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The dependences of phase velocity and dispersion on trabecular thickness and spacing in trabecular bone-mimicking phantoms

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Abstract

Frequency-dependent phase velocity was measured in trabecular-bone-mimicking phantoms consisting of two-dimensional arrays of parallel nylon wires (simulating trabeculae) with thicknesses ranging from 152 – 305 microns and spacings ranging from 700 – 1000 microns. Phase velocity varied approximately linearly with frequency over the range from 400 to 750 kHz. Dispersion was characterized by the slope of a linear least-squares regression fit to phase velocity vs. frequency data. The increase in phase velocity (compared with that in water) at 500 kHz was approximately proportional to the 1) square of trabecular thickness, 2) inverse square of trabecular spacing, and 3) volume fraction occupied by nylon wires. The first derivative of phase velocity with respect to frequency was negative and exhibited nonlinear, monotonically decreasing dependences on trabecular thickness and volume fraction. The dependences of phase velocity and its first derivative on volume fraction in the phantoms were consistent with those reported in trabecular bone.

Keywords

bone; trabecular; cancellous; velocity; dispersion

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I. INTRODUCTION

Bone sonometry is now an accepted method for diagnosis of osteoporosis (Laugier, 2004). Speed of sound (SOS) in trabecular bone is highly correlated with bone mineral density (Rossman *et al.,* 1989, Tavakoli and Evans, 1991, Zagzebski *et al.*, 1991, Njeh *et al.*, 1996, Laugier *et al.*, 1997, Nicholson *et al.*, 1998, Hans *et al.*, 1999, Trebacz, and Natali, *et al.*, 1999), which is an indicator of systemic osteoporotic fracture risk (Cummings *et al.*, 1993). Calcaneal ultrasonic measurements (SOS combined with broadband ultrasonic attenuation or BUA) have been shown to be predictive of hip fractures in women in prospective (Hans *et al.*, 1996, Bauer *et al.*, 1997, Huopio *et al.,* 2004) and retrospective (Schott *et al.*, 1995,

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Turner *et al.*, 1995, Glüer *et al.*, 1996, and Thompson *et al.,* 1998) studies. SOS and BUA have also been shown to be as effective as central dual energy x-ray absorptiometry in identification of women at high risk for prevalent osteoporotic vertebral fractures (Glüer *et al.*, 2004).

Despite the clinical utility of SOS, the mechanisms responsible for variations of SOS in trabecular bone are not well understood yet. This paper describes a phantom study designed to provide insight into the relationship between SOS and trabecular microarchitecture. This includes an investigation of the role of microarchitecture in determining dispersion. Unlike soft tissues, which typically exhibit positive dispersion (phase velocity increasing with ultrasonic frequency) (O'Donnell *et al.,* 1981), trabecular bone exhibits negative dispersion (Nicholson *et al.,* 1996; Strelitzki and Evans, 1996; Droin *et al.*, 1998; Wear, 2000a; Wear, 2001a).

II. METHODS

A. Phantoms

Seven phantoms consisting of parallel nylon wires (simulating trabeculae) in two-dimensional rectangular grid arrays (custom-built by Computerized Imaging Reference Systems, Norfolk, VA) were interrogated. See Figure 1. The nylon wire diameter corresponded to trabecular thickness, which in the standard nomenclature for bone histomorphometry is denoted by Tb.Th (Parfitt *et al.,* 1987). Four values for Tb.Th were used: 152 µm, 203 µm, 254 µm, and 305 µm. (These values correspond to 0.006", 0.008", 0.010", and 0.012", which are readily available nylon wire thicknesses.) See Table 1. The mean value for Tb.Th for human calcaneus is 127 µm (Ulrich, 1999).

Trabecular spacing, s, is given by

$$s = \mathrm{Tb.Sp} + \mathrm{Tb.Th} \tag{1}$$

where Tb.Sp is trabecular separation. Four values for s were used: 700 µm, 800 µm, 900 µm, and 1000 µm. The mean value for Tb.Sp in human calcaneus is 684 µm (Ulrich, 1999), which corresponds to a mean value for s equal to 684 µm + 127 µm = 811 µm.

The volume fraction, VF, occupied by wire (trabeculae) is given by

$$VF = \frac{\pi(Tb.Th/2)^2}{s^2} \tag{2}$$

VF in bone is often denoted by BV/TV, the ratio of bone volume to tissue volume (Parfitt *et al.*, 1987). Porosity, β, is given by $\beta = 1 - \mathrm{VF}$. The range of VF spanned by the seven phantoms (1.8 – 11.4%) roughly corresponds to the range reported for human calcaneus, 2 – 14% (Wear, 2005).

The grid arrays were immersed in a water tank so that water filled the spaces between the wires. This phantom design was somewhat simplistic in that it 1) substituted nylon for mineralized bone and water for marrow, 2) contained only rod-like structures and not platelike structures that are also known to exist in trabecular bone, and 3) was perfectly periodic unlike trabecular bone, which is far less regular in structure. Its relevance, as discussed below, depended on its ability to reproduce frequency-dependent phase velocity properties similar to those observed in trabecular bone.

Some justification for the substitution of water for marrow is provided by the fact that the longitudinal sound speed in water (1480 m/s) is probably commensurate with that in marrow. Measurements of sound speed in isolated marrow are difficult to come by, but sound speeds in most soft tissues fall in the range from 1400 – 1600 m/s (Duck, 1990). Many *in vitro* experiments in bone are performed with water instead of marrow and yield results consistent with *in vivo* measurements. Nicholson and Bouxsein (2002) compared phase velocities in marrow-filled and water-filled human calcaneus *in vitro*. They found a good correlation ($r^2 = 0.77$) between the two but somewhat higher values in water (1563 ± 25 m/s vs. 1520 ± 36 m/s). Hoffmeister *et al.* (2002a) found no significant difference between the two in bovine trabecular tibia.

The longitudinal sound speed in nylon (2600 m/s) is somewhat lower than that for mineralized bone material (2800 – 4000 m/s, near 500 kHz) (Duck, 1990) but still far greater than that for water or marrow. In addition, nylon wires exhibit frequency-dependent scattering similar to that exhibited by trabecular bone (Wear, 2004).

A previously reported phantom design, consisting of cubic granules of gelatin immersed in epoxy, has been shown to be useful for the prediction of the dependences of phase velocity, dispersion, and attenuation on porosity of trabecular bone (Clarke *et al.*, 1994; Strelitzki *et al.*, 1997). One advantage of the parallel-nylon-wire-in-water design is that it allows straightforward investigation of the effects of Tb.Th and s on phase velocity and dispersion.

