SOLUS | SMART OPTICAL AND ULTRASOUND DIAGNOSTICS OF BREAST CANCER

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Deliverable 2.1: Definition of paradigms representing exemplary breast lesions cases

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Abbreviations

ACR: American College of Radiology

BI-RADS: Breast Imaging-Reporting and Data System

NIR: Near-infrared

US: Ultrasound

1. Introduction

The goal of this deliverable is to provide a set of paradigms that represent the clinical problem under study in SOLUS. They aim at offering simplified scenarios – yet as close as possible to real situations – to be used to mimic the *in vivo* situation in simulations (*in silico*) and in the laboratory (on phantoms). These paradigms (consisting in a set of optical properties, composition, geometry) will be also exploited for extensive validation of the reconstruction algorithms, sub-systems, and finally the SOLUS system.

From the point of view of optics, the problem of identifying (a limited number of) paradigms representing malignant and benign lesions in breast tissue is a complex one.

The composition of breast tissue itself (even **healthy breast tissue**) is highly heterogeneous, and that reflects markedly on its optical properties. Major tissue constituents are characterized by significantly different optical properties, especially absorption, as highlighted in Figure 1 for oxy- and deoxy-haemoglobin, water, lipids and collagen, which are major tissue absorbers in the red and near-infrared (NIR) spectral range and will be object of evaluation by the SOLUS instrument.

As shown, the absorption properties also vary strongly with wavelength, making the identification of "typical" breast tissue properties assessed in multi-wavelength studies more complex.

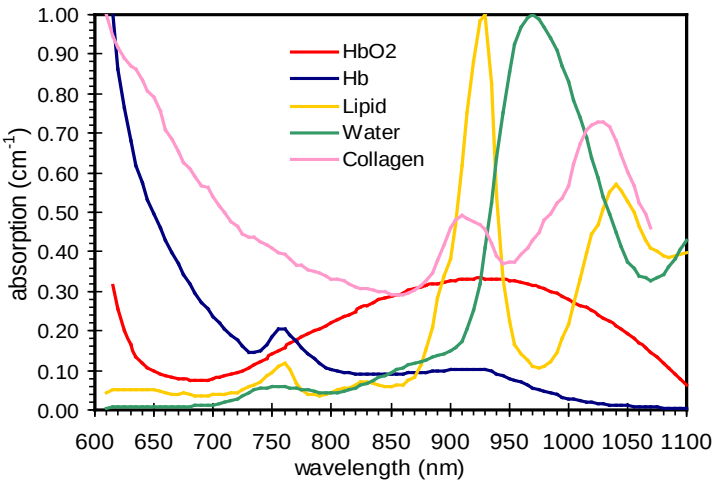

Figure 1: Absorption properties of major breast tissue constituents

Remarkable heterogeneity is observed as both intra-subject and inter-subject variability.

Intra-subject variability is often due to the presence of a higher amount of fibro-glandular tissue in external breast quadrants as compared to internal ones, but spatial variations in tissue composition are observed also on a smaller, more local (sub-centimetre) scale, as confirmed by the typically heterogeneous appearance of x-ray-mammograms.

Inter-subject variability mostly reflects breast density, and can lead to absorption differences of up to a factor of 3 at some wavelengths (typically on the absorption peak of water around 975 nm, as shown in the following), in agreement with marked differences observed in x-ray mammograms (mostly sensitive to attenuation from water) as a function of the amount of fibro-glandular tissue.

Breast lesions can differ significantly from one another in **composition, shape, size, depth** within tissue. As already described here above for the surrounding healthy "background" tissue, in particular the variability of lesion composition reflects into the variability of optical properties, especially absorption. Scattering is mostly (even though not uniquely) affected by the presence of liquid lesions (*e.g.*, liquid cysts).

2. Methodology

Several studies available in the literature report information on the optical characterization of breast, namely healthy breast tissue and/or malignant and benign breast lesions. A database was generated including information on the optical properties of breast tissue and breast lesions, classified as malignant

or benign, at all available wavelengths in the range of 600-1100 nm, as published in recent review papers [1–4] and in the references cited therein.

The database was then used to extract average tissue and lesion properties.

The standard deviation values reported in Section 3 refer to the spread of average values among studies, not to the data variability within a single study.

A significant variability is expected, due to tissue variability and measurement different conditions. However, few data, which resulted to differ strongly (typically, more than 2 STD) from the average of what reported in the literature, were excluded from the database.

The optical properties of healthy breast tissue surrounding the lesion ("background" tissue) can vary significantly. To quantify variations that can be expected in real measurement conditions, data from a study performed by POLIMI on 200 women were considered [5], as no other studies were found in the literature, carried out on a significant number of subjects and at wavelength >900 nm, where variations are more marked.

