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An ultrasonic caliper device for measuring acoustic nonlinearity

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Abstract

In medical and industrial ultrasound, it is often necessary to measure the acoustic properties of a material. A specific medical application requires measurements of sound speed, attenuation, and nonlinearity to characterize livers being evaluated for transplantation. For this application, a transmission-mode caliper device is proposed in which both transmit and receive transducers are directly coupled to a test sample, the propagation distance is measured with an indicator gage, and receive waveforms are recorded for analysis. In this configuration, accurate measurements of nonlinearity present particular challenges: diffraction effects can be considerable while nonlinear distortions over short distances typically remain small. To enable simple estimates of the nonlinearity coefficient from a quasi-linear approximation to the lossless Burgers' equation, the calipers utilize a large transmitter and plane waves are measured at distances of 15-50 mm. Waves at 667 kHz and pressures between 0.1 and 1 MPa were generated and measured in water at different distances; the nonlinearity coefficient of water was estimated from these measurements with a variability of approximately 10%. Ongoing efforts seek to test caliper performance in other media and improve accuracy via additional transducer calibrations.

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Keywords: acoustic calipers, liver transplant, nonlinear acoustics, B/A

1. Introduction

In diagnostic and therapeutic applications of medical utrasound, there is a general need for knowing the acoustic properties of tissue. Although many measurements have been made (Duck, 1990), available data are not consistent

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and were compiled from studies using different measurement techniques. Beyond a general interest in the acoustic properties of tissue, we are pursuing a specific project to use ultrasound for characterizing donor livers for transplantation. Despite efforts to expand the donor pool there is still a discrepancy between the availability of transplantable organs and the need for them (Orman et al., 2013; Wertheim et al., 2011). In particular, hepatic steatosis (fatty liver disease) is considered a primary risk factor in transplanted livers and can therefore result in organ nonuse (McCormack et al., 2011; Spitzer et al., 2010). Although there is interest in expanding the donor pool by using organs with a higher degree of steatosis, consistent measurements of steatosis are typically not available. The current gold standard for potential donor liver evaluation is histological biopsy, which is an inherently subjective and invasive process; moreover, because biopsies are often not performed, decisions are often based on visual inspection by the surgeon.

We seek to develop an ultrasonic caliper device capable of quantitatively characterizing liver tissue. The potential of such measurements was investigated by Sehgal et al. (1986), who used sound speed and nonlinearity measurements to infer the fatty and non-fatty composition of liver tissue. To build on this approach, we also aim to quantify the amount of fat that exists in small or large droplets. Small, sub-micron sized droplets (*i.e.*, microsteatosis) are metabolically different from large droplets and potentially much less problematic in transplants. Toward this end, dispersion calculations (Evans and Attenborough, 2002) for ultrasound propagation in a medium comprising fatty and non-fatty components suggest that micro-steatosis may be detectable from attenuation measurements at sub-megahertz frequencies. To measure ultrasonic sound speed, nonlinearity, and attenuation in transplant applications, we propose to develop a transmission-mode caliper device such as the one pictured in Fig. 1. Notably, this basic hardware design is comparable to that used for *in vivo* nonlinearity measurements by Zhang and Dunn (1987).

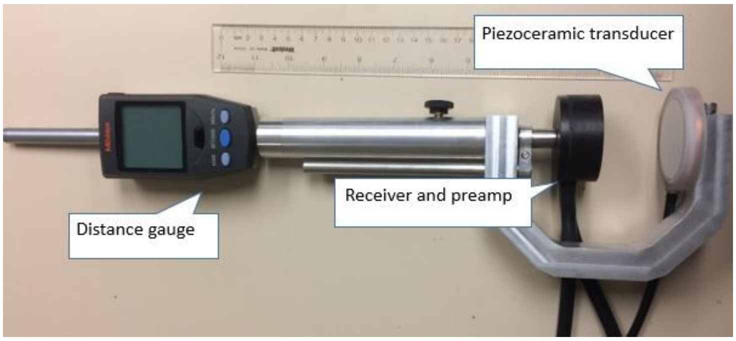

Fig. 1. Photo of the proposed hardware for an acousic calipers.

