Photoacoustics 10 (2018) 48–53

Contents lists available at ScienceDirect

Photoacoustics

journal homepage: www.elsevier.com/locate/pacs

Research article

Imaging of blood flow and oxygen state with a multi-segment optoacoustic ultrasound array

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ARTICLE INFO

Article history:
Received 12 January 2018
Received in revised form 3 April 2018
Accepted 23 April 2018
Available online 27 April 2018

Keywords:
Optoacoustic imaging
Ultrasonography
Multimodal imaging
Photoacoustics
Color Doppler

ABSTRACT

Changes in hemodynamic parameters are directly linked to biological function and physiological activity. Characterization of hemodynamics is commonly performed by Doppler ultrasound, which provides accurate measurements of blood flow velocity. Multi-spectral optoacoustic tomography is rapidly undergoing clinical translation fostered by its unique and complementary capacity for label-free mapping of the blood volume and the distribution of oxy- and deoxy-hemoglobin in blood. Here we report on a hybrid optoacoustic and ultrasound imaging approach that enables multi-modal imaging of blood flow and oxygen state using a multi-segment detector array. We further demonstrate rendering of multi-modal pulse-echo ultrasound, multi-spectral optoacoustic tomography, and color Doppler images from carotid artery of a healthy subject.

1. Introduction

Simultaneous measurement of multiple hemodynamic parameters is of high importance for the understanding of tissue function and disease progression. Hemodynamic responses are normally produced in response to physical or organ activity, environmental changes as well as neural activity to guarantee proper oxygen delivery to tissues [1,2]. Majority of cardiac and vascular disorders are similarly related to systemic hemodynamic dysfunction, so that hemodynamic measurements are essential in their timely diagnosis and treatment monitoring [3]. Color Doppler ultrasound (US) has arguably become the gold standard for mapping the distribution of blood flow. Handheld US scanners are extensively employed in the clinics for diagnosing blood clots, defects in heart valves, blockage in arteries and numerous other conditions [4]. Owing to its unique capability for non-invasive label-free mapping of the distribution of oxy- and deoxy-hemoglobin deep in living tissues, multi-spectral optoacoustic tomography (MSOT) has recently found widespread use in preclinical imaging applications [5,6] and is undergoing rapid clinical translation in various point-of-care diagnostic applications, such as melanomas [7,8], inflammatory bowel (Crohn's) disease [9], breast abnormalities [10], thyroid cancer [11,12] or peripheral vascular diseases [13].

Efficient integration between MSOT and US in a hybrid hand-held scanner is expected to further accelerate clinical translation of MSOT and significantly enhance imaging performance of the stand-alone systems by simultaneously delivering their highly complementary contrasts. While a number of possible hybridization approaches have been previously suggested [14–18], such an efficient combination is inherently challenged by the fundamentally different excitation and image formation strategies behind the two modalities. Recently, a hand-held probe based on a multi-segment detector array combining linear and concave segments with different inter-element pitch has been reported [19,20]. The different parts of the array provide optimized performance for each modality, hence enabling accurate multi-modal optoacoustic and pulse-echo US imaging. The linear segment may additionally be exploited for other US modes, such as Doppler US.

Here we adopted the multi-segment array approach in order to achieve multi-modal MSOT, pulse-echo US and color Doppler imaging in a hand-held mode. The experimental performance of the multi-modal approach is further showcased by imaging the carotid artery region of a healthy volunteer, where Doppler US is commonly used for the detection of vascular abnormalities, such as stenosis or intraluminal turbulence [21].

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https://doi.org/10.1016/j.pacs.2018.04.002

2. Methods

2.1. Experimental setup

The main system components used for the acquisition of MSOT and US data have been described elsewhere [19,20]. In short, for the MSOT data acquisition, a pulsed Nd:YAG-pumped optical parameter oscillator (OPO) laser source (InnoLas Laser GmbH, Krailling, Germany) is operated at 25 Hz repetition rate, a peak pulse energy of 25 mJ at 730 nm, and a wavelength in the 680–900 nm range tunable on a pulse-by-pulse basis. The excitation light is guided to the specimen via a custom-made fiber bundle (CeramOptec GmbH, Bonn, Germany) resulting in an incident fluence of <10 mJ/cm^2 at the skin surface for the entire wavelength range of interest, well below the maximum permissible exposure limits recommended by the ANSI standards [22].

The transducer array employed in this study (Imasonic SaS, Voray, France) has nominal Tx/Rx bandwidth of 60% around 7.5 MHz central frequency. It combines segments of linear (L) and concave (C) geometry (Fig. 1a). The L segment consists of 128 elements with 0.25 mm (1.25λ) inter-element pitch while the two C segments each have 64 elements with their individual elements separated by a pitch of 0.6 mm (3λ). The concave segments lie on a 40 mm radius arc and all their elements are cylindrically focused at a distance of 38 mm within the common imaging plane. The elements of the linear segment are focused at 34 mm distance from the active aperture.

The OA signals collected by the array probe were digitized by a custom-made data acquisition system (Falkenstein Mikrosysteme GmbH, Taufkirchen, Germany) at a sampling rate of 40 MS/s. The signals were subsequently transferred to a designated PC station using a 1-Gbit Ethernet connection. Image reconstruction was performed using OpenCL-based GPU code.

