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Pulsed laser diode based photoacoustic tomography system using multiple acoustic reflector based single element ultrasound transducers

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ABSTRACT

Conventional photoacoustic tomography (PAT) systems use bulky, expensive Q-switched Nd:YAG lasers which limits its usage in clinics. The low repetition rate of these lasers makes them not suitable for real-time imaging as well. Compact pulsed laser diodes (PLD) are being currently used for PAT systems due to their high repetition rates and compact in size. These lasers can be mounted inside the PAT circular scanning geometry making the PAT system more portable. Using acoustic reflector based single-element ultrasound transducer (SUTR), the scanning radius can be reduced thereby making the PAT system more compact. In this work, we present a portable, high frame rate, more compact second generation PLD-PAT system using eight SUTRs in circular scanning geometry. This system provides high frame rate of ~1 Hz. We demonstrate the performance of this system using phantom imaging studies.

Keywords: pulsed laser diode, acoustic reflector, single element ultrasound transducer, multiple ultrasound transducers, photoacoustic tomography

1. INTRODUCTION

Photoacoustic imaging (PAI) is an emerging biomedical imaging modality having great potential for preclinical research and clinical practice. It's a hybrid technique combining optical imaging with ultrasound detection.¹⁻⁴ PAI works on the basis of photoacoustic effect phenomenon: when a nano second pulsed laser is incident on a biological sample, the diffused light through the tissue gets absorbed by the intrinsic chromophores present such as oxy-haemoglobin, deoxy-haemoglobin, water, lipids etc. As the tissue absorbs the optical energy, it gets heated up and there is a local temperature rise in the order few milli degrees. This rise in temperature results in thermoelastic expansion of the tissue within thermal and stress confinements. This results in generation of pressure waves known as photoacoustic (PA) waves. These PA waves can be detected using an ultrasound transducer placed at the tissue boundary. In PA tomography (PAT)/PA computed tomography (PACT), several reconstruction techniques can be used to map the optical absorption inside the tissue with the initial pressure rise distribution.⁵⁻¹³ PAI is employed in various applications such as small animal whole body imaging,¹⁴ molecular imaging,¹⁵ thyroid imaging,¹⁶ carotid imaging,¹⁷ sentinel lymph node imaging,¹⁸ tissue engineering,¹⁹ monitoring of blood oxygenation and deoxygenation levels²⁰ and so on.²¹⁻²³

Traditional PACT systems use Q-switched Nd:YAG laser which are bulky, expensive, and low-repetition-rate (~10–100 Hz), coupled with an optical parametric oscillator (OPO)/dye laser as excitation source and a single-element ultrasound transducer (SUT) or an array transducer for PA signal detection. These bulky lasers require vibration-isolation optical table to produce optimum laser output of ~100 mJ energy per pulse. Though portable high-pulse-energy OPO lasers (e.g., OPOTEK) are available in the market, they are even more expensive compared to conventional OPO lasers. One SUT needs several minutes to obtain single cross-sectional PA image due to low-repetition-rates which inhibits imaging speed of the PAT system. Hence, imaging of rapidly changing biological phenomena cannot be obtained dynamically. To overcome this limitation, custom made full-ring array transducers can be employed. The state-of-the-art single-impulse PACT system reported a frame rate of 50 Hz.² But these custom-made array transducers need

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complex back-end parallel signal amplifiers and digitizer electronics. This requirement increases the overall cost of the PACT system. Therefore, clinical translation of PAT systems remains as a challenge.

Due to the higher pulse-repetition rate (kHz), compact size and low cost compared to conventional Nd:YAG/OPO lasers, pulsed laser diodes (PLDs)²⁴⁻²⁷ or light emitting diodes (LEDs)^{28, 29} are being used for PA imaging in recent years. *In vivo* brain imaging,³⁰ rheumatology,³¹ high-frame rate imaging using array transducers³² and the diagnosis of cardiovascular disease³³ was successfully demonstrated using a PLD-based PAT imaging system. Mounting the PLD inside the PAT scanner and using single SUT, a first-generation portable PLD-PAT system was developed,²⁵ and *in vivo* imaging was demonstrated in 5 s scan time³⁰ using this system. Conventionally the SUT is being used horizontally. This arrangement takes lot of space as the SUT rotates in larger scanning radius. An acoustic-reflector-augmented single-element ultrasound transducer (SUTR) can be used to reduce the scanning radius and thereby the size of the PAT scanner by placing it vertical direction instead of horizontally. The performance of the SUTR was demonstrated for phantom and *in vivo* imaging and compared with that of SUT using an OPO-PAT system.³⁴ Frame rate can be further improved by using multiple SUTs instead of single SUT,^{35, 36} and by using continuous scanning method instead of stop-and-go scanning method.³⁷ By consolidating all these techniques, we developed PLD-PAT system using 8-SUTRs and PLD laser inside the PAT scanner. We have characterized this system in terms of the spatial resolution and imaging depth using phantom (point source and chicken breast) studies.

Fig. 1 (a) Schematic diagram of PLD-PAT experimental set up with multiple SUTRs. SUTR : Acoustic reflector augmented single-element ultrasound transducer; AMP : amplifier; SM: stepper motor; DAQ: data acquisition card, LDU: Laser driving unit, PLD: Pulsed laser diode; CSP: circular scanning plate (b) Circular arrangement of 8 SUTRs at 45 degree interval (c) Photograph of point source phantom (d) Photograph showing LDPE tube filled with blood placed on top of chicken tissue.

