Real-time *in vivo* photoacoustic and ultrasound imaging

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Abstract. A real-time photoacoustic imaging system is designed and built. This system is based on a commercially available ultrasound imaging system. It can achieve a frame rate of 8 frames/sec. Vasculature in the hand of a human volunteer is imaged, and the resulting photoacoustic image is combined with the ultrasound image. The real-time photo acoustic imaging system with a hybrid ultrasound probe is demonstrated by imaging the branching of subcutaneous blood vessels in the hand. [DOI: 10.1117/1.3005421]

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Blood vessels play a key role in homeostasis, growth, and repair of tissue. Knowledge on the presence of blood vessels, and the content of hemoglobin and its degree of oxygenation, yield crucial information regarding various applications in medicine, ranging from oncology to dermatology.

A promising new technique to obtain both anatomical and functional information about the vascular bed is photoacoustic imaging. In photoacoustic imaging, a pressure transient is generated on absorption of a short pulse of light by a tissue chromophore (e.g., hemoglobin). Measurement of the pressure waves at the tissue surface enables reconstruction of the absorbed energy distribution, which yields information on the hemoglobin concentrations.

Recently, photoacoustic imaging has successfully been applied to *in vivo* imaging of blood vessels in small animals[1–3] and humans.[4–8]

Clinical application of photoacoustic imaging is hampered by its long imaging time, which leads to patient discomfort, movement artifacts, and consequently a low temporal resolution. Photoacoustic imaging systems based on a commercial ultrasound system are a logical next step toward clinical introduction. Systems reported in the literature that could be used for *in vivo* imaging in reflection mode (i.e., illumination and detection at the same side of the tissue) required a multi-channel data-acquisition system and a computer to reconstruct the images.[5,9]

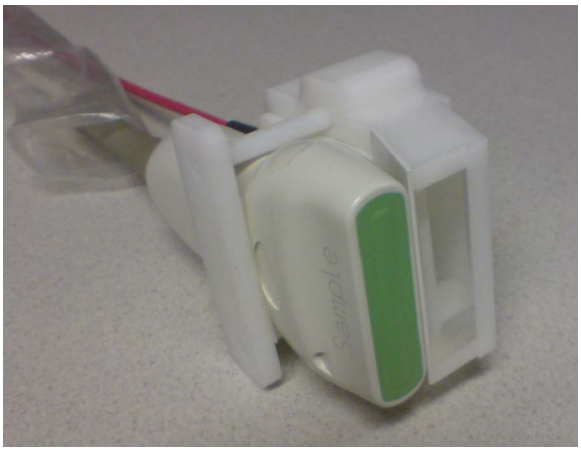

Fig. 1 Optical system attached to an existing ultrasound probe.

We present an approach in which we do not need this additional data-acquisition system and computer, as we utilize the data acquisition as well as hardware-implemented image reconstruction of a conventional ultrasound imaging system. The developed system is able to reconstruct the photoacoustic images of *in vivo* vasculature in real time with a frame rate of 8 frames/sec. As this photoacoustic imaging system is based on a commercial ultrasound system, it provides hybrid photoacoustic and ultrasound imaging without the need for additional algorithms and hardware to capture the signals and reconstruct the images.

An ultrasound imaging system (Picus, ESAOTE Europe BV, Maastricht, the Netherlands) was modified to synchronize the data acquisition with the firing of the laser. In addition, the emission of the ultrasound could be switched off during photoacoustic imaging. To detect the (laser-generated) ultrasound, a linear array (L10-5, 40 mm, 128 elements, 7.5-MHz central frequency, 75% −6-dB bandwidth) was connected to this ultrasound imaging system.

An optical system was developed that could be connected to this linear array (Fig. 1) to construct a hybrid photoacoustic-ultrasound transducer. Through this optical system, an area of tissue with a size of 5×20 mm^2 was illuminated with light pulses from an Nd:YAG laser (Diny pQ, IB laser, Berlin, Germany) with an energy of 1.9 mJ/pulse, a pulse repetition frequency of 1000/s, and a pulse duration of 8 ns.

The photoacoustic and ultrasound images were reconstructed using the traditional hardware-implemented delay-and-sum beam forming algorithm of the ultrasound system, and were displayed in real time on the screen of the ultrasound system. These images consisted of 128 lines (A-scans). The images were presented by plotting the rectified rf data in a 2-D image plane (B-scan). In this way, the upper and lower part of the blood in the lumen of the vessels is visualized.[10] Reading 128 lines (B-scan) at a laser pulse-repetition rate of 1 kHz resulted in an image acquisition time of 128 msec for a single frame (frame rate 8 frames/sec), which is an enormous improvement in temporal resolution compared to re-