B. Ultrasonic Methods

A Panametrics (Waltham, MA) 5800 pulser/receiver was used. Samples were interrogated in through-transmission in a water tank using a pair of coaxially-aligned Panametrics 500 kHz, broadband, 0.75” diameter, unfocused transducers. The propagation path between transducers was 3” (7.62 cm). Received radio frequency (RF) signals were digitized (8 bit, 10 MHz) using a LeCroy (Chestnut Ridge, NY) 9310C Dual 400 MHz oscilloscope and stored on computer (via GPIB) for off-line analysis. Seven measurements (of ten RF lines each) were obtained on each phantom. Phantoms were removed from the tank and then repositioned between measurements.

Frequency-dependent phase velocity, $c_p(f)$, was computed using

$$c_p(f) = \frac{c_w}{1 + \frac{c_w \Delta\phi(f)}{2\pi f d}} \tag{3}$$

where f is frequency, $\Delta\phi(f)$ is the difference in unwrapped phases (see next paragraph) of the received signals with and without the phantom in the water path, d is the phantom thickness (12.7 mm), and c_w is the temperature-dependent speed of sound in distilled water given by (Kaye and Laby, 1973)

$$c_w = 1402.9 + 4.835T - 0.047016T^2 + 0.00012725T^3 m/s \tag{4}$$

and T is the temperature in degrees Celsius. Temperature, measured with a digital thermometer, was 19.5° for these measurements, which meant that c_w was 1480 m/s.

The unwrapped phase difference, $\Delta\phi(f)$, was computed as follows. Fast Fourier Transforms (FFT's) of the digitized received signals were taken. The phase of the signal at each frequency was taken to be the inverse tangent of the ratio of the imaginary to real parts of the FFT at that frequency. Since the inverse tangent function yields principal values between $-\pi$ and π, the phase had to be unwrapped by adding an integer multiple of 2π to all frequencies above each frequency where a discontinuity appeared.

Dispersion was characterized by the slope, dc_p/df, of a linear least-squares regression fit of $c_p(f)$ vs. f over the range from 400 to 750 kHz, which roughly corresponded to the system −6 dB bandwidth.

III. RESULTS

Figure 2 shows measurements of phase velocity (c_p) vs. frequency for one phantom. Phase velocity declined quasi-linearly with frequency for all phantoms.

Figure 3 shows measurements of c_p(500 kHz) vs. Tb.Th for four phantoms with a constant value of s (800 μm). A quadratic fit, c_p(500 kHz) = 1477 + 502[Tb.Th(mm)]^2 m/s, is also shown.

Figure 4 shows measurements of c_p(500 kHz) vs. s for four phantoms with a constant value of Tb.Th (152 μm). A curve fit, c_p(500 kHz) = 1482 + 5.5/[s(mm)]^2 m/s, is also shown. The functional forms of the curve fits in Figures 3 and 4 suggest that c_p(500 kHz) - c_w is approximately proportional to VF. (See Equation 2.)

Figure 5 shows measurements of c_p(500 kHz) vs. VF on all seven phantoms. A linear fit, c_p(500 kHz) = 1479 + 387(VF) m/s, is in good agreement with the data.

Figure 6 shows measurements of dc_p/df vs. Tb.Th for four phantoms with a constant value of s (800 μm). A power law fit, $dc_p/df = -10{,}700$[Tb.Th(mm)]$^{4.8}$ is also shown. The fact that the exponent is so far removed from 2 suggests that, unlike change in phase velocity, dc_p/df is not simply proportional to VF.

Figure 7 shows measurements of dc_p/df vs. s for four phantoms with a constant value of Tb.Th (152 μm). A meaningful curve fit to this data is precluded by small values of dc_p/df, relatively large error bars, and small variation in dc_p/df, observed over the range of s studied.

Figure 8 shows measurements of dc_p/df vs. VF for all seven phantoms. A power law fit, $dc_p/df = -5950\text{VF}^{2.4}$ is also shown. Unlike the case with phase velocity, the relationship between dc_p/df and VF is nonlinear. Values for dc_p/df ranged from −2 to −35 m/sMHz, which is consistent with values reported in human calcaneus *in vitro*. See Table 2.

IV. DISCUSSION

Phase velocity in trabecular-bone-mimicking phantoms is a linear, monotonically increasing, function of volume fraction. This seems to be true regardless of whether changes in volume fraction arise from changes in trabecular thickness or changes in trabecular spacing. Phase velocity in human calcaneus is also highly influenced by volume fraction. In this case, phase velocity varies nonlinearly, but still increases monotonically, with volume fraction. The variation may be predicted accurately using Biot theory (Wear *et al.*, 2005). Similar findings have been reported for bovine trabecular bone (Williams, 1992; Hosokawa and Otani, 1997; Hosokawa and Otani, 1998; Haire and Langton, 1999, Lee *et al.*, 2003, Mohamed *et al.*, 2003). An earlier application of Biot theory to trabecular bone was reported by McKelvie and Palmer (1991).

The first derivative of phase velocity with respect to frequency, dc_p/df, in trabecular-bone-mimicking phantoms is a nonlinear, monotonically decreasing function of volume fraction. Measurements of dc_p/df in phantoms may be compared with previously reported measurements of dc_p/df in human calcaneus (Wear, 2000a) plotted vs. estimates of volume fraction based on an assumption of constant bone material density (Wear *et al.*, 2005), shown in Figure 9. There is too much scatter in the human calcaneus data to allow confident conclusions regarding the functional dependence of dc_p/df on volume fraction. Nevertheless, the human data in Figure 9 largely fall within the range of the phantom data in Figure 8. For trabecular bovine tibia interrogated in the mediolateral orientation, dispersion has been reported to be a linear, monotonically decreasing function of density (Waters *et al.,* 2005, Figure 6). Although dc_p/df may potentially carry important diagnostic information, dc_p/df measurements in bone, even *in vitro*, tend to exhibit high variability. *In vivo* application of this measurement would be very challenging with currently available techniques.

The physical mechanism responsible for negative dispersion in the nylon wire phantoms is unknown. It has been shown, however, that negative dispersion in media consisting of alternating parallel slabs of two components may be predicted with the so-called “stratified model” (Brekhovskikh, 1980 and Hughes *et al.,* 1999). The stratified model predicts values of dc_p/df commensurate with those observed in polystyrene / water phantoms and in human calcaneus *in vitro* (Wear, 2001a). The modified Biot-Attenborough theory (Lee *et al.*, 2003) and the Kramers-Kronig relations (Waters, 2005) have successfully modeled dispersion in bovine trabecular bone.

