Abstract — Second harmonic imaging systems transmit relatively low frequency pulses, e.g., 2.5 MHz, and image the frequency-doubled second harmonic generated by acoustic nonlinearity. Imaging the second rather than the first harmonic eliminates significant wavefront aberration and attenuation on the forward path, narrows the beam, and suppresses sidelobes. This technique is used successfully in commercial medical imaging systems and may become dominant in the near future. However, system optimization requires a better understanding of second harmonic generation by focused ultrasound pulses in tissue. Data and simulations are presented quantifying aberration and second harmonic generation by two-dimensional ultrasound beams in realistic tissue models. A pseudo-spectral solver is used to achieve very high accuracy over long paths through lossy, nonlinear abdominal wall and liver.

INTRODUCTION

Superficial tissue structure, e.g., skin, fat, and muscle, produces pulse distortions or aberrations that reduce contrast and lateral resolution of medical ultrasonic imaging systems. There are, of course, compelling clinical and economic reasons for trying to improve the tissue-compromised image quality.

Partial recovery of contrast and resolution has been demonstrated using aberration correction schemes [1-3]. However, they generally require data from two-dimensional (2D) imaging arrays, which are still in the research stage [4]. 1D array data are inadequate for these schemes because of wavefront averaging over the fixed-focus elevation dimension. 1.5D arrays may provide an intermediate solution [5, 6].

Another way to improve image quality is by utilizing harmonic distortion or shocking of the pulse, whereby images are created from second (or higher) harmonic signals continuously generated by the intrinsic nonlinearity of acoustic propagation in soft tissue. This harmonic imaging method [7-9] is suitable for 1D arrays with sufficient bandwidth to transmit a moderate first harmonic signal and receive the weak second harmonic with adequate sensitivity.

Much has been written about second harmonic imaging since 1980 when Muir and Carstensen [10] first demonstrated that conventional imaging arrays produced significant nonlinear effects. These are impressive in water, where absorption is less than 0.1% that of tissue. For example, Fig. 1 shows water pulse measurements from an Acuson linear array with 7 cm fixed elevational focus. It is driven uniformly in azimuth by a 4-cycle RF signal with 2.5 MHz center frequency. Peak-to-peak pressure 2 mm from the lens is 1.3 MPa, which is a typical clinical value. The upper graph in Fig. 1 shows pulse waveforms at 0.2, 5, and 6 cm (time shifted for plotting). Shocking is obvious towards the 7 cm elevation focus. The lower graph is a cross-plot of amplitude spectra, showing strong harmonic generation (integer multiples), as well as interesting intermediate peaks. In tissue, less dramatic but significant second and third harmonics are generated at clinical drive levels.

Today, major medical ultrasound companies sell harmonic imaging systems based on conventional array/system technology. These first generation systems will eventually be replaced by a second generation utilizing more specialized transducers and a better understanding of second harmonic generation (SHG) in vivo. Therefore, one step towards second generation systems is to develop a more comprehensive picture of SHG by focused pulses in aberrating tissue.

Figure 1. Experimental data showing harmonic generation in water by a 1D, fixed-focus medical array.
Computer simulations in realistic tissue models can provide useful information on the SHG/aberration process. They require accurate solutions of the scalar (acoustic), full wave equation in heterogeneous, lossy, nonlinear media. The principal difficulty in practical tissue models is the long propagation distance. For example, over a 10 cm direct or round-trip path, 5 MHz waves propagate 333 wavelengths. At such ranges, typical finite element (FE) or finite difference (FD) algorithms, e.g., [11, 12], distort signals unacceptably. They use lower order space and time derivative approximations to achieve modeling versatility and efficiency rather than ultimate numerical accuracy.

The pseudospectral code described in [13] can satisfy all of the above simulation requirements. Alternatively, the KZK and related methods [14, 15] could be used. However, KZK-type methods are not as robust in inhomogeneous media and only capture forward and limited off-axis propagation due to the underlying paraxial (parabolic wave equation) basis. Omnidirectional solutions are important because of the fundamental role that backscatter and reflection play in the imaging process, as well as for completeness in acoustic power and intensity studies.

Realistic models of abdominal wall morphology are critical to aberration studies. Careful measurements of abdominal wall sections by Hinkelman [16, 17] are the basis for the following model studies.

**PSEUDOSPECTRAL WAVE SOLVER**

Time-domain numerical solutions of the bioacoustic equation involve step-by-step integration in time and evaluation of spatial derivatives at each step. Solutions must include radiation boundary conditions, nonlinearity, and frequency-dependent absorption.

