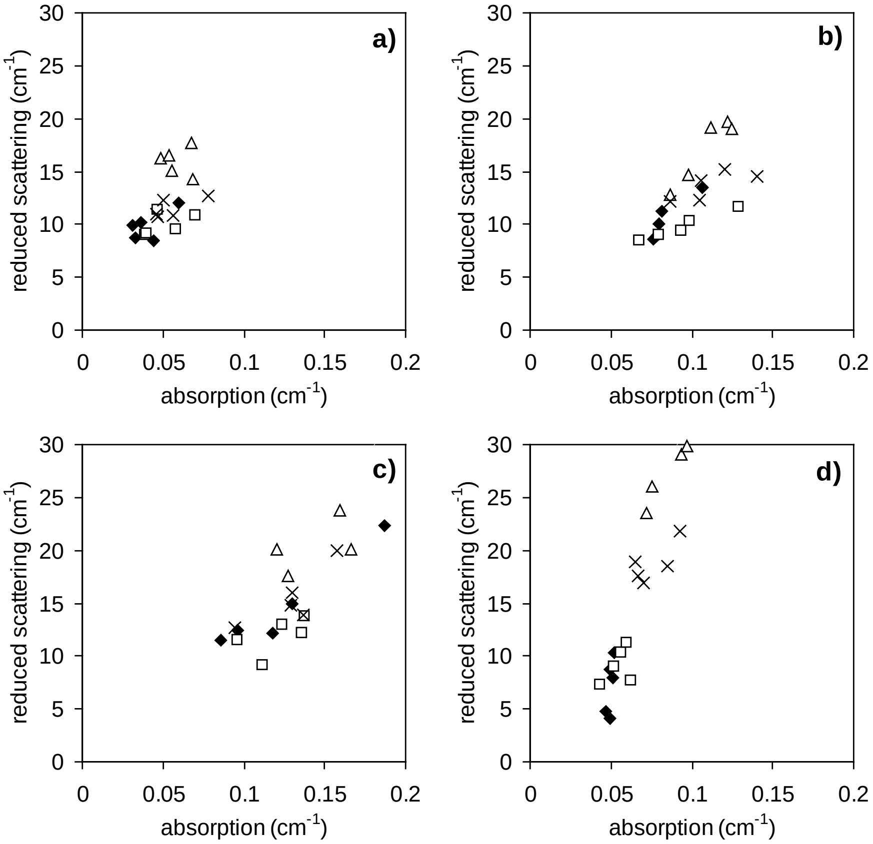

Fig.3 Optical coefficients for 26 (a), 28 (b), 39 (c), and 50 (d) years old volunteers measured with the diode laser system.

diamond - 1cm @ 660nm; square -1.5 cm @660nm; triangle - 1 cm @ 785 nm; cross - 1.5cm @ 785nm;

4. CONCLUSION

In conclusion, we have derived the optical properties of the breast of 4 healthy volunteers on 5 locations both for reflectance and transmittance geometries. Key differences were found among subjects related to the breast structure in terms of a higher or lower abundance of the fibrous and glandular tissue. Also, changes were observed on the same subject between reflectance and transmittance data and among reflectance spectra for various inter-fiber distances. These variations were correlated to the different regions and consequently breast structures visited by photons.

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