The LUCA device - Laser and Ultrasound Co-Analyzer for Thyroid Nodules

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ABSTRACT

We present the current status of the LUCA project whose aim is to develop an innovative device combining ultrasound and diffuse optics for an improved screening of the thyroid cancer.

Keywords: thyroid cancer, near-infrared diffuse optical spectroscopy, diffuse correlation spectroscopy, time resolved spectroscopy, multimodal imaging.

1. INTRODUCTION

Thyroid cancer is a major and growing health challenge with more than five hundred thousand new cases diagnosed worldwide annually [1]. The goal of the thyroid screening (>2 million screenings/year in Europe) is to identify high-risk nodules for malignancy, for further, more invasive evaluation and potentially a surgical intervention, and to avoid missing any malignant nodules. After an initial ultrasound screening, which is poor in sensitivity and in specificity, depending on the suspected type of the nodule, the most common tool to test malignancy is ultrasound-guided fine needle aspiration biopsy (FNAB) of the suspicious nodule. However, the effectiveness of the FNAB in thyroid cancer is also limited. A large number of non-diagnostic and/or false positive FNAB results lead to unnecessary surgeries [2]. The high prevalence of thyroid nodules (up to 76% of the population if screened with ultrasound) implies that even modest improvement in strategies to characterize lesions could have a great impact - not only in terms of better therapeutic outcomes, but also in terms of a more efficient use of health resources. This calls for new modalities and biomarkers to be introduced for an increased sensitivity and specificity of the screening process.

The LUCA project aimed to tackle this need by developing a point-of-care device for the screening of thyroid nodules. The device is based on near-infrared diffuse correlation spectroscopy (DCS) [3] and time-resolved spectroscopy (TRS) [4] combined with an ultrasound system (US) [5] and a probe that enables multimodal data acquisition. LUCA device allows the retrieval at the same time of information about tissue hemodynamics (microvascular blood flow, blood oxygenation), chemical constitution (scattering spectrum, collagen, water and lipid concentrations) as well as anatomy. This may overcome the shortcomings of present techniques assuring a better screening for malignant nodules. LUCA-project involves a multidisciplinary team of eight partners, including end-users in endocrinology and radiology, three research groups in the field of optics, opto-electronics and bio-photonics and industry players with a background in development of innovative photonic and ultrasonic components and medical devices. The first phase of the project was focused on the development and construction of new, low cost and high quality opto-electronic components, while the second phase on implementation and clinical validation of the LUCA device.

Here, we present the current status of the LUCA-project (36 months from the beginning).

2. THE LUCA DEVICE

There are four main technologies involved in the LUCA device: US, DCS, TRS and the multimodal probe. Furthermore, the LUCA device will exploit a dedicated module for the data analysis.

-The Ultrasound technology is the current standard technology used in the screening of thyroid cancer (EXAPad, IMV Imaging – U.K.). For this technology the focus is on the innovation challenges involved in the integration of the extra information provided by the optical module and the new hybrid probe. In this respect a specific software interface was developed to exchange information with the optical and post-processing modules.

-DCS and TRS have reached commercial-level maturity as independent solutions. TRS is used for the determination of chromophore concentrations such as oxy/deoxy-hemoglobin, water, lipid and collagen [4]. The DCS system measures deep tissue micro-vascular blood flow [3]. The LUCA DCS module is characterized by a custom fiber coupled laser system and a 16 channel detection system, based on four synchronized four channel autocorrelators. The newly custom developed components allows a reduction of the costs of 5-10 times with respect of a standard DCS system. The 8-wavelength LUCA TRS module exploits eight custom fiber-coupled pulser diode lasers, Silicon Photomultipliers (SiPM) detectors, and a two channel time-correlated single-photon counting system based on Time-to-Digital Converter (TDC). The cost for all TRS sub-systems is about five times lower than equivalent systems based on commercially-available sub-components.

-The hybrid optics/US probe acquires optical and US data and deliver them independently to each module. The probe contains DCS and TRS source and detector fibers, the US transducer and two laser safety controls (i. e. a manual button and a contact sensor).

-Data analysis has a dedicated module inside LUCA device consisting in a computer with a dedicated graphic processing unit (GPU) for calculations. A NIRFAST [6] toolbox for TRS has been implemented, while a NIRFAST toolbox for DCS has been completely developed for the LUCA project. The data analysis system processes the output provided by LUCA device to calculate hemodynamics and components related to a selected region of interest (i. e. the thyroid nodule)

