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Deep imaging with low-cost photoacoustic tomography system with pulsed diode laser

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ABSTRACT

Optical imaging beyond a few mm inside biological tissue is a challenging task due to the light scattering inside the biological tissue. Photoacoustic tomography (PAT) breaks this depth limit of optical imaging by combining light and sound. Over the last few years PAT has emerged as a viable deep tissue imaging modality and created lot of attention to the medical imaging community. However, the cost, size and time consuming image acquisition of the PAT system is deterrent to its translation to real clinical applications. So, there is a need for inexpensive, compact, simple, fast PAT imaging system for easy adoption by the clinical practitioners. Nanosecond pulsed laser diodes could help to bring down the cost, size and image acquisition time and make PAT attractive for deep tissue imaging of optical contrast with high resolution. In this work, we present our findings on using a low-cost pulsed diode laser for deep tissue imaging with photoacoustics. The PAT system was tested on tissue phantoms to verify its potential imaging depth demonstration. Up to 3 cm deep inside chicken breast tissue we were able to see photoacoustic signals and up to 2 cm deep we were able to image successfully.

Keyword: Photoacoustic tomography, Hybrid imaging, Deep tissue imaging, Pulsed diode laser.

INTRODUCTION

Among many existing medical imaging modalities optical imaging is very promising as it uses non ionising radiation. However, the penetration depth of optical imaging is very limited in biological tissue due to light scattering.¹ Beyond ~1 mm inside biological tissue it is very difficult to focus light photons. As a result all the high resolution pure optical imaging modalities like two photon microscopy, optical microscopy, optical coherence tomography can image only up to a depth of ~1 mm. However, using diffused photons one can achieve imaging depth up to 7-10 cm inside biological tissue, but at the cost of low-resolution. Using diffused optical tomography such high imaging depth has been shown but the resolution is only 0.5-1 mm.² The optical depth limit was broken with the arrival of photoacoustic imaging, which is a hybrid imaging combining optical with ultrasound imaging.³⁻⁷ It is one of the rapidly growing noninvasive, in vivo imaging technique owing to its deep penetration depth, combining high ultrasound spatial resolution with high soft tissue optical absorption contrast. It is a combination of the best features of pure ultrasound imaging and pure optical imaging.⁸ Since ultrasound scattering is two to three orders of magnitude less than optical scattering in biological tissue, photoacoustic imaging can break through the fundamental limitation existing in pure optical imaging. In photoacoustic imaging a short pulsed laser light illuminates the tissue. Due to light absorption by the intrinsic absorber in the body (e.g., blood, melanin, even water), there is a local temperature rise (in the order of milli degree). Then as a result of thermoelastic expansion pressure waves are generated in the form of ultrasound waves and come out of the tissue. Ultrasound transducers (detectors) receive the ultrasound waves [known as photoacoustic (PA) waves] around the tissue surface. In Photoacoustic tomography (PAT) typically a single element detector receives the PA signals around the object (tissue sample) in full circle. Reconstruction techniques are used to map the initial pressure rise in the object which is in turn correlated to the absorption coefficient of the object.⁹⁻¹⁴

The photoacoustic effect was invented more than a century back. However, until recently its application in biological imaging was very limited. Then with the advent of high energy pulsed lasers made efficient photoacoustic wave generation inside biological tissue and thus making it easier to build photoacoustic imaging systems. The applications of PAT are varied and include blood vessel imaging, Sentinel lymph node imaging, breast cancer detection and various others.¹⁵⁻²⁰ It is also possible to do functional photoacoustic imaging with

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tunable laser sources. Thus quantification of oxygen saturation level, total haemoglobin concentration, blood flow etc. are possible using photoacoustic imaging. Functional photoacoustic imaging can help in early cancer diagnosis. Blood is an intrinsic contrast in our body. However, when the contrast from the blood is not strong enough other exogenous contrast agents can be used to enhance the signal contrast. There are a plethora of contrast agents both organic dyes as well as inorganic ones.²¹⁻²⁹ Contrast agents can also help in targeted molecular imaging, which is again a key in early cancer diagnosis.

Due to its high penetration depth of few centimetres and good spatial resolution we can use PAT to image the soft tissues in the body and obtain the structural as well as functional details. The system uses only non-ionising radiation in the near infrared region thus making it more suited for the repetitive usage unlike Magnetic resonance imaging or Computed tomography which uses harmful radiation. In the near-infrared region the light penetrates much deeper in the tissue. As a result for deep tissue imaging near-infrared (NIR) wavelengths are preferred. Typically a Nd:YAG pump laser either pumps a dye laser or a OPO laser to generate pulsed NIR wavelength laser beam. So far, these types bulky lasers have been used in the PAT setup making this kind of system bulky, expensive, and slow (typical pulsed repetition rate for such lasers is 10-20 Hz).³⁰ Also, the bulky laser would mean that it needs a bulky cooling system and hence making its portability an issue and less favourable for clinical application.³¹ There is a great need to develop a system which is compact, affordable, portable and have a high speed.³² Also a smaller and portable system would be more beneficial from the clinical point of view, as there would be ease of handling for the physicians and the low cost is also an added advantage.

