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Solid heterogeneous phantoms for multimodal ultrasound and diffuse-optical imaging: an outcome of the SOLUS project for standardization

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ABSTRACT

In the last decade, multimodal imaging raised increasing interest to overcome the limits of single techniques and improve the diagnostic potential during the same examination. This gives rise to the need for phantoms and procedures for standardizing performance assessment of the multimodal instrument. The SOLUS[1] project adopts this methodology with the aim to build a multimodal instrument (based on diffuse optics -DO-, shear wave elastography -SWE-, and ultrasound imaging -US-) to increase the specificity of breast cancer diagnosis. Here we propose a long-lasting phantom based on silicone material (easier to manipulate with respect to other material for bimodal phantom such as polyvinyl alcohol, PVA) and suitable for both diffuse optical imaging/tomography and ultrasound acquisitions, designed within the SOLUS project. To achieve this goal, we explored a new silicone material for diffuse optics and ultrasound (Ecoflex 00-30), creating a new fabrication recipe and demonstrating its suitability for multimodal imaging if coupled to another silicone elastomer (Sylgard 184), featuring similar optical and acoustical performances except for the echogenicity. The main advantage of the proposed phantom is the capability of tuning independently optical and acoustical performances, thus allowing one to mimic a wide range of clinical scenarios.

Keywords: diffuse optical spectroscopy, diffuse optical tomography, ultrasound, phantom, multimodal imaging

1. INTRODUCTION

In the last years, scientists and industrials working in the biophotonics field have pushed towards the standardization of the procedures for performance assessment of newly developed instruments in order to ensure the objective comparison of the effectiveness of different systems. To achieve that goal, a series of tests should be defined, as well as the key parameters to be evaluated. Within this need for standardization, years ago the diffuse optics community started to define protocols for the assessment of the basic hardware performances (BIP protocol[2]) as well as the capability of systems to detect and quantify an inhomogeneity and recover optical properties of an homogeneous medium (nEUROPt and MEDPHOT protocols, respectively[3,4]). Together with the protocols, new phantoms were developed to perform the tests[4,5]. However, to the best of our knowledge, up to now neither protocols nor specific phantoms dedicated to their implementation have been developed for diffuse optical tomography.

Recently, many works were published on the combination of different imaging techniques to improve the diagnosis of several diseases. In particular, ultrasound (US) imaging was proposed in conjunction with diffuse optics (DO) for diagnostic breast imaging[6]. In this context, the SOLUS project[1] (a 4-year EU funded H2020 project started in November 2016) aims to build a multimodal imaging system to improve the specificity of the diagnosis of breast cancer, combining B-mode US imaging to derive morphologic information, SWE for tissue stiffness, DO for tissue composition. Such a system will also use the US information to improve the spatial resolution and chromophores quantification[7,8] of the tissues constituents obtained using DO.

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To mimic the breast and to test the performances achievable with both DO and US, there is the need to build multimodal phantoms with different optical properties (to be retrieved by DO) and echogenicity (to be imaged by US) that should be tuned independently. The phantoms should also be heterogeneous, to mimic lesions in breast tissue, and long-lasting, for convenient and reliable use. To meet these requirements, we conceived, developed, and characterized a phantom kit (with different geometrical parameters such as inclusions sizes and depths), where the optical and acoustical properties can be set independently. Here we present a subset of the phantom kit and its characterization, assessing its suitability for combined US and DO acquisitions under proper conditions as detailed in section 2.

2. PHANTOM PREPARATION

To build a phantom suitable for US measurements we need two materials featuring different echogenicity. To obtain long-lasting phantoms, we use a silicon rubber (Ecoflex 00-30, Smooth-On, Inc. PA, USA, “Eco” in the following) and a silicone elastomer (Sylgard S184, Dow Corning Corp. CA, USA, “Syl” in the following). Eco was used to prepare one bulk (thickness = 40 mm, with cavities to host inclusions) and 3 slab as top layers (thickness = 25 mm, 15 mm and 5 mm). It is a new material for DO phantoms, thus requiring to develop a recipe to get the desired optical properties (here, absorption coefficient μ_a = 0.1 cm^{-1} and reduced scattering μ_s’= 10 cm^{-1} at 690 nm). Syl was used to obtain inclusions (volume = ~1 cm^3 and 6 cm^3) with a different echogenicity with respect to the bulk and/or different optical properties (here μ_a = 0.2 cm^{-1} and μ_s’ = 10 cm^{-1} at 690 nm). For both materials, titanium (IV) oxide powder (Sigma Aldrich, USA, in the following “TiO_2”) and toner powder (Infotec, Toner Black 46/l) were added in calibrated quantities to give the desired scattering and absorption coefficient. As absorber we use toner powder, since it shows flat absorption over the spectral range of 600-1100 nm. To avoid any refractive index and/or acoustical impedance mismatch, a calibrated mixture of liquid Eco with TiO_2 was used as a matching fluid between contact surfaces (e.g. in the cavities hosting the inclusions).

