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Research article

The application of frequency-domain photoacoustics to temperature-dependent measurements of the Grüneisen parameter in lipids

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ABSTRACT

The Grüneisen parameter is an essential factor in biomedical photoacoustic (PA) diagnostics. In most PA imaging applications, the variation of the Grüneisen parameter with tissue type is insignificant. This is not the case for PA imaging and characterization of lipids, as they have a very distinct Grüneisen parameter compared with other tissue types. One example of PA applications involving lipids is the imaging and characterization of atherosclerotic plaques. Intravascular photoacoustic (IVPA) imaging is a promising diagnostic tool that can evaluate both plaque severity and composition. The literature for IVPA has mainly focused on using the difference in absorption coefficients between plaque components and healthy arterial tissues. However, the Grüneisen parameters for lipids and their behavior with temperature have not been well established in the literature. In this study we employ frequency-domain photoacoustic measurements to estimate the Grüneisen parameter by virtue of the ability of this modality to independently measure *both* the absorption coefficient and the Grüneisen parameter through the use of the phase channel. The values of the Grüneisen parameters of some lipids are calculated as functions of temperature in the range 25–45 °C.

1. Introduction

Biomedical photoacoustics features excellent contrast and functional imaging. The wavelength based optical absorption coefficient of tissue facilitates a variety of photoacoustic (PA) applications in imaging and characterization of tissues. Nevertheless, the PA signal also depends on the Grüneisen parameter and the optical fluence, in addition to the absorption coefficient [1,2]. The foremost subject of biomedical PA functional imaging has been blood, the Grüneisen parameter of which has a very small dependence on hemoglobin concentration [3]. Therefore, its effect on the estimation of parameters such as blood oxygen saturation is minimal. However, the temperature dependence of the Grüneisen parameter has incentivized the use of PA as a tool to monitor tissue temperature [4–9]. On the other hand, knowledge of the Grüneisen parameter is critical for estimating the sensitivity of PA imaging. In fact, one of the effective methods for determining the Grüneisen parameter is via PA measurements [3,10,11]. For instance, the Grüneisen parameter of subcutaneous porcine fat has been measured by the PA method and was reported to be 0.69 at 22 °C [3]. Furthermore, a technique for measuring the Grüneisen parameter was suggested which relied on the time-resolved transient PA signal [12,13]. In this technique the exponential slope of the rising signal edge provides the value of the optical absorption coefficient and the total amplitude yields the Grüneisen parameter. Related to this research, PA has also been employed to measure the acoustic properties, sound speed and ultrasonic attenuation, of tissue and several lipids [14–16].

One of the promising applications of biomedical photoacoustics is the diagnosis of coronary artery disease. This disease is characterized by the narrowing of coronary arterial vessels by atherosclerotic plaques. The buildup of plaque can restrict blood flow and significantly increase the risk of acute coronary events, such as myocardial infarction, due to plaque dislodging and leading to a clog. The early detection of the severity of plaque build-up is an important predictor for patients with atherosclerosis [17]. In addition, assessment tools that allow for

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direction evaluation of coronary stenosis have better diagnostic value than indirect evaluation tools, such as a stress test [18]. Currently, coronary angiography, intravascular ultrasound (IVUS), and intravascular optical coherence tomography (IV-OCT) are possible diagnostic techniques [19,20]. However, these techniques cannot accurately evaluate the composition or inflammation of plaque to determine its vulnerability [21]. Intravascular photoacoustic (IVPA) imaging is an emerging spectroscopic diagnostic tool that can illuminate the conformation and composition of atherosclerotic plaques [22–29]. In contrast to other techniques such as coronary angiography, IVPA does not require the use of radioactive contrasting dyes. This minimally invasive technique uses the difference in optical absorption coefficients of the various constituents of tissues to characterize their components [27]. For example, Allen et al. [24] have demonstrated the potential of using 1210 nm and 980 nm lasers to differentiate between healthy arterial walls and plaques due to their different absorption coefficients at these two wavelengths.

The Grüneisen parameter is a thermodynamic property that varies with temperature. Tian et al. [30] showed that the Grüneisen parameters of blood and lipids are highly different in their temperature-dependence: the Grüneisen parameter of blood increases with temperature while that of lipids decreases with temperature in the physiological temperature range [30]. The use of the different behavior of the Grüneisen parameter with temperature has been suggested for characterization of atherosclerotic plaques. It has been shown that for the adventitia, the PA signal would increase with temperature, while that for fatty plaque would decrease with increasing temperature [31]. While the spectroscopic feature of IVPA based on differences in absorption coefficients has been extensively studied, the potential of using the difference in the Grüneisen parameter has not been well explored. This can potentially result in the development of novel approaches for the assessment of atherosclerosis. It should be emphasized that the difference between the Grüneisen parameters of healthy tissues and lipids is larger than that of their absorption coefficient differences [24,27], therefore, the effect of this parameter cannot be ignored. One potential way for exploiting this difference is by measuring the photoacoustic (PA) response of atherosclerotic vessels at two different temperatures. For a healthy tissue, the PA signal would increase with temperature while for plaque constituents, such as cholesterol, it would decrease [31]. The change in temperature can be achieved clinically through ultrasound waves, by flushing blood vessels with a low-temperature fluid, or with an endovascular cooling catheter that inserts a balloon filled with a low temperature fluid into the blood vessel [32]. However, the Grüneisen parameters of lipids have not been well established in the literature but have been reported to be between 0.7 and 0.9 [3,10].

