Preclinical photoacoustic imaging endoscope based on acousto-optic coaxial system using ring transducer array

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Received April 1, 2010; revised May 28, 2010; accepted June 8, 2010; posted June 16, 2010 (Doc. ID 126347); published June 29, 2010

We developed and fabricated a preclinical photoacoustic imaging endoscope (PAIE) with an acousto-optic coaxial structure for cavity imaging that integrates a Plexiglas tube, an optical fiber, a ring transducer array, a taper reflector, and an ultrasonic coupling medium. A photoacoustic image for a section of pig colorectal tissue embedded in a transparent gelatin phantom was reconstructed. Furthermore, human colorectal cancer and normal colorectal tissue were imaged *ex vivo* with a contrast ratio of ~2.3. Experimental results demonstrate that the PAIE has potential for detecting colorectal cancer in clinical use.

OCIS codes: 170.2150, 110.5120, 170.1420.

Photoacoustic (PA) imaging utilizing excitation from a pulsed laser energy source is a noninvasive imaging method [1,2]. In recent years, PA imaging has attracted considerable attention, and it has been successfully applied in tumor vascular imaging [3], brain functional imaging [4], and detection of breast tumors [5]. It provides structural and functional imaging *in vivo* with optically scattered biological tissue. However, because the imaging resolution can be inadequate at large depths, applications of the above are not related to imaging of internal organs, such as the wall of the stomach, esophagus, and intestines. In fact, endoscopic PA imaging can obtain the internal organ image; therefore, it was necessary to develop endoscopic PA imaging for detecting lesions of internal organs.

Over the past three years, endoscopic PA imaging technology has been developed and applied. Sethuraman *et al.* used an intravascular PA imaging (IVPA) system to image rabbit arteries *ex vivo* with a commercial intravascular ultrasound probe [6]. The presence of inflammation in the atherosclerosis plaque was detected by the IVPA system [7]. Yang *et al.* reported a PA endoscopy microscopy system with a single ultrasonic transducer for PA signal collection, and a rat abdominal surface was imaged *in situ* [8]. The above systems need to rotate the detector or mirror to receive PA signals in a 2π view.

To curtail the time of signal acquisition, we have newly designed and fabricated a fast preclinical photoacoustic imaging endoscope (PAIE) based on a ring transducer array. The sound, light, and ring transducer array are coaxial, the structure of which makes the PAIE receive the PA signals in a 2π view without rotating the ultrasound transducer. The ring transducer array is connected with the parallel acquisition system, and PA signals from all elements are collected simultaneously. The parallel acquisition system can collect data quickly; the acquisition time of a set of data is only 0.05 s.

Figure 1(a) shows the schematic of the new PAIE. It includes a Plexiglas tube (polymethyl methacrylate), a ring transducer array with 64 elements, a taper reflector, an optical fiber (core diameter of 0.6 mm, NA = 0.22), and an ultrasonic coupling medium with water and glycerin. The length and the diameter of the Plexiglas tube are 95 mm and 30 mm, respectively. The vertex angle of the taper reflector shown in Fig. 1(b) is ~123°, the length and diameter of which are 15 mm and 10 mm, respectively. The ring transducer array shown in Fig. 1(c) is hollow, and the optical fiber is inserted in the hole as the excitation light source. The resonance frequency of the ring transducer array is 6 MHz with a −6 dB bandwidth of 60%. Its inner and outer diameters are 5 mm and 10 mm, respectively. The sensitivity of the ring transducer array is 1.8 μV/Pa. The optical fiber and the ultrasonic coupling medium are separated by the transparent plastic film to prevent contact between each other. The energy density of the pulse laser is ~20 mJ/cm^2.

In the PAIE system, a Nd:YAG (yttrium aluminum garnet) laser (Brilliant B, Big Sky) with a wavelength of 1064 nm, output of 8 ns pulse width, and repetition rate of 20 Hz is used, and the laser is transmitted with an optical fiber. The laser reflected by the taper reflector is formed into a ring beam to irradiate the sample, and the PA signal is generated due to thermal expansion.

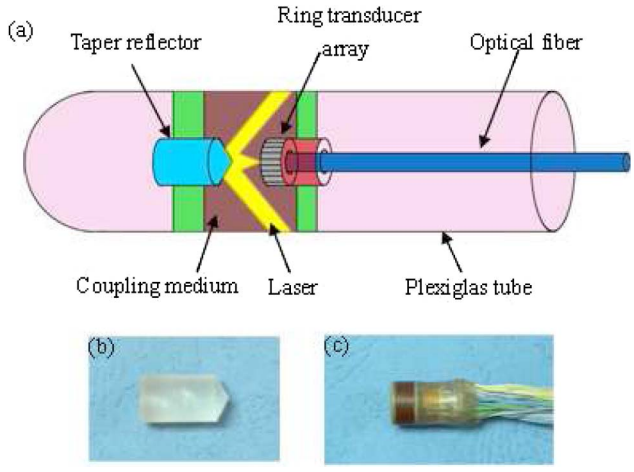

Fig. 1. (Color online) (a) Schematic of the PAIE. (b) Photograph of the taper reflector. (c) Photograph of the hollow ring transducer array.

