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Ring-shaped confocal photoacoustic computed tomography for small-animal whole-body imaging

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ABSTRACT

We report herein a novel three-dimensional photoacoustic computed tomography (PACT) system for small-animal whole-body imaging. The PACT system, based on a 512-element full-ring ultrasonic transducer array, was cylindrically focused and capable of forming a two-dimensional image in 1.6 seconds. The pulsed laser could either illuminate directly from the top or be reshaped to illuminate the sample from the side. Top illumination was mainly used for mouse brain and mouse embryo imaging. Side illumination provided *in vivo* anatomical images of an adult mouse. By translating the mouse along the elevational direction, the system provided serial cross-sectional images.

Keywords: Photoacoustic computed tomography, small-animal imaging, whole-body imaging, focal-line image reconstruction

1. INTRODUCTION

Due to the widespread use of animal models for human disease studies, small-animal imaging plays an increasingly important role in biomedical research. Previously, the majority of small-animal whole-body imaging systems were based on magnetic resonance imaging (MRI) or X-ray computed tomography (X-ray CT) for anatomic evaluation, and positron emission tomography (PET) for functional evaluation. However, these imaging techniques have their own limitations, for instance, X-ray CT and PET utilize ionizing radiation, which may be carcinogenic and will confound experimental results in oncology, and MRI requires a very high magnetic field and long imaging time (more than one hour) for small-animal imaging.

Recently, photoacoustic imaging emerged as a promising tool for small-animal imaging [1, 2]. By combining optical sensitivity and ultrasonic imaging depth scalability, this hybrid technology provides high-resolution images beyond the diffusion limit of optical microscopic imaging technologies. Over the past few years, several array-based photoacoustic whole-body imaging systems have been proposed, including 64-element arc array [2, 3], 64-element half-ring array [4], and 128-element hemisphere array [5]. However, these systems have either limited boundary coverage or a long data acquisition time, which limits their applications on pre-clinical research. In this report, we present a novel whole-body imaging system based on a 512-element full-ring ultrasonic transducer array.

2. SYSTEM DESIGN

Figure 1 shows the schematic diagram of the system. The key components include a 512-element full-ring ultrasonic transducer array, a 64-channel data acquisition (DAQ) system, and two laser systems.

The 512-element full-ring transducer array (Imasonic, Inc.) has a central frequency of 5 MHz and a reception bandwidth greater than 80%. The piezocomposite elements were spaced with a lateral pitch of one wavelength (0.3 mm) and a kerf of 0.1 mm. The array element was mechanically shaped into an arc to produce an axial focal depth of 19 mm within the imaging plane. The combined foci of all elements generate a central imaging region of 20 mm diameter and 1 mm thickness. The elevation focus and the small pitch enable each array element to be treated as a point detector in a two-dimensional (2D) image reconstruction. During the experiment, signals acquired from all 512 elements were first amplified and selected by a custom-designed connector board consisting of 512 preamplifiers, 64 8:1 multiplexers, and

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64 post-amplifiers, and then digitalized by a 64-channel data acquisition system [6]. The two stage amplification achieves a total gain of 60 dB. Due to the 8:1 multiplexing, the current system can acquire one frame of data per 1.6 seconds.

The excitation source consists of two lasers. An optical parametric oscillator (OPO) laser, tunable from 400 to 680 nm and 740 to 2000 nm, and a Ti:sapphire laser, tunable from 680 to 900 nm. The laser beam was first homogenized using a ground glass, and then passed through a conical lens to form a ring-shaped light. The ring-shaped light was then focused using an optical condenser made from acrylic to project a light band around the animal. The thickness of the light band was 5 mm, and the diameter was determined by the cross-sectional diameter of the animal. By removing the conical lens and the optical condenser, the system can also provide planar top illumination for brain [7] and embryo imaging [8].

