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Temperature Dependence of Harmonics Generated by Nonlinear Ultrasound Beam Propagation in Water: A Simulation Study

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***Abstract*—Nonlinear ultrasound beam propagation is exploited in various biomedical applications of ultrasound. In this work, the feasibility of using harmonic pressure amplitudes generated by nonlinear ultrasound propagation in noninvasive temperature estimation has been studied. The nonlinear propagation of a 30-cycle Gaussian-envelop sinusoidal pulse in water was simulated. The ultrasound source had a pressure amplitude of 0.35 MP from a flat circular transducer of 22 mm diameter with three different center frequencies of 1 MHz, 2.5 MHz and 5 MHz. The simulations were performed using a numerical solution of Khoklov-Zabolotskaya-Kuznetsov (KZK) nonlinear wave equation with temperature dependent medium parameters. The water temperature was assumed to increase from 20°C to 60°C in the simulations. Using empirical published data, the medium's parameters including sound speed, density, absorption coefficient and nonlinearity parameter (B/A) were modeled as a function of temperature in the simulations. The harmonic amplitudes were analyzed at axial distances from the transducer where the last pressure maximum occurs for each temperature. The pressure amplitudes of the fundamental frequency, the second and the third harmonics changed by 0.2% and 9.1%, -6.1% and 17.5%, -11.8% and 30.3% for pulses with transmit frequencies of 1 MHz and 5 MHz, respectively, due to the temperature change. The harmonics were weakly affected by temperature for the transmit pulse with a center frequency of 2.5 MHz. It is concluded that temperature estimation based on changes in the nonlinear harmonics is feasible with transmit frequencies higher than 3 MHz. The large changes in the harmonics as a function of temperature show that this could potentially be a basis for an ultrasound-based thermometry method.**

Keywords— Noninvasive thermometry, nonlinear ultrasound, harmonics, KZK simulation.

I. Introduction

A. Motivation

In cancer thermal therapy the tissue temperature is increased to levels where the controlled treatment of cancer cell can be achieved. There are two types of cancer thermal therapy that are clinically approved: hyperthermia and thermal ablation [1]. In hyperthermia, the temperature of the tumor tissue is increased up to 43°C. Hyperthermia enhances the effectiveness of other cancer treatment modalities such as radiation therapy and chemotherapy. In thermal ablation, the temperature is increased to above 55°C in order to cause direct coagulation necrosis in the tumor tissue. Different devices have been used to deliver heat to the tissue such as ultrasound, microwave and radio frequency [1].

Regardless of the treatment type or the heating device, thermal therapy lacks a simple and robust non-invasive and real-time temperature monitoring technique. The goal of this study is to develop a simple ultrasound-based real-time tissue-temperature monitoring technique with clinically acceptable accuracy and spatial resolution. Monitoring and controlling the tissue temperature distribution during thermal therapy will help to maintain the target tumor tissue temperature and to reduce damage to surrounding healthy tissues.

Ultrasound is an attractive option for temperature mapping since it is non-ionizing, portable, inexpensive, and it has relatively simple signal-processing requirements. Several ultrasonic techniques have been proposed for noninvasive tissue thermometry [2]. In order to noninvasively estimate the tissue temperature using ultrasound, a temperature sensitive acoustic parameter is required. The tissue temperature could be estimated by knowing the temperature dependence of the parameter and tracking changes in that parameter during heating.

B. Nonlinear Ultrasound Thermometry

Acoustic pulses with relatively high-pressure (a.k.a a finite-amplitude wave) progressively get distorted as they propagate and this results in the generation of higher harmonics. This effect increases with frequency, source pressure and focusing the beam [3]. Finite-amplitude effects of nonlinear propagation of ultrasound beam are used in various diagnostic applications of ultrasound [4, 5].