2. Methods

Nonlinear acoustic propagation is a well-known phenomenon characterized by distortion of the shape of an acoustic waveform as it propagates in a nonlinear medium. The nonlinearity comprises convective nonlinearity as well as the impact of higher-order terms in the medium's equation of state, which cause parts of the waveform at higher pressures to propagate faster than those at lower pressures (Hamilton and Blackstock, 1998). Previous work by Bjørnø (1986) suggests an estimation accuracy on the order of ±5% can be achieved for the coefficient of nonlinearity for biological fluids. There are two basic approaches for such measurements: the thermodynamic method and the finite-amplitude method. Though the thermodynamic method is considered to be more accurate, it is not viable for measuring tissues *in vivo*. Here we use the finite-amplitude method, which relies on a calibration of source output and direct measurement of waveform distortion over a known propagation distance. Typically, the finite-amplitude approach is implemented by using the amplitude of the second-harmonic component of the distorted waveform to quantify the nonlinearity of the medium.

For the present application, a key challenge is to accurately measure nonlinearity over a relatively short propagation distance (15–50 mm) using a transmitting transducer with a fundamental frequency below 1 MHz. Our basic approach is to use a large transmitting transducer such that measurements can be made in the plane-wave regime and diffraction effects can be ignored. However, for the geometry and frequency of interest, the plane-wave regime will be realized for only a few acoustic cycles, during which the real transducer output will be transient in nature.

Accordingly, it is necessary to analyze nonlinear waveform distortions in the time domain. To that end, we first define an expression for estimating the nonlinearity from an arbitrary transient waveform. Then we use a known solution for lossless nonlinear propagation of plane waves to demonstrate the performance of this expression for estimating nonlinearity. Finally, we use a transducer designed for the calipers depicted in Fig. 1 to generate finite-amplitude waveforms in water and glycerol to experimentally test the approach in the regime of interest.

2.1. Model

The nonlinear propagation of plane waves is commonly described by Burgers' equation (Hamilton and Blackstock (1998)):

$$\frac{\partial p}{\partial x} - \frac{\beta}{\rho_0 c_0^3} p \frac{\partial p}{\partial \tau} = \frac{\delta}{2c_0^3} \frac{\partial^2 p}{\partial \tau^2} \tag{1}$$

where $p(x, \tau)$ is pressure, x is propagation distance, β is the coefficient of nonlinearity, c_0 is sound speed, ρ_0 is density, and $\tau = t - x/c_0$ is a retarded time coordinate. Note that the nonlinearity of a medium is often expressed as B/A, where A and B are coefficients of nonlinear terms in the Taylor series expansion of the equation of state. By definition, $\beta = 1 + B/2A$. In Eq. (1), the right-hand side captures attenuation with δ representing the diffusivity of sound. As a plane wave at an initial point $p_1(\tau) = p(0, \tau)$ propagates to an arbitrary second point, the waveform shape $p_2(\tau) = p(x, \tau)$ becomes distorted. It is now convenient to define $\hat{p} = p_2 - p_1$ as the nonlinear component of the distorted waveform. If we neglect attenuation and waveform distortions $\hat{p}$ are small, then Eq. (1) is readily integrated to yield

$$\hat{p} = x \cdot \frac{\beta}{2\rho_0 c_0^3} \frac{\partial p_1^2}{\partial \tau} \tag{2}$$

From this expression, if waveforms p_1 and p_2 are measured in conjunction with the propagation distance x, then the coefficienct of nonlinearity β can be readily calculated. In practice, we estimate β from a set of measurements by selecting the value that provides the optimal least-squares fit between the left- and right-hand sides of Eq. (2).

While Eq. (2) is sufficient if attenuation can be neglected, we note from Zhang and Dunn (1987) that attenuation can be accounted for using the modified estimate

$$\beta' = \beta \cdot \exp\left[\left(\alpha_1 + \frac{\alpha_2}{2}\right) x\right] \tag{3}$$

Here, α_1 and α_2 are the attenuation coefficients of the medium evaluated at the fundamental frequency and the second harmonic, respectively.