There are various geometries along which the scanning can be performed. We use the circular scanning where the transducer is rotated around the object in a circular motion recording the signals at various positions.¹⁴ A simple delay-and-sum method for image reconstruction using a back projection algorithm is generally used as we are more focused on the structural information rather than quantitative images.⁹ Though the system doesn't provide real time imaging it is the fastest method available for this type of imaging. To focus more on the quantitative image reconstructions, iterative image reconstructions or system matrix-based image reconstructions can also be used. However, in this work we will only focus on the time-domain back projection implementation. Also, time-domain back projection- based reconstruction is faster than the system matrix-based approach.

In this work, a pulsed diode laser is used to irradiate the object. Since the pulsed diode laser in general has lower pulse energy, we wanted to test its capability of generating photoacoustic signals from deep tissue. A single element ultrasound detector was used for the study. For the imaging purpose a simple reconstruction algorithm is used to map the absorption map of the object. Hair phantom in water is used to test the performance of the imaging system. We have quantified the signal-to-noise ratio (SNR), resolution, and the imaging depth.

EXPERIMENTATION AND RESULTS

First we tested the ability to generate photoacoustic (PA) signal by the pulsed diode laser. A NIR pulsed diode laser (Quantel DQ-Q1910-SA-TEC) of ~803 nm wavelength, pulse energy ~1.45 mJ per pulse at a very high pulse repetition rate of 7 kHz was used as the PA excitation source. The laser is capable of producing ~136 nano second pulses. We used a 2.25 MHz center frequency 13 mm active area diameter nonfocused ultrasound transducers (UST) for the detection of the PA signal. To synchronize the acquisition of the data, same function generator (HTRONIC FG 250D) was used to trigger both the laser as well as the data acquisition system. The PA signal was first amplified with a pulse/receiver amplifier (Olympus, 5072PR) and then digitized and recorded using a data acquisition card (Gage, CompuScope 4227) connected with a desktop computer. We performed experiments on mouse blood/ink sample inside LDPE tube (inner diameter: 590 μm , wall thickness: 190 μm). Two LDPE tubes, one filled with black ink (Parker, France) and the other one filled with mouse blood were prepared for this experiment. The transducer and the LDPE tubes were mounted in a transparent container (made out of Perspex) filled with water. The tube, placed at ~4 cm distance from the laser window, was irradiated with pulse energy density of ~0.85 mJ/cm² in the beam area 2×0.85 cm². The PA signal received by the UST was band pass filtered (1-10 MHz) and amplified with 50 dB gain. Finally, the signal was digitized by a DAQ card at 50 Ms/s and stored in the computer. A total of 14,000 A-lines (2 sec) were collected. To measure the penetration-depth capabilities of the system, LDPE tube filled with black ink or blood was embedded in the chicken breast tissue (CBT). The tube was still kept the same distance 4 cm from the laser window. The LDPE tube was embedded in the middle of the tissue sample. PA signals were collected when the tube was placed at 1, 2, or 3 cm deep from the laser illuminated tissue surface. The generated PA signal also needs to travel 1, 2, or 3 cm inside the attenuating chicken breast tissue before it is received by the transducer.

Figure 1a shows the PA signals averaged 700 times (0.1 sec) of the black ink. We can clearly see the PA signal generated from up to a depth of 3 cm inside chicken breast tissue. Of course with increase in depth the PA signal amplitude drops. In the inset the PA signal from the ink tube in water is shown. Figure 1b shows the similar experimental data but with blood filled tube. The PA signal generated by black ink is as strong as that generated by blood which indicates that they have similar optical absorption coefficients at ~ 803 nm.

Figure 1: Photoacoustic signal from (a) ink, (b) mouse blood inside a low-density polyethylene (LDPE) tube with inner diameter: $590 \mu\text{m}$ and wall thickness: $190 \mu\text{m}$. A 2.25 MHz center frequency 13 mm active area diameter nonfocused ultrasound transducers was used for the detection of the PA signal. The LDPE tube was embedded in the middle of the tissue sample. PA signals were collected when the tube was placed at 1, 2, or 3 cm deep from the laser illuminated tissue surface. The generated PA signal also needs to travel 1, 2, or 3 cm inside the attenuating chicken breast tissue before it is received by the transducer. In the inset the PA signal from tube inside water is shown. There was no chicken breast tissue for the PA signal in the inset.

