Measurements of ultrasonic backscatter coefficients in human liver and kidney *in vivo*

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Ultrasonic backscatter coefficients, in the range of 2.0–4.0 MHz, were measured in normal human livers and kidneys *in vivo*. In liver, data were acquired and analyzed from 15 normal volunteers and 19 patients with hepatitis. No significant difference between normal and chronic hepatitis was found. The power-law fit to the backscatter coefficient in normal liver as a function of frequency was $\eta(f)=4.5\times10^{-5} f^{1.6}$ cm^{-1} Str^{-1}. This is comparable to that measured by other investigators in *in vitro* preparations of human and animal liver and to that measured by two other teams of investigators in *in vivo* human liver. In kidney, data were acquired from 11 normal volunteers. The power-law fit to the backscatter coefficient in normal kidney was $\eta(f)=2.3\times10^{-5} f^{2.1}$ cm^{-1} Str^{-1}. This is in the range of that measured by other investigators in *in vitro* preparations of human and animal kidney. In order to assess the system dependence of *in vivo* abdominal organ backscatter coefficients, measurements were performed using two different ultrasonic data-acquisition systems. The two systems exhibited close agreement. © *1995 Acoustical Society of America.*

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INTRODUCTION

The ultrasonic backscatter coefficient is a useful parameter that describes the scattering efficiency, as a function of ultrasonic frequency, of a tissue or material. Many *in vitro* experiments have been performed to demonstrate its utility for characterization of heart,[1] liver,[2–7] and kidney.[4,5,8,9] These measurements are often performed in a water tank. Under such conditions, complicating factors such as attenuation and distortion of the ultrasonic beam due to tissues lying between the transducer and region of interest are removed.

In vitro measurements tend to be more accurate in some sense than *in vivo* measurements because of the absence of intervening tissues. However, the tissue of interest is often either dead or not in the same state that it would be *in vivo* and therefore may exhibit altered ultrasonic properties. Moreover, in order to have clinical utility, measurements need to be performed *in vivo*.

There are many reports documenting measurements of the backscatter coefficient in healthy liver but not many for diseased liver. The work of Bamber and Hill,[2] however, indicates that solid tumors in human liver exhibit smaller backscatter coefficients than normal liver. Zagzebski and co-workers[10] and O'Donnell and Reilly[11] have published estimates of the backscatter coefficient from normal human volunteers *in vivo*. Measurements on normal liver *in vitro* have been reported by Nicholas[3] (human), Nassiri and Hill[6] (human), Fei and Shung[5] (bovine), and Campbell and Waag[7] (calf).

There is much evidence to support the notion that backscatter coefficients can be useful in characterizing kidney. Insana and co-workers[12] have performed measurements on dog kidneys *in vivo*. Their work suggests that at lower frequencies (2.5–5.0 MHz) Bowman's capsules are the dominant scatterers (in the cortex) and at higher frequencies (5.0–10.0 MHz) glomerular arterioles dominate. In addition, the integrated backscatter coefficient is elevated under ischemic conditions. Scatterer size was estimated from the frequency dependence of the backscatter coefficient.[13] Under ischemic conditions, scatterer size was found to exhibit a significant decrease at diagnostic frequencies and a significant increase at higher frequencies. Scatterer size also exhibited a significant decrease at low frequencies during acute obstruction of the kidney under diuresis. Earlier work by these investigators showed an anisotropy in backscatter from dog kidney *in vitro*.[8] Fei and Shung have published measurements of bovine kidney cortex *in vitro*.[5]

In studies of human kidney *in vitro*, Turnbull and co-workers[9] have observed elevated backscatter in renal angiomyolipoma. Garra and co-workers[14] measured backscatter coefficients in human kidneys *in vivo* and reported estimates of scatterer size (obtained from the frequency dependence of the backscatter coefficient) and the integrated backscatter coefficient. Scatterer size was found to be useful in the detection of parenchymal structural change in diffuse renal disease[14] and was found to correlate with glomerular diameter. The integrated backscatter coefficient was less useful.

