Sensitivity study of the acoustic nonlinearity parameter for measuring temperatures during High Intensity Focused Ultrasound treatment

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The aim of High Intensity Focused Ultrasound (HIFU) is to locally increase the temperature in a body. For an adequate application of the treatment it is important to measure non-invasively the temperature profiles in the heated region. Most efficiently, this is done with the same modality as being used for heating. Consequently, the preferred measuring method should rely on the temperature dependence of an acoustic medium parameter. The goal of this study is to determine which parameter is most sensitive to temperature changes. To find the most suitable parameter, the temperature dependence of the acoustic medium parameters for water are investigated. Since measured values of the acoustic nonlinearity parameter $\frac{B}{2A}$ parameter are only known for a few coarsely distributed temperature values, it has been synthesised from a two-dimensional function describing the speed of sound versus temperature and pressure. Results show that the $\frac{B}{2A}$ parameter is far more sensitive for temperature changes than the other parameters, except for the acoustic absorption coefficient. Comparison with $\frac{B}{2A}$ values found in literature confirms the idea that nonlinear acoustics is a favorite candidate to measure temperature profiles.

1 Introduction

The aim of High Intensity Focused Ultrasound (HIFU) is to obtain a thermal energy flow into the body in order to increase the temperature locally. This increase in temperature can be used for thermal ablation therapy during cancer treatment. A compact overview of research activities in this area are presented in [1, 2, 3].

During the propagation of the ultrasound wave field the acoustic medium parameters (density and compressibility) change locally due to deformations that come along with the high amplitude pressure wave field. Due to this nonlinearity, higher harmonics of the acoustic wave field are generated. The amplitudes of these harmonic wave fields depend on the acoustic nonlinearity parameter $\frac{B}{2A}$. A good overview of the theory of nonlinear acoustics is given by Beyer [4] and Hamilton and Blackstock [5].

It is observed by many authors that the effect of nonlinear acoustics plays a signifcant role during treatment. The most noticeable effect is the spatial shift of the region with maximum temperature as expected from linear acoustics. This shift is amongst others caused by changes in the frequency spectrum during treatment.

In order to increase the efficiency of the treatment it is important to control these effects and to obtain precise knowledge about the temperature profiles in the region of interest. Preferably, these profiles are measured non-invasively and with the same apparatus as is being used to increase the temperature. For situations where HIFU is the treatment modality the preferred measuring method should therefore rely on changes in the acoustic medium parameters, i.e. the speed of sound (or density and compressibility), the acoustic absorption coefficient, the acoustic nonlinearity parameter, the volume coefficient of thermal expansion or the specific heat constant.

To the best of the authors' knowledge, so far only *i)* the speed of sound, *ii)* the acoustic absorption coefficient and *iii)* the volume coefficient of thermal expansion have been used actively to measure temperature [6]. Fortunately, as the acoustic nonlinearity parameter $\frac{B}{2A}$ is known to be temperature dependent [7, 8] and the effect of non-linear propagation has proved to be significant, nonlinear acoustics can form the basis for an additional technique to measure temperature.

In order to determine which acoustic medium parameter should form the basis for the prefered method to measure temperature non-invasively we compare the temperature dependence of the acoustic nonlinearity parameter with the three acoustic medium parameters currently used. It should be noted that water has been used as the medium under investigation, since representative values for all parameters under investigation are not well reported in literature for human tissues.

1.1 Theory

The propagation and scattering of nonlinear acoustic wave fields is well described via the Westervelt equation [5, 9] which reads

$$\nabla^2 p(\vec{r},t) - \frac{1}{c_0}\partial_t^2 p(\vec{r},t) + \frac{\delta}{c_0^4}\partial_t^3 p(\vec{r},t) = -\frac{\beta}{\rho_0 c_0^4}\partial_t^2 p^2(\vec{r},t) + \nabla\cdot\vec{f}(\vec{r},t) - \rho_0\partial_t q(\vec{r},t), \quad (1)$$