2.2. Experiments

Transient pressure waveforms with a center frequency of 667 kHz were generated by a flat piezoceramic transducer 50 mm in diameter. The transducer was driven by a class D amplifier with supply voltages between 50 and 350 V. Using a 14-bit digitizer (Gage Razor 14, DynamicSignals LLC, Lockport, IL), waveforms were measured with a capsule hydrophone (Model HGL-0200, Onda Corp., Sunnyvale, CA). This hydrophone was calibrated at 667 kHz by substitution with a calibrated fiber optic hydrophone (Model FOPH 2000, RP Acoustics, Leutenbach, Germany). With these components, measurements were acquired in a tank of deionized, degassed water at a temperature of 18°C. All propagation distances were inferred from the sound speed in water at this temperature and measurement of the time-of-flight for waveform propagation. In addition, to estimate β in glycerol, a 35 mm thick drum with 0.5 mm acoustic rubber windows was submerged in the tank in the propagation path.

To implement the method described in Section 2.1, a low-amplitude measurement at driving voltage V_{lo} in the plane-wave regime was used to represent the shape of the undistorted waveform p_0 at the source. The size of the flat transducer in conjunction with the desired propagation range from 15–50 mm constrained the plane-wave regime to a time window corresponding to about three acoustic cycles. Each high-amplitude waveform p_2 at known propagation distance x was measured directly at a driving voltage V_{hi}. The corresponding source pressure p_1 was then calculated by assuming linear transducer behavior and scaling the waveform shape p_0 by the ratio V_{hi}/V_{lo}.

3. Results

A measured nonlinear signal $\hat{p}$ is shown in Fig. 2. In this example, a $\hat{p}$ amplitude of about 0.03 MPa was achieved using a source pressure of about 1 MPa. In order to estimate β reliably, measured waveforms were averaged over 1,000 realizations to reduce noise in the signal. Using the least-squares method proposed in Section 2.1, a best-fit value of β was estimated to match the measured $\hat{p}$ signal from Fig. 2. This estimation was well-behaved with a clearly defined convergence at a minimum error as shown in Fig. 3. In water, measurements produced estimates $\beta = 3.35 \pm 0.3$ over distances from 15–50 mm in 5 mm intervals. For comparison, Hamilton and Blackstock (1998) reported a table of β values for water at temperatures from 0–100°C. Interpolation at 18°C yields a value of 3.45. Figure 4 shows experimentally estimated values of β over multiple days across the aforementioned distance range.

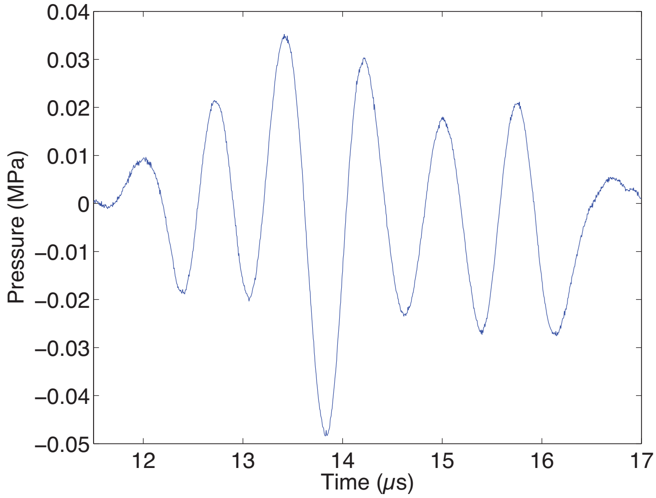

Fig. 2. An example of the nonlinear signal $\hat{p}$ as measured in water at 15 mm.