In the work described in this paper, backscatter coefficients are estimated from human liver and kidney *in vivo*. A standard exponential correction is applied to compensate for attenuation of intervening layers of tissue (e.g., skin, muscle,

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and fat). Measurements are reported for liver from normal volunteers and from patients with chronic hepatitis. Measurements in normal liver are compared with those by Zagzebski and co-workers (Ref. 10, 1993) and O'Donnell and Reilly (Ref. 11, 1985) *in vivo* and with measurements by others *in vitro*. Measurements in kidney are compared with *in vitro* measurements by other investigators. In order to investigate the system dependence of *in vivo* backscatter coefficient measurements, results obtained using two different ultrasonic data-acquisition systems are compared.

I. METHODS

A reference phantom method for measuring ultrasonic backscatter coefficients described by Zagzebski and co-workers[10] was used in this study. Other methods for quantifying ultrasonic backscatter have been described by Sigelmann and Reid,[15,16] O'Donnell and Miller,[17] Lizzi and co-workers,[18] Campbell and Waag,[19] and Madsen and co-workers.[20–22] In addition, numerous applications (some involving modifications which decrease complexity at the cost of decreased generality) of these techniques have been published.[23–27] With the reference phantom method, spectra obtained in tissues are compared with spectra obtained from a phantom with known scattering and attenuation properties. The region of interest (ROI) has the same size, shape, and position for both measurements. With this method, the effects of diffraction and the transducer electromechanical response on estimates of backscatter coefficient are removed.

Data were compensated for attenuation due to intervening tissues between the transducer and the ROI as described by Zagzebski and co-workers[10] and Garra and co-workers.[14,28] Unfortunately, measurements on each individual subject were not available. Therefore, average values were used for tissue thicknesses for skin, fat, and muscle. These average values were obtained by performing measurements from ultrasound B-scan images on 13 normal individuals and 13 patients with hepatitis. The resulting thicknesses (mean±standard deviation) for skin (d_s), fat (d_f), and muscle (d_m) were $d_s=1.8\pm0.3$ mm, $d_f=3.9\pm1.9$ mm, and $d_m=11.9\pm4.0$ mm (normals) and $d_s=2.0\pm0.5$ mm, $d_f=2.7\pm1.5$ mm, and $d_m=12.6\pm3.9$ mm (patients with hepatitis). The attenuation coefficients for skin, fat, and muscle were assumed to be 1.5, 0.46, and 0.51 dB/cm MHz,[29] respectively. The value used to compensate for attenuation in the liver was 0.5 dB/cm MHz.[10,30] This is the value measured by Garra and co-workers in normal volunteers and in patients with chronic hepatitis.[30] The value used to compensate for attenuation in the kidney was 0.38 dB/cm MHz[1.19] (which corresponds to an average between values measured parallel and perpendicular to the predominant nephron orientation by Insana and co-workers[8]).

The formula used to compute the tissue backscatter coefficient as a function of frequency $\eta_t(f)$ was

$$\eta_t(f)=\eta_p(f)\frac{S_t(f)}{S_p(f)}\times\exp\left[-4\alpha_p(f)z+4\sum_{i=1}^{n}\alpha_i(f)z_i\right],$$

where $\eta_p(f)$ is the reference phantom backscatter coefficient, and $S_t(f)$ and $S_p(f)$ are the average power spectra measured from tissue and phantom, respectively. *In vivo* measurements are presumed to involve n tissues (including the tissue of interest) with attenuation coefficients $\alpha_i(f)$ (nepers per unit distance) and thicknesses z_i. The reference phantom attenuation coefficient is $\alpha_p(f)$ and z is the distance from the transducer to the center of the ROI.

Two clinical ultrasonic imaging systems were used to acquire the data. One was an ATL Ultramark 8 with a 3.5-MHz annular array transducer. Data acquired with this system were digitized (11 bits) at 12.0 MHz. The second system was a Diasonics DS-20. The center frequency of the circular (diameter=19 mm) focused transducer for this system was 3.5 MHz. rf signals were digitized (8 bits) at 22.1 Msamples/s. The −6-dB bandwidths for both systems were approximately 1.0 MHz.

