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SOLUS: Multimodal System Combining Ultrasounds and Diffuse Optics for Tomographic Imaging of Breast Cancer

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Abstract: An innovative multimodal system for breast imaging was developed combining in a single probe B-mode ultrasound, shear-wave elastography and multi-wavelength time-domain diffuse optical tomography. The clinical validation is ongoing aiming at improving the diagnostic specificity.

1. Introduction

One in 8 women will develop breast cancer in her lifetime. Screening mammography is key to reduce mortality for breast cancer but has limitations. A major one is the high false positive rate, leading to a huge number of further needless examinations, including biopsies, that are presently being performed after a false positive mammogram.

The SOLUS project [1], funded by the European Commission in the H2020 framework, aims at improving the specificity of breast cancer diagnosis non-invasively for the patients' quality of life and for the sustainability of the healthcare systems. To reach its goal, SOLUS has developed a multimodal imaging system that combines in a single probe the capability to perform B-mode ultrasound (US, for morphologic information), shear-wave elastography (SWE, for stiffness) and multi-wavelength time-domain diffuse optical tomography (DOT, for tissue composition – water, lipids, and collagen content – and blood parameters – total hemoglobin content and oxygen saturation).

Each optical measurement point in the probe is represented by an optode, developed to offer state-of-the-art performance in very compact size. Besides being the key element of the multimodal imaging system, the optode is also a stand-alone device to perform time domain multiwavelength diffuse optical measurements.

The multimodal SOLUS system is presently being tested in clinics on the discrimination between malignant and benign breast lesions. Initial results, even though quantitatively limited, seem promising.

2. The multimodal imaging system

To perform the two US techniques the SOLUS system relies on a high-end commercial instrument (Aixplorer Mach 30 by Hologic SuperSonic Imagine S.A.), while the multimodal probe was designed and realized as part of the project. That included the design of all components of the optode (picosecond pulsed laser driver to operate at 8 wavelengths, wide area time-gated silicon photomultiplier detector, and dedicated acquisition electronics) and their integration in the optode.

Eight optodes are arranged around the US transducer, 4 on each long side, and water cooling guarantees optimal operation temperature on the probe front end (in contact with the patient's skin) and internally, for reliable operation of the electronics. The probe is also equipped with a position sensor and a contact sensor. A second screen and a dedicated PC complete the optical part of the system.

3. Procedures for the clinical validation

The initial clinical validation foresees the acquisition of multimodal data on 40 patients: 20 with malignant and 20 with benign lesions. Written informed consent is obtained from all enrolled subjects.

On each subject, measurements are performed at four locations: i) along the main axis of the lesion; ii) on the lesion, orthogonal to the previous measure; iii) on the healthy tissue in the same breast; iv) on the healthy tissue in the contralateral breast. Each acquisition includes B-mode US, Color Doppler, SWE, and DOT. The full procedure requires approximately 15 min. Five more minutes are needed to display the results of preliminary DOT analysis. Up to now, 16 lesions (5 malignant and 11 benign) were analyzed. Each subject is examined by three radiologists, to provide us with feedback on system ergonomics and general usability, and to test the independence of the results from the operator.

4. Initial clinical results

US-guided DOT reconstructions based on the diffusion approximation are performed to estimate optical properties at the eight wavelengths (640-1050 nm) and tissue composition (oxy- and deoxy-hemoglobin, water, lipids, and collagen) using spectrally constrained global data analysis. Figure 1 (left) shows an example of segmentation carried out to derive the morphologic prior from the US image and sections along orthogonal directions of the US-guided DOT reconstruction of collagen concentration.

On average malignant lesions are characterized by stronger absorption than benign lesions at all wavelengths (Figure 1, right). Based on the Mann-Whitney U-test, the difference is statistically significant (generally, $p < 0.001$) at all wavelengths except for 675 nm. When tissue composition is considered, only total hemoglobin content shows highly significant difference [tHB(M) > tHb(B) with $p < 0.001$]. However, work is still in progress to best apply the spectrally constrained analysis on data obtained with the complex SOLUS system (time-gated detection, strong signal level variation depending on source-detector separation, etc.).

Even though a limited dataset was available, two decision methods exploiting machine learning were tentatively applied to classify the lesions based on optical data: i) a support vector machine (SVM) and ii) logistic regression (LR). The results obtained are summarized in Table 1. The specificity is encouraging, while a very low sensitivity was obtained. The estimate is certainly affected by the limited dataset. To try to reduce the effects of that limit, the two orthogonal measurements performed on the same lesion as well as measurements carried out by different radiologists were all considered as independent data. That may at least in part have biased the results.

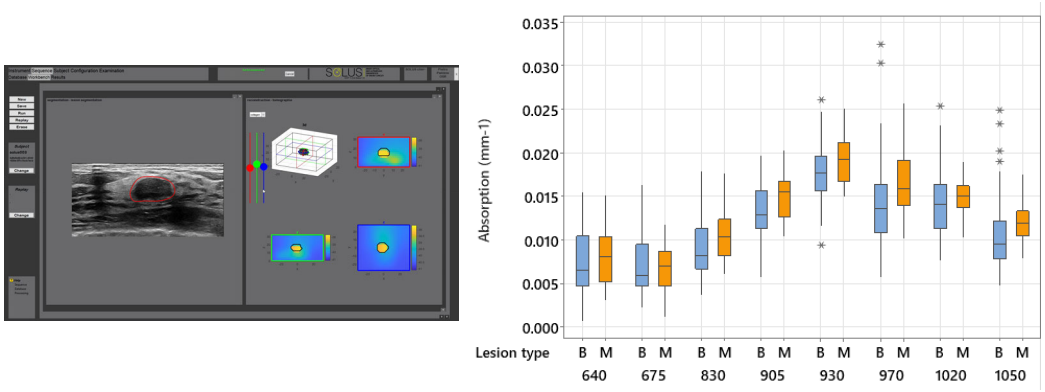

Figure 1 - Left: US segmentation and DOT sections as displayed on the SOLUS monitor.
Right: Absorption properties of malignant (M) and benign (B) lesions at all examined wavelengths (in nm).

Table 1 - Lesion classification

	SVM	LR
Sensitivity	0.57	0.54
Specificity	0.91	0.93

Patients are being enrolled and work is ongoing to improve the data analysis, especially on the estimate of tissue composition. Furthermore, the multimodal probe presently used in clinics suffers from the failure of some detectors, which reduced its performances. A new probe was developed and is about ready to replace the first one. So, more (and higher quality) data will be available soon. Furthermore, for now we focused on optically derived information, while, for a sounder evaluation of the diagnostic potential of the multimodal SOLUS approach, we need to exploit also B-mode US and SWE.

5. Acknowledgment

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6. References

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