where $p(\vec{r},t)$ is the acoustic pressure with spatial coordinate $\vec{r}$ and temporal parameter t, c_0 is the small-signal speed of sound of the homogeneous background medium, ∂_t is the temporal derivative, δ is the diffusivity of sound, β is the coefficient of nonlinearity, ρ_0 equals the small-signal density of the medium and $\vec{f}(\vec{r},t)$ and $q(\vec{r},t)$ are the volume density of volume force and the volume density of volume injection rate respectively. Note that the subscribt "0" is used for parameter values under ambient conditions. The first term on the right hand side of Eq. (1) is the nonlinearity term which can be understood as a contrast source term; local changes in the acoustic medium parameters caused by the time-varying acoustic wave field will act as a contrast for the wave field itself. This effect manifests itself by the formation of harmonic wave fields. The coefficient of nonlinearity is defined as

$$\beta = 1 + \frac{B}{2A}, \quad (2)$$

where the parameter $\frac{B}{2A}$ is the leading order finite amplitude correction to the small-signal speed of sound parameter c_0 [5]. In order to show its relation with temperature the parameter is expressed as

$$\frac{B}{2A} = \rho_0 c_0 \left.\frac{\partial c}{\partial p}\right|_{p_0,T} + \frac{\alpha_T c_0 T_0}{c_p \rho_0}\left.\frac{\partial c}{\partial T}\right|_{p,T_0}, \quad (3)$$

where α_T is the volume coefficient of thermal expansion, c_p the specific heat at constant pressure and T the absolute temperature of the medium [8]. From Eq. (3)

it becomes clear that acoustic nonlinearity parameter $\frac{B}{2A}$ consists of two contributions, of which the first one is based on isothermal pressure changes,

$$\left(\frac{B}{2A}\right)_1 = \rho_0 c_0 \left.\frac{\partial c}{\partial p}\right|_{p_0,T}, \tag{4}$$

while the second one is based on isobaric temperature changes,

$$\left(\frac{B}{2A}\right)_2 = \frac{\alpha_T c_0 T_0}{c_p \rho_0} \left.\frac{\partial c}{\partial T}\right|_{p,T_0}. \tag{5}$$

One can understand these terms as the relative increase in the phase velocity caused by variations in pressure, Eq. (4), and temperature, Eq. (5), [7, 8].

A qualitative examination of the temperature dependency of the nonlinearity parameter requires a model for the speed of sound as a function of temperature and pressure. Various models exist, of which the ones presented in [10, 11] are the most well known. However, the temperature range we are interested in exceeds these models. Therefore, we have used the model of Wilson [12] instead. Models describing the coeficient of thermal expansion and the absorption coefficient as a function of temperature, as well as the remaining acoustic medium parameters, are based on measured values and obtained from literature [10, 11, 13].

2 Results

First the volume density of mass $\rho = \rho_0(T)$, the volume coefficient of thermal expansion $\alpha = \alpha_T(T)$, the acoustic absorption coefficient α_a/f^2, and the specific heat constant $c_p = c_p(T)$ have to be obtained for a range of temperature values. This is done by interpolating a set of measured values, obtained at atmospheric pressure [13, 14]. The results are shown in Fig. 1.

The speed of sound $c = c_0(T, p)$ is know to be both temperature and pressure dependent. Various models exist which describe the speed of sound as a function of temperature and pressure based on least square curve fitting of a set of measurements to a polynomial function. The most well known are from Belogol'skii *et al.* [10] which is only valid up to 40°C and from Bilaniuk *et al.* [11] which is only valid at atmospheric pressure. Consequently, we use the less known model developed by Wilson [12] which is based on measurements over the temperature range 0.9 to 91.2°C and the pressure range 0.1 to 96 MPa. This is the same model which Beyer used to compute $\frac{B}{2A}$ for a limited number of temperatures [8]. The resulting speed of sound as function of temperature and pressure is shown in Fig. 2. The results clearly reveal that changes in the speed of sound are dominated by variations in temperature.

Next, the gradient of the speed of sound function $c_0 = c_0(T, p)$ is computed along the pressure axis to obtain $\left(\frac{B}{2A}\right)_1$ for isothermal pressure changes and along the temperature axis to obtain $\left(\frac{B}{2A}\right)_2$ for isobaric temperature changes. The results are shown in Fig. 3. Note that the contributions from the isobaric temperature changes are much higher than the contributions from the isothermal pressure changes.