Strelitzki *et al.* (1997) reported measurements of c_p(600 kHz) and dc_p/df in phantoms consisting of cubic gelatin granules suspended in epoxy. Comparison of the present study with Strelitzki *et al.*’s work is complicated by the facts that 1) the two phantom designs used different materials, and 2) the phantom sets spanned different, non-overlapping, ranges of volume fraction. Streliztki *et al.* examined a range of VF from 17 – 54% while the present study examined a range from 1.8 – 11.4%, which was chosen to approximate the range reported in human calcaneus, 2 – 14% (Wear, 2005). As in the present study, Strelitzki *et al.* found phase velocity to increase with VF, but they observed a quadratic rather than a linear variation. Contrary to the present study, they found dc_p/df to increase with VF. Extrapolation of Strelitzki *et al.*’s nonlinear trend to VF = 0 (where dc_p/df would be expected to be near 0), however, would suggest dc_p/df decreasing with VF at low values for VF (<10%), consistent with the present study.

The data reported in the present paper suggest that for certain simple alterations in microarchitecture (changes in Tb.Th and s), c_p and dc_p/df are primarily determined by volume fraction. For more complicated alterations, this may not hold. For example, many studies have demonstrated a substantial anisotropy of SOS in trabecular bone (Nicholson *et al.*, 1998; Hosokawa and Otani, 1998; Hans *et al.*, 1999, Hughes *et al.*, 1999; Luo *et al.*, 1999; Hoffmeister *et al.*, 2000; Hoffmeister *et al.*, 2002a; Hoffmeister *et al.*, 2000b), suggesting that the physical arrangement of the trabeculae, and not just the quantity of trabecular material, influences SOS. In clinical calcaneal-based bone sonometry, however, the mediolateral orientation is always used, and the degree of microarchitectural alteration encountered in diagnostic applications can be expected to be more subtle than the comparatively drastic difference measured in anisotropy studies (e.g. medio-lateral vs. antero-posterior vs. supero-inferior orientations). Consequently, the simple alterations considered in the present phantom study may be relevant to the clinical situation.

Under conditions when phase velocity (c_p) and dc_p/df are primarily determined by VF, group velocity (c_g) must also be primarily determined by VF. This may be seen by considering the relationship between the two velocity measures (Duck, 1990, Equation 4.2),

$$c_g = \frac{c_p}{1 - \frac{f_c}{c_p}\left(\frac{dc_p}{df}\right)} \tag{5}$$

Many clinical and laboratory measurements of SOS in bone, however, are neither phase nor group velocity. They are based on time-of-flight measurements of broadband pulses through bone in which a designated marker (e.g. a zero-crossing or a threshold) on the pulse waveform is designated to measure pulse arrival time. Rather than using the pulse envelope maximum (as would be required for c_g), it is common in bone sonometry to choose a marker closer to the leading edge of the pulse. SOS measurements obtained in this way differ from c_g by an amount that increases monotonically with attenuation (Wear, 2000b; Wear, 2001b). This discrepancy is negligible for soft tissues but substantial for highly-attenuating media such as bone. Therefore, the dependence of SOS on volume fraction may be expected to differ somewhat from that for c_p or c_g. Nevertheless, Luo *et al.* (1999), using a finite-difference simulation based on the 2-D elastic wave equation in conjunction with a threshold near the leading edge for time-of-flight estimation, also predicted a close, monotonically increasing, relationship between velocity and volume fraction in trabecular bone. Nicholson *et al.* (2001) found that the correlation between volume fraction and c_p(600 kHz), r = 0.86, was very close to the correlation between volume fraction and signal velocity (SOS based on the pulse leading edge as an arrival time marker), r = 0.88, in human calcaneus *in vitro.*

The present study may help explain findings by other researchers investigating relationships between phase velocity and microarchitecture. Nicholson *et al.* (2001), reporting measurements on 69 human calcaneal trabecular bone cubes, found moderate correlations between c_p(600 kHz) (mediolateral orientation) and Tb.Th (r = 0.49) and between c_p(600 kHz) and Tb.Sp (r = −0.47). As expected, the signs of these correlation coefficients are consistent with the phantom measurements of the present study. (Figures 3 through 5 and Equation 2 suggest, however, that Tb.Th^2 and s^{-2} may have been more appropriate independent variables in the regression analysis than Tb.Th and Tb.Sp). More important, Nicholson *et al.* found a high correlation between c_p(600 kHz) and VF (r = 0.86) but that multivariate regression models to predict c_p(600 kHz) from VF and Tb.Th or Tb.Sp did not significantly increase that correlation coefficient. In other words, phase velocity contains little or no information regarding Tb.Th or Tb.Sp beyond that already contained in VF. Chaffai *et al.* (2002) reported similar findings in human calcaneus. (Chaffai *et al.* actually used bone mineral density rather than VF as an independent variable. These two parameters, both of which are essentially reflections of quantity of bone, were highly correlated with each other in Chaffai *et al.*'s study, however, with r = 0.92.) The present phantom study offers an explanation for the results of Nicholson *et al.* and Chaffai *et al.* As can be seen in Figure 5, c_p(500 kHz) in phantoms is highly correlated with VF but is relatively insensitive to the particular combination of Tb.Th and s that produce VF.

In this investigation, the dependences of phase velocity and its first derivative (with respect to frequency) on trabecular thickness, trabecular spacing, and volume fraction were measured in phantoms, yielding insight into relationships between frequency-dependent phase velocity and microarchitecture in bone. The phantom design allowed easy separation of effects due to changes in trabecular thickness from those due to changes in trabecular spacing. The dependences of phase velocity and its first derivative on volume fraction in the phantoms were consistent with those reported in trabecular bone. The measurements in phantoms help explain why previous investigators have found in multiple regression analyses that trabecular thickness and trabecular spacing carry little predictive information regarding phase velocity beyond that carried by volume fraction alone.

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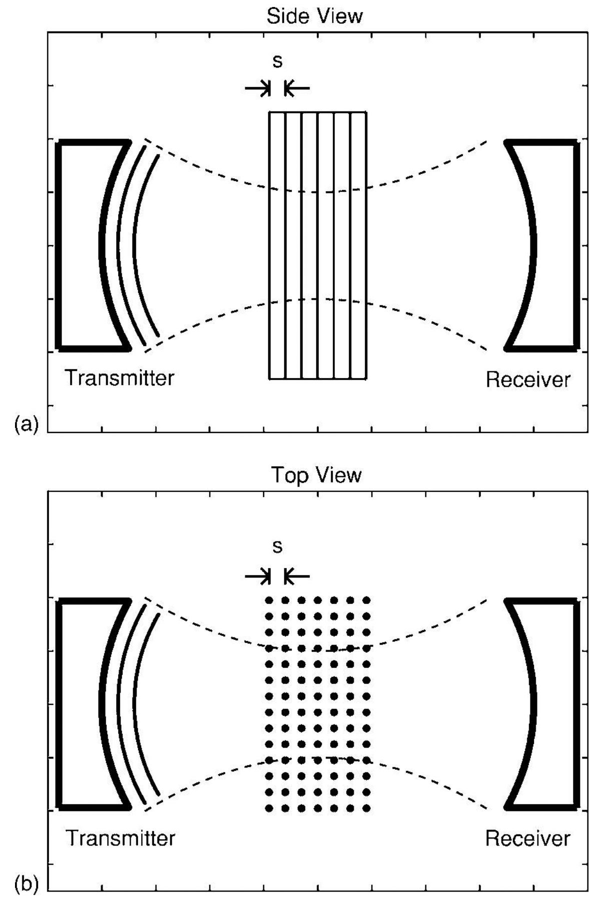

Figure 1.
a) Side view and b) top view of experimental setup.