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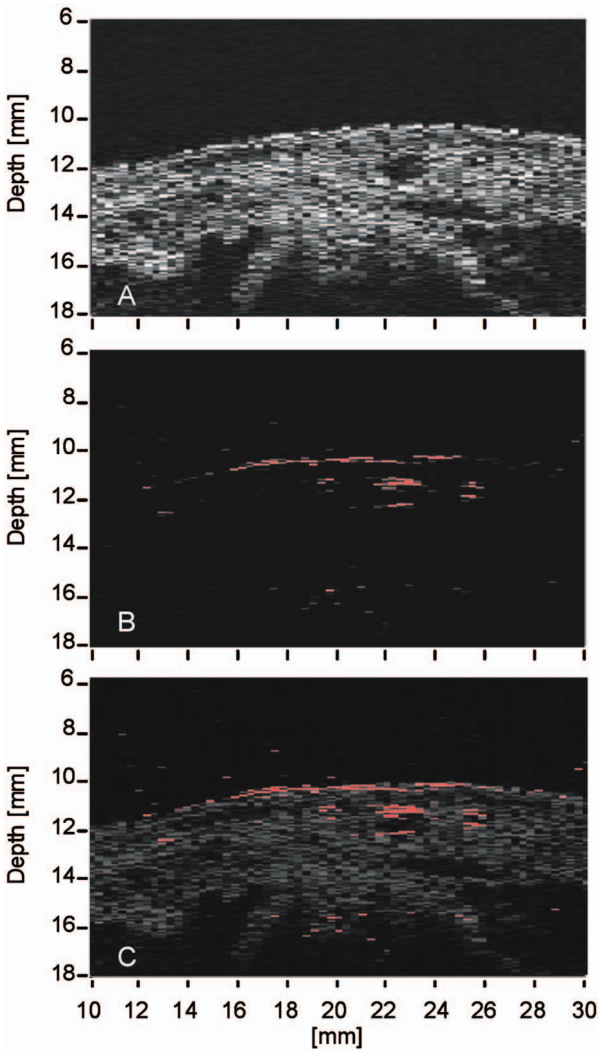
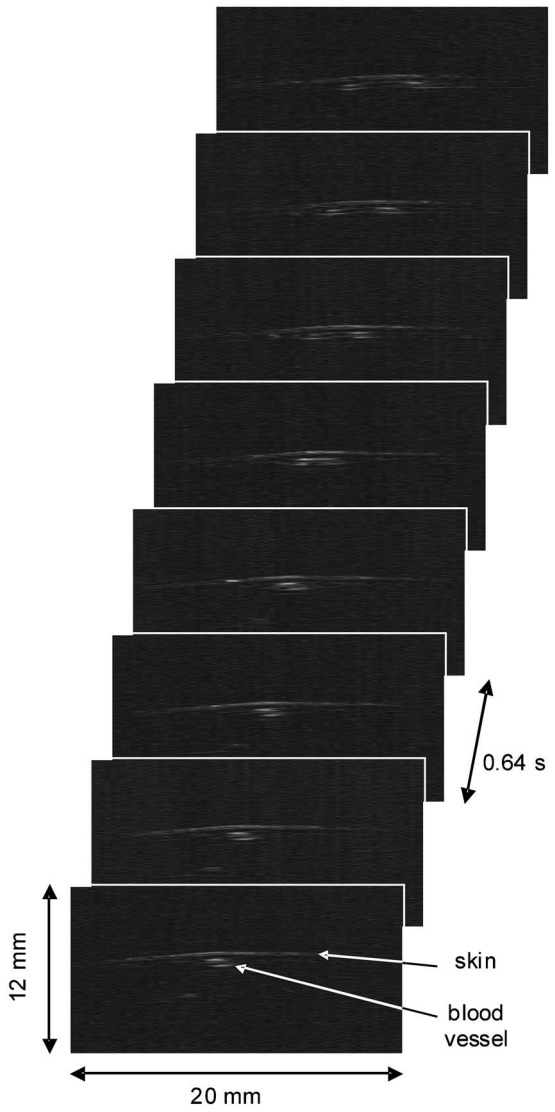


Fig. 2 Images of the dorsal side of the left hand of a human volunteer: (a) ultrasound image, (b) photoacoustic image, (c) combined image. The acquisition time for the images was 128 msec (8 frames/sec).



Video 1 Real-time photoacoustic imaging of the dorsal side of the left hand of a human volunteer. In this image, frames 0, 5, 10, 15, 20, 25, 30, and 35 are shown to visualize the branching of a single vessel into two blood vessels. The time between these frames was 0.64 sec. (QuickTime, 900 kb). [URL: http://dx.doi.org/10.1117/1.3005421.1].

ported *in vivo* photoacoustic imaging times in the order of 2 min for a single B-scan.[6,8] The images were stored on a personal computer by acquiring the rf data of the individual image lines (A-scans) with an oscilloscope card (NI5112, 8-bits, 100 MS/sec, National Instruments, Austin, Texas). To view these stored images, no additional image-reconstruction algorithms are required.

Combined ultrasound and photoacoustic imaging was performed on the dorsal side of the hand of a human volunteer. To ensure the acoustic coupling between the skin and the photoacoustic-ultrasound probe, the hand was immersed in water. The gap between the probe and tissue surface was about 11 mm. The resulting images are presented in Fig. 2.

