Published in final edited form as:

IEEE Int Ultrason Symp. 2012 October 7; 2012: 1–4. doi:10.1109/ULTSYM.2012.0231.

Characterization of nonlinear ultrasound fields of 2D therapeutic arrays

Petr V. Yuldashev^{2,4}, Wayne Kreider¹, Oleg A. Sapozhnikov^{1,2}, Navid Farr¹, Ari Partanen³, Michael R. Bailey¹, and Vera Khokhlova^{1,2}

¹Center for Industrial and Medical Ultrasound University of Washington Seattle, USA

²Physics Faculty Moscow State University Moscow, Russia

³Philips Healthcare, Cleveland, OH, USA

⁴LMFA UMR CNRS 5509, Ecole Centrale de Lyon, F-69134 Ecully Cedex, France

Abstract

A current trend in high intensity focused ultrasound (HIFU) technologies is to use 2D focused phased arrays that enable electronic steering of the focus, beamforming to avoid overheating of obstacles (such as ribs), and better focusing through inhomogeneities of soft tissue using time reversal methods. In many HIFU applications, the acoustic intensity *in situ* can reach thousands of W/cm² leading to nonlinear propagation effects. At high power outputs, shock fronts develop in the focal region and significantly alter the bioeffects induced. Clinical applications of HIFU are relatively new and challenges remain for ensuring their safety and efficacy. A key component of these challenges is the lack of standard procedures for characterizing nonlinear HIFU fields under operating conditions. Methods that combine low-amplitude pressure measurements and nonlinear modeling of the pressure field have been proposed for axially symmetric single element transducers but have not yet been validated for the much more complex 3D fields generated by therapeutic arrays. Here, the method was tested for a clinical HIFU source comprising a 256-element transducer array. A numerical algorithm based on the Westervelt equation was used to enable 3D full-diffraction nonlinear modeling. With the acoustic holography method, the magnitude and phase of the acoustic field were measured at a low power output and used to determine the pattern of vibrations at the surface of the array. This pattern was then scaled to simulate a range of intensity levels near the elements up to 10 W/cm². The accuracy of modeling was validated by comparison with direct measurements of the focal waveforms using a fiber-optic hydrophone. Simulation results and measurements show that shock fronts with amplitudes up to 100 MPa were present in focal waveforms at clinically relevant outputs, indicating the importance of strong nonlinear effects in ultrasound fields generated by HIFU arrays.

Keywords

HIFU; therapeutic arrays; nonlinear propagation effects; acoustic characterization; shock fronts; numerical modeling

I. Introduction

Currently, medical ultrasound is used for either diagnostic or therapeutic purposes. Diagnostic ultrasound is widely used in clinical practice. Therapeutic applications are less prevalent, though many treatments are in the process of development. A clinical example is shock wave lithotripsy (SWL), which is used to break up renal calculi. A wide class of therapies that use ultrasound to either thermally ablate or mechanically fractionate tissue is known as HIFU – high intensity focused ultrasound [1-2].

In any medical ultrasound application it is important to know how acoustic energy is delivered to tissues in order to ensure safety and efficacy of the treatment. Relevant measurement standards are available for diagnostic ultrasound, but remain in development for therapeutic applications that utilize high acoustic intensities [3]. Such measurements are often termed ‘exposimetry’ and are derated to estimate *in situ* pressures in biological tissue [4-5].

The quantitative characterization of high intensity fields poses technical challenges related to both the acquisition and derating of exposimetry data. Challenges in acquiring exposimetry data are related to the nature of intense nonlinear acoustic fields, which are characterized by highly localized focal regions and pressure waveforms with shocks. Direct measurement of such fields poses stringent hydrophone requirements in terms of bandwidth, resistance to damage, and size of the sensitive region. Moreover, scanning a hydrophone throughout a 3D volume can be impractical for capturing small scale features associated with high frequencies.

To address exposimetry challenges, a method that combines measurements and modeling for characterizing the performance of ultrasound sources has been proposed [6]. In this paper, the approach was tested for a phased-array source designed for clinical HIFU therapies (Sonalleve V1 3.0T, Philips Healthcare). The scope of this work includes calibration measurements to define an acoustic hologram as well as array output power levels; modeling of the nonlinear acoustic field in water, using the hologram to provide realistic boundary conditions; and comparison of modeling results with independent hydrophone measurements at the focus that were collected over a wide range of clinically relevant output power levels.

