# CHAPTER 9
# CONCLUSIONS AND FUTURE WORK

During the course of this investigation, many observations were made about the estimation of the *in vivo* power spectrum as it applies to estimating the characteristic size of the tissue microstructure. In this final chapter, the conclusions derived from all of the observations are summarized. Then, future goals for extending the work and applying the conclusions are discussed.

## 9.1 Conclusions from Current Investigation

For the estimation of the characteristic size of the tissue microstructure, the *in vivo* power spectrum can be determined to sufficient accuracy by estimating the total attenuation along the propagation path over the frequency range used to estimate the scatterer size. Hence, most of the work in this investigation attempted to solve for the scatterer size and total attenuation simultaneously. However, before solving for these two parameters, the effects of focusing on the estimation of the scatterer size were considered while assuming that the attenuation was known so that the results of the investigation could later be applied to clinically relevant fields. By assuming that the velocity potential fields near the focus could be modeled as a three-dimensional Gaussian distribution, focusing could be corrected by using a new generalized attenuation-compensation function that accounted for focusing, windowing, and attenuation.

The new generalized attenuation-compensation function was then compared to the traditional attenuation-compensation functions that neglected focusing along the beam axis using computer simulations and phantom experiments. The generalized attenuation-compensation function yielded improvements in size estimation accuracy as high as 100% over the traditional attenuation-compensation functions. However, errors from the

choice of the attenuation-compensation function when estimating the radius of the glass beads were much less significant than the same errors when estimating the radius of a Gaussian scatterer due to the stronger frequency dependence of the form factor for the glass bead scatterer. Likewise, the improvement provided by the new generalized attenuation-compensation function decreased as the wavelength dependence of $w_z$ was reduced. In addition, the simulations and phantom experiments had agreement better than 2.5% provided that the same type of scatterers and sources were being compared.

After verifying the new generalized attenuation-compensation function, two distinct algorithms for estimating the scatterer size and total attenuation simultaneously were evaluated. For both algorithms, the evaluation was done using weakly focused sources and relatively small window lengths so that the generalized attenuation-compensation function could be simplified. The first algorithm was termed the Gaussian Transformation algorithm. This algorithm estimated the scatterer size from the change in the approximate Gaussian bandwidth and estimated the total attenuation from the downshift in the frequency corresponding to the main spectral peak after compensating for the scatterer size. The algorithm's performance was reasonable for very small attenuations, but the accuracy of the scatterer size estimate quickly degraded with increasing attenuation. The failure was a result of the algorithm assuming that the spectrum was perfectly Gaussian when in fact real spectra are better described by a Rayleigh distribution that goes to zero at zero frequency.

The second algorithm evaluated did not make any assumptions about the transmitted spectrum and was termed the Spectral Fit algorithm. The Spectral Fit algorithm was initially tested using Gaussian scatterers with an $a_{eff}$ of 25 μm and using a spectrum where the peak of the spectrum was located near 8 MHz. With this size scatterer, the performance (i.e., accuracy and precision) of the basic Spectral Fit algorithm was reasonable for attenuations less than 0.8 dB/cm/MHz, SNR's for 23 dB to 28 dB, and window lengths of 8 mm. The limiting factor of the performance was a lack of precision with increasing noise, decreasing window length, and increasing attenuation. Hence, the rest of the investigation focused on improving the precision of the Spectral Fit algorithm.

After introducing the Spectral Fit algorithm, four different signal processing strategies were investigated with the hope of improving the precision of the Spectral Fit algorithm. Once again, the strategies were tested using Gaussian scatterers with an $a_{eff}$ of 25 μm and using a spectrum where the peak of the spectrum was located near 8 MHz. The first strategy averaged together estimates from different window lengths. Then, homomorphic signal processing was attempted to smooth the spectra before the minimization. The third strategy involved taking the RF echoes in different combinations and then averaging the results together. Finally, the frequency dependence of the form factor was varied, estimates were obtained at each assumed form factor, and a final estimate was extrapolated from the results for each assumed form factor. In all four cases, the signal processing did not improve the precision of the Spectral Fit algorithm. Hence, it does not appear that robust estimates of tissue microstructure can be obtained by new signal processing techniques alone.