The ultrasound image [Fig. 2(a)], based on the reflection of ultrasound pulses, visualizes different tissue structures. In the photoacoustic image [Fig. 2(b)], the absorbed energy distribution is displayed, visualizing the contour of the skin as well as blood vessels inside the tissue. The largest blood vessel (axial diameter 1.2 mm) that is observed in the photoacoustic image (x=22 mm, depth=12 mm) is also visible in the ultrasound image as a black region (low reflection of ultrasound). The presence of the smaller vessel (x=25 mm, depth=12 mm, axial diameter 0.6 mm) is less predominant in the ultrasound image, but it is clearly visualized in the photoacoustic image. The even smaller vessel (x=13 mm, depth=12.5 mm, axial diameter about 0.2 mm) is not visible in the ultrasound image. In Fig. 2(c), the ultrasound and photoacoustic images are combined into a single image. At a depth of about 16 to 18 mm, in the center of the image, a photoacoustic signal is observed. This is most likely a reflection of the photoacoustic signals of the superficial blood vessels (in the image at a depth of about 12 mm) at the underlying bone. The bone is visualized as a semicircular structure with low ultrasound intensity in the ultrasound image x=16–26 mm; depth =15 to 18 mm).

In Video 1, the branching of vessels at the dorsal side of

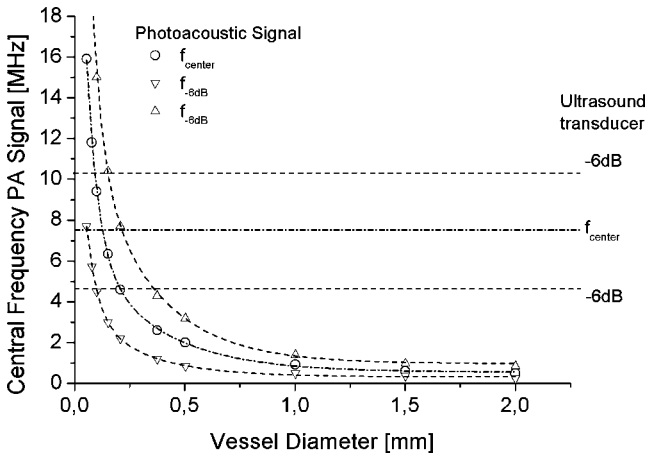


Fig. 3 Central frequency and −6-dB bandwidth of the photoacoustic signal as a function of vessel diameter. The central frequency and −6-dB bandwidth of the 7.5-MHz transducer are plotted as well (horizontal dashed lines).

the left hand of a human volunteer is shown in real time with a frame rate of 8 frames/sec.

To image vessels with a diameter of 0.6 to 1.2 mm, the bandwidth of the transducer that has been used in this study was not optimal. In Fig. 3, the −6-dB frequency range of the photoacoustic signal[10] is plotted versus the blood vessel diameter, along with the frequency range of the ultrasound transducer. From this figure, it can be concluded that the transducer that was used is mainly suited for imaging vessels with a size of about 100 μm. The large vessels that were observed in the images (diameter 0.6 to 1.2 mm) have a central frequency that lies well outside the bandwidth of the transducer. However, these vessels were well visible in the images. The bandwidth of the smaller vessel with a diameter of about 0.2 mm matches well with the bandwidth of the ultrasound transducer. To further improve the images, a larger bandwidth is preferred or, if one is solely interested in imaging vessels with a diameter in the order of 1 mm, a transducer with a lower central frequency should be chosen.

Compared to the systems reported in the literature,[5,9] the system described here has the advantage that it is based on a conventional ultrasound system, not requiring a 128-channel high speed digitizer in combination with a personal computer to capture the data and reconstruct the images. For a single image we need 128 laser pulses. To achieve a frame rate of 8 frames/sec, this implies that a laser is needed with a repetition rate of 1 kHz. This relatively large repetition rate has consequences for the maximum permitted exposure, as described in the International Electrotechnical Commission (IEC) laser safety standard.[11] For measurements lasting longer than 10 s, the MPE is limited to 1 mJ/cm^2.

While the probe in this study would need further optimization for frequency range and sensitivity, this work makes clear that photoacoustic imaging can easily be added to a conventional ultrasound system as an additional contrast mechanism without the need for additional acquistition and processing means.

We have presented a combined photoacoustic and ultrasound-imaging system that can reconstruct images in real time and that can achieve a frame rate of 8 frames/sec, for a photoacoustic B-scan composed of 128 A-scans. *in vivo* imaging of vasculature was shown, as well as combined photoacoustic and ultrasound imaging. In ultrasound images, blood vessels show up as voids, which may not be distinguishable from other structures with low ultrasound reflection. As photoacoustic imaging is able to visualize vasculature with a high contrast, it finds potential application in medicine, ranging from angiogenesis assessment (e.g., the ability of tissue to heal or of the tumour to sustain itself and grow), to dermatogy (e.g., port wine stain treatment). The shown addition of real-time photoacoustics to a commercial ultrasound system is an important step towards clinical application. In fact, this demonstration brings us to the threshold of introducing photoacoustics as an add-on modality to conventional ultrasound devices.

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