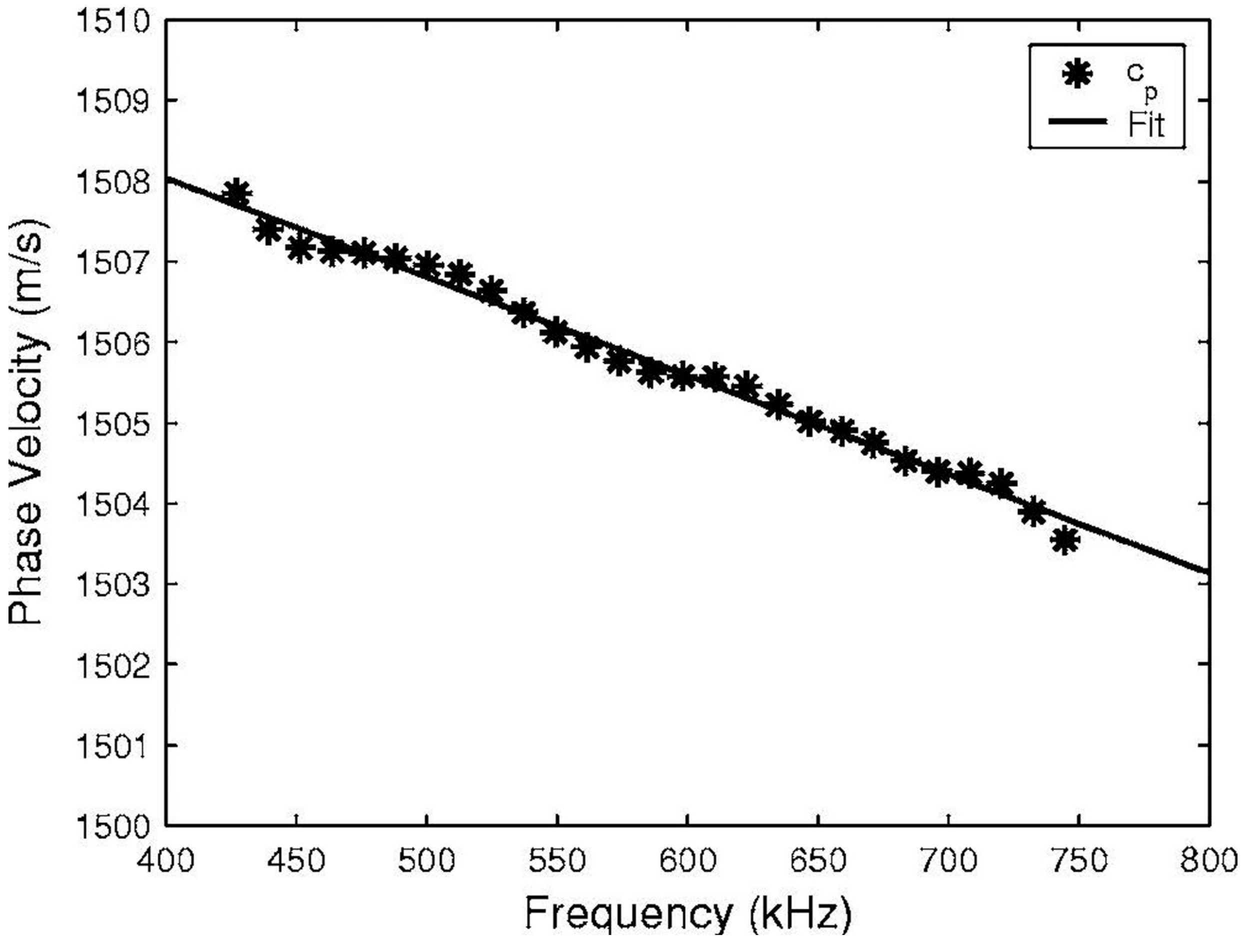

Figure 2.

Measurements (*) of phase velocity (c_p) vs. frequency for phantom with Tb.Th = 254 microns and s = 800 microns. A linear least-squares regression fit to the data is also shown (solid line).