The reference phantom used in conjunction with the ATL system was a tissue-like slurry containing glass beads and graphite in agar particles suspended in a water–alcohol solution.[31,32] The attenuation coefficient was measured to be $0.30\,f^{1.28}$ dB/cm.

The reference phantom used in conjunction with measurements made with the Diasonics system consisted of graphite particles embedded in agar. The diameters of these particles were in the range from 5 to 20 μm and were much smaller than the wavelength of sound used (approximately 430 μm). Rayleigh scattering resulted (backscatter coefficient proportional to f^4). The attenuation coefficient was 0.57 dB/cm MHz.

The phantom used to test the backscatter coefficient measurement method consisted of glass beads embedded in agar. (This phantom shall be referred to as the "test phantom" to distinguish it from the reference phantoms.) The diameters of the beads ranged from 180 to 212 μm. The scatterer number density was 2.0 per cubic mm. The speed of sound was measured to be 1556 m/s. The attenuation coefficient was measured to be $0.115\,f^{1.72}$ dB/cm. Data from five different ROIs (2 cm×2 cm) were obtained. Backscatter coefficient estimates, as functions of frequency, from the five ROIs were averaged.

Region of interest sizes in humans were generally about 8 mm×10 mm in kidney and 24 mm×30 mm in liver. Data from liver were acquired using the Diasonics system. Data were acquired from 15 normal human livers (generally five or six ROIs per subject) and 17 patients with chronic hepatitis (again, generally five or six ROIs per subject). In the kidney, two sets of data (one using the ATL system and the other using the Diasonics system) were acquired for each normal human subject. Only one ROI was acquired per subject, from the renal cortex/cortico-medulary junction of the right kidney using the right lobe of the liver as an acoustic window as described previously.[14]

The biopsy results for the 17 patients with chronic hepatitis were as follows. Seven had chronic persistent hepatitis or mild chronic active hepatitis. Ten were judged to exhibit moderate (as opposed to mild) chronic active hepatitis. Patients were also graded with respect to severity of cirrhosis. Six showed no signs of cirrhosis. Seven exhibited mild, early

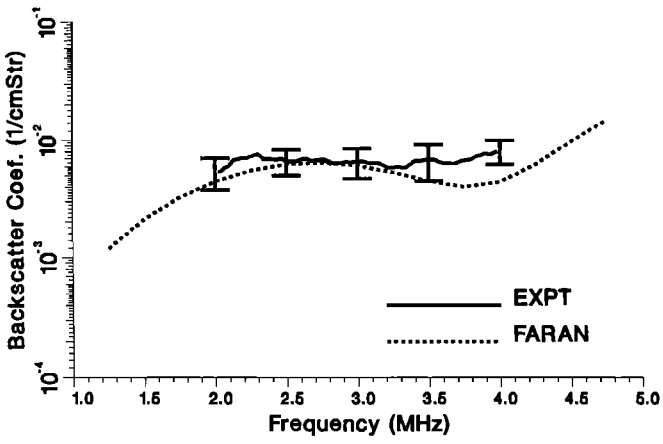

FIG. 1. Measurement of the backscatter coefficient, as a function of frequency, of the test phantom with the ATL data-acquisition system. Also shown (dashed line) is the theoretical backscatter coefficient, computed from the theory of Faran (see Ref. 34). This phantom consisted of glass beads with diameters ranging from 180 to 212 μm embedded in agar. Error bars denote standard deviations of measurements.

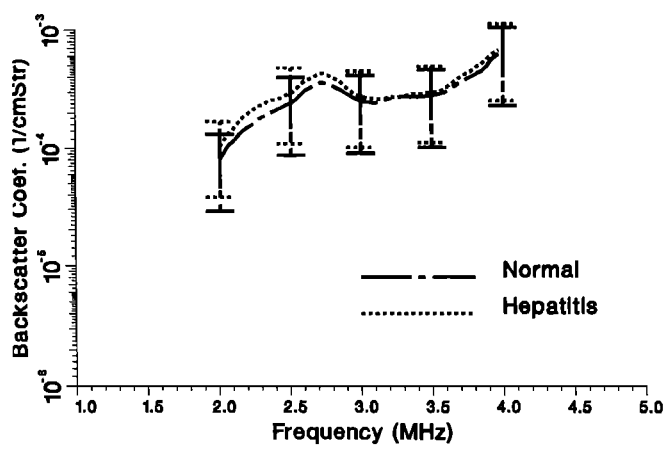

FIG. 2. Measurements of average backscatter coefficients from a set of 15 normal human livers *in vivo* and from a set of 17 patients with chronic hepatitis. This data was acquired with the Diasonics data-acquisition system. The two groups show little difference in backscatter coefficient. Error bars denote standard deviations of measurements.