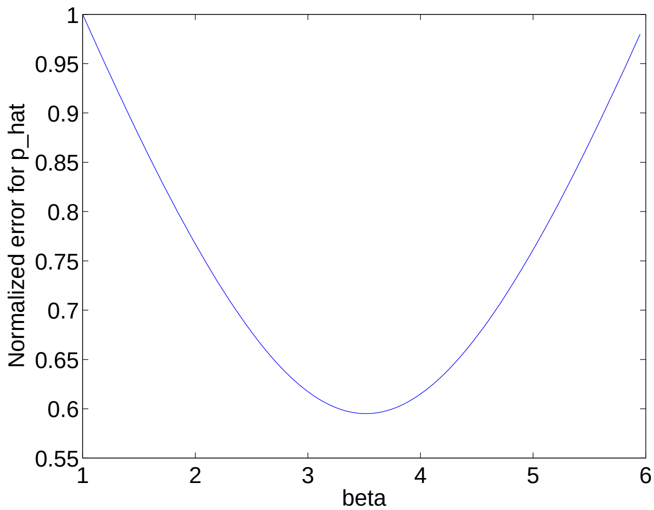

Fig. 3. Normalized error in estimating $\hat{p}$ as a function of β at 15 mm.

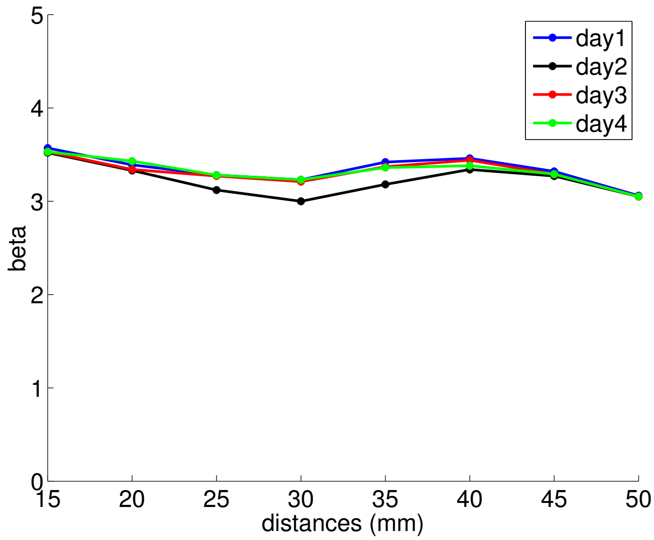

Fig. 4. Estimation of β across distance range

In glycerol, measurements produced an estimate $\beta = 5.0$ in the absence of attenuation. However, unlike water, glycerol has non-negligible attenuation. Using available values for glycerol's attenuation at 667 and 1334 kHz (Kaye & Laby Online, Version 1.0, 2005), we use Eq. (3) and obtain the improved estimate of $\beta = 5.75$. This value compares favorably to a reported value of 6.0 for pure glycerol at 20°C (Khelladi et al., 2009). In addition, we note that the drum used to contain the glycerol possessed 0.5 mm thick "windows" that impacted measurements. When filled with water, we found that the drum itself decreased β estimates on the order of 5%.

4. Conclusion

For both water and glycerol, the proposed approach for estimating nonlinearity was robust when p_2 amplitudes were high enough to introduce significant distortion relative to baseline noise in the hydrophone measurements. Here we used source pressures near 1 MPa in addition to waveform averaging, though we expect that this maximum pressure amplitude could be reduced with a different combination of averaging and source pressures represented by p_1 and p_2. Parameter estimates were relatively accurate and repeatable – *i.e.*, within 10% of reported values at any given measurement distance. Note that a significant portion of this variability can be attributed to ~10% variability for the hydrophone calibration, which is needed to quantify absolute source pressures. In addition, it was found that measurements in water across the entire range from 15–50 mm were consistent within 8% of the average value. This measurement variability in homogeneous media is somewhat larger than that of 3% as reported in measurements used to characterize liver tissue using a thermodynamic approach (Sehgal et al., 1984, 1986). Future work will include consideration of higher-order terms in the approximation represented by Eq. 2 in order to obtain more consistent β estimates over the entire measurement range. In addition, we will build and calibrate receivers designed to facilitate the acquisition of nonlinearity, sound speed, and attenuation measurements for planned *ex vivo* and *in vivo* studies.

Acknowledgements

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