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Super-contrast photoacoustic resonance imaging

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Abstract

In this paper, a new imaging modality, named photoacoustic resonance imaging (PARI), is proposed and experimentally demonstrated. Being distinct from conventional single nanosecond laser pulse induced wideband PA signal, the proposed PARI method utilizes multi-burst modulated laser source to induce PA resonant signal with enhanced signal strength and narrower bandwidth. Moreover, imaging contrast could be clearly improved than conventional single-pulse laser based PA imaging by selecting optimum modulation frequency of the laser source, which originates from physical properties of different materials beyond the optical absorption coefficient. Specifically, the imaging steps is as follows: 1: Perform conventional PA imaging by modulating the laser source as a short pulse to identify the location of the target and the background. 2: Shine modulated laser beam on the background and target respectively to characterize their individual resonance frequency by sweeping the modulation frequency of the CW laser source. 3: Select the resonance frequency of the target as the modulation frequency of the laser source, perform imaging and get the first PARI image. Then choose the resonance frequency of the background as the modulation frequency of the laser source, perform imaging and get the second PARI image. 4: subtract the first PARI image from the second PARI image, then we get the contrast-enhanced PARI results over the conventional PA imaging in step 1. Experimental validation on phantoms have been performed to show the merits of the proposed PARI method with much improved image contrast.

Introduction

Photoacoustic (PA) imaging is a fast-developing imaging modality in recent decades based on PA effect, which refers to the ultrasound generation induced by the optical absorption and thermoelastic expansion [1, 2]. Up to now, majority of the PA imaging studies rely on the nanosecond high peak power pulsed laser source (e.g. Q-switched Nd:YAG laser) to induce wideband PA signals, which reveal the optical absorption contrast of the imaging target [3-7]. Some important applications of the conventional PA imaging include measurements of oxy- and deoxy-hemoglobin in blood for oxygen saturation mapping, melanoma detection, breast cancer screening, exogenous nanoparticles for contrast-enhanced imaging, etc. [8-14]. Although multi-wavelength laser source could provide rich spectroscopic optical absorption contrast, the detection sensitivity is always a bottleneck in real scenarios due to limited absorption of the target, deep penetration, and ultralow conversion efficiency from optical absorption to PA generation. To overcome the sensitivity limit, expensive and bulky high-power pulsed laser has to be utilized to achieve sufficient SNR of PA signal. In recent years, low-power intensity modulated laser source has also been explored for PA imaging with chirp and continuous-wave (CW) modulations [15-19], which however still suffers low image contrast when optical absorption of the target is similar [20].

In this paper, PA resonance imaging (PARI) is proposed utilizing multi-burst laser illumination to induce PA resonant signal with enhanced SNR and narrower bandwidth. Under same peak power, PA resonant signal could be clearly enlarged than the single laser pulse induced PA signal due to its resonating phenomenon. In addition, by sweeping the modulation frequency, different kinds of materials could exhibit different resonance frequencies, which provide another dimension of contrast beyond optical absorption. More interestingly, by selecting the optimum modulation frequency for different targets, the reconstructed image could selectively visualize the target of interest, and suppressing the undesired background after applying differential imaging. Next, the principle of the PARI method will be introduced, and experimental results will be demonstrated to show its feasibility for super-contrast imaging capability.

Results

The physical principle of PARI is based on the PA resonance effect [21]. When the target is illuminated with by a multi-burst intensity-modulated light source, it will experience optical absorption, localized heating and thermal expansion. Modelling a small enough viscid target as an ideal point source, the induced PA signal $p(t)$

follows the expression [21, 22]:

$$\frac{\partial^2}{\partial t^2} p(t) + a^2 \frac{\xi + \frac{4}{3}\eta}{\rho} \frac{\partial}{\partial t} p(t) + a^2 c^2 p(t) = \Gamma \frac{\partial H(t)}{\partial t} \quad (1)$$

where a is the propagation phase constant, ρ is the tissue density, η is the shear viscosity, ξ is the bulk viscosity, and c is the speed of sound. Γ is the Grüneisen constant expressed as $\Gamma = \beta c^2 / c_p$, where β is the thermal expansion coefficient, and c_p is the constant pressure heat capacity per unit mass. $H(t) = \mu_a \Phi(t)$ is the heating function from the laser illumination, where μ_a is the optical absorption coefficient of the target, and $\Phi(t)$ is the optical fluence rate.

It is clearly showing that Eq. (1) is a second order differential equation driven by the source term $\Gamma \times \partial H(t) / \partial t$, which could be straightforwardly modelled as a second-order oscillator, such as a damped mass-spring model or a resistor-inductor-capacitor resonance circuit. With some mathematical derivations, the resonance frequency and quality factor of the second-order oscillator could be expressed as [21]:

$$\omega_r = \sqrt{a^2 c^2 - \frac{1}{2} \left(a^2 \frac{\xi + \frac{4}{3}\eta}{\rho} \right)^2} \quad (2)$$

$$Q = \frac{\rho^2 c^2}{a^2 \left(\xi + \frac{4}{3}\eta \right)^2 - \frac{1}{2}} \quad (3)$$

From Eq. (2) and Eq. (3), it is observed that both resonance frequency and quality factor of the oscillation target are functions of physical properties beyond optical absorption. In addition, it is expected that when the modulation frequency of the laser source matches the resonance frequency of the target, the SNR of the PA resonant signal could be enhanced by Q times.

Fig. 1. The illustration of the proposed PARI method. (a) Conventional PA imaging using pulsed laser, (b) PA resonance spectroscopy of target and background. (c) PARI images utilizing the resonance frequency of target and background separately, and the contrast-enhanced PARI image after subtraction.