cirrhosis. Two patients showed moderate cirrhosis. The remaining two were judged to have severe cirrhosis.

"Effective scatterer size" was estimated using the method developed by Insana and co-workers[13,33] which involves computation of the intensity form factor (proportional to the Fourier transform of the correlation function) for the scattering medium. The form-factor data were then least-squares fitted to a functional form derived from the assumed correlation function. For tissue data, the correlation function was assumed to be Gaussian. For test phantom data, a correlation function corresponding to spherical scatterers[13] was used rather than a Gaussian function. From the width of the best-fit correlation function, the effective scatterer size could be estimated.

II. RESULTS

Figure 1 shows measurements of the backscatter coefficient, as a function of frequency, of the test phantom using the ATL acquisition system. This phantom consisted of glass beads with diameters ranging from 180 to 212 μm embedded in agar. Also shown (dashed line) is the theoretical backscatter coefficient (based on the theory of Faran[34]). Over the useful band of the transducer (2.0–4.0 MHz), the measurements are in fair agreement with theory. The estimate of effective scatterer size, derived from the ultrasound data, was 167 ± 1 μm (mean$\pm$standard deviation). Explanations for discrepancies between measurements and actual or theoretical values include: (1) There are several simplifying approximations underlying the backscatter coefficient estimation algorithm;[10] (2) the wavelength of ultrasound used (430 μm) was large relative to the error in scatterer size estimate; (3) there are uncertainties involved in the phantom manufacturing process; (4) the Faran theory is based upon spherical scatterers while the beads in the test phantom were irregularly shaped.

Figure 2 shows measurements of average backscatter coefficient from 15 normal human livers *in vivo* and 17 patients with chronic hepatitis. The values from the two groups were very similar. The means and standard deviations of the measurements at 3 MHz were $2.9\pm1.8\times10^{-4}$ (normal) and $3.2\pm2.0\times10^{-4}$ $cm^{-1}\,Str^{-1}$ (hepatitis). (Note that standard deviation is a function of ROI size and number of ROIs per subject.) The standard deviations for the measurements are far greater than the separation between the two groups. The measured effective scatterer sizes were 245 ± 32 μm for normals and 246 ± 32 μm for chronic hepatitis.