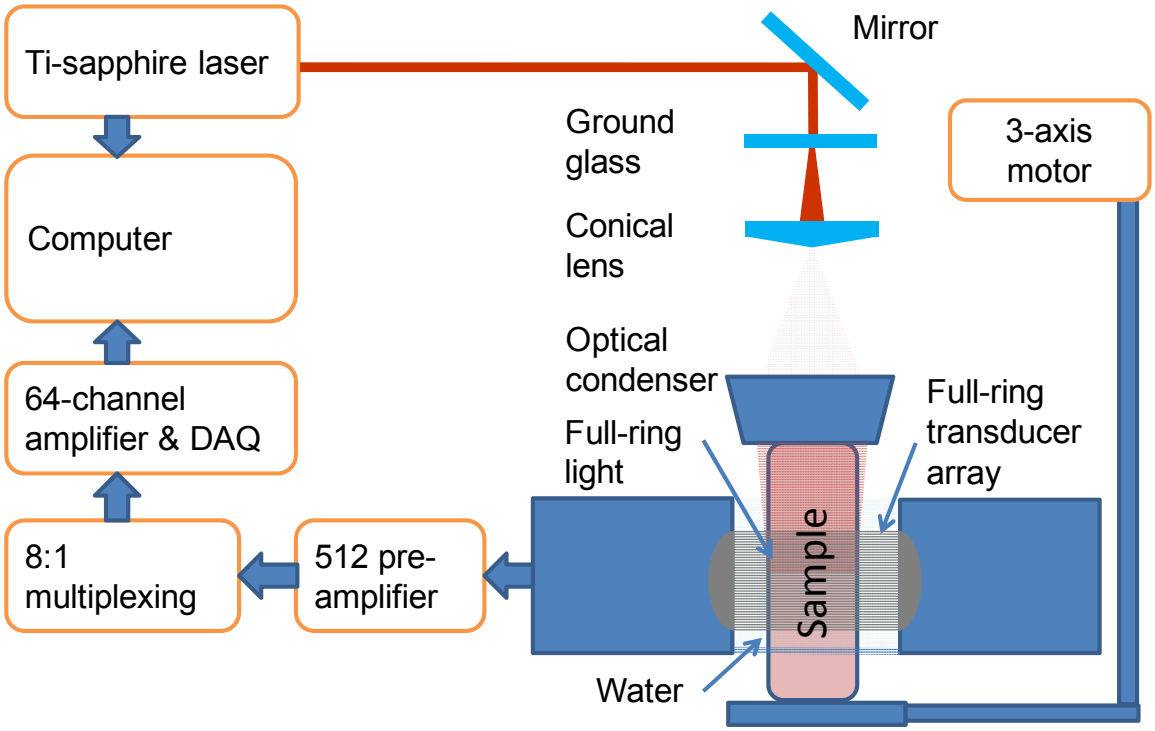


Figure 1. Schematic diagram of the photoacoustic computed tomography system for small-animal whole-body imaging.

3. IMAGE RECONSTRUCTION

Due the elevation focus of the transducer element, the detector cannot be treated as a point detector in a three-dimensional (3D) image reconstruction. Instead, we can treat the focal line of the detector as an auxiliary line for applying appropriate delays in the 3D image reconstruction [8]. As shown in figure 2, to compute the delay of a point A in the 3D space, we first project A to the *x*-*y* plane (B). Point B is then connected to the center point of the transducer (C), crossing the focal line at point D. We then connect A and D, and extend the line to reach the transducer at E. The line AE is always perpendicular to the transducer surface (CD=DE), and is used for calculating the delay time between the imaging point A and the transducer. In the 3D image reconstruction, the original time-domain photoacoustic signals from each transducer are back-projected into the 3D imaging space based on the calculated delay time, and are then summed to form the reconstructed image [8, 9].

