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Initial examples of the SOLUS multimodal potential

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ABSTRACT

We present initial evidence of the SOLUS potential for the multimodal non-invasive diagnosis of breast cancer by describing the correlation between optical and standard radiological data and analyzing a case study.

Keywords: breast cancer, lesion classification, multimodal imaging, non-invasive imaging, time-resolved diffuse optical tomography, ultrasounds, color doppler, shear wave elastography.

1. INTRODUCTION

The SOLUS project aims at improving specificity in the detection of breast cancer with a multimodal non-invasive approach [1]. Its goal is to reduce the number of unnecessary biopsies by correlating findings retrieved through 4 different techniques: the well-established B-mode Ultrasound (US) and Color Doppler (CD), the emerging but already commercial Shear Wave Elastography (SWE), and the innovative multi-wavelength time-resolved Diffuse Optical Tomography (DOT). A successful implementation of the multimodal approach would help improve the patients' quality of life and save financial resources.

So far, we have processed the data collected during the clinical trial at the San Raffaele Hospital (Milan, Italy) focusing on optical information only. We have already obtained interesting results regarding absorption and composition parameters for the discrimination of malignant and benign lesions.

In this work, we present the first attempt of correlation between optical and standard radiological data to prove the strength of multimodality. First, we show a correspondence between the most significant optical parameters and the BI-RADS scores of the lesions. Then, we describe a case example, where the support of SWE and DOT has been crucial. Finally, we update the sensitivity and specificity values adding new US-based predictors to the previous lesion classification performed through machine learning that involved only optical data.

2. MATERIALS AND METHODS

2.1 The SOLUS probe

The cutting-edge technological novelty introduced by SOLUS is the first ever miniaturization of multi-wavelength time-resolved DOT. This has been possible thanks to the expertise in photonics and imaging of the project partners, who designed and fabricated the so-called "smart optode" [2], a stand-alone module containing 8 picosecond pulsed lasers (640, 675, 830, 905, 930, 970, 1020, 1050 nm), a wide-area fast-gated Silicon Photomultiplier and an integrated Time-to-Digital converter [3]. 8 smart optodes are arranged on the sides of a regular ultrasound transducer for US, CD and SWE (Aixplorer Mach 30 by Hologic SuperSonic Imagine S.A.) yielding a handheld multimodal probe for medical imaging.

2.2 The SOLUS database

The SOLUS database is very rich, because 48 different images (12 for each technique) are collected from each patient. In fact, the enrolled subjects are analyzed by 3 radiologists to assess operator independence and each physician acquires B-mode US, CD, SWE and DOT data on 4 different locations to evaluate the contrast between lesion and healthy tissue (lesion main axis, its orthogonal axis, the healthy tissue ipsilaterally and contralaterally). Up to now, 6 malignant and 16

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benign lesions larger than 1 cm have been considered. Among the 22 lesions, 12 belong to BI-RADS 2 category, 3 to BI-RADS 3, 5 to BI-RADS 4 and 2 to BI-RADS 5. Suspicious lesions have been verified via histology after the SOLUS examination.

2.3 The SOLUS performance based on DOT data

An initial performance assessment limited to US-guided DOT data from these 22 patients has already been performed [4]. DOT reconstructions employed the Born approximation of the diffusion equation in heterogeneous settings. Average values for the absorption and composition parameters of the lesions were computed based on the 3D extrapolation from the segmentation implemented on the B-mode image. The 12 DOT acquisitions for each patient were (not rigorously) considered as independent in order to expand the dataset. The absorption and composition parameters were then selected as predictors for a machine learning algorithm devoted to lesion classification, that returned a sensitivity of 91% and a specificity of 75%. Also, the Mann-Whitney U test indicated oxy-haemoglobin and lipids for composition and the wavelengths 640, 830, 905, 1050 nm as the most significant parameters for lesion discrimination.

2.4 Lesion characterization through non-invasive imaging

The techniques available in the SOLUS probe provide different kinds of information:

- US: morphological insight such as shape, spiculation and orientation of the lesion [5].
- CD: vascularization.
- SWE: stiffness.
- DOT: physiological insight about tissue composition, in terms of haemoglobin, water, lipids and collagen concentrations.

A malignant lesion is generally characterized by irregular borders, spiculated and/or angular margins, it may be vascularized, stiff and dense [5]. From an US perspective, density is linked to the echo pattern, while from the optical point of view it means higher content of blood, water and collagen and a lower content of lipids with respect to the surrounding healthy tissue [6].

Based on the US features, lesions can be classified into BI-RADS categories (Breast Imaging-Reporting and Data System [7]) to rank the probability of malignancy:

- BI-RADS 1: no lesions
- BI-RADS 2: benign finding
- BI-RADS 3: probably benign finding (short interval follow-up suggested)
- BI-RADS 4: suspicious for malignancy (biopsy should be considered)
- BI-RADS 5: highly suggestive of malignancy (appropriate action should be taken)

SWE is often used to downstage the BI-RADS of a suspect lesion, *i.e.* improve specificity, which is the ultimate goal of SOLUS. DOT should corroborate such intent, adding quantitative physiological information.