Figure 3 shows measurements of the backscatter coeffi-

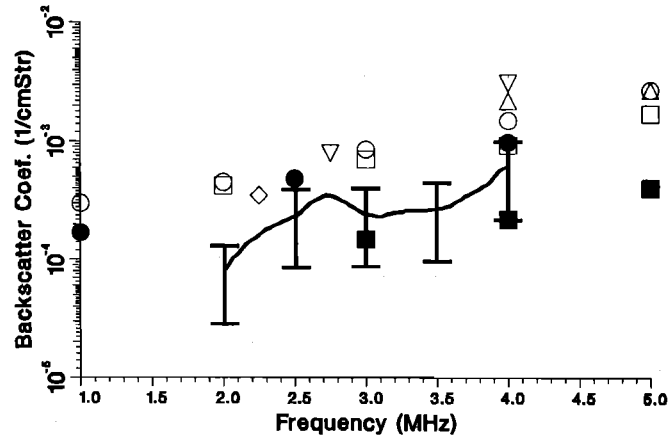

FIG. 3. Measurements of backscatter coefficient in liver. The solid curve represents the data acquired in this study on human liver *in vivo*. The remaining data points represent measurements made by other researchers. The downward pointing triangles (▽) correspond to measurements made by Zagzebski and co-workers on human liver *in vivo* (see Ref. 10). The diamond (◇) corresponds to the measurement made by O'Donnell and Reilly in human liver *in vivo* (see Ref. 11). The solid circles (●) are measurements performed by Bamber and Hill (see Ref. 2) on excised human liver. The open circles (○) are measurements by Nicholas (see Ref. 3) on excised human liver. The open squares (□) correspond to measurements by Fei and Shung (see Ref. 5) on excised bovine liver. The solid squares (■) are measurements by Campbell and Waag (see Ref. 7) on calf liver. The upward pointing (△) triangles are from Nassiri and Hill's (see Ref. 6) measurements on excised human liver. Error bars denote standard deviations of measurements.

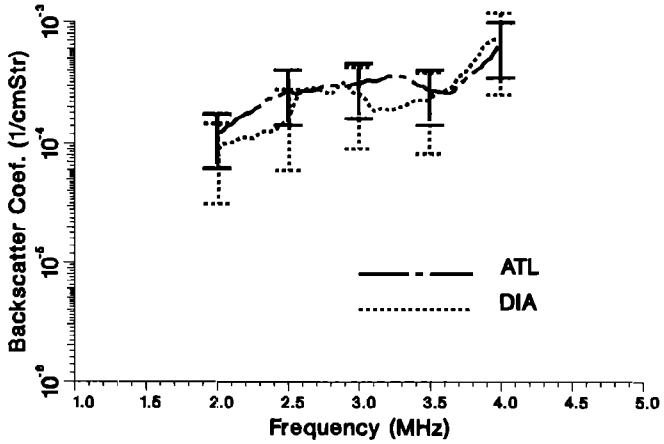

FIG. 4. Measurements of average backscatter coefficient from 11 normal human kidneys *in vivo*. Again the two systems (ATL and Diasonics) exhibited close agreement. The backscatter coefficient showed a gradual increase with frequency in the range of frequencies used. The backscatter coefficient was approximately 10^{-4} cm^{-1} Str^{-1}. Error bars denote standard deviations of measurements.

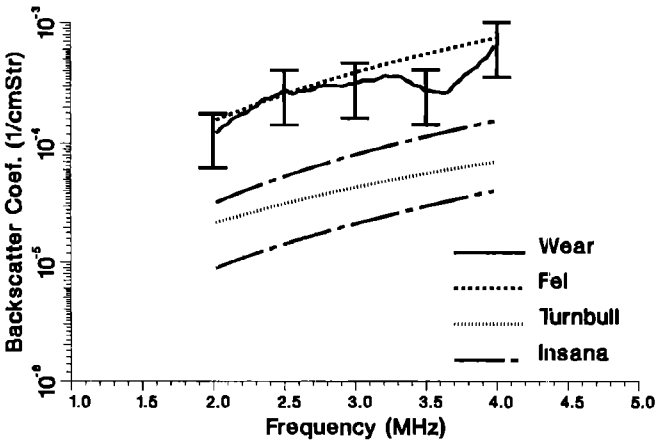

FIG. 5. Measurement of backscatter coefficient in kidney. The solid curve represents the data acquired in this study on human kidney *in vivo*. The other curves are power-law fits obtained by other researchers for their data. The dashed curve corresponds to data acquired by Fei and Shung on excised bovine kidney (see Ref. 5). The dotted curve corresponds to measurement by Turnbull *et al.* on excised human kidney (see Ref. 9). The chain-dash curves correspond to measurements made by Insana and co-workers on excised dog kidney both *parallel* (lower curve) and *perpendicular* (higher curve) to the predominant nephron orientation (see Ref. 8). Error bars denote standard deviations of measurements.

cient in liver. The solid curve represents the data acquired in this study on human liver *in vivo*. The remaining data points represent measurements made by other researchers. The measurements performed in this study tend to be somewhat lower than most of the others. Only the measurements by Campbell and Waag are lower. (Differences among the measurements by Campbell and Waag and the others include the following: Measurements were actually obtained for 165-deg scattering rather than 180 deg. Measurements were obtained from calves rather than other animals. A different data analysis algorithm was used.)