Pulse-echo US signal acquisition was performed by four 64-channel PCIe acquisition boards (two transmit and two receive boards) custom-built by S-Sharp Corporation, Taiwan. The acquired signals were transferred to the main motherboard, where CUDA-based image reconstruction on a high-level GPU was performed and the images were ultimately transferred as binary raw data files via Ethernet to the main PC. Switching between OA ("receive-only") and US ("transmit-receive") imaging modes was facilitated through a custom-made programmable multiplexing unit (MUX) connected to the transducer array and controlled via a laser-triggered signal from the OA data acquisition system. Any possible acquisition conflict was avoided by allocating strictly defined non-overlapping time windows for the OA and US data recording and processing [20]. Moreover, frame time-stamping enables clearly differentiating the incoming data streams from the different modalities. Only the latest frames with the closest time stamps are overlaid for the multi-modal representation.

Two basic operation modes were enabled by the acquisition hardware, namely, (1) interleaved MSOT and pulse-echo US by means of synthetic transmit aperture (STA) beamforming or (2) interleaved MSOT and duplex US (color Doppler combined with pulse-echo US) by means of dynamic receive focusing (DRF) beamforming, also known as B-scan mode. Switching between the two modes was performed manually.

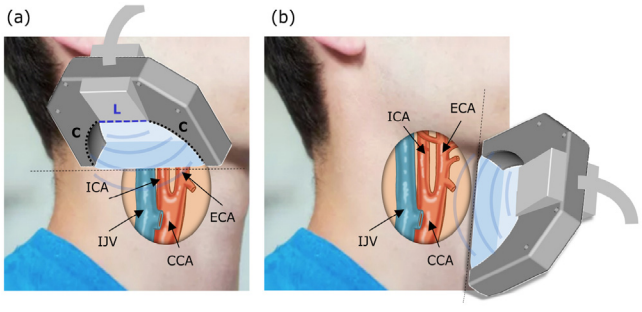

Fig. 1. Geometry of the multi-modal (MSOT, pulse-echo US, and color Doppler) image acquisition with the multi-segment probe in a) transverse and b) longitudinal planes. ICA: internal carotid artery; ECA: external carotid artery; IJV: internal jugular vein; CCA: common carotid artery.

2.2. MSOT imaging

For the MSOT image formation, the optoacoustic signals acquired with all the 256 multi-segment array elements were first pre-processed with a band-pass finite impulse response (FIR) filter (0.05 and 10 MHz cut-off frequencies) and deconvolved with the simulated electrical impulse response of the transducer, obtained using a 2D Gaussian function assuming a detector center frequency of 7.5 MHz, a bandwidth of 60%, and a sampling frequency of 40 MS/s. Two-dimensional OA images were then reconstructed with a standard back-projection algorithm in a field of view (FOV) of 17×30 mm (150 μm pixel size).

For spectral unmixing, the OA images were acquired at seven wavelengths (700, 730, 760, 780, 800, 825, and 850 nm) in order to accurately sample the absorption spectrum profiles of the endogenous chromophores of interest. To minimize the negative effect of motion on the unmixing accuracy, the probe was kept still during acquisition of the multi-wavelength data. Alternatively, motion artefacts in multi-spectral imaging can be effectively averted by using microsecond-delayed triggering of multiple lasers [23], which was however not attempted in the current study. The distributions of oxy- and deoxy-hemoglobin were subsequently rendered by means of spectral fitting of unaveraged single-wavelength images to the known absorption spectra of oxy- and deoxy-hemoglobin [24], and the resulting 2D maps of the specific chromophore distribution were visualized using pseudo-color coding. This type of visualization does not permit quantitative evaluation of blood oxygen saturation but rather intended for visualizing the distribution of oxy- and deoxy-hemoglobin.

2.3. Pulse-echo STA US and duplex US image acquisition

In the pulse-echo US mode, single-cycle 20 Vpp bipolar pulses at 7 MHz frequency were transmitted. The 128 elements of the linear array segment were used for US image formation by employing a synthetic transmit aperture (STA) focusing technique [25]. The concave parts of the array were not considered for US image formation as those would introduce grating-lobe artefacts associated to the large inter-element pitch of the concave segments [20]. The method was realized by sequential pulse transmission from individual elements and detection of the back-scattered echoes with all the array elements. The sampled channels were then stored to build 128 low-resolution images (LRIs) corresponding to each event of an unfocused emission of an ultrasonic pulse from a single element and acquisition of the resulting echoes by all the other elements. The LRIs were formed using delay-and-sum (DAS) beamforming within a FOV of 17×30 mm with a pixel size of 200 μm. The LRIs from subsequent transmit events were coherently summed to form a final high-resolution image (HRI). The LRIs add up at points where the isochronal lines, i.e. those connecting pixels with the same time of flight, overlap on a real scatterer. At other locations, the individual images add incoherently resulting in a much lower signal level. In this way, the STA algorithm synthetically focuses both the transmitted and back-scattered fields throughout the entire image. In our experiments, the synthetically focused beam intervals were set to 200 μm.