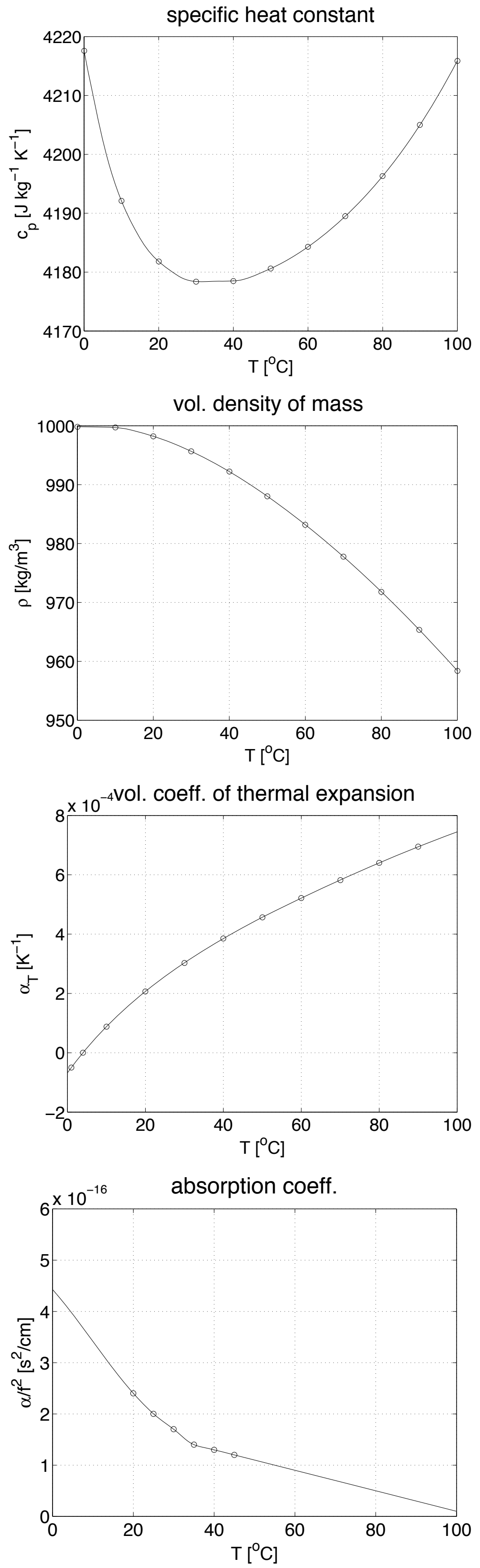

Figure 1: From top to bottom: specific heat constant $c_p(T)$, volume density of mass $\rho_0(T)$, volume coefficient of thermal expansion $\alpha_T(T)$ and acoustic absorption coefficient α_a/f^2 as a function of temperature.

Combining the outcome for $\left(\frac{B}{2A}\right)_1$ and $\left(\frac{B}{2A}\right)_2$ results in the required acoustic nonlinearity parameter $\frac{B}{2A}$ as a function of temperature and pressure, see Fig. 4. The computed $\frac{B}{2A}$ values are in agreement with the results obtained by Beyer [8] and Hagelberg *et al.* [15], see

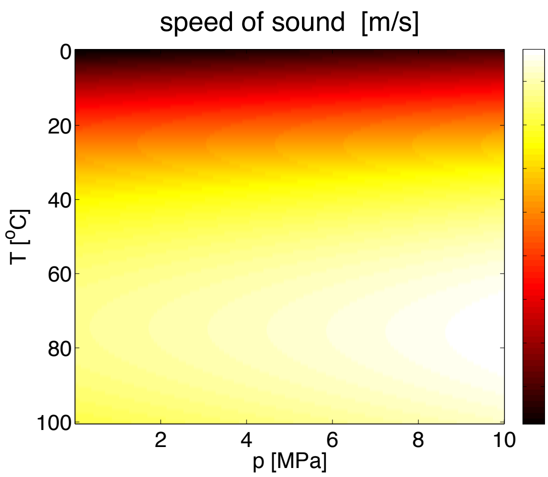

Figure 2: The speed of sound of water as function of pressure and temperature [10, 11].