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The PA signal is detected by the ring transducer array and then collected by the parallel acquisition system. The data are stored by a personal computer. The radial and transverse resolutions of the PAIE system were measured by experiments, and they are ~0.32 mm and ~2.4 mm, respectively.

The components of the parallel acquisition system consist of an analog signal processing board and a digital signal processing board. The 64-element ring transducer array is connected with the parallel acquisition system by the RDL-156 ZIF connector. The 64-channel PA signals are sent to the analog signal processing board and processed by amplification and two antialiasing filters, and then the analog signals are sent to the digital signal processing board for analog-to-digital conversion. After analog-to-digital conversion, the digital PA signals are collected and temporarily stored by a temporary staging module controlled by the laser Q-switched signal. When the data acquisition is completed, the data are transferred to the personal computer through the USB interface for data processing and storage. The parallel acquisition system is working at a sampling rate of 40 MHz.

Colorectal cancer, with a high death rate, is one of the most common malignant tumors in the world, ranking third among malignant tumors after lung cancer and breast cancer [9]. It is important to detect colorectal cancer using a fast and noninvasive imaging method so that the patients can be treated immediately. PA imaging may satisfy these conditions, owing to its imaging principle. The relationship between PA pressure and the optical absorption coefficient of the tissue follows the formula [10,11]

$$p = \frac{\beta v^2}{C_p} \mu_a E_0 \eta, \tag{1}$$

where p is the PA pressure (unit Pa), β is the thermal coefficient of volume expansion (unit K^{-1}), v is the sound speed (unit m/s), C_p is the specific heat (unit J/g K), μ_a is the optical absorption coefficient (unit mm^{-1}), E_0 is the absorbed energy density of the short pulse laser (unit mJ/cm^2), and η is the percentage of absorbed energy. The optical absorption coefficients of normal human colorectal and colorectal cancer tissue are 0.043 mm^{-1} and 0.163 mm^{-1} at a wavelength of 1065 nm, respectively [12]. The different optical absorption coefficient causes different amplitude of the PA pressure, and further leads to the contrast of the reconstructed image difference. Based on the discussion mentioned above, the PA imaging model can be used to detect colorectal cancer.

To verify that the PAIE system can accomplish fast endoscopic PA imaging in a 2π view without rotating the ultrasound transducer, *ex vivo* pig colorectal tissue was imaged in the experiment. When the PAIE was assembled, the relative positions of the taper reflector, ring transducer array, optical fiber, and Plexiglas tube were adjusted so that their axes would overlap, which can make the taper reflector provide uniform circular illumination for the targeted tissues. Figure 2(a) is a photograph of the *ex vivo* pig colorectal tissue embedded in the transparent gelatin phantom. To improve the resolution of the PA image, a limited-view filtered mean backprojection reconstruction algorithm was used for the reconstruction of the image [13]. Figure 2(b) shows the reconstructed PA image with high contrast. We estimate that the maximum thickness of the pig colorectal wall is about 2.8 mm. The red-dotted line in Fig. 2(b) indicates the position where the PAIE was inserted. Because of the nonuniform absorption distribution of the colorectal wall, the PA image has a different contrast at different positions.

To demonstrate the colorectal cancer detection ability of the PAIE system, the experiment of distinguishing normal human colorectal tissue and colorectal cancer tissue was performed. Normal human colorectal tissue and colorectal cancer tissue samples were obtained from patient colorectal resections, which were removed from a previously diagnosed colon. They were cleaned with 0.9% sodium chloride irrigation solution and embedded in the transparent gelatin phantom. A photograph of the sample is shown in Fig. 3(a); the thicknesses of the normal colorectal tissue and colorectal cancer tissue were from ~2 mm to ~5.5 mm. The PA signals are shown in Fig. 3(b), and the amplitude of the PA signal generated by colorectal cancer tissue is higher than that of normal colorectal tissue. The reason is that the optical absorption coefficient of colorectal cancer tissue is higher than that of normal colorectal tissue. Figure 3(c) is the reconstructed PA image of the samples. Clearly, the contrast of colorectal cancer tissue and normal colorectal tissue has a difference in Fig. 3(c). The contrast ratio of the colorectal cancer tissue and normal colorectal tissue is ~2.3, which is calculated by the ratio of pixel values shown in the shaded bar. Two more samples of human colorectal cancer tissue and normal colorectal tissue have been used for the experiment to demonstrate that the system can detect colorectal cancer *ex vivo*. The contrast ratios of the colorectal cancer tissue and normal colorectal tissue are ~2.1 and ~2, respectively. These results can prove that the PAIE system is able to detect human colorectal cancer *ex vivo*, based on the difference in the optical absorption coefficients between normal human colorectal tissue and colorectal cancer tissue.

