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SOLUS: A Smart OpticaL and UltraSound device for the diagnostics of breast cancer

G. MAFFEIS(1)(*), A. PIFFERI(1), A. DALLA MORA(1), L. DI SIENO(1), R. CUBEDDU(1), A. TOSI(2), E. CONCA(2), A. GIUDICE(3), A. RUGGERI(3), S. TISA(3), A. FLOCKE(4), B. ROSINSKI(5), J.-M. DINTEN(6), M. PERRIOLLAT(6), C. FRASCHINI(7), J. LAVAUD(7), S. ARRIDGE(8), G. DI SCIACCA(8), A. FARINA(9), P. PANIZZA(10), E. VENTURINI(10), P. GORDEBEKE(11) and P. TARONI(1)

(1) *Politecnico di Milano, Dipartimento di Fisica - Milano, Italy*
(2) *Politecnico di Milano, Dipartimento di Elettronica, Informazione e Bioingegneria - Milano, Italy*
(3) *Micro Photon Devices Srl - Bolzano, Italy*
(4) *iC-Haus GmbH - Bodenheim, Germany*
(5) *Vermon SA - Tours, France*
(6) *Commissariat à l'Energie Atomique et aux Energies Alternatives, Laboratoire d'Electronique et de Technologie de l'Information - Grenoble, France*
(7) *Hologic Supersonic Imagine SA - Aix en Provence, France*
(8) *University College London, Department of Computer Science - London, UK*
(9) *Consiglio Nazionale delle Ricerche, Istituto di Fotonica e Nanotecnologie - Milano, Italy*
(10) *Scientific Institute (IRCCS) Ospedale S. Raffaele, Breast Imaging Unit - Milano, Italy*
(11) *European Institute for Biomedical Imaging Research - Wien, Austria*

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Summary. — SOLUS is a H2020 funded project devoted to the design, development and testing in clinics of a Smart OpticaL and UltraSound device for the diagnostics of breast cancer. The collaboration of all partners allowed the first integration of time domain multi-wavelength diffuse optical tomography and commercial B-mode ultrasound imaging, color doppler and shear wave elastography in a handheld probe. The initial results of the clinical validation of the SOLUS system now ongoing on patients with breast lesions are presented.

1. – Introduction

SOLUS is a European project in the framework of the Horizon 2020 programme devoted to the design, development and testing in clinics of a Smart Optical and Ultrasound device for the diagnostics of breast cancer [1]. Smartness stems from purpose (*i.e.*, discrimination of benign and malignant lesions), method (*i.e.*, non-invasive characterization of tissue) and technology (*i.e.*, a multimodal and compact device). The collaboration of all partners allowed indeed the first integration of time domain multi-wavelength diffuse

(*) E-mail: giulia.maffeis@polimi.it

optical tomography (DOT) and commercial ultrasound (US), color doppler (CD), and shear wave elastography (SWE) in a hand-held multimodal probe. These techniques provide information about tissue composition in terms of constituents' concentrations, morphology, vascularization and stiffness, respectively. After being assembled, the instrument has been thoroughly characterized in laboratory on phantoms mimicking the optical and ultrasound properties of breast tissue. Early results of the clinical validation of the SOLUS system now ongoing at San Raffaele Hospital (Milan) on patients with breast lesions will be presented.

2. – Materials and methods

2˙1. *Diffuse optics.* – The innovative part of the probe is time domain multi-wavelength DOT, which relies on diffuse optics. Diffuse optics studies light propagation in turbid media like biological tissues, and can have different implementations [2]. For example, in time domain, in reflectance geometry, light pulses at different wavelengths are injected into the tissue, and output pulses are collected on the same surface, at a certain distance. During propagation, pulses get modified in amplitude, broadening, and delay, due to the absorption and scattering properties of tissue, as described by coefficients μ_a and μ_s.

Once output pulses are collected, the use of multiple wavelengths allows the estimation of the tissue composition through absorption and of its micro-structure thanks to scattering. Operatively, first tissue optical properties μ_a and μ_s are inferred by solving the diffusion equation under diffusion approximation. As a second step, the constituents' concentrations and a and b scattering parameters can be retrieved from the Lambert-Beer law and the Mie empirical model (eq. (1)). In the case of breast, the constituents of interest are oxy- and deoxy-hemoglobin, water, lipid and collagen, while a and b scattering parameters provide information on the size and density of tissue discontinuities, respectively [3]:

$$\mu_a(\lambda) = \sum_i \epsilon_i(\lambda) C_i; \quad \mu_s'(\lambda) = a \left(\frac{\lambda}{\lambda_0} \right)^{-b}, \tag{1}$$

λ is the wavelength, ϵ_i the extinction coefficient, C_i the i-th constituent's concentration, $\mu_s' = \mu_s(1-g)$ the reduced scattering coefficient, g the anisotropy factor, $\lambda_0 = 600\,\mathrm{nm}$ the reference wavelength.