Fig. 5. Their results are computed in the same way as we do using data measured by Wilson [12] and Holton [16] respectively.

Prior to starting hyperthermia treatment with HIFU, the background temperature is known and equals $T_0 = 37^o$C. Hence, only the temperature increase in the region of intereast is of importance and should be measured. Consequently, it is more relevant to investigate the relative changes as a function of temperature of the above parameters than their absolute values. Therefore this relative change is computed for the temperature range of $T = 30 - 70^o$C. The results are shown in Fig. 6. As reference temperature $T_0 = 37^o$C has been used. For reference, the absolute values of each parameter for the most important temperatures ($T = 37^o$C and $T = 42^o$C) are presented in Table 1.

Table 1: The acoustic medium parameters the acoustic nonlinearity parameter $\frac{B}{2A}$, speed of sound c_0, the volume density of mass ρ_0, the volume coefficient of thermal expansion α_T, the acoustic absorption coefficient α_a/f^2 and the specific heat constant c_p at temperatures of $T = 37^o$C and $T = 42^o$C.

parameter	value	
	$T = 37^o$C	$T = 42^o$C
$\frac{B}{2A}$ (computed)	2.71	2.75
c_0	1524	1532
ρ_0	993.3	991.4
α_T	$0.36{\cdot}10^{-3}$	$0.40{\cdot}10^{-3}$
α_a/f^2	13.5	12.6
c_p	4178	4179

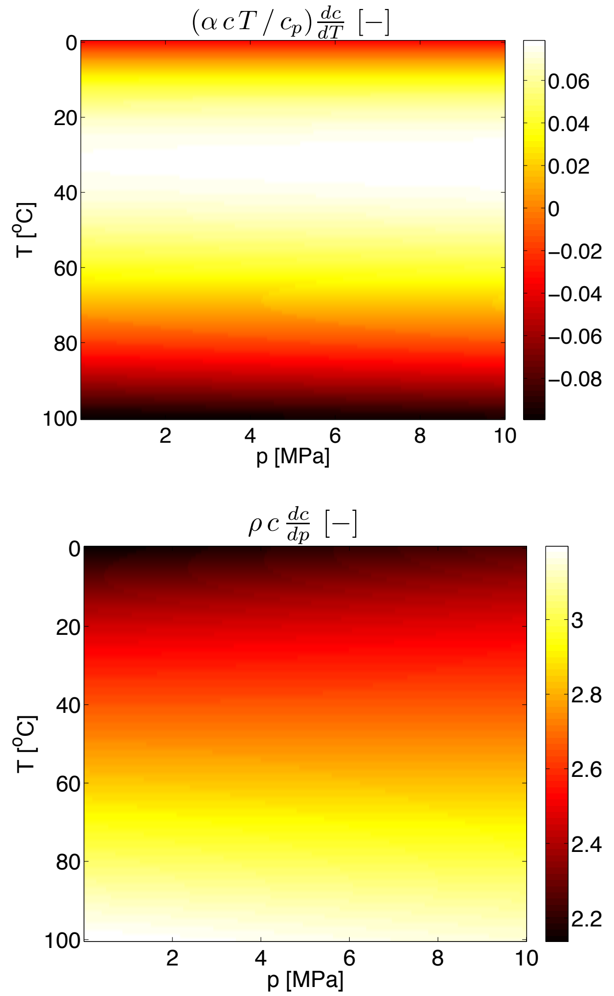

Figure 3: The contributions to the nonlinearity parameter $\frac{B}{2A}$ from (top) isothermal pressure changes and (bottom) isobaric temperature changes.

3 Discussion and conclusion

High Intensity Focused Ultrasound (HIFU) is used to increase the temperature in a tumor for hyperthermia cancer treatment. In order to achieve this temperature increase high pressure fields are required resulting in a nonlinear propagation of the acoustic pressure wave field. For an adequate application of the treatment it is important to measure non-invasively the temperature profiles in the heated region. Most efficiently, this is done with the same modality as being used for heating. Consequently, the preferred measuring method should rely on the temperature dependence of some acoustic medium parameter.

In this paper we investigated the degree of sensitivity to changes in temperature for various acoustic medium parameters. The sensitivity analysis has been done for water due to the fact that values for these parameters are not well documented for human tissue.