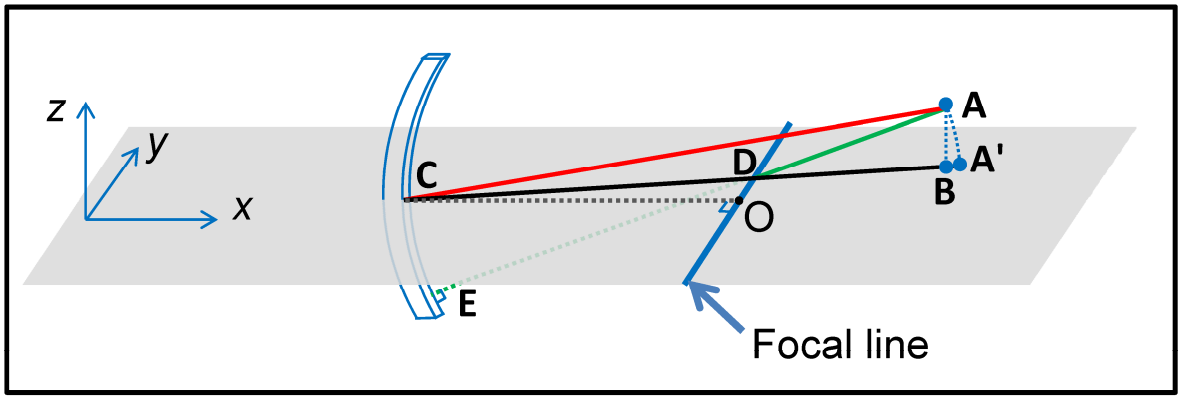
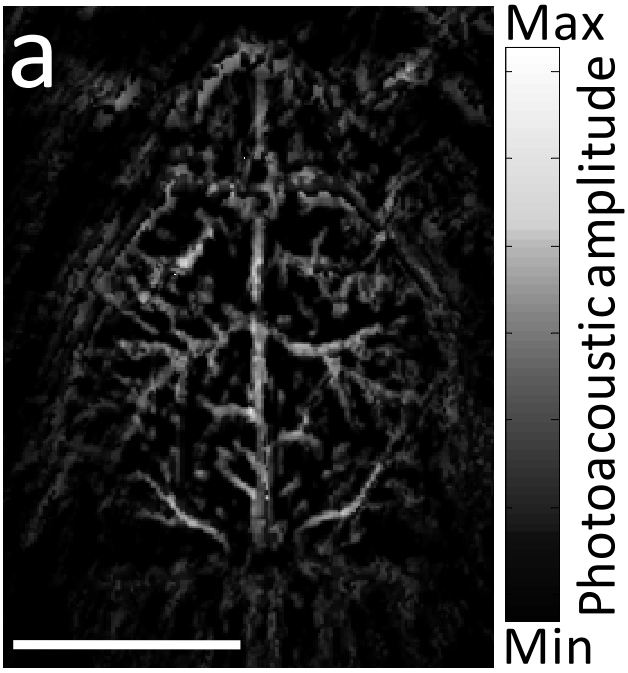