When the different signal processing strategies failed to improve the precision, different frequency ranges, $\Delta ka_{eff}$ values, and initial frequencies were investigated by performing simulations with different scatterer sizes, half-space attenuations, source bandwidths, and levels of additive electronic noise. The accuracy and precision of the attenuation estimate were consistently improved by increasing the frequency range while the accuracy and precision of the scatterer size estimate were consistently improved by increasing $\Delta ka_{eff}$. The improvement observed explained the dependence of precision on half-space attenuation and electronic noise that was observed in the initial simulation studies using Gaussian scatterers with an $a_{eff}$ of 25 μm and a spectrum where the peak was located near 8 MHz. In addition, the Spectral Fit algorithm was shown to exhibit a peak in the deviation of the attenuation estimate versus initial frequency that was shown to be correlated with the frequency location of the peak in the backscattered spectrum. The occurrence of the deviation peak may be useful in the future to improve the precision if it is not an artifact of the simulation.

After establishing the dependence of the precision on the frequency ranges, $\Delta ka_{eff}$ values, and initial frequencies, the dependence was investigated further by analyzing the average squared difference (*ASD*) surface (i.e., difference between backscattered spectrum and reference spectrum modified by scatterer size and total attenuation) over

which the Spectral Fit algorithm finds the minimum when estimating the scatterer size and total attenuation. The analysis was done using both the simulated waveforms as well as ideal surfaces corresponding to a derived expression for the *ASD* surface. The analysis of the *ASD* surface demonstrated that the precision of the estimation scheme was directly related to the prominence of the minimum for the surface. In addition, the precision of the attenuation estimate was related to the shape of the parabolic trough along which the minimum always occurred. The minimum of the *ASD* surface became more pronounced (better precision) for larger $\Delta ka_{eff}$ ranges, larger frequency ranges, and smaller spectral variances. Also, the parabola describing the parabolic trough of the *ASD* surface was narrowed with larger initial frequency (poorer precision for attenuation estimate). Hence, the analysis of the *ASD* surface was in agreement with the simulation results regarding $\Delta ka_{eff}$ range, frequency range, and initial frequencies below the deviation peak. The results for initial frequencies greater than the deviation peak were found to be inconsistent with *ASD* analysis, once again indicating a limitation in the current theory or perhaps a simulation artifact.

## 9.2 Future Directions for *In Vivo* Power Spectrum Estimation

After completing the current investigation, it was clear that there were many aspects of the problem that needed to be investigated in more detail. More work could certainly be done on estimating the *in vivo* power spectrum as it applies to estimating the size of the tissue microstructure. In addition, the basic principles of the work could be extended to other applications. Both types of future work are briefly discussed in this section.

### 9.2.1 Future work on size estimation

Although much of the groundwork for the *in vivo* spectral estimation problem for size estimation was presented in this thesis, there are many aspects that still need to be addressed. One aspect of considerable interest is the source dependence of the attenuation deviation peak versus initial frequency used in the estimate. Because the current theory does not explain this peak, the first step would be to confirm that it is not just an artifact of the simulation by performing a phantom experiment with a real

ultrasound source. Before the phantom experiment can be performed, however, more simulations need to be run using glass beads (the scatterers in phantoms) instead of Gaussian scatterers. Some of the results in Chapter 3 demonstrated that the estimation of glass bead radii is not as affected by errors in the attenuation-compensation function. Hence, the performance of the Spectral Fit algorithm may be slightly different, probably improved, when using glass beads for the scatterers. As a result, the deviation peak may not be as pronounced for these glass beads, and the simulations are required so that the properties of the peak can be anticipated facilitating the design of the phantom experiment.

Assuming that the existence of the deviation peak is real and not just a strange artifact of the simulation, two other investigations should be conducted. From a theoretical point a view, the scattering equations need to be analyzed in greater detail so that the properties of the deviation peak can be expressed mathematically. Any mathematical derivations would then assist in the development of a spectral coding scheme to capitalize on the dramatic improvement in precision/accuracy after the deviation peak. Currently, this improvement cannot be used due to the low signal levels on this part of the backscattered spectrum.

If the deviation peak is only an artifact of the simulation, then the only definitive way to obtain reasonable estimates of scatterer size and total attenuation simultaneously is to use large frequency and $\Delta ka_{eff}$ ranges. However, the bandwidth of most sources would not allow for adequate estimates to be made using a single source. Hence, multiple sources covering different frequency ranges would need to be used and the resulting RF echoes combined in a single algorithm. Although multifrequency probes do not present a manufacturing difficulty, the combination of the different RF echoes may be difficult because the ultrasound beams from the different sources may not expose exactly the same tissue region. Hence, the spatial resolution may be reduced because the region exposed by all of the sources must be assumed to have the same scatterer size if the waveforms are combined under the current theory.