II. Methods

The approach employed here for HIFU source calibration in water utilizes low-amplitude hydrophone measurements in the linear propagation regime in combination with nonlinear modeling. Specific steps of the approach can be listed as follows:

1. At a low output level, measure the linear pressure magnitude and phase over a plane region in front of the source using a calibrated hydrophone. Such measurements represent a 2D hologram of the full 3D sound field and can be used to mathematically reconstruct the pattern of vibrations on the surface of the source [7].
2. At a near-source location, measure the linear pressure magnitude across a range of clinically relevant output levels, including the level used in Step 1. The

measurement location should be away from any local nulls, while also being close to the source to minimize the possibility of nonlinear propagation effects. This single point measurement allows the source output at various settings to be related to the output level used for the hologram measurements in Step 1.

3. Simulate the nonlinear acoustic field using the pattern of source vibrations from Step 1 and the output measurements from Step 2 to define model boundary conditions by scaling the magnitude of the hologram. Nonlinear modeling of the full 3D field generated by an array transducer is possible though computationally intensive [8].

A. Experimental Arrangements

The ultrasound source characterized in this paper is part of a Sonalleve V1 3.0T MR-HIFU system (Philips Healthcare, Cleveland, OH) at the Bio-Molecular Imaging Center at the University of Washington (Seattle, WA). The HIFU source includes a phased-array transducer with 256 elements arranged on a spherically curved surface with a 120 mm radius of curvature. Each circular element is 6.6 mm diameter, while the aperture of the entire array is 127.8 mm. The source operates at 1.2 MHz and is able to produce up to 800 W of acoustic power.

The overall experimental arrangement used for hydrophone measurements is shown in Fig. 1. A cylindrical acrylic tank with an inside diameter of 184 mm was attached to the top of the patient table and filled with degassed water. The transducer was surrounded by oil that was separated from the degassed water by a mylar membrane with a thickness of 50 μm . The aperture plane of the transducer was placed 5 mm below the membrane. The oil at room temperature has sound speed 1380 m/s and density 840 kg/m³.

B. Hydrophone Measurements

All hydrophone measurements were acquired using a custom LabVIEW program (National Instruments; Austin, TX, USA). The program controlled the following elements: movement of the hydrophone using a 3D positioner (NF90 motor controllers, Velmex Inc.; Bloomfield, NY, USA); triggering of the HIFU array using a function generator (Model 33250A, Agilent Technologies, Inc.; Santa Clara, CA, USA); and capturing of the hydrophone signal using a digital oscilloscope (Model LT344, LeCroy Corp.; Chestnut Ridge, NY, USA). Two different hydrophones were used to accommodate both low-amplitude and high-amplitude waveforms.

Calibration measurements from Step 1 and Step 2 of the method were taken at low amplitudes using an HGL-0200 capsule hydrophone (Onda Corporation; Sunnyvale, CA, USA). This hydrophone is designed for measurements from 1–20 MHz and pressures up to several MPa at the array's operating frequency of 1.2 MHz. Its sensitive area is a PVDF membrane with a 200 μm diameter. Measurements with this hydrophone included a scan in a plane 40 mm in front of the focus as well as a series of measurements at a single, near-source location to compare acoustic output levels at different settings. The hologram area was 86.4 mm square with a step size of 0.6 mm, which is less than half of a wavelength to eliminate the possibility of spatial aliasing.

Independent validation measurements of focal waveforms over a broad range of output levels were made with a fiber-optic probe hydrophone (Model FOPH 2000, RP Acoustics; Leutenbach, Germany). This hydrophone measures pressure changes in the fluid at the tip of a 100 μm optical fiber and has a stated bandwidth up to 100 MHz. Deconvolution of the signal according to manufacturer's impulse response data was applied.

C. Modeling Nonlinear Acoustic Propagation

In this paper, propagation of 3D nonlinear acoustic continuous waves was simulated using the Westervelt equation [9]:

$$\frac{\partial^2 p}{\partial \tau \partial z} = \frac{c_0}{2} \Delta p + \frac{\beta}{2\rho_0 c_0^3} \frac{\partial^2 p^2}{\partial \tau^2} + \frac{\delta}{2c_0^3} \frac{\partial^3 p}{\partial \tau^3} \quad (1)$$

Here t is time; $\tau = t - z/c_0$ is retarded time; $p = \frac{1}{2} \frac{\partial^2}{\partial x^2} + \frac{1}{2} \frac{\partial^2}{\partial y^2} + \frac{1}{2} \frac{\partial^2}{\partial z^2}$; and x and y are spatial coordinates lateral to the propagation distance z . Finally, ρ_0 , c_0 , β and δ are the density, ambient sound speed, nonlinearity coefficient, and absorption coefficient of the medium, respectively. Values of the physical parameters in Eq. (1) were chosen to represent the experimental measurement conditions in water: $\rho_0 = 998 \text{ kg/m}^3$, $c = 1485 \text{ m/s}$, $\beta = 3.5$, $\delta = 4.33 \times 10^{-6} \text{ m}^2/\text{s}$.