3. Results

3.1. Optical properties of healthy breast tissue and lesions

Average optical properties of healthy breast tissue and breast lesions are shown in Table 1 (absorption) and Table 2 (reduced scattering). For the absorption, data could be obtained for both malignant and benign lesions, while scattering information was available only malignant lesions.

Table 1: Average absorption properties of different tissue types as a function of wavelength*

	635 nm	**670 nm**	**685 nm**	**785 nm**	**905 nm**	**930 nm**	**975 nm**	**1060 nm**
Healthy	0.062 (0.010)	0.036	0.042 (0.000)	0.042 (0.005)	0.108 (0.003)	0.176	0.127 (0.039)	0.095
Malignant	0.238	0.091 (0.028)	0.124 (0.056)	0.093 (0.048)	0.201	0.262	0.276	0.181
Benign	0.177 (0.015)		0.115 (0.012)	0.095 (0.007)	0.159 (0.015)	0.213 (0.013)	0.237 (0.011)	0.136 (0.013)

*When available, standard deviations are reported in parentheses to quantify variability among studies.

Table 2: Average reduced scattering properties of different tissue types as a function of wavelength*

	635 nm	**670 nm**	**685 nm**	**785 nm**	**905 nm**	**930 nm**	**975 nm**	**1060 nm**
Healthy	13.2 (0.3)	10.5	12.6 (0.4)	10.2 (1.2)	10.9 (0.7)	10.2	10.8 (1.3)	9.4
Malignant		15.6 (2.9)	15.0	13.8 (3.1)				

*When available, standard deviations are reported in parentheses to quantify variability among studies.

To allow easier visualization of the differences (with wavelength and tissue type), average absorption data reported in Table 1 are also displayed in Figure 2.

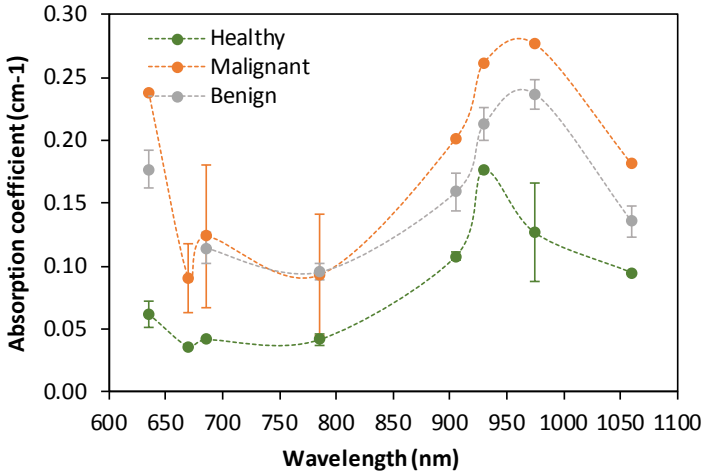

Figure 2: Average absorption properties of healthy breast tissue, malignant and benign breast lesions, based on literature data as reported in Table 1.

3.2. Healthy breast tissue as a function of breast density

Figure 3.A shows the average absorption spectra of different breast tissue types, from almost entirely fat (BI-RADS 1) to extremely dense (*i.e.*, with a high percentage of fibro-glandular tissue, BI-RADS 4).

Figure 3.B displays the average reduced scattering spectra for the different categories of breast density, showing that, even though to a minor extent than absorption, also scattering changes significantly with wavelength and with breast tissue type. It should be taken into account that the signal level depends strongly on the scattering properties, with a minor increase in scattering leading to a remarkable reduction in the diffusely reflected signal.

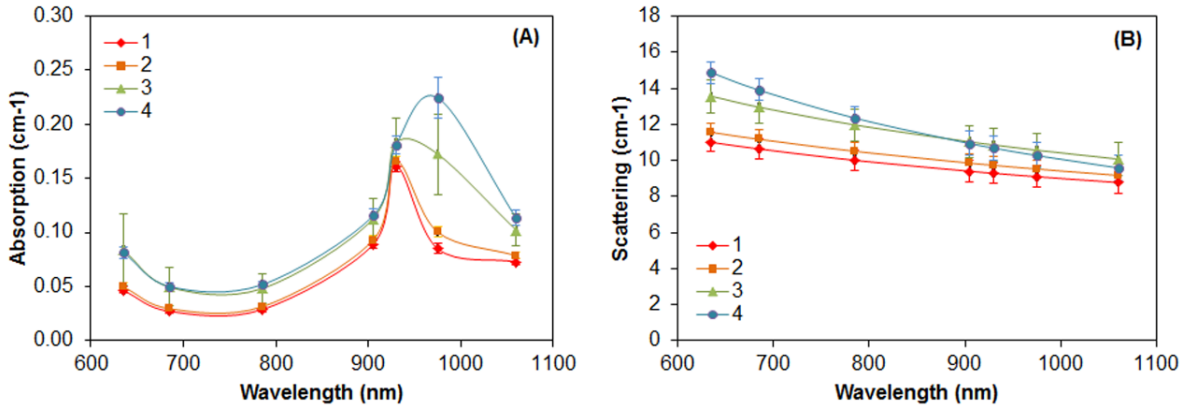

Figure 3: Average absorption (A) and reduced scattering (B) spectra of breast from fully adipose (BI-RADS category 1) to extremely heterogeneous (BI-RADS category 4). Reproduced from [5].