A number of studies showed that the acoustic nonlinearity parameter (B/A) is highly temperature dependent and it could be considered as a basis for noninvasive temperature estimation [6, 7]. The B/A is about four times more temperature sensitive compared to the speed of sound and thermal expansion in water [6]. Liu *et al.* demonstrated that the B/A increases about 40% and 55% in porcine fat and liver, respectively, as the temperature was raised from 20°C to 60°C [7].

van Dongen and Verweij simulated the nonlinear propagation of acoustic waves in glycerol with the lossless Burgers equation [6]. They showed that the harmonics pressure amplitudes are temperature dependent and they could potentially be a suitable parameter for noninvasive ultrasound thermometry. However, the Burgers equation is the simplest model that describes the combined effect of nonlinearity and absorption for progressive plane waves of finite amplitude. Both [8] simulated an acoustic plane wave propagating in water in order to study the temperature dependence of harmonics. The simulations were performed using two different solutions of Burgers equation known as Key-Beyer and Fubini for lossy and lossless media, respectively. A monochromatic source with a frequency of 1 MHz and pressure of 1 MPa was used in the study. The author showed that the harmonics are weakly sensitive to temperature and a minimum in the harmonic pressure value occurs at around 45°C.

The Khoklov–Zabolotskaya–Kuznetsov (KZK) equation is a well-established model for finite-amplitude beam propagation [3, 9-11]. The KZK equation is a parabolic approximation of the Westervelt nonlinear wave equation that consists of terms to account for diffraction, absorption and nonlinearity. The diffraction term accounts for the finite dimensions of the source and the attenuation term considers the heat conduction and viscosity of the medium. The nonlinear term accounts for the nonlinear propagation of the finite-amplitude wave.

In this study, nonlinear ultrasound beam propagation simulations were performed using a time-domain numerical solution of a modified KZK nonlinear wave equation that accounts for temperature dependent medium parameters. The main objective of this study is to investigate and understand the temperature dependence of acoustic harmonics generated by nonlinear ultrasound beam propagation in water in a simulation study, considering the effects of absorption, diffraction and nonlinearity. The results will be used to theoretically predict the transmit signal frequency range for which the acoustic harmonics can be used as suitable acoustic parameters for noninvasive ultrasound thermometry.

II. Methods

A modified version of the KZK nonlinear differential equation based on H. Hasani *et al.* work [10] was used in which temperature dependence of the medium parameters were included in the model. The dimensionless form of the temperature dependent KZK equation for unfocused sources could be given as:

$$\frac{\partial P}{\partial \sigma} = \frac{1}{4(1+\sigma)^2}\int_{-\infty}^{\tau}\left(\frac{b}{a}\frac{\partial^2 P}{\partial X^2} + \frac{a}{b}\frac{\partial^2 P}{\partial Y^2}\right).d\tau' + A(T)\frac{\partial p^2}{\partial \tau^2} + \frac{N(T)}{1+\sigma}\left(P\frac{\partial p}{\partial \tau}\right) \quad (1)$$

where P is the transformed source pressure amplitude defined as $P = (1+\sigma)(p/p_0)$ which p is the sound pressure in the Cartesian coordinates and p_0 is the source pressure amplitude. $\sigma = z/z_0$ is the dimensionless z axis relative to the Rayleigh distance ($z_0 = \omega_0 ab/2c_0$) for a source with characteristic sizes of a and b in the x and y directions with an angular frequency of ω_0. X and Y are the transformed transverse coordinates ($X = x/a$, $Y = y/b$) and T is the temperature. $A = \alpha_0 z_0$ is the absorption parameter, α_0 is the pressure absorption coefficient, $N = z_0/z_s$ is the nonlinear parameter, z_s is the plane-wave shock formation distance at frequency ω_0 defined as $z_s = \rho_0 c_0^3/\beta\omega_0 p_0$ which c_0 and ρ_0 are the small signal speed of sound and the medium density, respectively. τ is the transformed retarded time defined as $\tau = \omega_0 t'$ where t' is the retarded time ($t' = t - z/c_0$). The terms on the right-hand side of Equ. (1) account for diffraction, nonlinearity, and thermoviscous absorption, respectively.