The frequency dependences for all measurements are roughly comparable. The power-law fit to the normal data was $\eta(f)=4.5\times10^{-5} f^{1.6}$ cm^{-1} Str^{-1} (where f is measured in MHz). The frequency dependence (exponent of the power law) is comparable to that reported by other investigators from *in vitro* experiments. Nicholas reported $\eta(f)=2.7\times10^{-4} f^{1.2}$ cm^{-1} Str^{-1} for excised human liver.[3] Nassiri and Hill reported $\eta(f)=3.2\times10^{-4} f^{1.4}$ cm^{-1} Str^{-1} for excised human liver.[6] Fei and Shung reported $8.4\times10^{-5} f^{2.0}$ cm^{-1} Str^{-1} for excised bovine liver.[5] Some caution must be exercised in comparing frequency dependences estimated in different studies as the various power-law fits have been performed across different ranges of ultrasonic frequency.

Figure 4 shows measurements of average backscatter coefficient from 11 normal human kidneys *in vivo*. The two systems (ATL and Diasonics) exhibited close agreement. The backscatter coefficient was generally in the range between 10^{-4} and 10^{-3} cm^{-1} Str^{-1} and exhibited a gradual increase with frequency in the range of frequencies used.

Figure 5 shows estimates of the backscatter coefficient in kidney. The values obtained here are near the high end of the range reported by other investigators. The average backscatter coefficient estimates were $3.1\times10^{-4}\pm1.5\times10^{-4}$ (ATL) and $2.3\times10^{-4}\pm1.5\times10^{-4}$ cm^{-1} Str^{-1} (Diasonics). These are roughly comparable to values reported by Insana and co-workers on *perfused* dog kidney (between 1.0×10^{-4} and 2.0×10^{-4} cm^{-1} Str^{-1} for frequencies between 2.5 and 5.0 MHz [see Figs. 4(c) and 7(c) in Ref. 11] and are a little higher than that reported by Garra and co-workers[14] for normal human kidney *in vivo* ($7.8\pm4\times10^{-5}$ cm^{-1} Str^{-1}).

The frequency dependence of the backscatter coefficient was evaluated by performing a power-law fit to the data. The resulting fitted function was $\eta(f)=2.3\times10^{-5} f^{2.1}$ cm^{-1} Str^{-1}. This frequency dependence of 2.1 (exponent of the power law) is comparable to what other researchers have reported from *in vitro* experiments. The power-law fits by other researchers are $3.1\times10^{-5} f^{2.3}$ cm^{-1} Str^{-1} (Fei and Shung[5]), $6.6\times10^{-6} f^{1.7}$ cm^{-1} Str^{-1} (Turnbull and co-workers[9]), and $1.9\times10^{-6} f^{2.2}$ cm^{-1} Str^{-1} (Insana and co-workers[8]). The estimates for effective scatterer size were 232 ± 29 μm (mean$\pm$standard deviation) for ATL measurements and 211 ± 57 μm for Diasonics measurements.

III. DISCUSSION

Backscatter coefficients have been measured in human liver and kidney *in vivo*. The measurements in liver with hepatitis and in kidney represent the first such measurements in humans *in vivo* reported. In kidney, comparable results were obtained using two different clinical ultrasonic data-acquisitions systems and two very different reference phantoms.

The measurements in liver presented here were somewhat lower than those reported by Zagzebski and co-workers[10] and O'Donnell and Reilly.[11] Much of the discrepancy may be attributable to the high sensitivity of backscatter coefficient estimates to choices of values for attenuation coefficients used to compensate for overlying tissues. For example, Zagzebski and co-workers used 1.3 dB/cm MHz for muscle (0.5 dB/cm MHz was used in the present paper) and 0.6 dB/cm MHz for fat (0.46 dB/cm MHz

was used in the present paper). In both studies, the value used for liver was 0.5 dB/cm MHz. If the attenuation values of Zagzebski and co-workers[10] are utilized, the two sets of measurements are in better agreement. At 2.75 MHz, the values obtained are $1.4\pm0.9\times10^{-3}$ (present paper) and $7.9\pm2.3\times10^{-4}$ cm^{-1} Str^{-1} (Zagzebski and co-workers[10]). At 4.0 MHz, the values obtained are $4.6\pm2.9\times10^{-3}$ (present paper) and $3.1\pm1.7\times10^{-3}$ cm^{-1} Str^{-1} (Zagzebski and co-workers[10]).