4. Discussion and Conclusion

4.1. Optical properties

The experimental conditions of the studies reported in the literature vary markedly from one another.

They explored different wavelengths in the range of 600 to 1100 nm, with most information collected at wavelengths shorter than 850 nm. Actually, a consistent amount of information on the optical properties of both healthy tissue and lesions above 900 nm has been published only by POLIMI.

Different measurement geometry (reflectance, with different source-detector distance, or transmittance) were used, probing different tissue volumes.

Different theoretical models were applied for the interpretation of optical data: homogeneous models, perturbative approaches, tomographic reconstructions with or without morphologic *a priori* information.

All these features are expected to affect at least to some extent the estimated optical properties, especially - but not only - when lesions are considered. An example is likely represented by the absorption and scattering data at 670 nm, which are lower than expected, leading to an apparent minimum in both absorption and reduced scattering spectra.

Few general observations can be made:

- The absorption is generally lower below 850 nm than at longer wavelengths.
- The scattering decreases progressively with wavelength.
- As compared to healthy breast tissue, breast lesions are characterized by both higher absorption and higher reduced scattering at all wavelengths.
- In turn, malignant lesions seem to present higher absorption than benign ones.
- Quantitative information on the scattering properties of benign lesions is not available. Still it should be mentioned that, depending on their nature, solid benign lesions might have higher/lower scattering than healthy tissue, while liquid benign lesions (typically cysts) are expected to have lower scattering. So a clear trend cannot be envisaged.

Taking these features into account, an attempt was made to reduce the number of parameters that characterize breast lesions and healthy tissue from an optical point of view.

For the **absorption** properties:

- Two wavelength ranges were identified: $\lambda < 850$ nm and $\lambda > 850$ nm
- Only two tissue types were considered: lesions (including malignant and benign ones) and healthy (background) tissue.

This led to the average absorption properties summarized in Table 3.

Table 3: Average absorption properties

	Absorption coefficient (cm^{-1})	
	λ < 850 nm	**λ > 850 nm**
Healthy	0.046 ± 0.012	0.126 ± 0.035
Lesions	0.128 ± 0.055	0.208 ± 0.046

For the **reduced scattering** properties, changes with tissue type and wavelength are more limited, and over the entire spectral range 600-1100 nm the situation can be approximated as summarized in Table 4.

Table 4: Average reduced scattering properties

	Reduced scattering coefficient (cm-1)
Healthy	11.1 ± 1.3
Lesions	14.8 ± 0.9

4.2. Morphologic information

In the multi-modal SOLUS instrument, morphologic information will be provided by ultrasound (US) imaging. Still, for the purpose of simulations of optical measurements and preliminary phantom studies, it may be useful to identify representative values/ranges as follows.

Shape: The lesion shape, orientation and margins are key diagnostic features for US imaging, and their categories and related diagnostic meaning are clearly identified in the ACR BI-RADS® Atlas [6]. For optical imaging/tomography, a **round** shape can be considered as a first approximation.

Size: Breast lesions can span over a broad range of sizes. The clinical protocol of the SOLUS feasibility study (Deliverable 5.1) sets an inclusion criterion on the minimum lesion size (≥1 cm), while no indications are given on the maximum lesion size. In view of experimental optical data acquisition and interpretation, the minimum size is definitely more critical than the maximum one, thus lesions of **at least 1 cm** size should be considered. To identify a range that covers frequently observed lesion sizes, **3 cm** could be taken as the **maximum size**.

Depth: Lesion depth can anywhere from the tissue surface (skin) to several centimetres deep within tissue, where maximum depth depends also on breast size. However, two considerations can be made to limit the range:

- The multimodal SOLUS acquisition will be performed in reflectance geometry, following the procedure routinely used for US imaging (with the subject lying in a supine or supine oblique position, with the corresponding arm raised behind the head or neck to reduce breast thickness and movement).
- The depth of view of US probes for clinical breast imaging is typically of 4-5 cm.

Taking these observations into consideration and based on typical US images of breast lesions:

- For the minimum lesion size of 1 cm: the centre of the lesion could be located at a typical depth of **1.0 ± 0.5 cm**.
- For bigger lesions: the top of the lesion could be located at a typical depth of **1.5 ± 0.5 cm**.

5. References

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