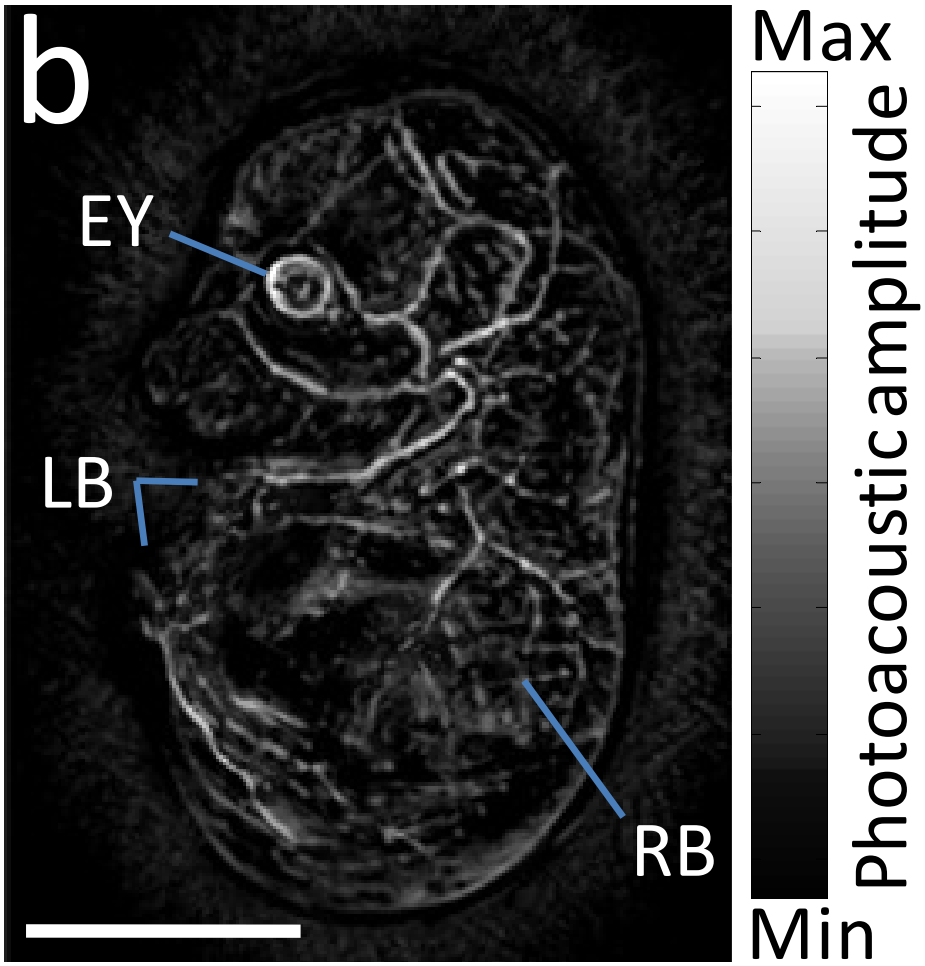