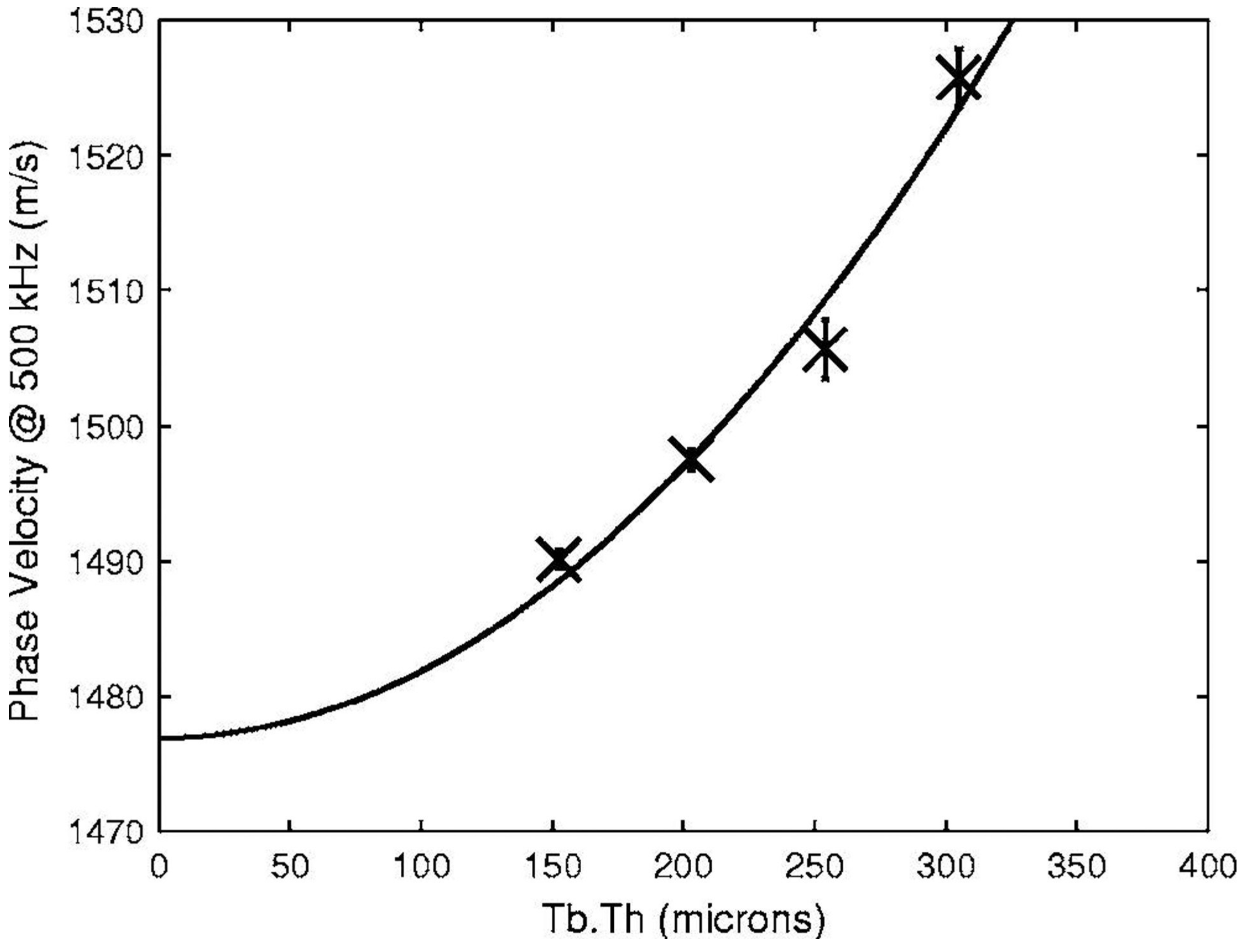

Figure 3.

Phase velocity at 500 kHz vs. Tb.Th for four phantoms with s = 800 microns. Error bars denote standard deviations. A quadratic fit, c_p(500 kHz) = 1477 + 502[Tb.Th(mm)]^2 m/s, is also shown.

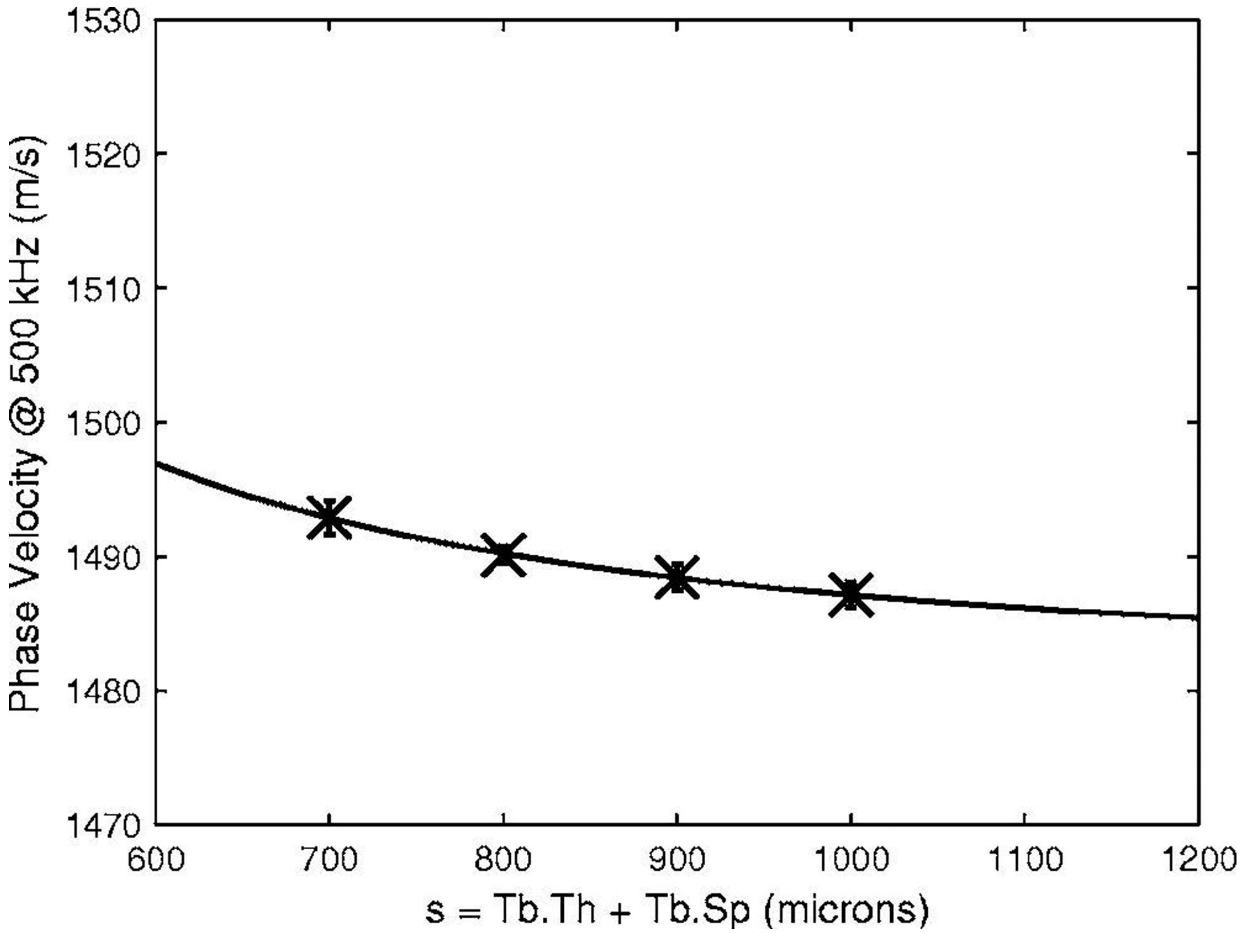

Figure 4.

Phase velocity at 500 kHz vs. s for four phantoms with Tb.Th = 152 microns. Error bars denote standard deviations. A curve fit, c_p(500 kHz) = 1482 + 5.5/[s(mm)]^2 m/s, is also shown.