The pseudospectral (PS) method provides an extremely accurate approximation of spatial derivatives in homogeneous media using FFTs on a uniform FD mesh [18]. It yields almost perfect spatial accuracy even at 2 nodes per wavelength. Numerical errors are introduced at material interfaces. However, for the low contrasts typical of soft tissue, numerical experiments show that PS spatial derivatives are adequate at 4-5 nodes per wavelength.

The price for high PS spatial accuracy is a space-periodic domain. Thus, solutions exhibit wraparound at the boundaries, i.e., waves effectively exit one side and enter the opposite side. Berenger’s PML boundary condition [19] is used to circumvent wraparound by forcing the solution to be “periodically small” at the boundaries. The remaining drawback of domain periodicity is that waves are most conveniently introduced as initial conditions rather than boundary conditions.

For accurate time-domain calculations, explicit time integrators are appropriate. The first version in [13] used the 4th order Runge Kutta integrator, which is robust, convenient and reasonably accurate. 2nd order methods like leapfrog were unacceptable for long range propagation. It was noted that the 4th order Adams Bashforth integrator offered advantages. Recent work by Ghrist et al. [20] demonstrated that staggering the 4th order Adams Bashforth integrator (ABS4) improves both accuracy and stability relative to Runge Kutta. Here, staggering means evaluating velocity at full time steps and pressure at half time steps. The ABS4 method yields a factor of 4-6 reduction in parallel computation time relative to Runge Kutta. Note that starting values are obtained from Runge Kutta with ½ of the ABS4 timestep.

Acoustic nonlinearity is due to the pressure density (constitutive) behavior. Expanding in a power series and retaining the first two terms yields the widely accepted “B/A” model, namely,

\[
\rho = -K \left( \nabla \cdot u + \frac{1}{2A} \left( \nabla \cdot u \right)^2 \right)
\]

where \(K\) is the bulk modulus. This is implemented in the PS solver. Other nonlinear models, e.g., more general power laws, are easily incorporated, but the third order differences with the B/A model are not of concern here.

Various relaxation models have been used for absorption in PS solvers, e.g., see [13]. The general version is implemented here, following the formulation in [21] and [22]. Multiple relaxation frequencies are used to accurately model power law frequency dependence. A least squares fitting procedure chooses model parameters for an optimal fit over a specified frequency range. Two mechanisms are adequate over the 2-6 MHz range considered here. This is illustrated in Fig. 2, showing fits to power laws with exponents 0.6, 1.0 and 1.4.

![Figure 2. Least squares fits of attenuation power laws from 2 to 6 MHz using two relaxation frequencies.](image-url)

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**Figure 2.** Least squares fits of attenuation power laws from 2 to 6 MHz using two relaxation frequencies.
The PS algorithm described above yields an accurate, complete wave solver. Fine-tuning of the implementation is possible, but potential gains appear less than a factor of 5. Therefore, for current PCs and workstations, simulations of 300+ wavelength models are restricted to 2D. Similar 3D simulations are only feasible on a massively parallel machine with O(1000) processors. Fortunately, a great deal of information can be gained from 2D simulations.

**TISSUE AND FINITE DIFFERENCE MODELS**

Ultrasonic pulses are propagated through four abdominal wall model sections labeled MS1-MS4. MS1 is a piecewise homogenous approximation of an abdominal wall as shown in the top panel of Fig. 3. MS2, MS3 and MS4 are shown in subsequent figures and were extracted from actual tissue cross-sections [17]. Material properties in Table 1 are from [23]. Water was assumed linear and tissues were simulated with B/A (2nd order) nonlinearity and a two-mechanism relaxation model.

Models MS1, MS2 and MS3 simulate a 2.5 MHz transducer with 1.5 cm aperture and 5 cm geometric focus. MS4 simulates a 2 cm aperture and 10 cm geometric focus. The pulse was generated by bending a plane wave to the appropriate radius of curvature and setting initial conditions on pressure and velocity in the water layer.

<table>
<thead>
<tr>
<th>Tissue/Material</th>
<th>(\rho) [kg/m(^3)]</th>
<th>(V) [m/sec]</th>
<th>B/A</th>
<th>Loss [dB/cm/MHz(^b)]</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>1000</td>
<td>1500</td>
<td>5.0*</td>
<td>0.002*</td>
<td>2.0</td>
</tr>
<tr>
<td>Fat</td>
<td>928</td>
<td>1427</td>
<td>10.0</td>
<td>0.75</td>
<td>1.0</td>
</tr>
<tr>
<td>Connective</td>
<td>1100</td>
<td>1537</td>
<td>7.87</td>
<td>1.125</td>
<td>1.0</td>
</tr>
<tr>
<td>Muscle</td>
<td>1041</td>
<td>1571</td>
<td>7.5</td>
<td>0.55</td>
<td>1.0</td>
</tr>
<tr>
<td>Liver</td>
<td>1050</td>
<td>1577</td>
<td>6.75</td>
<td>0.4</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* set to zero in simulation

Models MS1-MS3 are 2x8 cm with PML boundaries on all sides to simulate an infinite domain. They were discretized at 256 x 1024 cells, producing a cell size of 0.0078125 cm, or 4 cells per wavelength at the second harmonic. The pulse was propagated through the model for 5000 timesteps at 0.2 of the Courant (stability) number, chosen for accuracy rather than stability. The simulations required about 2 hours each on an SGI Origin 2000, using 6 of the 8 available processors. Parallel efficiency was about 80%, i.e., the simulations would have required 10 hours each on a single CPU machine.