Previous diffuse optical measurements found that lesions are generally characterized by higher content of blood, water and collagen with respect to healthy tissue, which is more adipose. Also, the difference in composition in malignant lesions is even more marked than in benign ones. The breast tissue assessment through DOT thus allows distinguishing among different lesion types [4].

2˙2. *Experimental setup.* – In the last years, diffuse optical technologies experienced a strong boost. Up to 2015, time domain multi-wavelength diffuse optical systems were of the size of a fridge, but since then volumes significantly reduced, until SOLUS set the ambitious goal to shrink everything in few centimeters cube. Indeed, the SOLUS probe is a compact hand held device that contains a regular US transducer and 8 optodes (fig. 1), including components designed and developed specifically for this device thanks to the expertise in imaging and photonics of the partners. The main components of each optode are the fast-gated Silicon PhotoMultiplier (SiPM) detector, 8 pulsed diode lasers in the

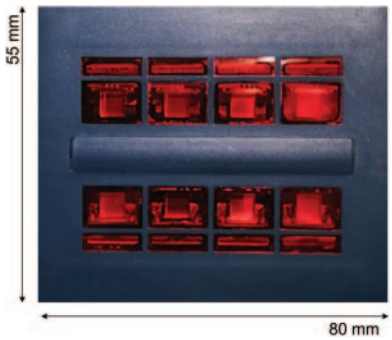

Fig. 1. – Front end of the SOLUS probe. The 8 optodes flank the US transducer.

red and infrared spectral range (640, 675, 830, 905, 930, 970, 1020, 1050 nm) and an integrated Time-to-Digital-Converter [5]. The wavelengths have been selected according to the absorption spectra of the constituents of interest. The crossed optical paths due to the multiple source-detector couples allows for a 3D characterization of the tissue concerned.

2˙3. *Clinical protocol*. – A SOLUS acquisition is a sequence of B-mode US, CD, SWE and DOT. These techniques give complementary information, but there is a special connection between B-mode US and DOT: in fact, at the end of each sequence, the operator records the position and the shape of the lesion by marking its contours on the US image, so to give *a priori* geometrical constraints to DOT. This improves localisation and quantitation of tomography itself. For each patient, the sequence is repeated at 4 different locations: lesion main axis, orthogonally to the previous position, far from the lesion on the same breast and on the contralateral breast in mirrored position. This is needed because optical assessments are based on the contrast between lesion and healthy tissue. Also, different views enable a more complete assessment of the lesion. So far, 22 patients have been recruited, 16 benign and 6 malignant cases.

2˙4. *Data analysis*. – The US-based segmentation and 3D extrapolation allow identifying 2 regions on the image: the one that delimits the lesion, and the surrounding breast tissue. The computation of average values for absorption and constituents' concentrations helps discriminate benign from malignant lesions. Focusing on lesion values, even though the dataset is limited, an initial attempt of classification was performed by exploiting machine learning techniques, in particular a K nearest neighbours algorithm. The quality of the outcome is measured in terms of sensitivity and specificity. The first represents the percentage of malignant lesions correctly recognised as such, while the second represents the percentage of benign lesions correctly recognised as such. At this preliminary stage, analysis is referred to optical data only, focusing on composition.

3. – Results

The boxplot in fig. 2 displays the absorption properties of malignant and benign breast lesions as a function of wavelength. Even though distribution partly overlaps, it can be observed that the median absorption of malignant lesions is always higher than in benign ones, as expected.

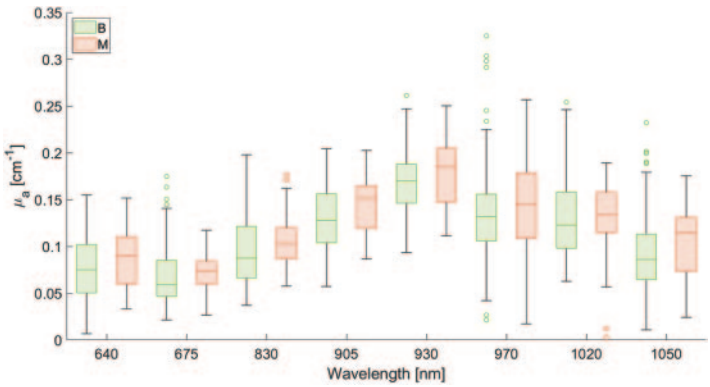

Fig. 2. – Comparison of the absorption coefficient of benign (green) and malignant (red) lesions.

As regards lesion classification, the machine learning algorithm returned 91% sensitivity, while specificity is 75%, in line with the other imaging modes.

4. – Conclusion

In conclusion, SOLUS aims at a more specific non-invasive diagnosis of breast cancer by means of a multimodal tomographic system. The initial results obtained only on optical data are promising, but the dataset is becoming richer and richer thanks to the ongoing clinical trial, and the future inclusion of information obtained from all US techniques will give the possibility of improving analysis and better define performances.

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