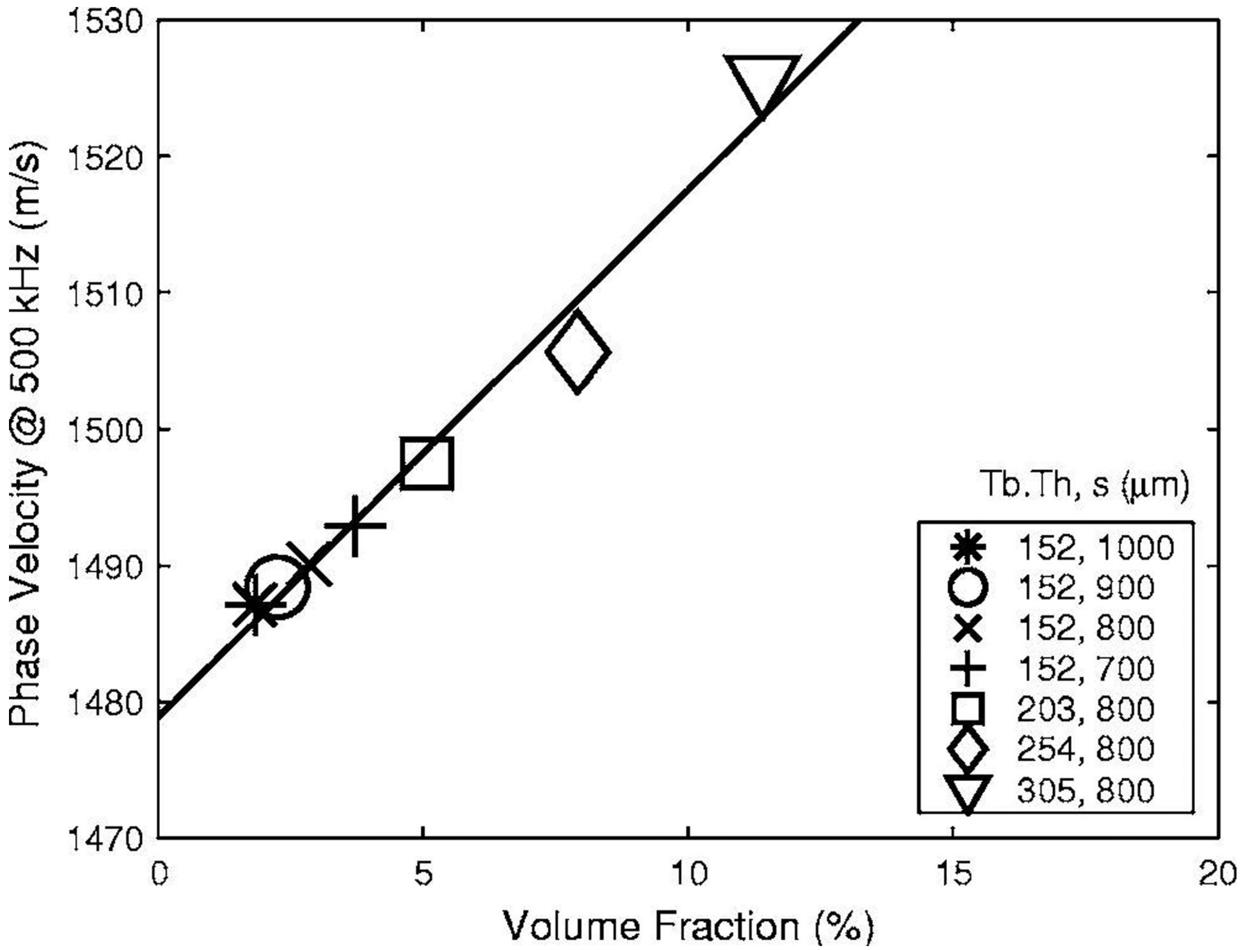

Figure 5.
Phase velocity at 500 kHz vs. volume fraction for all seven phantoms. A linear fit, c_p(500 kHz) = 1479 + 387(VF) m/s, is also shown.

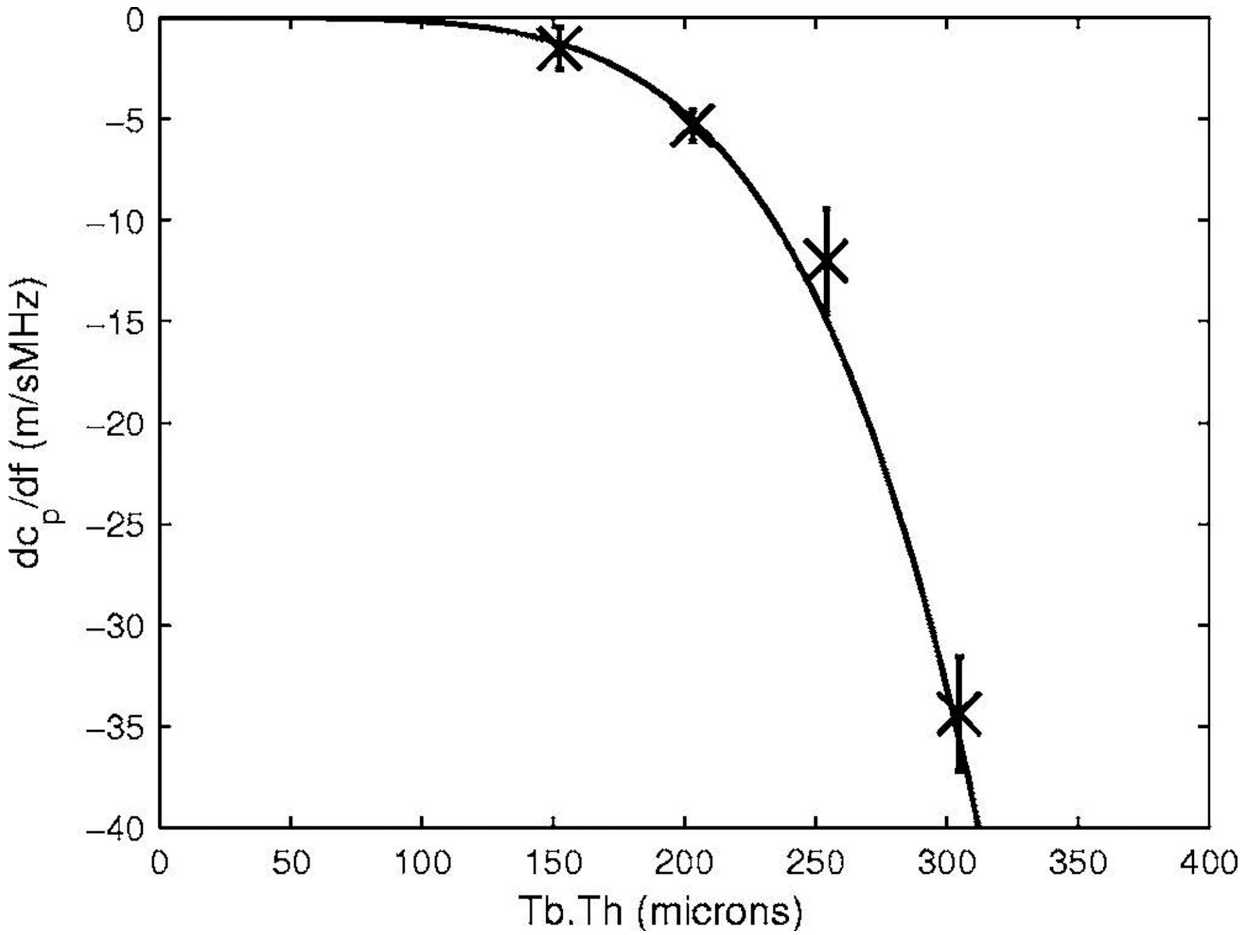

Figure 6.