In this paper, we investigate the PA method for an estimation of the Grüneisen parameter of lipids. We employ frequency-domain (or Fourier-domain, FD) PA to evaluate the absorption coefficient and the Grüneisen parameter of lipids. The methodology and various techniques of FD-PA for spectroscopic probing and imaging have been discussed before, where the main subject was the evaluation of the blood oxygenation level [33–37]. Furthermore, we report the Grüneisen parameter of some lipids such as mineral oil, castor oil, olive oil, glycerin as well as cholesterol and cholesteryl oleate. The values of Grüneisen parameters of lipids have been reported at room temperature and in the entire physiological temperature range.

2. Theoretical background

The utilization of IVPA is based on the generation of PA signals through irradiation by a laser beam. The pulsed laser creates a transient thermoelastic expansion of the target tissue. This expansion generates a PA wave that is detected by an ultrasonic transducer. The amplitude of the PA signal (p_o) is approximated by [1,2]:

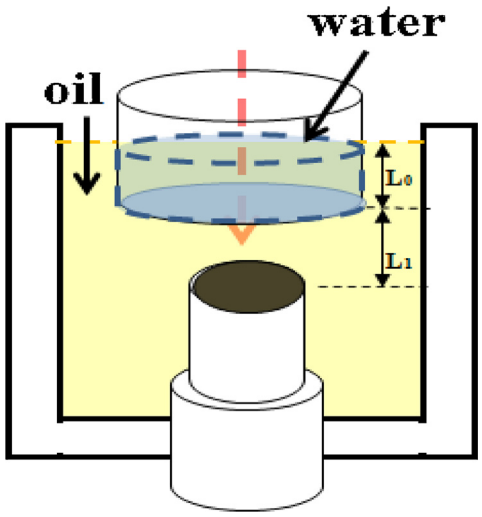

Fig. 1. Schematic of the PA signal generation.

$$p_0 \approx \Gamma \mu_a F \tag{1}$$

where Γ is the Grüneisen parameter, μ_a is the absorption coefficient, and F is the light fluence. The Grüneisen parameter is defined as

$$\Gamma = \frac{\beta c_a^2}{C_p} \tag{2}$$

where β is the isobaric volume expansion coefficient, c_a is the sound speed and C_p is the specific heat. Eq. (1) is a very useful approximation for PA functional imaging. However, the direct proportionality of the pressure amplitude to both μ_a and Γ, prevents the estimation of the Grüneisen parameter directly from the PA signal. One solution would be to measure the absorption coefficient independently, for instance, via a purely optical method and use the PA effect to measure the Grüneisen parameter. Another limitation of Eq. (1) is that it does not account for acoustic attenuation. A more rigorous method to relate the absorption coefficient and the PA signal requires a priori knowledge of the geometry and the optical fluence reaching the absorber. It can be shown that the 1D transmission-mode PA pressure spectrum of a two layer material (Fig.1) is given by [38]:

$$\tilde{p}_a(L_1, f) = \frac{\Gamma\, e^{-\mu_{eff} L_0} e^{-\alpha(f) L_1}}{\left(1 + \frac{\rho_s c_s}{\rho_a c_a}\right)} \left(\frac{\mu_a (\mu_a \frac{\rho_s c_s}{\rho_a} + j\omega)}{(\mu_a c_a)^2 + \omega^2} \right) e^{-j\frac{\omega L_1}{c_a}} \tilde{I}_0(f) \tag{3}$$

where the tilde indicates the Fourier transform operation; ω is the angular frequency, $\omega = 2\pi f$; c_a (c_s) is the speed of sound in the absorbing liquid and in the interfacial water; ρ_a (ρ_s) is the density of the absorbing liquid (water); μ_a is the absorption coefficient of the absorbing liquid; μ_{eff} is the effective optical attenuation coefficient of water; α is the acoustic attenuation of oil; L_0 and L_1 are the thickness of the water column and the distance of the transducer from the absorbing liquid (e.g. oil) surface respectively; I_o is the incident laser intensity before attenuation. For a short pulse, negligible acoustic attenuation and approximately similar acoustic impedance of the two liquids, it can be shown that Eq. (3) reduces to Eq. (1). However, in a more general case, the transient detected by the transducer is:

$$V_{tr}(t) = \frac{\Gamma\, \mu_a e^{-\mu_{eff} L_0}}{\left(1 + \frac{\rho_s c_s}{\rho_a c_a}\right)} \int_{-\infty}^{+\infty} \left(\frac{\mu_a \frac{\rho_s c_s}{\rho_a} + j\omega}{(\mu_a c_a)^2 + \omega^2} e^{j\omega(t - \frac{L_1}{c_a})} e^{-\alpha(f) L_1} \tilde{I}_0(f) \tilde{H}_{tr}(f) \right) df \tag{4}$$

where H_{tr} is the transfer function of the transducer. Eq. (4) helps account for the effect of factors such as the limited bandwidth of the transducer and acoustic attenuation. It should be noticed that acoustic