To develop the PA resonance effect towards an imaging modality PARI, there are several procedures to be conducted as shown in Fig. 1. Step 1: Perform conventional PA imaging by modulating the laser source as a short pulse. Identify the location of the target and the background (Fig. 1(a)). Step 2: Characterize the resonance frequencies of the target and background by sweeping the modulation frequency of the laser source. (Fig. 1(b)). Step 3: Choose the resonance frequency of the target as the modulation frequency of the laser source, perform imaging and get the first PARI image. Then choose the resonance frequency of the background as the modulation frequency of the laser source, perform imaging and get the second PARI image. Finally, subtract the first PARI image from the second PARI image, then we get the contrast-enhanced PARI results over the conventional PA imaging in step 1 (Fig. 1(c)).

Fig. 2. The experimental setup of the PARI method demonstration. FC: function generator; LD: laser diode; FC: fiber coupler; ConL: condenser lens; BS: beam splitter; PD: Photodiode UT: ultrasound transducer; LNA: low-noise amplifier.

Results

The dark-colored grass jelly phantom with a 1-mm-diameter black rubber wire inserted 1 mm below the top surface was used to mimic the biological tissues with different mechanical properties, where the jelly served as background and the black wire served as target. The frequency responses of the jelly and black wire were characterized by sweeping the laser modulation frequency from 840 kHz to 1340 kHz with a step size of 10 kHz and the normalized peak-to-peak values of PA signal at each frequency were recorded to construct the PA resonance spectra as shown in Fig. 3(a). Six cycles were used during each frequency sweep with a repetition rate of 1 kHz. The resonance peaks of the jelly and black wire can be clearly identified at 930 kHz and 1140 kHz, respectively. Fig. 3(b) shows the PA waveforms from the black wire at resonance and the typical single-pulse-induced PA signal, where the signal amplitude enhancement of about ~ 2 times can be clearly observed for resonance PA signal. A small area ($1\text{ cm} \times 1\text{ cm}$) of the phantom containing the black rubber wire was then scanned with a step size of $200\text{ }\mu\text{m}$ which is indicated by the dashed white box in Fig. 3(c). The resolution is $\sim 300\text{ }\mu\text{m}$ which is mainly determined by the size of laser focusing point. The images were reconstructed by taking the peak-peak value at each pixel. The target-resonance 2D image and conventional pulsed PA image are shown in Fig. 3(c) and 3(d). The quantitative contrast of PARI is 4.65:1 while the

conventional PA imaging has a contrast of 2.85:1 shown in Fig. 3(e), indicating the merit of contrast improvement of PARI over conventional single-pulse-induced imaging.

Fig. 3. (a) The PA resonance spectra of jelly background (blue) and black wire target (red). (b) PA waveforms of black wire at resonance (dashed red line) and single-pulse-induced PA signal (solid blue line). (c) PARI at target resonance. (d) Conventional PA image. (e) Quantitative contrast comparison of Fig. 3(c) and 4(d).

Conclusion

In conclusion, we have developed and demonstrated a novel super-contrast imaging modality named PARI, using both phantom and *ex vivo* tissues. The contrast enhancement at resonant frequency of a certain target was validated experimentally. More remarkably, by selecting optimum modulation frequencies for target and background, the contrast improvement is even more pronounced in differential images, and selective visibility of desired target is also achievable. *In vivo* experiment is also expected to be feasible, aiming to differentiate malignant and benign tumor tissues based on their different mechanical properties such as viscosity, elasticity and density [23]. Although the PA resonance signal generated by a CW laser is much weaker compared to a pulsed laser which may cause difficulty for *in vivo* experiment and real application, highly sensitive lock-in detection can be applied here thanks to the narrowband nature of resonance signal. Apart from that, chirp-modulated laser can also be employed to improve the SNR to a comparable state with pulsed laser source. Moreover, chirp-based excitation can be utilized for fast imaging of PARI avoiding

the frequency sweeping individually, which will be studied in the future work. The proposed PARI method provides a super-contrast imaging modality with high selectivity, going beyond the conventional absorption-only PA imaging.

Methods

The experimental setup of the PARI imaging. As shown in Fig. 2, the input square wave signal with 6 cycles and tunable modulation frequency as well as 1 kHz repetition rate is generated by a function generator (33250A, Agilent), which is connected to a custom-designed current driver. The output of the driver is then fed to a laser diode (L808P1000MM, Thorlabs, wavelength: 808 nm, power: 1 W) with fiber coupling. The output light from the fiber (MHP550L02, Thorlabs) is then collimated and focused by condenser lens (LB1471, Thorlabs) on the sample with a spot size of $\sim 500\ \mu\text{m}$ diameter. Meanwhile, a beam splitter (BSF10-B, Thorlabs) and photodiode (DET10A, Thorlabs) are utilized to monitor the laser intensity variation. An ultrasound transducer (V303SU, Olympus) with 1 MHz central frequency is placed close to the sample to detect the PA resonance signals. A water tank with a window covered by thin and transparent polyethylene membrane film at the bottom is in contact with the sample and transducer is immersed in water tank for optimum optical and acoustic coupling. The PA resonance signals are firstly amplified by a low-noise amplifier (5662, Olympus) with 54 dB gain, and then recorded by an oscilloscope (WaveRunner 640Zi, LeCroy) with 100 MSPS sampling rate. The optical path and ultrasound transducer are fixed on a 2D translational stage, which enables raster-scanning of the sample to render 2D and 3D images.

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