Model MS4 extended 4x16 cm and was discretized at the same element size, requiring 512x2048 cells. This model was run for 10,000 timesteps and required 18 hours, again using 6 CPUs.
graphical definition only pulse compression is plotted in greyscale. Circular diffracted waves from the edges of the insonified region are apparent. These edge diffractions are produced by any finite transducer, although details differ. In the third snapshot note the reflections and diffractions from the muscle interface. The PML boundaries have accurately removed outgoing waves at the sides of the model with no spurious reflections. In the fourth snapshot, the pulse has reached the geometric focus. Fig. 4 compares the amplitude spectrum of the pulse at its geometric focus with that of the input signal (arbitrarily scaled). A significant second harmonic at 5 MHz and a weaker, essentially undamped, subharmonic (rectified pulse) near 0.5 MHz are apparent.

Figures 5, 6 are analogous to Figs. 3, 4 except that piecewise homogeneous model MS1 is replaced by MS2, an actual abdominal cross-section. The fine structure produces considerable diffuse scattering relative to the idealized model. Dropouts or shadow regions are also evident in later snapshots. The amplitude spectrum in Fig. 6 is quite similar to that in Fig. 4, but is weakened by backscatter.

ABERRATION AND SECOND HARMONIC GENERATION

Figure 7 displays the harmonic amplitude distributions obtained by Fourier transforming the pulse at each point in model MS1. The transforms are smooth, as shown in Fig. 4, so that similar distributions would be found for frequencies near the first and second harmonics. The fingers or feathers, i.e., sidelobes, in the first are due to interference between the direct pulse

Figure 5. Snapshots of pulse propagation through a typical abdominal wall model section (MS2) from [16].

Figure 6. Amplitude spectrum of pulse at the geometric focus in abdominal wall model (MS2), compared to spectrum of input pulse.

Figure 7. Spectral amplitude distribution of first and second harmonic over piecewise homogeneous tissue model section (MS1) and quantified on centerline. (1.5 cm aperture and 5 cm geometric focus).
and the edge diffractions. Standing waves are obvious in the layers. The second harmonic emerges as the pulse propagates (disregard the initial conditions artifact). Note how the second harmonic develops through the tissue layers, with a sharper focus and minimal diffraction. Diffraction moves the first harmonic focus to about 4 cm, while the second harmonic focus is deeper.

Figures 8–10 display the same information for the inhomogeneous tissue models. MS2, Fig. 9, distorts both first and second harmonic foci and shifts them laterally. This is caused by fat marbling in the muscle layer. MS3, Fig. 8, shows less effect because the fat is layered between the muscle and liver tissue.

The corresponding wavefront deformations are given by the phase spectra. For example, Fig. 11 plots phase spectra at 2.5 and 5 MHz for MS3 over an expanded region around the foci. This demonstrates the complexity of second harmonic wavefronts.

**DISCUSSION AND CONCLUSIONS**

The pseudospectral method is a powerful tool for studying ultrasonic pulse propagation through tissue. Material nonlinearity, attenuation and fine structure are accurately modeled in 2D. Large scale (hundreds of wavelengths) 3D simulations require 1000x more computational resources than current PCs or workstations can provide. Massively parallel machines may provide a brute force solution to this dilemma. Fortunately, 2D simulations suffice for understanding many of the issues. Since, the azimuthal direction is frequently used for beam scanning rather than focusing, in these cases 2D simulations will be quantitative.

Pulses were modeled through three abdominal wall cross-sections and one homogeneous layered model for comparison. Fourier transforms of signals illustrate second harmonic generation as the pulse propagates. The focal shifting and distortion induced by real structure relative to the baseline layered model are readily apparent. By simulating a representative selection of tissue models, it should be possible to evaluate strategies for optimizing both the second harmonic beam and aberration correction schemes.
Figure 11. Example of phase aberration in MS3. The phase spectrum plots are at 2.5 MHz (left) and 5 MHz (right). These are over the focal region between the vertical lines drawn in the model plot (above).

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REFERENCES