2. MATERIAL AND METHODS

The schematic of the PLD-PAT system is shown in Fig. 1(a). A PLD laser (QD- Q1924-ILO-WATER) was used to deliver laser pulses at of ~107 ns pulse width at ~816 nm wavelength 2 KHz rate onto the sample. A laser driving unit (LDU) was used to control the PLD laser. LDU consists of a water cooling system, a 12V power supply (Votcraft, PPS-11810), and a variable power supply (EA-PS 8160-04 T) to change the laser power, and a function generator (RIGOL

DG1022) to control the pulse repetition rate (up to 2000 pulses per sec). The laser energy density of 0.17 mJ/cm^2 , well below the ANSI safety limit³⁸ for a scan time of 1 s (0.94 mJ/cm^2) was maintained. Eight unfocused SUTRs (SUT: V309-SU/U8423013, augmented with 45° acoustic reflector: F102, Olympus NDT) of 5 MHz central frequency with 70% fractional bandwidth and 13 mm active area diameter were used to acquire the generated PA waves. All eight SUTRs were placed around the sample at 45° intervals in a circle [Fig. 1(b)]. Each transducer rotates 45° around the sample to acquire the PA data in full circle. We compared the 8-SUTRs data with that of 1-SUTR data (rotating for one full circle (360°)). Around the sample in case of point source phantom [Fig. 1(c)]. Two different scan speeds of 30 deg/s and 45 deg/s, were used for comparison. The acquired PA signals were amplified by using low-noise-signal amplifiers by 48 dB (Mini-circuits, ZFL-500LN-BNC) and stored inside a Windows operating desktop (Intel Xeon, 3.7 GHz 64-bit processor, 16 GB RAM) using an eight-channel data acquisition (DAQ) card (Spectrum, M2i.4932-exp). All the PA data were acquired at 25 MHz sampling rate. To synchronize the DAQ with laser pulse excitation, a transistor–transistor logic (TTL) signal from the function generator was used. PA data in all the cases were averaged into 200 A-lines before reconstruction for better comparison purpose. A simple delay-and-sum reconstruction method was used for mapping initial pressure rise distribution.

3. RESULTS AND DISCUSSION

Fig. 2 Reconstructed images of point source phantom. (a, b) Reconstructed images obtained using 1-SUTR for scan times of 8 s and 12 s respectively. (c, d) Reconstructed images obtained using 8-SUTRs for scan times of 1 s and 1.5 s respectively. Color bar is shown for all images on the left. Scale bar is shown in (a).

Figure 2 shows the reconstructed cross-sectional PA images of a point source phantom made using pencil leads of ~ 0.5 mm diameter: one is kept approximately at scanning center and other four are at $\sim 90^\circ$ degree interval [Fig. 1(c)]. Figures 2(a), 2(b) show the cross-sectional reconstructed PA images for the PA data obtained using one SUTR rotating around 360° for different scan times of 8 s and 12 s, respectively whereas Figs. 2(c), 2(d) show the reconstructed cross-sectional PA images for the PA data obtained using eight SUTRs rotating 45° around the sample for scan times of (8/8) s, and (12/8) s, respectively. Signal-to-noise ratio (SNR) was used to compare the quality of the images obtained using 8-SUTRs with that of images obtained using 1-SUTR. For each reconstructed image, SNR was calculated as $SNR(dB) = 20 \log_{10}(V/n)$, where V is the average PA amplitude of the target object and n is the standard deviation of the background noise. The SNR levels for the reconstructed images obtained for 1 s and 1.5 s scan period (28.94 dB and 28.81 dB) were

similar to that of the reconstructed images obtained for 8 s and 12 s scan time (28.38 dB and 28.68 dB), respectively. Hence, a highest frame rate of 1 Hz (1 s per frame) was obtained using the second generation PLD-PAT system. The resolution of this system was calculated from the edge spread function (obtained from center point) and was found to be $\sim 180 \mu\text{m}$.

Fig. 3 Deep tissue imaging of blood tube embedded inside chicken breast tissue. (a-c) PAT images at depths of 1 cm, 2 cm and 3 cm respectively for a scan time of 1 s. (d) Signal to noise ratio of blood at various depths. Color bar is shown for all images on the left. Scale bar is shown in (a).

Next, a study was conducted to determine the imaging depth of the second generation PLD-PAT system. A low-density polyethylene (LDPE) tube filled with rat blood was placed on chicken breast tissue, as shown in Fig. 1(d). Stacked layers of chicken breast tissue were placed on top of the LDPE tube to image blood at different depths of 1 cm, 2 cm, and 3 cm. PA data were acquired at all depths for scan times of 1 s using eight SUTRs. The reconstructed cross-sectional PA images of blood for 1 s scan time at different depths of 1 cm, 2 cm, and 3 cm can be seen in Figs. 3(a), 3(b), and 3(c), respectively. SNR was calculated for blood at depths of 1 cm (22.6 dB), 2 cm (19.3 dB) and 3 cm (7.4 dB) and is shown in Fig. 3(d). From this we can show that till 3 cm deep inside the tissue (*in vitro*) we can image using this second generation PLD-PAT system. With the help of photoacoustic contrast agents,³⁹⁻⁴⁴ the imaging depth can be further improved.

3. CONCLUSIONS

In this work, we have demonstrated a compact, portable, cheap desktop pulsed laser diode based PAT imaging system. A cross sectional imaging of 1 s per frame was shown using multiple acoustic reflector based single element ultrasound transducers. Image quality in terms of SNR was also maintained and spatial resolution of $\sim 180 \mu\text{m}$ (with 5 MHz unfocused UST) was achieved. Spatial resolution is not affected by the longer pulse width of the PLD (107 ns) due to the low frequency ultrasound detection in PAT (typically 1–10 MHz). Spatial resolution can further be improved by using a PLD with low pulse width and high-frequency transducer. An imaging depth of 3 cm can be achieved (*in vitro*) using this second generation PLD-PAT system, which is deeper than previously reported.

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