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Thermally Enhanced Photoacoustic Radar Imaging of Biotissues

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Abstract The signal-to-noise ratio (SNR) and imaging depth of photoacoustic (PA) imaging remain limited for clinical applications. The temperature can influence PA signals; the SNR of PA signals can be increased at higher temperatures. Therefore, the imaging quality and depth can be improved by the assistance of heating. Experimental results showed that the maximum imaging depth can be doubled by raising the temperature of the absorbers (*ex-vivo* beef muscle) uniformly from 20 °C to 41 °C, and the SNR can be increased 53 % from 20 °C to 45 °C.

Keywords Frequency-domain photoacoustic · Imaging depth · Signal-to-noise ratio · Temperature-enhanced imaging

1 Introduction

Imaging depth and signal-to-noise ratio (SNR) are important issues in biomedical imaging systems. The light intensity decreases exponentially with depth because of strong scattering and absorption in biological tissues. Near-infrared wavelengths have a lower absorption coefficient and a relatively low scattering cross section in biotissues, so the optical window in the 700 nm to 900 nm range allows light to penetrate relatively deeply. Furthermore, the PA signal can be enhanced by contrast agents, such as Indocyanine Green (ICG) dye [1]. Even though these methods can improve the SNR and imaging depth significantly, contrast agents are not without health risks and are, therefore, invasive. The desire for deep subsurface breast cancer imaging is so

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prevalent that new depth enhancement imaging methodologies are constantly sought for better and easier diagnosis [1].

Photoacoustics (PA) has been used for temperature monitoring. At higher temperatures the PA signal is stronger [2]; therefore, noninvasive material heating along with PA probing can enhance PA signals. Studies showed that raising the temperature to 41.8 °C in human body tissues for a period of time is generally safe [3]. In this study, a thermally enhanced frequency-domain photoacoustic imaging system has been developed. *Ex-vivo* beef muscles were used for experimental studies of imaging depth and SNR.

2 Theoretical Background

The photoacoustic response from a subsurface chromophore in biotissues depends on the photon propagation mechanism. Theoretical analysis of photoacoustic generation in liquid and solid materials can be found from previous studies [4]. The frequency-domain photoacoustic technique uses frequency-modulated continuous wave (CW) laser beams which, upon absorption, generate temperature oscillations in a sample and produce acoustic pressure waves [5]. In the case of slow heat conduction and ideal matching of the acoustic impedance with a coupling medium, the PA spectrum of the response pressure wave is [5]

$$p(r', \omega) = \frac{\Gamma}{2} \frac{\mu_{\mathrm{a}}}{\mu_{\mathrm{a}} c_{\mathrm{a}} + \mathrm{i}\omega} I(r', \omega), \tag{1}$$

where μ_{a} (m^{-1}) is the absorption coefficient, $\omega = 2\pi f$ where f (Hz) is the PA response frequency spectrum, c_{a} ($\mathrm{cm}\cdot\mathrm{s}^{-1}$) is the speed of sound, Γ is the Gruneisen parameter, and I ($\mathrm{J}\cdot\mathrm{m}^{-2}$) is the deposited optical energy. The Gruneisen parameter is defined as

$$\Gamma = \frac{c_{\mathrm{a}}^2 \beta}{C_p}, \tag{2}$$

where β ($^{\circ}C^{-1}$) is the volumetric thermal expansion coefficient and C_p ($\mathrm{J}\cdot\mathrm{kg}^{-1}\cdot{}^{\circ}\mathrm{C}^{-1}$) is the specific heat capacity at constant pressure.

The matched-filter pulse compression method has been introduced in photoacoustic radar (PAR) in order to give the frequency-domain PA signal necessary depth resolution and adequate SNR [5]. The cross-correlation output is

$$R(t) = \int_{-\infty}^{+\infty} s(\tau) \cdot r(t+\tau) \mathrm{d}\tau = \Im^{-1} \left\{ \tilde{s}(f) \cdot \tilde{r}^*(f) \right\}, \tag{3}$$

where $s(t)$ and $r(t)$ are the detected signal and the reference signal, respectively, and $\Im^{-1}$ denotes the inverse Fourier transformation.