3. PHANTOM CHARACTERIZATION

The US characterization of the phantoms was done using an SL18-5 ultrasonic probe on an Aixplorer v11 system, (Supersonic Imagine, S.A., France) operating in Fundamental mode with customized preset (i.e. demodulation frequency 5 MHz transmit and receive, voltage 72 V, and 2 half cycles). The speed of sound within the Eco or Syl material was measured at 980 m/s using a pulse-echo substitution method and this value has been set on the ultrasound imager for image reconstruction. To compare other US properties of the Syl/Eco we used the 040GSE phantom (Computerized Imaging Reference Systems, Inc., Virginia, USA) as a reference. The optical images of the phantom were taken using a time domain imager for mammography[9,10] (scanning grid: 85 x 110 mm with 1 mm step to cover the whole phantom, for each pixel the integration time was set to 100 ms). The contrast was computed for each pixel using the nEUROPt[3] protocol definition, i.e. the number of counts between the current pixel and a homogeneous part of the phantom (a 10 x 10 mm^2 area where there is no effect of the inclusion).

The phantom characterization should demonstrate the following features: i.1) the Eco/Syl material shows an echogenicity reasonably comparable to commercially available ultrasound phantoms, i.2) that Eco and Syl materials exhibit significantly different echogenicity levels to show background/inclusion ultrasound contrast and i.3) a sufficient low US attenuation; ii) the optical properties (i.e. the addition of toner and TiO_2 particles) of both Syl inclusions and Eco bulk phantom are not affecting the US image quality; iii) the different material used (i.e. showing different echogenicity) for inclusions and bulk should not affect DO imaging (i.e., no optical contrast should be detected when the optical properties of Eco and Syl are the same).

Eco and Syl feature different echogenicity among them (i.e. -8.3 dB and -32.9 dB respectively, where CIRS 040GSE is taken as the 0 dB reference, see requirement i.2), while they show a similar attenuation coefficient (3.1 dB/cm/MHz vs 3.2 dB/cm/MHz respectively). Although those values do not match CIRS 040GSE attenuation level of 1.1 dB/cm/MHz, they are still compliant with requirement i.3. A relative echogenicity level of -8.3 dB is sufficiently high to be displayed on an ultrasound image at 5 MHz, whereas a -32.9 dB echogenicity level appears as black and can be used to mimic a hypoechoic lesion behavior (requirement i.1). The proposed materials can be considered suitable for multimodal phantoms since they fulfill the ultrasound requirements i.1 to i.3 (this guarantees enough ultrasound contrast compatible with the chosen acquisition geometries) while keeping the same optical properties (optical spectra of Eco and Syl have been demonstrated to be the same provided that the recipe is well calibrated, data not shown).

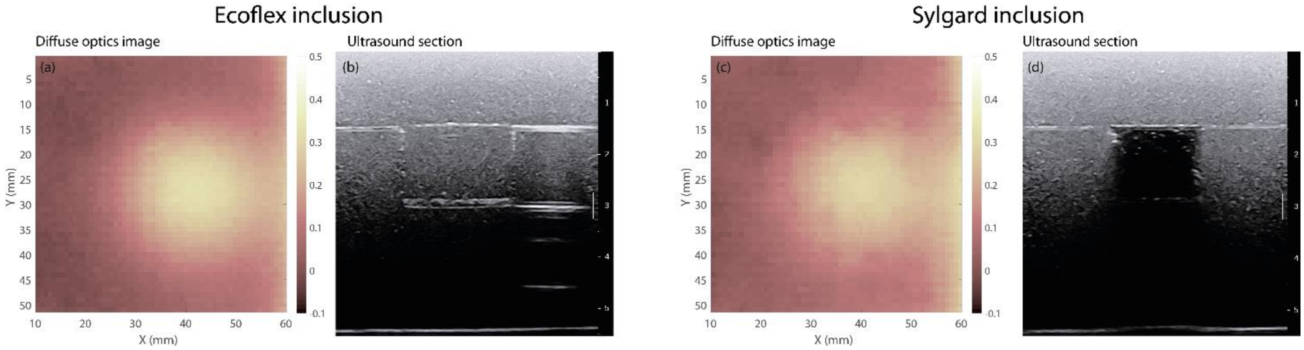

Figure 1. DO images -(a) and (c)- and US section -(b) and (d)-.

As expected, from the DO image it is not possible to distinguish between Eco and Syl inclusions (see (a) and (c)), meaning that the two materials produced exactly the same optical perturbation (i.e. contrast) if the optical properties are matched. On the other hand, even if the optical properties are different (i.e. different concentration of toner for Eco inclusion and Eco bulk, in this case) the Eco inclusion is not seen at US as the echogenicity of the material is not affected by the absorber (same results were obtained with TiO_2 addition, data not shown). The capability to see a perturbation using the US is connected to the choice of the material. Indeed, looking at picture (d) the inclusion is clearly visible and it is represented as a hypoechoic volume. It is also possible to notice that the thickness of the top layer (15 mm) is correctly retrieved.

To conclude, we developed a recipe for long-lasting silicon-based inhomogeneous phantoms, whose optical and acoustical characteristics can be tuned independently, thus allowing one to simulate different clinical scenarios were new multimodal systems can be challenged.

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