Nonlinear propagation of a 30-cycle pulse in water with source pressure amplitude of 0.35 MPa from a flat circular transducer of 22 mm diameter was simulated. The center frequency of the excitation pulse was set to 1 MHz, 2.5 MHz and 5 MHz for three different set of simulations. The source pressure waveform was a Gaussian envelope pulse given as:

$$P = exp\left[-\left(\frac{\tau}{30\pi}\right)^2\right] sin\tau \quad (2)$$

In order to replicate the effects induced by raising temperature in water from 20°C to 60°C, the values of four acoustic medium parameters at each temperature were employed as an input to the simulation codes.

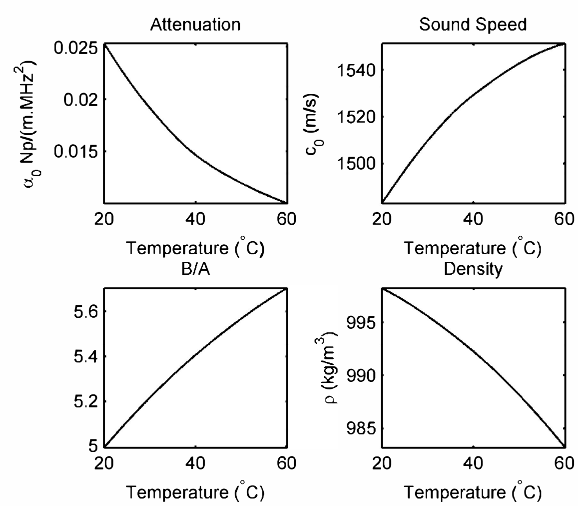

Fig. 1. The (a) attenuation coefficient [11], (b) speed of sound [11], (c) B/A [12], and (d) density [6] as functions of temperature for water.

The values of sound speed, medium's density, absorption coefficient and the B/A as a function of temperature in water were obtained from published data in the literature [6, 11, 12] and are shown in Fig. 1. At each simulation run, the acoustic pressure pulse was computed at the last maximum distance. The last maximum distance is the axial distance from the transducer where the last pressure maximum occurs. The last maximum distances for the three center frequencies of 1 MHz, 2.5 MHz and 5 MHz occurred at 8.5 cm, 18 cm and 32 cm, respectively.

The harmonic pressure amplitudes were obtained by calculating the frequency spectrum of the pulse using the Fourier transform. The change in the amplitudes of the fundamental frequency (P_1), the second (P_2) and the third (P_3) harmonics were analysed at each simulated water temperature from 20°C to 60°C with an increment of 4°C.

III. RESULTS

Fig. 2 illustrates the percentage change in the pressure amplitudes of fundamental frequency and the harmonics with respect to the initial temperature (20°C) for pulse transmit frequencies of 1, 2.5 and 5 MHz. The percentage change in P_1, P_2 and P_3 due to this 40°C temperature rise is summarized in Table I for all three transmit signal frequencies.

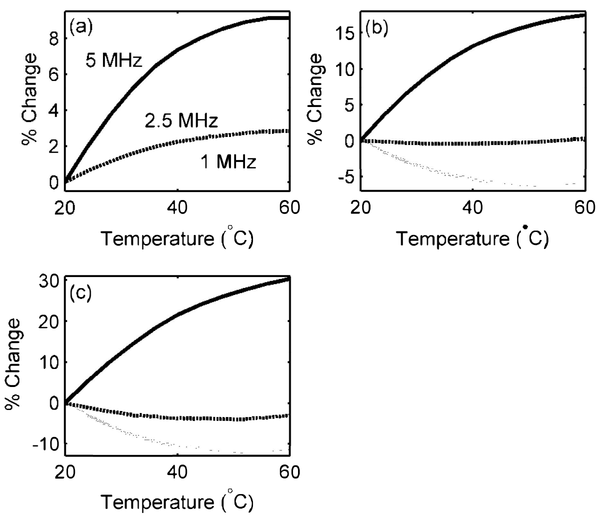

Fig. 2. Changes in (a) the fundamental frequency, (b) the second, and (c) the third harmonics as a function of temperature with respect to the initial temperature (20°C) for pulses with transmit frequencies of 1 MHz (gray dotted), 2.5 MHz (black dotted) and 5 MHz (black solid).