3. RESULTS

The boxplots in Figure 1 show how the absorption coefficients at 640, 830, 905 and 1050 nm on the first row and the oxy-haemoglobin and lipid concentrations on the second correlate with the lesion BI-RADS. Except for BI-RADS 2, all parameters show an increasing trend with malignancy, while lipids a decreasing one, as expected. Applying the Mann-Whitney test to consecutive classes, the p-value is lower than $1.1\ 10^{-4}$ for absorption (2 vs 3, 3 vs 4, 4 vs 5) and $3.2\ 10^{-4}$ for composition (2 vs 3, 3 vs 4). BI-RADS 2 always appears similar to BI-RADS 4 and indeed, they are not significantly different except for oxy-haemoglobin. Population unbalance might have played a role in this unexpected behavior.

Let us now consider a case example of the multimodal approach. Figure 2 depicts the US and SWE images of a lesion initially classified as BI-RADS 4. In fact, the lesion appears not well-defined, with irregular and indistinct borders at B-mode US. However, for CD it is not vascularized and SWE does not highlight the presence of stiff tissue. Also, the machine learning algorithm based on DOT classified it as benign, as later confirmed by the histology. Then, the lesion has been downgraded to BI-RADS 3 and, in a future where SWE and DOT are affirmed imaging modalities, the patient would have been spared a needless biopsy.

Such considerations based on lesion borders irregularity, vascularization and stiffness have been applied also to all the other patients, adding 3 new binary predictors to the classifier. The consequent sensitivity and specificity became almost perfect. Of course, this result is biased by the non-independence of samples and the still small database, but represents an indication of improvement implying that multimodality can be a strength of non-invasive imaging

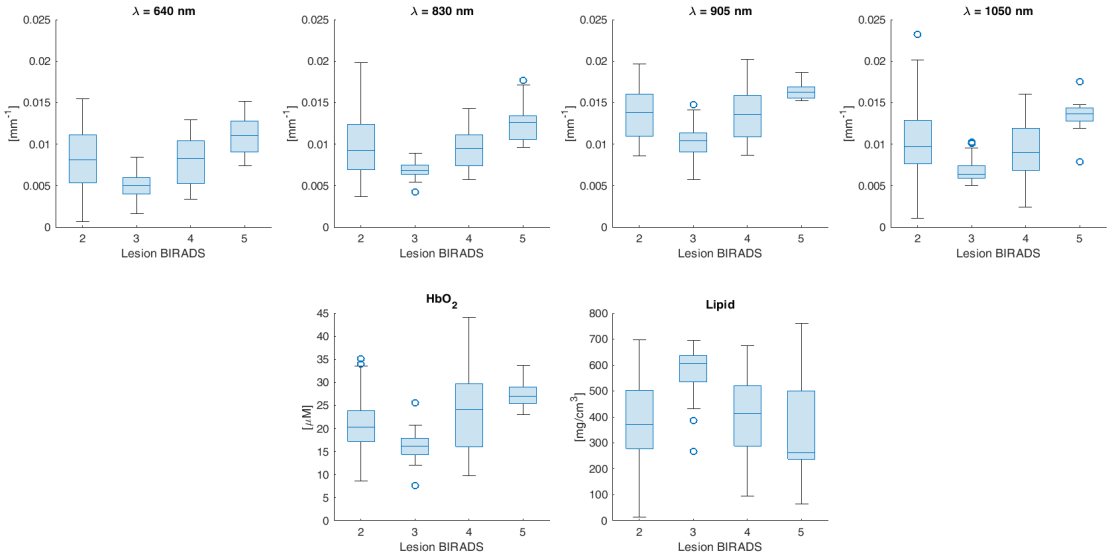

Figure 1: Boxplots for absorption coefficients at 4 wavelengths and 2 constituents concentrations based on lesion BI-RADS.

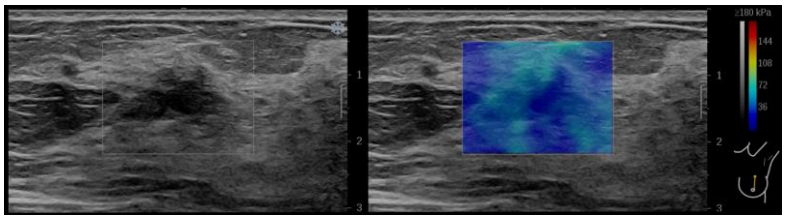

Figure 2: B-mode US and SWE images of a 1.55 cm lesion, recognized as fibroadenoma at histology.

4. CONCLUSION

In this work, we moved the first steps into the multimodal database of SOLUS. We showed some correlations between DOT data and standard radiological data (lesion BI-RADS) and we gave an example of how the combination of techniques is more robust than the single ones. A systematic and rigorous processing of data is required, but initial results are promising.

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