The encouraging photoacoustic signal in the chicken breast tissue sample was very encouraging. Therefore, we continued our experiment to see if deep-tissue imaging can also be done. For the imaging we used photoacoustic tomography system in the orthogonal illumination mode. Orthogonal photoacoustic tomography is known for deep-tissue imaging. In PAT the detector is rotated around the sample using a stepper motor (Lin Engineering, Silverpak 23C) and a homebuilt mechanical scanner. A simple MATLAB based program was used to control the data acquisition, stepper motor motion and also the reconstruction of the PA data. Figure 2a shows the tissue phantom used to study the imaging performance of the system. For PAT typically low frequency transducers are used, as they are best suited for deep tissue imaging. Therefore in this study we used the same 2.25 MHz center frequency non-focused 13 mm active area diameter detector. Two LDPE tubes (length ~ 10 mm), one filled with mouse blood and the other ICG (indocyanine green) was placed on top of the chicken breast tissue and it was covered with another layer of chicken breast tissue with thickness 1 and 2 cm for two experiments. ICG solution was prepared to have absorption peak around ~ 800 nm wavelength light.

Various imaging speed was tested by controlling the transducer rotation speed. We tested 10 second, and 20 seconds imaging speed. Figures 2b and 2c shows reconstructed PAT images of the cross-sectional image of the phantom for 20 sec and 10 sec scanning speed, respectively, when the tubes are buried inside 1 cm thick chicken breast tissue. Figures 2d and 2e shows reconstructed PAT images of the cross-sectional image of the phantom for 20 sec and 10 sec scanning speed, respectively, when the tubes are buried inside 2 cm thick chicken breast tissue. All our reconstruction was done using a simple delay-and-sum back projection reconstruction algorithm in MATLAB.

It is clearly evident from the Figures 2 that even with 2 cm deep-tissue we were able to reconstruct back the optical absorption map using PAT with reasonable SNR and resolution. Most traditional PAT systems use bulky Nd:YAG pump lasers with high pulse energy. However, with portable and small pulsed diode laser also we were able to image 2 cm deep inside biological tissue. The imaging speed is also improved over other existing PAT system. For certain applications, the image resolution obtained with the short time scanning is just good enough and would be sufficient. Traditional lasers used for PAT has a pulse repetition rate in the order of 10-20 Hz. As a result to collect enough no of PA signals around the object the transducers need to rotate the sample slowly. As a result the image acquisition time is quite slow. Typically several minutes are needed for full rotation. However, with the use of high repetition rate pulsed diode laser we can collect data very fast (10 s) and still obtain a very good quality PAT image. This is close to 10 fold improvement in terms of imaging speed.

Figure 2: (a) photograph of the chicken breast tissue phantom used for the imaging study. Two LDPE tubes filled with blood and ICG was placed on top of the chicken breast tissue, then it was covered with 1 cm and 2 cm thick chicken breast tissue layer. (b) Reconstructed PAT images with 20 sec scanning time, (c) 10 sec scanning. (d-e) same as b and c but with 2 cm chicken breast tissue layer. A 2.25 MHz center frequency ultrasound transducer was used for PAT data collection.

Laser Safety Limit: When PAT is used to image subjects in vivo, the maximum permissible pulse energy and the maximum permissible pulse repetition rate are governed by the ANSI laser safety standards.³³ The safety limits for the skin depend on the optical wavelength, pulse duration, exposure duration, and exposure aperture. In the spectral region of 700–1050 nm, the maximum permissible exposure (MPE) on the skin surface by any single laser pulse should not exceed $20 \times 10^{2(\lambda-700)/1000}$ mJ/cm² (where λ is the wavelength in nm). At 803 nm, for example, the MPE is 32.1 mJ/cm². In our imaging system, the pulsed diode laser provides ~1.4 mJ pulse energy and the laser beam spread over an area ~4 cm² (1.5 cm X 2.5 cm). Therefore, the laser fluence is around 0.35 mJ/cm². Thus, the fluence is well within the ANSI MPE. In addition, if the same area on the skin is exposed to laser light for more than 10 s, the mean irradiance should not exceed 200 mW/cm² in the 700–1400 nm region. However, we show that with 5 s imaging time we are able to obtain high SNR PAT images, therefore, do not require long time laser exposure.

CONCLUSION

In this work, we showed that using a high repetition rate low cost pulsed diode laser we can image deep-inside the tissue noninvasively the optical absorption map using photoacoustic tomography. We have shown strong photoacoustic signal from blood and black ink 3 cm deep inside the chicken breast tissue. We have also shown cross-sectional imaging capability as deep as 2 cm inside chicken breast tissue both with blood as well as ICG. The imaging speed was also significantly higher than the other PAT system which uses a traditional Nd:YAG pump lasers as illumination source.

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