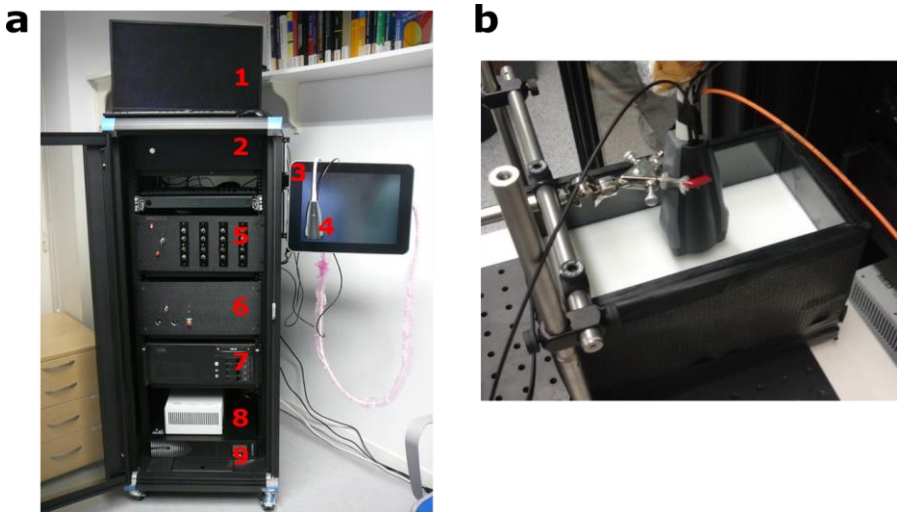

Figure 1. (a) The LUCA device: 1- Optical main module monitor; 2- Optical main module; 3- US module; 4- Multimodal optical-US probe; 5- DCS module; 6- TRS module; 7- Processing unit (NIRFAST); 8- Medical grade isolation transformer; 9- Uninterruptible power supply (UPS) unit. (b) Experimental setup for preclinical phantom testing.

3. PRECLINICAL TESTS

Before the clinical testing campaign (starting in spring 2019), the integrated LUCA device has been tested with dedicated liquid phantoms (Figure 1 (b)), suitable for all the technologies involved in LUCA. The phantoms are made of

water/glycerol solutions, with Lipofundin as scattering element [7]. In Figure 2 we report exemplary results of the standard phantoms tests we performed, consisting in simultaneous US, DCS and TRS acquisitions. In Figure 2 (a) it is reported an US image with a region of interest (ROI) highlighted (a syringe tube tip). In the LUCA measurement protocol, the US image together with the selected ROI shape and the acquired optical data is sent to the NIRFAST module for the post-process analysis. Figure 2 (b) reports the capability of the LUCA device of detecting changes in the particle Brownian diffusion coefficient D_b in phantom with different viscosities (i. e. changes in blood flow index). Figures 2 (c) and (d) reports the measured absorption and reduced scattering coefficients, obtained both with a real time diffusion model fitting, and with the NIRFAST post process fitting. All the measurements performed with LUCA well reproduce the expectations of the theory.

In this talk, we will present the current status of the LUCA-project, focusing on the technological advances of components and device, and preclinical tests.

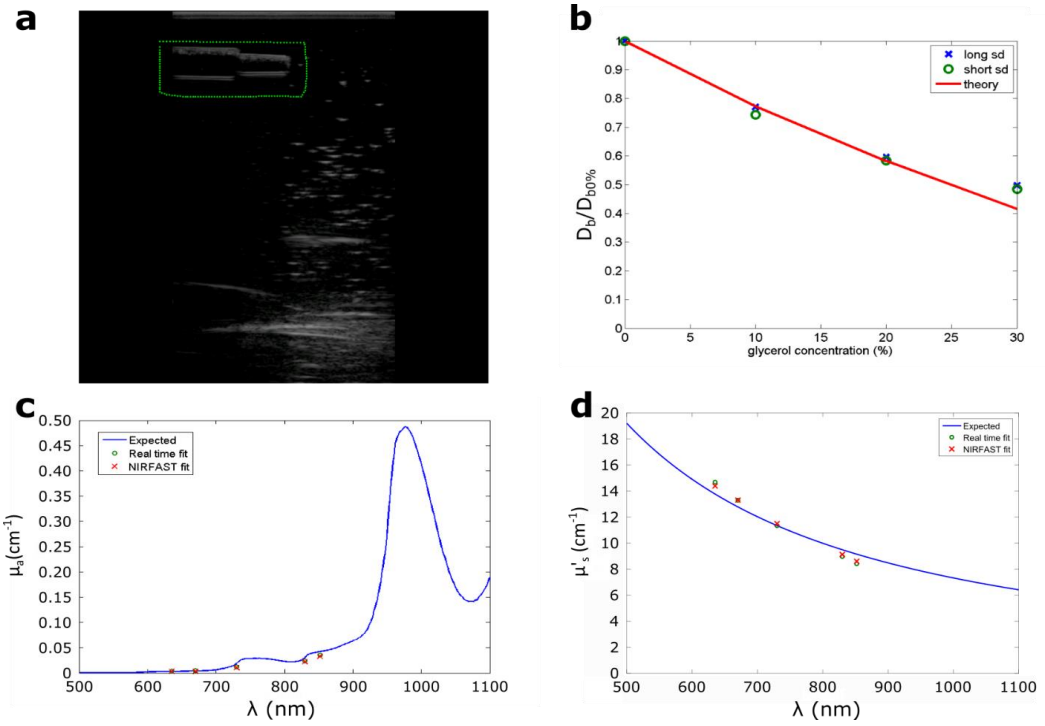

Figure 2. (a) Processed US image delimitating the region of interest (a syringe tube tip); (b) Ratio of the measured D_b of 4 different phantom with different viscosities measured considering the two different source-detector fibers separation allowed by the LUCA probe (long s-d separation 2.5 cm, short s-d separation 1.5 cm); (c) Absorption coefficient measured at 5 wavelengths together with the expected water absorption; (d) Reduced scattering coefficient measured at 5 wavelengths together with the expectations [7]. Green and red symbols are related to real time semi-infinite diffusion model fitting and NIRFAST post process fitting respectively.

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