The first derivative of phase velocity with respect to frequency, dc_p/df, vs. Tb.Th for four phantoms with s = 800 microns. Error bars denote standard deviations. A power law fit, dc_p/df = −10,700 [Tb.Th(mm)]$^{4.8}$ is also shown.

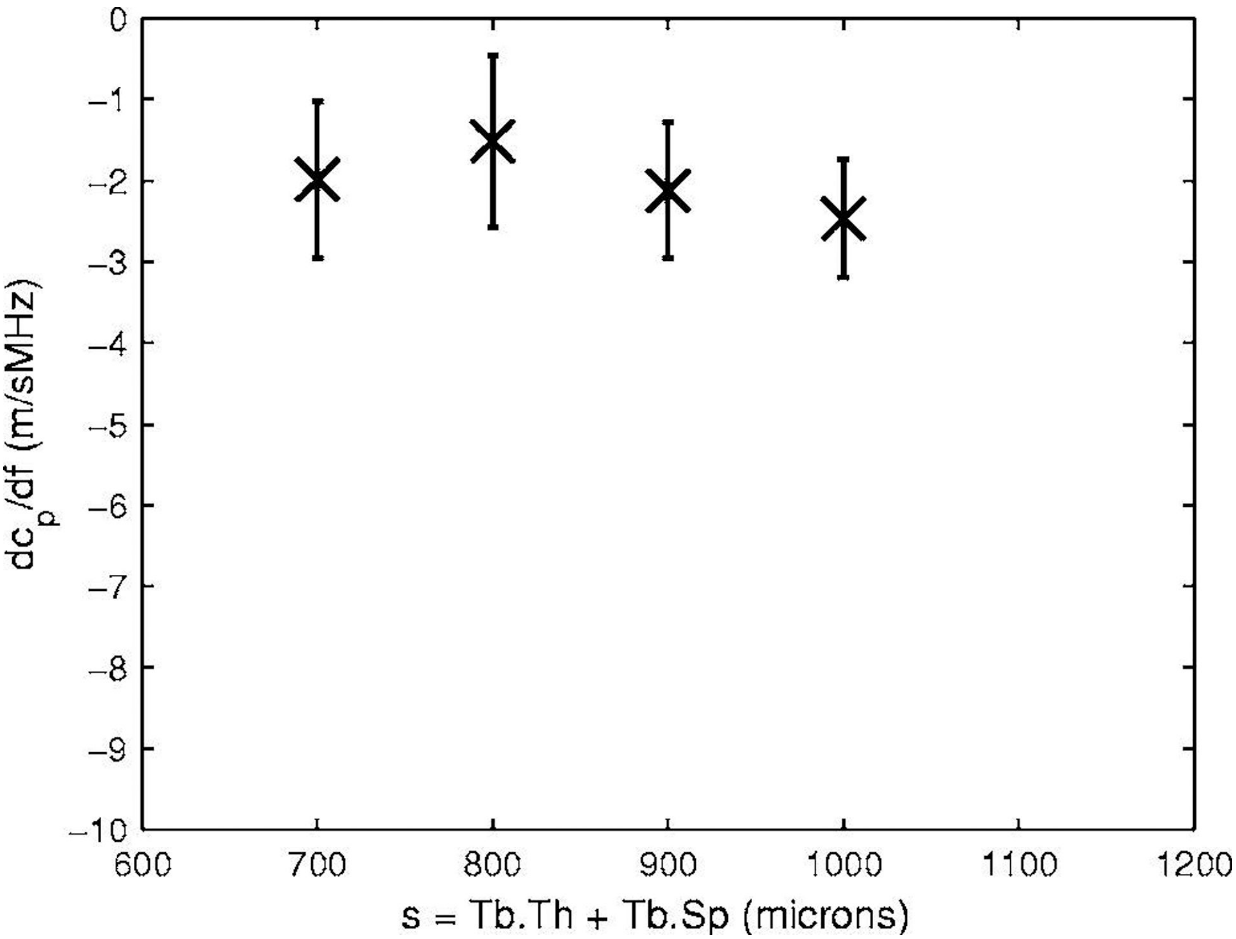

Figure 7.

The first derivative of phase velocity with respect to frequency, dc_p/df, vs. s for four phantoms with Tb.Th = 152 microns. Error bars denote standard deviations.

