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In-vivo handheld optoacoustic tomography of the human thyroid

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ABSTRACT

We interrogated the application and imaging features obtained by non-invasive and handheld optoacoustic imaging of the thyroid in-vivo. Optoacoustics can offer complementary contrast to ultrasound, by resolving optical absorption-based and offering speckle-free imaging. In particular we inquired whether vascular structures could be better resolved using optoacoustics. For this reason we developed a compact handheld version of real-time multispectral optoacoustic tomography (MSOT) using a detector adapted to the dimensions and overall geometry of the human neck. For delivering high-fidelity performance, a curved ultrasound array was employed. The feasibility of handheld thyroid MSOT was assessed on healthy human volunteers at single wavelength. The results were contrasted to ultrasound and Doppler ultrasound images obtained from the same volunteers. Imaging findings demonstrate the overall MSOT utility to accurately retrieve optical features consistent with the thyroid anatomy and the morphology of surrounding structures.

1. Introduction

Multispectral optoacoustic tomography (MSOT) can visualize functional and molecular parameters of tissue at high resolution while also reaching tissue depths of several mm to few cm [1]. Using targeted contrast agents the modality enables high sensitivity and specificity to molecular parameters of disease. Several studies have highlighted possible applications of the technique in a clinical context, including follicular thyroid carcinoma [2], cardio vascular disease [3,4] and arthritis [5]. MSOT thereby operates on optoacoustic images acquired at different optical excitation wavelengths to identify contrast agents that otherwise fail to generate sufficient signal strength to be discernible from the intrinsic background absorption (e.g. hemoglobin). In turn, optoacoustic images are produced by shining light of transient intensity onto tissue and detecting ultrasound signals generated by thermoelastic expansion of structures that have absorbed the incident light energy. By operating in the near-infrared, it was shown that vascular structures can be imaged up to 4 cm deep inside tissue. In particular, images of the human carotids [6] and other deep-seated vascular structures [7–9] have been shown.

Handheld implementation of MSOT is of particular interest in a clinical setting as it allows flexible utilization at the point of care. For this reason previous designs of handheld optoacoustic scanners attempted the extension of common linear ultrasound arrays by optical components (laser and light guides) to also enable combined optoacoustic and sonography imaging. In 2005 the first such system was introduced [10] with subsequent designs attempting various improvements to achieve better frame rates, penetration depth or signal-to-noise ratio [11–14]. Advantages of this design pattern include good availability of components such as detection arrays and acquisition electronics and simple co-registration with the sonographic image. On the other hand, the design suffers from low image quality due to strong artifacts and low transversal resolution (i.e. parallel to the array axis), which also limit the achievable imaging depth in tissue.

We have shown in [6] that the image performance in hand-held operation improves significantly when using curved ultrasound arrays, as opposed to linear arrays more commonly used in ultrasound imaging. Sonography employs beam-forming techniques to shape the excitation pulse and focus on the region of interest when detecting highly directive echo signals. In contrast, optoacoustic imaging has only limited capacity to actively determine the tissue volume to be excited, because photon scattering rapidly renders any light focused at the tissue surface diffusive. Furthermore, optoacoustic waves generally (i.e. in case of point sources) propagate in all directions and ideally require

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detection on a spherical surface completely enclosing the illuminated volume. Hence, the image quality achieved depends largely on the geometry of the detection array. Curved arrays allow the collection of a more complete projection data-set which can be employed together with model-based inversion algorithms [15] to more accurately represent the underlying light-absorption distribution.

Optoacoustic imaging, considered in handheld mode, can visualize a new set of human tissue features by resolving absorbing structures with resolution similar to the one achieved by clinical ultrasound imaging. In this work we interrogated features that could be visualized when imaging the thyroid. In particular we were interested in investigating anatomical markers associated with optoacoustic thyroid imaging and comparing the relative performance of optoacoustic and ultrasound imaging when focusing on anatomical and vascular structures.