An overview of the results are shown in Table 1. These results, in combination with the results presented in Fig. 6, clearly show that the acoustic nonlinearity parameter $\frac{B}{2A}$ is at least five times more sensitive to changes in temperature than speed of sound c_0, the volume density of mass ρ_0, the volume coefficient of thermal expansion α_T and the specific heat constant c_p. The re-

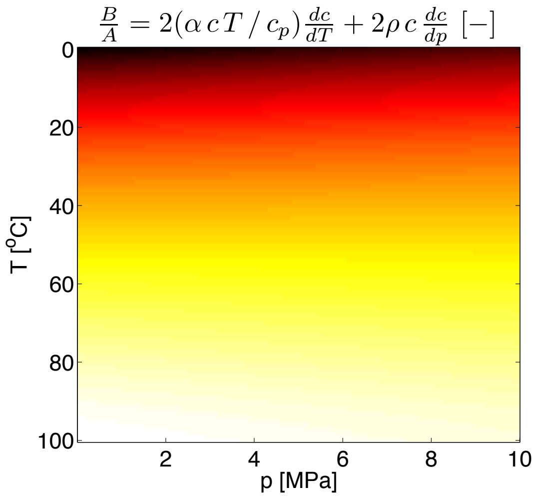

Figure 4: The computed nonlinearity parameter $\frac{B}{2A}$ as a function of pressure and temperature.

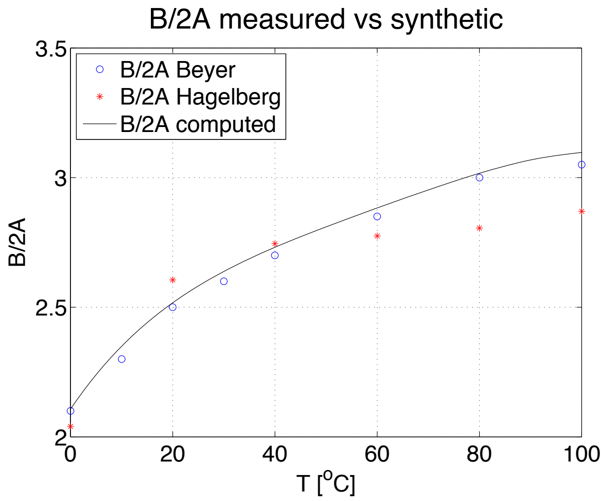

Figure 5: The computed nonlinearity parameter $\frac{B}{2A}$ at atmospheric pressure compared with values from literature [8, 15].

sults also show that the acoustic absorption coefficient α_a/f^2 is most sensitive to temperature changes.

Consequently, we conclude that the acoustic nonlinearity parameter $\frac{B}{2A}$ is a good parameter to use for measuring tissue temperature non-invasively by using ultrasound.

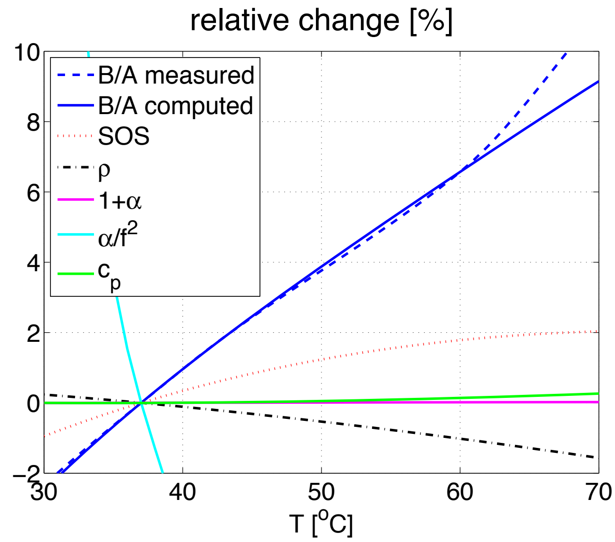

Figure 6: The relative change in the speed of sound (SOS), $\frac{B}{2A}$, ρ, α, α_a/f^2, c_p, with $T = 37^o$C and $p = 0.1$ MPa as reference pressure and temperature.

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