TABLE I. Percentage changes in p_1, p_2, and p_3 due to 40°C temperature increase from 20°C to 60°C.

Transmit signal frequency	% change in P_1	% change in P_2	% change in P_3
1 MHz	0.2%	-6.1%	-11.8%
2.5 MHz	2.8%	0.3%	3%
5 MHz	9.1%	17.5%	30.3%

IV. DISCUSSION

The results in Fig. 2 demonstrate that the pressure amplitudes of the second and the third harmonics are decreasing with temperature for the 1 MHz transmit signal. A minimum in the value of the harmonics occurs at around 52°C for transmit frequencies lower than approximately 2.5 MHz. The harmonics show the least sensitivity to temperature change at frequencies around 2.5 MHz. However, for higher transmit frequencies, the harmonics increase with temperature monotonically and the higher the frequency, the higher is the sensitivity of the harmonics to temperature.

This could potentially be due to the interplay between mechanisms of absorption and nonlinearity. The relative importance of absorption and nonlinearity in the KZK model is determined by the dimensionless parameters of nonlinearity (N) and absorption (A). The ratio of $\Gamma = N/A$ is defined as the Gol'dberg number [9], which gives a measure of balance between the nonlinear and the absorption processes. Duck stated that when $\Gamma \gg 1$ the nonlinear process dominates and when Γ is about 1.0, the effects of nonlinearity and absorption are comparable [5].

Fig. 3 shows the values and the percentage changes in A, N and the Gol'dberg number (Γ) as a function of temperature for three frequencies used in this study.

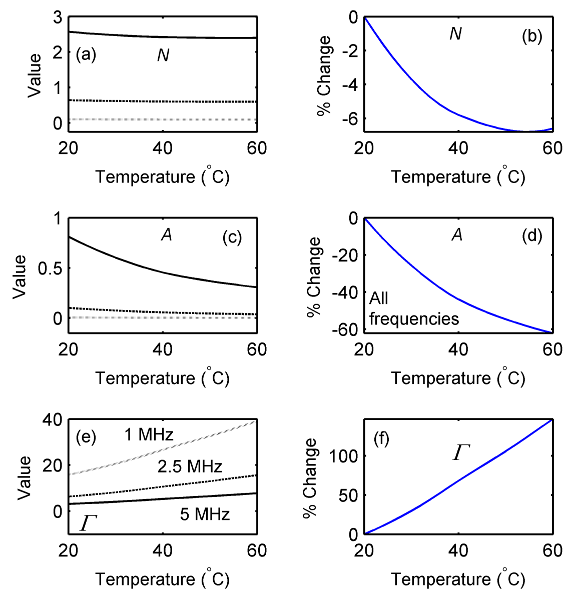

Fig. 3. The values (left) and the percentage changes (right) of (a) and (b) nonlinear parameter, (c) and (d) absorption parameter, (e) and (f) Gol'dberg number as a function of temperature for three frequencies used in this study.

As the temperature increases from 20°C to 60°C, A decreases by 60% whereas N decreases by 6%. A decrease in attenuation enhances the generation of harmonics but decrease in nonlinearity reduces the amount of wave distortion and creation of harmonics. At 1 MHz the Gol'dberg number is about 27 which shows that nonlinearity significantly dominates over absorption. Therefore, the trend of the harmonics with temperature is similar to that of the dimensionless parameter of nonlinearity (N) as shown Fig. 1 (a) and (b). As the frequency increases, the Gol'dberg number decreases and the absorption effect becomes stronger. Based on our results, 2.5 MHz is the frequency in which both mechanisms are comparable and the harmonics are almost unaffected by temperature change. At higher frequencies the absorption mechanism dominates over the mechanism of nonlinearity. Therefore, at frequencies higher than 2.5 MHz the harmonics increase monotonically with temperature due to the decrease in absorption and the slope of this increase becomes steeper at higher frequencies.

V. CONCLUSION

It is concluded that temperature estimation based on changes in nonlinear harmonics is feasible with transmit frequencies higher than 3 MHz. The large changes in the harmonics as a function of temperature indicate that this phenomenon could potentially be a promising basis for an ultrasound-based thermometry method.

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