Human tissues are heterogeneous; they contain water, proteins, nucleic acids, lipids, carbohydrates, and mineral components. Water determines the functional properties of tissues. For human skin the total water content is 65 %, and for abdominal muscles, it is up to 77 % [6]. In assessing the temperature dependence of the Gruneisen parameter, the

volumetric expansion coefficient β of water changes from 0.0002 °C^{-1} to 0.0003 °C^{-1} between 20 °C and 40 °C [7]. The specific heat capacity of water is 4.186 J·g^{-1}·°C^{-1} at 15 °C, and this value decreases only marginally to 4.178 J·g^{-1}·°C^{-1} at 40 °C [7]. The speed of sound in water increases with temperature from 1482 m·s^{-1} to 1529 m·s^{-1} from 20 °C to 40 °C [7]. These changes collectively lead to an increase of the Gruneisen parameter with temperature. Sigrist [8] demonstrated that PA signals increased with temperature between −2 °C and 5.6 °C in water, and other studies also showed that PA signals increased with temperature in biotissues [2]. However, the detailed relationship of the Gruneisen parameter of biotissues with temperature has not been investigated to date, specifically as a means of PA signal enhancement and this is the object of this report.

3 Experimental Results and Discussion

A CW diode laser emitting at 800 nm was used for our experiments (Fig. 1a). The laser beam size was 3.5 mm, and its output was current modulated with a driver. Four hundred linear frequency-modulated chirp signals (0.3 MHz to 1.3 MHz, 1 ms) were averaged at each measurement in order to increase the SNR. The chirp signals were generated by LabView software, uploaded to the digital card NI PXI-5421 and were synchronized with the data acquisition process. A focused ultrasound transducer (Panametrics-NDT, V314 with −6 dB range from 0.59 MHz to 1.2 MHz, focal distance of 50 cm) was employed as a detector of the photoacoustic signals. The detected signals were amplified by a preamplifier (Parametrics-NDT, 5676) first, and then were sent to the digital data acquisition card NI PXIe-5122 (National Instrument, Austin, Texas). Two thermocouples were employed for temperature measurements. One was used to measure the water temperature, and the other was used to measure the temperature of the tested sample (*ex-vivo* beef muscle).

The distilled water was slowly heated with a homemade heater to ensure that the heating was approximately uniformly distributed in a tank. The temperature was increased at a rate of approximately 1 °C· min^{-1}. The experimental results of uniform heating effects on the PA system are shown in Fig. 1d as mean values averaged over the aforementioned 400 measurements, along with the standard deviations. It can be seen that the PA signal amplitude increases with rising temperature in an approximately linear manner from 20 °C to 45 °C. The standard deviation shows an error of $<$10 %. The overall signal strength increase was about 157 % from 20 °C to 45 °C, and the increase was 12 % from 37 °C to 41 °C. The SNR was calculated as 19 dB at 20 °C, 27 dB at 37 °C, 28.4 dB at 41 °C, and 29 dB at 45 °C. The overall SNR increased by approximately 53 % from 20 °C to 45 °C, and the SNR increased by 5 % from 37 °C to 41 °C.

The specific heat capacity of beef muscle was measured by differential scanning calorimetry (DSC, Q2000, TA Instrument). The measurement results (Fig. 1b) showed the specific heat capacity increased with temperature from 25 °C to 50 °C. The speed of sound of beef muscle was measured by ultrasound transducers. One transducer was used as the transmitter, and another transducer was employed as the receiver. The delay time of the received and transmitted signals was recorded and measured by a computer.