Without direct measurement of muscle attenuation coefficient *in vivo* on each particular subject, it is not possible to know with absolute certainty which value to use. Ultimately, one must simply make an educated guess for the value. The value adopted in the present paper was that reported by Carson and co-workers[27] which corresponded to abdominal muscle and preperitioneal fascia (0.51 dB/cm MHz). Their application was compensation for attenuation in performing measurements on fetuses *in vivo*. The value used by Zagzebski and co-workers[10] is taken from measurements of freshly excised human gastrocnemius.[10,35]

It should also be noted that backscatter coefficient estimates will have a very sensitive dependence on the choices of value and functional form of attenuation coefficient for compensation in *liver*. Values ranging from 0.4 to 0.8 dB/cm MHz appear in the literature.[36] In addition, some investigators have reported nonlinear attenuation coefficient estimates in liver that vary as f^n where n ranges from 0.8 to 1.5.[36] For a typical round trip path length in liver of 14 cm, a change of 0.1 dB/cm MHz in assumed attenuation coefficient would result in a 4.2-dB change in estimated backscatter coefficient at 3.0 MHz!

Average backscatter coefficients, as functions of frequency, for normal subjects and patients with chronic hepatitis were roughly comparable. This finding disagrees with the often stated view that the liver in chronic hepatitis has decreased echogenicity and agrees with work showing little difference between the two states.[37,38] With the data-acquisition and analysis methods described in this paper, there would seem to be little hope for differentiating between normal and chronic hepatitis on the basis of backscatter coefficient. Improvements to the methodology, such as (1) direct *in vivo* measurements of attenuation, (2) accounting for individual variations in thicknesses of skin, fat, and muscle, and (3) a more general approach for measuring backscatter coefficient, may improve the likelihood of successful differentiation.

A study by Garra and co-workers[28] suggests that chronic hepatitis can be successfully differentiated from normal based on statistical properties of intensity of ultrasonic echoes. The parameters estimated in that study measured (1) the average spacing between regularly spaced scatterers in the liver (perhaps portal triads), (2) specular to diffuse backscatter ratio, and (3) variation of specular backscatter intensity.[39]

The absolute levels of measurements in normal kidney reported here are near the high end of the range reported in the literature for measurements in humans and animals. The frequency dependence (and therefore, effective scatterer size) was comparable to values computed by other investigators.

Estimates for effective scatterer size in kidney reported here (232 ± 29 μm, mean$\pm$standard deviation for ATL measurements and 211 ± 57 μm for Diasonics measurements) are in agreement with values reported by other researchers. Garra and co-workers measured 216 ± 35 μm from 18 normal kidneys *in vivo*.[14] Insana *et al.* measured 220 ± 15 μm (averaged over all angles of incidence) at low frequencies (2.5–3.5 MHz) in normal dog kidneys *in vitro*.[8] Subsequent experiments by Insana *et al.*[12] on *perfused* dog kidney indicate a substantial range of estimated effective scatterer sizes from about 140 to 250 μm [Figs. 4(a) and 7(a) in Ref. 12]. Differences between measurements reported here and those reported by Insana and co-workers may be attributable to differences between human and dog kidneys as well as differences between *in vivo* and *in vitro* conditions and numerous other variables. (Insana and co-workers have delineated many similarities and differences between human and dog kidney anatomy in Ref. 8, Sec. 2.1, p. 615.)

As shown in Fig. 4, it was possible to obtain highly consistent measurements of the backscatter coefficient *in vivo* with two different clinical data-acquisition systems and two very different reference phantoms. This result demonstrates the robust performance of the reference phantom method for measuring backscatter coefficients *in vivo*. This result is encouraging since the utility of backscatter coefficient measurements as a diagnostic tool is greatly enhanced if different researchers, using different systems, can meaningfully compare measurements.

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