2. Materials and methods

The optoacoustic system employed in this study was based on a previously described multispectral optoacoustic tomographic device [6] modified by improved illumination (laser and fiber bundle) and mechanical components for optimal water coupling and handheld operation. In particular, the previously chosen fiber bundle and optical diffuser combination was replaced by a custom tailored solution that provided a sharper illumination stripe on the skin surface. Fig. 1 shows the schematic of the handheld measurement probe, its implementation and operational use. The curved detector array consisted of 64 individual elements with a common radius of 40 mm and angular span of 172° within the x-y plane. Elements were mechanically focused in elevation (z-axis) and capable of detecting optoacoustic signals at frequencies of up to 7.5 MHz. The array was connected to a 12-bit custom made data acquisition (DAQ) system digitizing all channels in parallel at 40 MSamples/s. An in depth characterization of the array can be found in [15]. For optimal acoustic coupling the array cavity was filled with de-ionized water and sealed using acoustically and optically transparent foil. This highly flexible foil in combination with ultrasound gel, to lubricate contact between foil and human skin, enabled excellent coupling to the human body. A double O-ring sealing gasket ensured leak-proof operation. Optical excitation was provided by a (slow) tunable pulsed laser system, SpitLight 600 OPO (InnoLas Laser GmbH, Germany), which enabled a repetition rate of 10 Hz. Light delivery was facilitated by a custom made fiber bundle with rectangular output of $40 \times 0.9\,mm^2$ size (CeramOptec GmbH, Germany). The fiber bundle was mounted on the detection array such that an adjustable angle was formed to the x–y plane. For optimal results the beam was always directed at the array middle in z and illuminated an elongated stripe of approximately $50 \times 5\,mm^2$ size. The maximum light fluence measured on the tissue at the wavelength employed (800 nm) never exceeded $20\,mJ/cm^2$.

Image reconstruction from the digitized acoustic data was performed in two ways. During the measurement sessions live imaging was enabled using a delay and sum algorithm implemented on a high-performance graphics card (<30 ms/image). A reconstructed view of $40 \times 40\,mm^2$ at 600×600 pixels allowed optimal navigation and probe positioning during the measurement. To increase accuracy and image quality the same view was later reconstructed using a model-matrix inversion scheme [16], which had previously been shown to yield superior imaging results [17,18]. In addition optoacoustic images were post-processed by window and leveling to improve contrast.

In this study we focused on the thyroid lobes in healthy human volunteers. Fig. 2(a)shows a schematic anatomical depiction of a human thyroid in situ. We attempted cross-sectional imaging at the location marked "imaging plane". Two healthy female volunteers were imaged using the same detector and configuration, each scan following the same protocol. The measurement protocol was split in two imaging sessions, optoacoustic and ultrasound imaging. First an optoacoustic scan involved imaging of both lobes and the connecting isthmus to understand thyroid anatomy, depicted in Fig. 1(c). In a second session the same procedure was repeated using a commercial ultrasound system, Terason 2000+ (Teratech Corp., USA). The ultrasound scan revealed thyroid anatomy and included Directional Power Doppler to better visualize vasculature based on directional flow measurement.

3. Results

For each volunteer a large optoacoustic dataset was produced (>2000 images) and validated by Directional Power Doppler and echo-ultrasound, recording short image sequences at corresponding positions. For each ultrasound position a matching set of optoacoustic images could be identified by manual inspection. To facilitate a concise description of results, we show here the same position as indicated in Fig. 2(a) for both thyroid lobes, each from a different volunteer.

Fig. 2 further shows results from the left thyroid lobe of the first volunteer. The optoacoustic image, depicted in Fig. 2(b), allows immediate identification of large features characteristic of the anterior neck such as the carotid artery and the trachea, which appears round and dark as ultrasound cannot penetrate or escape from air filled cavities. Similarly, high vascularization within muscles allows identification of the sternocleidomastoid and an infrahyoid muscle. Although deeper seated the thyroid lobe can also be distinguished. In particular thyroid vascularization within the anterior part is clearly visible as indicated by the group of vessels surrounding marker 3. Vessels appearing as round bright dots traverse the imaging plain in a perpendicular angle while others, elongated or dashed in shape, cross through the imaging plane at lower angles. To validate these findings Fig. 2(c) depicts the corresponding echo-ultrasound image in grayscale with

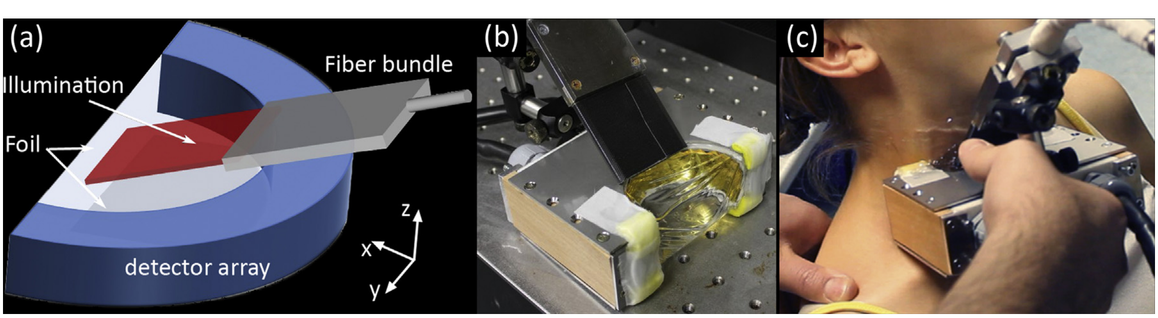

Fig. 1. Non-invasive handheld optoacoustic probe: (a) schematic, (b) implementation, (c) operational use.