The numerical solution to Eq. (1) was calculated using the method of fractional steps with an operator splitting procedure of second order [10]. According to this method, Eq. (1) was divided into simpler equations for diffraction, nonlinearity and absorption. The acoustic field was represented either in the time-domain or the frequency-domain using a finite Fourier series. The diffraction and absorption operators were calculated in the frequency domain. For each harmonic the angular spectrum method was employed to calculate diffraction and the exact solution accounted for absorption. The nonlinear operator at small distances from the source was solved in the frequency domain using a fourth-order Runge-Kutta method for the set of nonlinear coupled equations for harmonic amplitudes [11]. For shocked waveforms, a conservative time-domain Godunov-type scheme was used [12]. A more complete description of the numerical algorithm is given in [8].

Numerical simulations of three-dimensional nonlinear acoustic fields are computationally intensive, requiring long calculation times (typically 1 day) and large allocations of memory (RAM). In order to reduce memory requirements, the storage of harmonic amplitudes in memory was optimized by storing only several harmonics at the periphery of the beam and larger numbers near the focus. As a rule, from 32 to 72 GB of RAM were sufficient to perform the simulations even at high ultrasound intensities.

Boundary conditions for Eq. (1) were defined as a pressure field calculated from an experimentally measured hologram. The initial pressure field at the apex of the source ($z = 0$, see Fig. 2) was obtained by using the angular spectrum method to linearly backpropagate the field represented by the measured hologram obtained in Step 1 of the method. The pressure magnitudes at $z = 0$ were scaled according to near-source power calibration measurements (Step 2) and nonlinear forward propagation was then simulated starting from this plane (Step 3).

III. Results

To evaluate this approach for calibrating HIFU sources, focal waveforms from numerical simulations were compared to direct fiber optic hydrophone measurements for nominal acoustic powers ranging from 25 to 800 W. Several experimentally measured (red curves) and simulated waveforms (black curves) are presented in Fig. 3. These simulations show good agreement with the FOPH data for both quasilinear (Fig. 3a) and shocked waveforms (Fig. 3c). The intermediate case of incipient shock is also well captured (Fig. 3b). The results show that a modern therapeutic array at operating conditions can produce shocked waveforms in the focus with amplitudes over 100 MPa.

To summarize comparisons of simulations and measurements, peak positive and peak negative pressures are plotted in Fig. 4 for all measured output levels. The output levels are shown here in terms of the nominal source pressure $p_0 = \sqrt{2\rho_0 c_0 I_0}$, where a nominal source intensity I_0 is defined by dividing the total array power obtained from hologram by the area of the array elements. Experimental data were analyzed by averaging peak values over 8 acoustic cycles; mean values are plotted as circles, while vertical error bars depict the mean $\pm$ one standard deviation.

For peak positive pressures, simulations and measurements show good quantitative agreement. Simulations and measurements both track the formation of shocks as indicated by the steep slope in the curve near $p_0 = 0.25$ MPa. Across the entire range of output levels, simulation results remain within 6 MPa of the corresponding measured value. Normalized to the measured values, the largest discrepancy of about 10% occurs in the region where shocks develop and pressure amplitudes are very sensitive to the source pressure p_0 . For peak negative pressures, the differences between simulated and measured values remain less than 2 MPa, with a maximum relative discrepancy of 14%.

IV. Discussion/Conclusions

An approach using a combination of measurements and modeling was described for quantitatively characterizing the acoustic fields generated by HIFU sources. This approach utilizes linear field measurements to quantify the acoustic output level and to capture the pattern of vibrations at the transducer surface with acoustic holography. Such calibration measurements were then used to define boundary conditions for a 3D model of nonlinear propagation based on the Westervelt equation. This method was implemented and independently evaluated for a clinical HIFU array manufactured by Philips.