To our knowledge, this is the first work to develop a preclinical PAIE based on an acousto-optic coaxial system using a ring transducer array. Compared to the endoscopic PA imaging system with a single-element transducer, the PAIE system can collect a set of data without rotating the transducer. The optical absorption of the *in vivo* human normal colorectal tissue and colorectal cancer tissue was also different at the wavelengths from visible light to near-

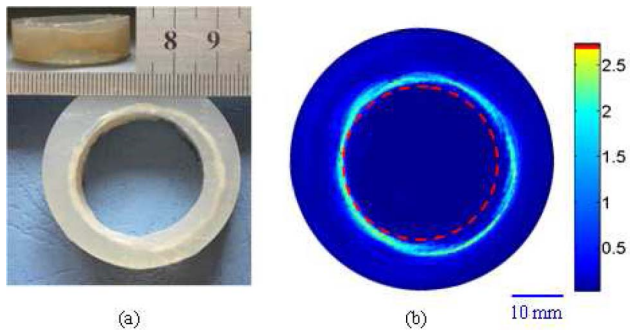

Fig. 2. (Color online) (a) Photograph of the *ex vivo* pig colorectal tissue embedded in the transparent gelatin phantom. (b) Reconstructed PA tomography of pig colorectal wall.

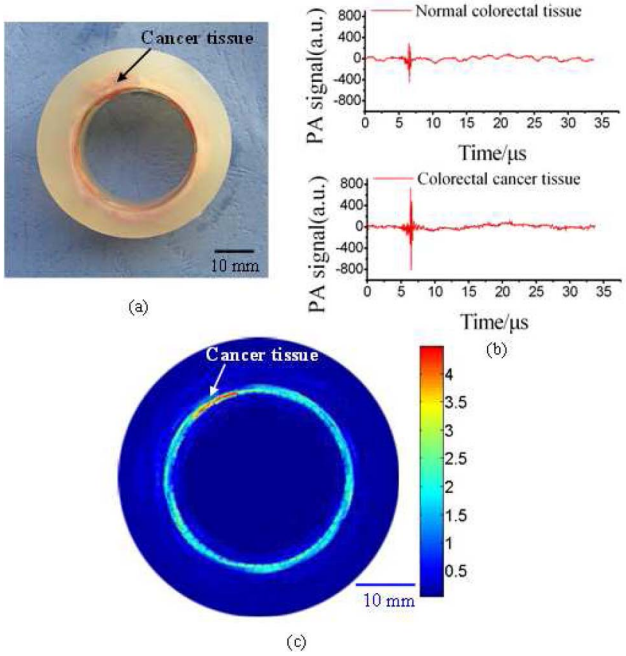

Fig. 3. (Color online) (a) Photograph of the test sample: normal human colorectal tissue and colorectal cancer tissue embedded in the transparent gelatin phantom. (b) PA signals of the human normal colorectal tissue and colorectal cancer tissue. (c) Reconstructed PA image of a section of human colon with cancerous tissue.

IR light [14]. The PAIE has the potential for detecting colorectal cancer tissue *in vivo* by suitable excitation wavelengths based on the native difference of optical absorption in the cancerous region. Concerning the limitation of the laser repetition frequency, it cannot achieve a real-time dynamic imaging. Therefore, to accomplish real-time dynamic imaging and apply it clinically in the future, a laser with a repetition frequency of 24 Hz or higher will have to be used. The size of the PAIE will have to be decreased in order to be used for endoscopic imaging in a much smaller cavity. When the diameter of the transducer array was decreased to 1–2 mm, it can be further used for IVPA: this is our next work.

In summary, we developed and tested a preclinical PAIE, which has a coaxial characteristic of light, sound, and ring transducer array. The PAIE system can collect the PA signals in a 2π view, simultaneously, without rotating the ultrasound transducer. Reconstructed PA image of pig colorectal wall was obtained *ex vivo* to testify the system imaging ability. Furthermore, *ex vivo* human normal colorectal, and colorectal cancer tissue was clearly distinguished by the system. This study shows that the PAIE system has potential for detecting colorectal cancer tissue *in vivo* based on the different optical absorption coefficient between normal colorectal tissue and colorectal cancer tissue.

This research is supported by the National Basic Research Program of China (2010CB732602), the Program for Changjiang Scholars and Innovative Research Team in University (IRT0829), the National Natural Science Foundation of China (NSFC) (30627003, 30870676), and the Natural Science Foundation of Guangdong Province (7117865).

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