In addition to the challenges associated with using multiple sources, just using large frequency ranges on real tissue will not be trivial. First, in the work presented in this thesis, the attenuation was always assumed to have a strict linear dependence on

frequency ($\alpha = \alpha_o f$) although the scatterer size estimates would still be valid when the attenuation had a general linear dependence ($\alpha = \alpha_o f + \alpha_b$). However, in real tissue, the attenuation has a power law dependence of the form $\alpha = \alpha_o f^n$ [*Jongen et al.*, 1986], where the value of *n* can vary from 1 to 2. Hence, a linear dependence ($\alpha = \alpha_o f + \alpha_b$) is only valid over a limited frequency range. For larger frequency ranges, the linear approximation would fail leading to inaccuracies in the estimate. Another challenge related to using larger frequency ranges on real tissue is that the form factor used to describe the tissue may only be valid over a certain range of frequencies. Recall that *Insana* and *Hall* [1990] showed that the radius of glass beads could no longer be estimated using the simple spherical shell form factor after a $ka_{eff}$ value of 1.2 due to the influence of shear waves. A similar phenomenon may also be associated with the scatterers in tissue. However, this cannot be determined until more is known about the structures in tissue responsible for the scattering.

One more challenge associated with larger frequency ranges that would be a problem even if the form factor for tissue was valid for all frequencies is the presence of scatterers with different sizes in the same tissue region. The current investigation only considered the estimation when a single size was present. This was done because normally a single size in the tissue will be dominant over a certain range of frequencies. However, if the frequency range is increased, the size estimate may be influenced by scattering structures on a different size scale.

Clearly, there are many issues that need to be investigated before the frequency range can be increased in real tissue experiments. However, it may be possible to improve the precision without drastically increasing the frequency although some increase may still be required. In this investigation, the total attenuation and scatterer size were estimated simultaneously for every resolution cell. However, the total attenuation should not be significantly different from one resolution cell to the next even though the scatterer size may change. Hence, it may be possible to smooth the variations in the attenuation estimate by averaging estimates from adjacent resolution cells improving the precision. The averaged attenuation estimates could then be used to find improved size estimates for each resolution cell individually. This idea needs to be tested

on real tissues so that the real variability in the total attenuation could be used to set the number of resolution cells over which the attenuation estimates would be averaged.

In addition to the challenges associated with implementing and improving the Spectral Fit algorithm, there were also some side issues that deserve further attention. First, the Spectral Fit algorithm was only implemented using weakly focused sources. Hence, the use of focused sources with the Spectral Fit algorithm still needs to be investigated. Before using focused sources, however, the importance of the local attenuation $\alpha_1$ in the generalized attenuation-compensation function needs to be determined. If the local attenuation is important, then an estimation of the local attenuation must be included in the Spectral Fit algorithm. Likewise, if errors in the local attenuation do not affect the accuracy of the estimates for the window lengths of interest, then the Spectral Fit algorithm can be implemented while only correcting for the focusing along the beam axis $w_z$ as measured in a water bath. Another issue that deserves more attention than is currently provided in the literature is the effect the scatterer number density has on the precision of both the traditional and Spectral Fit algorithms. Lastly, the computational efficiency of both the code used to simulate the backscattered waveforms as well as the code used to analyze the waveforms could be improved.

### 9.2.2 Future work on other applications

In addition to continuing the work on predicting the *in vivo* power spectrum for the purpose of estimating the characteristic size of the tissue microstructure, the method should also be applied to other applications in the future. One application for which some of the background work was included in the appendices of this thesis is the estimation of the heating at the skull/brain boundary of the developing skull. In Appendix G, the outer surface of a rat's skull was modeled as a flat plate at some arbitrary angle over the focal dimensions, and the effects of this assumption on estimating the power spectrum incident on the skull were evaluated. The model was found to be very good for a rat's skull. However, the microstructure of the developing human skull is very different than the fully developed rat's skull. Hence, before the results in Appendix G can be extended to developing humans, the RF echoes from a better animal model need

to be explored. A possible choice would be fetal pigs due to the developmental similarities.

Another application that should be investigated is the determination of the *in vivo* power spectrum to quantify ARFI measurements. In ARFI, the *in vivo* spectrum is needed in order to estimate the ultrasound intensity incident on the tissue region. For ARFI, the model would be the same as the form factor used when estimating the scatterer size. Hence, it would be natural to combine ARFI and the quantification of the tissue microstructure into a single measurement scheme.