Figure 2. Schematic of the 2D reconstruction, 3D direct reconstruction, and 3D focal-line reconstruction concepts. A: point of reconstruction. A': point A projected in 2D reconstruction. A'C: 2D reconstruction delay. AC: 3D direction reconstruction delay. AE: 3D focal-line reconstruction delay. *x*-*y*: 2D reconstruction plane. The focal line is perpendicular to the transducer plane (*x*-*z*).

4. RESUTLS

Figure 3a is an *in vivo* cortical vasculature image of an adult mouse with intact skin and skull. Figure 3b is an *ex vivo* image of a 15-day-old mouse embryo fixed in a gelatin gel. Figures 3a and 3b were acquired over a depth of 6 mm and 9 mm, respectively, and maximum-amplitude-projected along the elevation direction. The 3D focal-line reconstruction algorithm was utilized to generate these images. Figure 3c is an in vivo cross sectional image of an adult mouse. Figures 3a and 3b were acquired using the top illumination scheme, and figure 3c was acquired using the side illumination scheme.





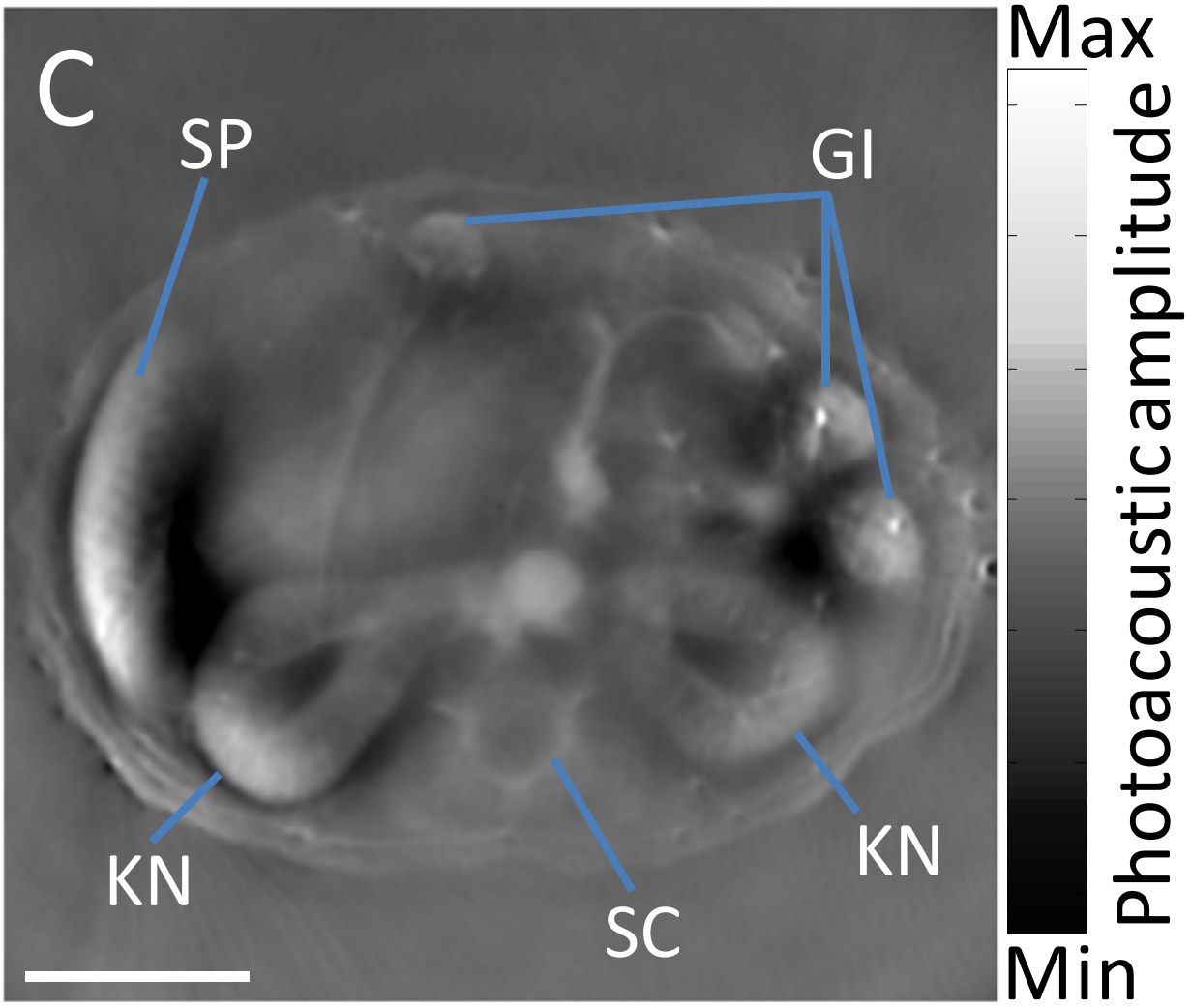


Figure 3. *In vivo* and *ex vivo* photoacoustic computed tomography images of mice. **a**. Maximum-amplitude-projection image of the cortical vasculature in a living adult mouse. **b**. Maximum-amplitude-projection image of a 15-day-old mouse embryo fixed in a gelatin gel. **c**. Cross-sectional image of a living adult mouse. EY, eye; GI, GI tract; KN, kidney; LB, limbs; RB, ribs; SC, spinal cord; SP, spleen. Scale bar, 5 mm.

5. CONCLUSION

A new small-animal whole-body imaging system has been developed based on the full-ring ultrasonic transducer array. The new system has an in-plane resolution of 0.1 mm and a frame rate of one frame per 1.6 seconds. Images of the mouse brain, embryo, and kidneys were successfully acquired using the system.

6. ACKNOWLEDGEMENTS

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