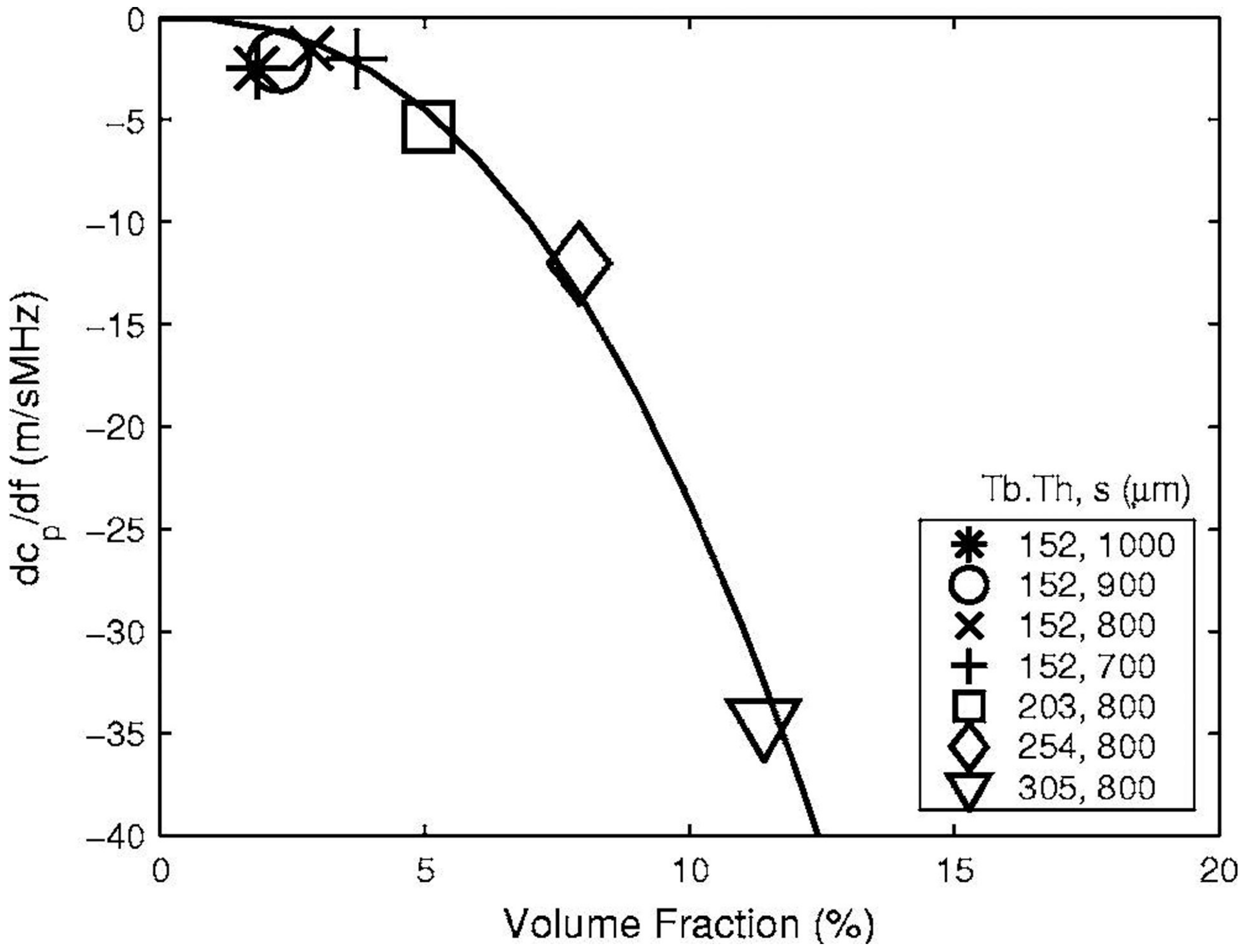

Figure 8.

The first derivative of phase velocity with respect to frequency, $\mathrm{d}c_p/\mathrm{d}f$, vs. volume fraction for all seven phantoms. A power law fit, $\mathrm{d}c_p/\mathrm{d}f = -5950\ \mathrm{VF}^{2.4}$ is also shown.

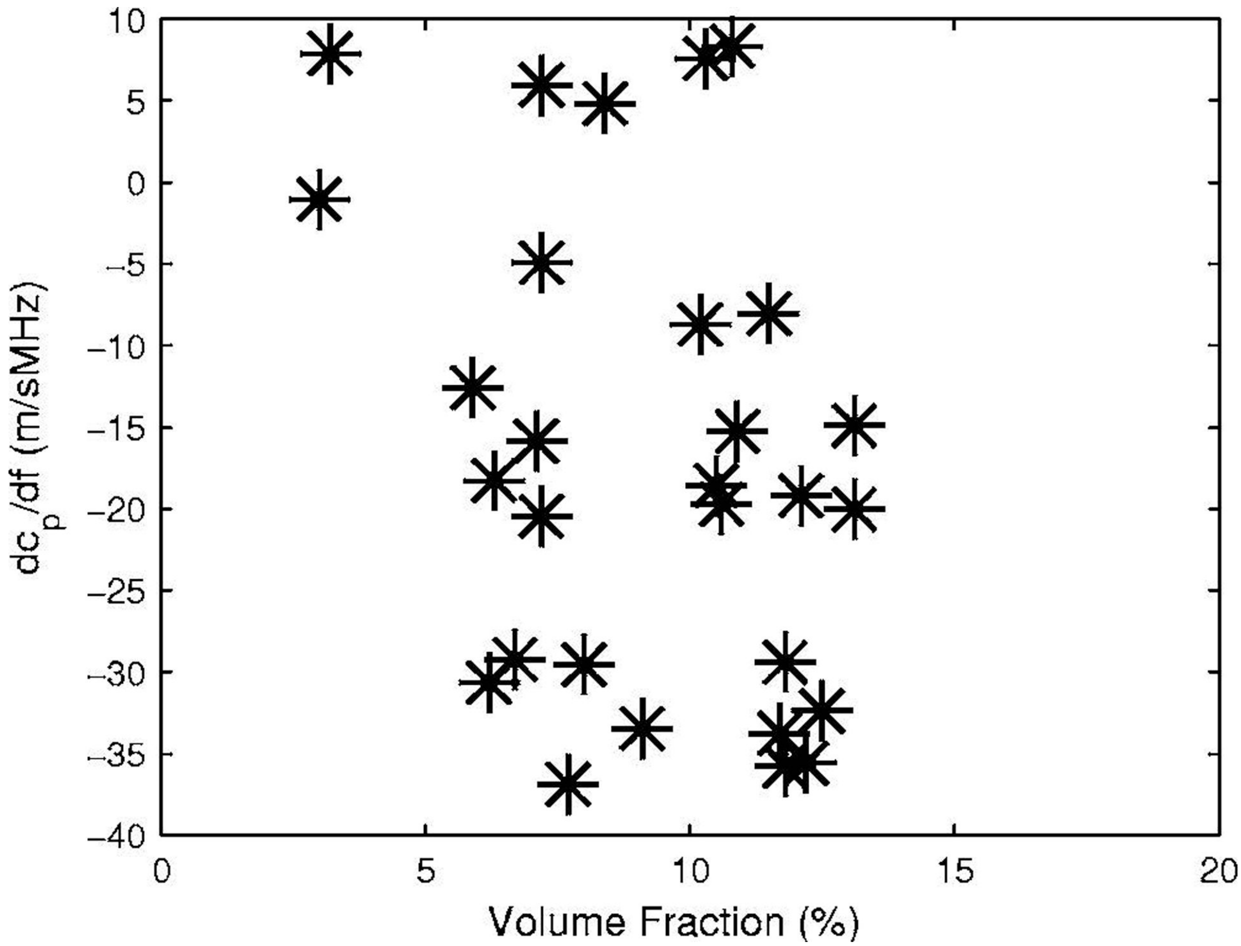

Figure 9.
The first derivative of phase velocity with respect to frequency, dc_p/df, vs. volume fraction in 30 human calcaneus samples.

Table 1.

Phantom properties.

Tb.Th (microns)	s = Tb.Th + Tb.Sp (microns)	Volume Fraction	Porosity
152	1000	0.018	0.982
152	900	0.022	0.978
152	800	0.028	0.972
152	700	0.037	0.963
203	800	0.051	0.949
254	800	0.079	0.921
305	800	0.114	0.886

Tb.Th is trabecular (nylon wire) thickness. The variable s is the inter-wire spacing, which is equal to the sum of Tb.Th and Tb.Sp (trabecular separation). The volume fraction (VF) is the fraction of volume occupied by nylon wire. Porosity = 1 – VF.

Table 2.

Estimates of the first derivative of phase velocity with respect to frequency, dc_p/df, in human calcaneus from Nicholson *et al.* (1996, Table 1), Strelitzki and Evans (1996, Table 2), Droin, *et al.* (1998, Table 1), and Wear (2000a, Table 1).

Author(s)	N	Frequency Range (kHz)	dc_p/df (mean ± standard deviation) (m/sMHz)
Nicholson *et al.*	70	200 – 800	−40
Strelitzki and Evans	10	600 – 800	−32 ± 27
Droin, Berger, and Laugier	15	200 – 600	−15 ± 13
Wear	24	200 – 600	−18 ± 15

N is the number of calcaneus samples upon which measurements were based.