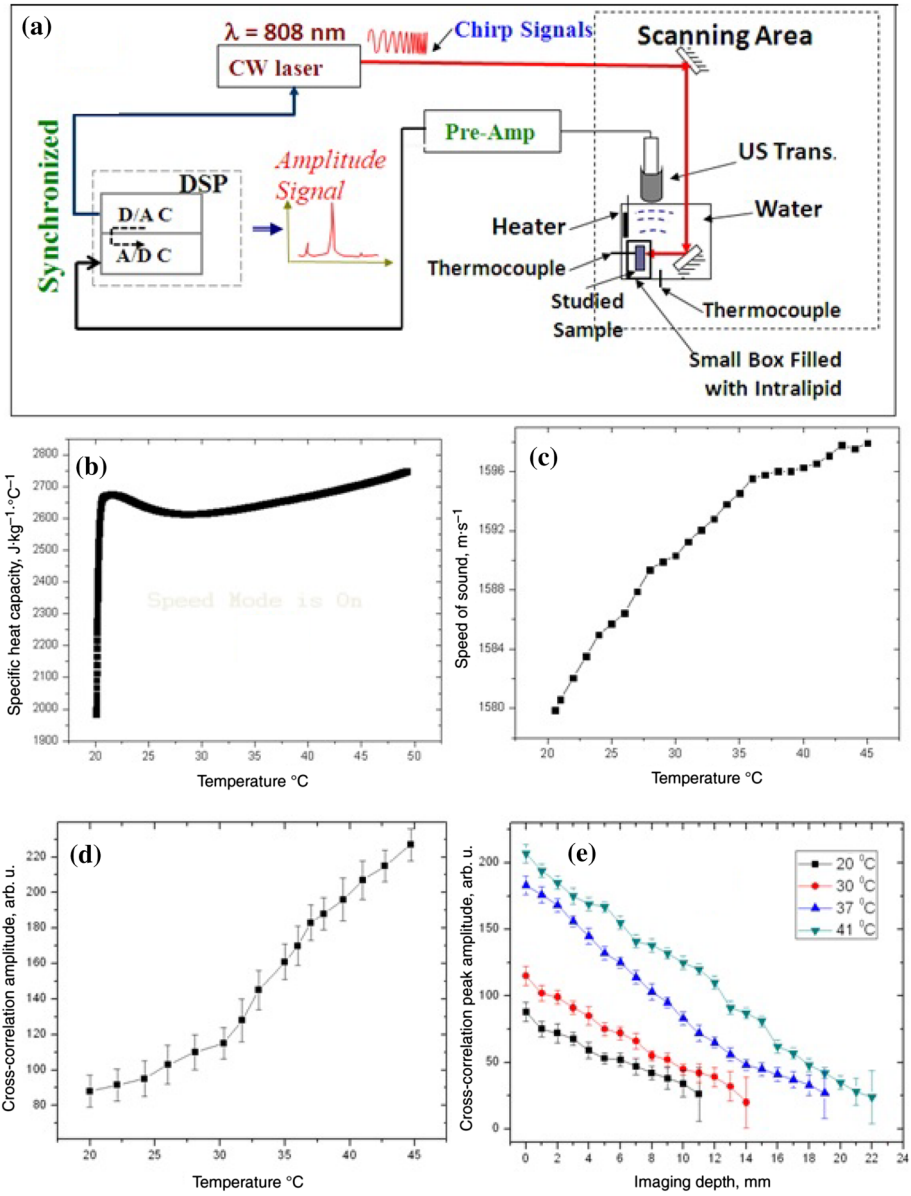

Fig. 1 (a) Functional diagram of the PAR system. (b) Specific heat capacity dependence on temperature. (c) Speed of sound dependence on temperature. (d) PAR signal cross-correlation dependence on temperature. (e) PAR signal cross-correlation peak imaging depth with temperature

The beef muscle was placed between these two transducers. With the known distance between the two transducers, the speed of sound was determined. The results showed that the speed of sound and the specific heat capacity both increased with temperature

(Fig. 1b, c). The speed of sound increased 1.1 % from 20 °C to 45 °C, and the specific heat capacity increased 5 % from 23 °C to 45 °C.

The experimental setup for an imaging depth enhancement study employed a box filled with 0.47 % intralipid solution as a scatterer [9]. The tested sample (*ex-vivo* beef muscle) was placed inside the box. The box moved with micrometer stages to simulate different absorber depths. In each case the foregoing heating experiment was repeated. Figure 1e shows the experimental results of the imaging depth study at various temperatures: between 20 °C and 41 °C, the maximum imaging depth doubled, increasing monotonically from 11 mm to 22 mm.

4 Conclusions

A detailed study of the temperature dependence of the parameters constituting the Gruneisen constant was undertaken, and experimental validation was performed using the PAR modality. The experimental results showed that the imaging depth in a PAR experiment using an intralipid solution as a scattering tissue-mimicking medium surrounding a biological absorber (beef muscle) increases with temperature, and it becomes doubled when the ambient temperature is raised from 20 °C to 41 °C. The signal strength and SNR also increased by over 157 % and 53 %, respectively, between 20 °C and 45 °C. Our results suggest that biomedical PA imaging can exhibit significant signal and SNR enhancement using external uniform heating of the probed tissues.

The monotonic increase of the speed of sound with temperature is one factor responsible for the increase of the PA signal with temperature. However, it can be offset by the change in the specific heat capacity which also increased with temperature, but because of its inverse relationship with the Gruneisen parameter, this increase leads to a non-linear photoacoustic pressure increase with temperature for beef tissue, as shown in Fig. 1d. The thermal expansion coefficient may also contribute to the increase of the PA signal with temperature, and it will be investigated in future work.

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