Results of this combined characterization approach were tested using independent hydrophone measurements. These complementary measurements confirm that nonlinear focal waveforms are accurately modeled. Simulations capture shock formation as well as shock amplitudes in excess of 100 MPa.

Clinical transducer arrays can operate in various configurations that are more complex than the case presented here without steering. Some variations in source behavior are possible, and they may not be taken into account in the programming of phases and amplitudes of array elements. At low acoustic amplitudes, such variabilities likely have little effect on the

resulting acoustic field. However, nonlinear fields can be considerably more sensitive to such factors. Though it may be extremely difficult to acquire accurate nonlinear measurements in such situations, simulations based on realistic boundary conditions can help to address these challenges by explicitly capturing the entire 3D field.

This work demonstrates the feasibility of using a combination of measurements and modeling to accurately calibrate the output of a clinical HIFU array source. This metrological approach can address the challenges of characterizing nonlinear HIFU fields in clinical situations and may be uniquely suited for meeting measurement standards that are being developed to ensure the clinical safety and efficacy of HIFU treatments.

Acknowledgments

This work was supported by the NIH (EB007643) and by the RFBR PICS 10-02-91062/CNRS 5603. Numerical simulations were performed on the SKIF “Chebyshev” and the “Lomonosov” clusters of the supercomputer center at Moscow State University

References

- [1]. Bailey MR, Khokhlova VA, Sapozhnikov OA, Kargl SG, Crum LA. Physical mechanisms of the therapeutic effect of ultrasound - (A review). *Acoust. Phys.* 2003; 49:369–388.
- [2]. Xu Z, Hall TL, Fowlkes JB, Cain CA. Effects of acoustic parameters on bubble cloud dynamics in ultrasound tissue erosion (histotripsy). *J. Acoust. Soc. Am.* 2007; 122:229–236. [PubMed: 17614482]
- [3]. Harris GR. Progress in medical ultrasound exposimetry. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 2005; 52:717–736. [PubMed: 16048175]
- [4]. Zeqiri B, Hodnett M. Measurements, phantoms, and standardization. *Proc. Inst. Mech. Eng. Part H-J. Eng. Med.* 2010; 224(H2, SI):375–391.
- [5]. Bessonova O, Khokhlova V, Canney M, Bailey M, Crum L. A derating method for therapeutic applications of high intensity focused ultrasound. *Acoust. Phys.* 2010; 56:376–385.
- [6]. Canney M, Bailey M, Crum L, Khokhlova V, Sapozhnikov O. Acoustic characterization of high intensity focused ultrasound fields: a combined measurement and modeling approach. *J. Acoust. Soc. Am.* 2008; 124:2406–4220. [PubMed: 19062878]
- [7]. Sapozhnikov OA, Pishchal'nikov YA, Morozov AV. Reconstruction of the normal velocity distribution on the surface of an ultrasonic transducer from the acoustic pressure measured on a reference surface. *Acoust. Phys.* 2003; 49:354–360.
- [8]. Yuldashev PV, Khokhlova VA. Simulation of three-dimensional nonlinear fields of ultrasound therapeutic arrays. *Acoust. Phys.* 2011; 57:334–343. [PubMed: 21804751]
- [9]. Westervelt P. Modeling the propagation of nonlinear three-dimensional acoustic beams in inhomogeneous media. *J. Acoust. Soc. Am.* 1963; 35:535–537.
- [10]. Zemp R, Tavakkoli J, Cobbold R. Modeling of nonlinear ultrasound propagation in tissue from array transducers. *J. Acoust. Soc. Am.* 2003; 113:139–152. [PubMed: 12558254]
- [11]. Khokhlova V, Souchon R, Tavakkoli J, Sapozhnikov O, Cathignol D. Numerical modeling of finite-amplitude sound beams: Shock formation in the near field of a cw plane piston source. *J. Acoust. Soc. Am.* 2002; 110:95–108.
- [12]. Kurganov A, Tadmor E. New high-resolution central schemes for nonlinear conservation laws and convection-diffusion equations. *J. Comput. Phys.* 2000; 160:241–282.

Fig. 1. Schematics of the measurement configuration with a custom tank mounted to the patient table.

Fig. 2.
Pressure magnitude at the initial plane of a boundary condition reconstructed from the measured hologram.

Fig. 3. Comparison of measured (red line) and simulated waveforms (black line) for several output levels.

Fig. 4.

Comparison of peak positive and peak negative pressures at the focus obtained in FOPH measurements as well as in simulations.