Design of HIFU transducers to generate specific nonlinear ultrasound fields

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Introduction and motivation
- nonlinear effects in therapeutic ultrasound fields

Hypothesis and theoretical models
- KZK equation, equivalent source model, Westervelt equation

Solving inverse problem
- multi-parametric solution to the KZK equation for focused ultrasound beams

Results
- determine transducer F-number, aperture, and initial intensity to achieve certain pressures and degree of nonlinear effects at the focus

Example of HIFU array design

Conclusions
Therapeutic applications of ultrasound

HIFU surgery:

- **Frequency**: 0.7 – 4 MHz, up to 20 MHz
- **Intensity in situ**: 500 – 30 000 W/cm²

**Major bioeffects in HIFU**

- **Thermal**: tissue heating due to absorption of ultrasound energy
  - Thermal dose for necrosis: 120-240 min at 43°C, 1 s at 56°C, 0.1 s at 59°C
- **Mechanical**: cavitation, shear stresses

High Intensity Focused Ultrasound = nonlinear acoustic fields
Motivation:

Some HIFU applications

- rely on the presence of shock fronts and their specific amplitudes at the focus
- are designed to avoid nonlinear effects and shocks
- rely on maximized peak negative pressure preferably without shocks

How to optimize transducer parameters to control the degree of nonlinear effects at the focus?
Nonlinear effects in HIFU

**Linear acoustics**
- focal pressure amplitude ($p_F$)
- broader focal zone

**Nonlinear acoustics**
- peak positive and negative pressures ($p_+ > p_-$)
- shock amplitude ($A_s$)
- narrower focal zone, enhanced heat deposition

Different effects in tissue:
- thermal coagulation
- boiling
- emulsification
- shear stresses
- immune response
- release of biomarkers

Nonlinear effects and resulting shocks are important in HIFU as they result in enhanced heating and additional nonthermal bioeffects
Example: boiling histotripsy (BH) method in HIFU
Mechanical tissue disintegration into subcellular debris

Pulsing protocol:
1 – 3 MHz, 10 – 20 ms pulses with shocks, 0.01 duty cycle, vapor bubble within each pulse

Shock amplitudes of $A_p > 60$ MPa are necessary to generate vapor cavities within each ms-long pulse

How to determine transducer parameters for most effective BH treatment?
Example: boiling histotripsy (BH) method in HIFU

Mechanisms of tissue disintegration into subcellular debris

Weak shock heating:

\[ q = \frac{\beta f_0 A_s^3}{6c_0^4 \rho_0^2} \]

Tissue at the focus reaches 100ºC in a few ms!

Canney M. et al., UMB 2009

Shock amplitude of 60 – 100 MPa are needed, how to choose transducer parameters?

Simon J.C. et al., PMB 2012
Hypothesis:

Pressure levels required for a certain degree of nonlinear effects to occur at the focus is mainly determined by transducer focusing angle (F-number).
Transducers with the same angular aperture

\[ f_0 = 1.5 \text{ MHz}, \quad F_{1,2,3} = 8; 12; 16 \text{ cm} \]

\[ F\text{-number} = 1.5 \]

Pressure waveforms at the focus focal length \( F = 8 \) and 16 cm for increasing source outputs

Transducers with the same \( F\text{-}number = \frac{F}{2a_0} \) generate shock fronts of the same amplitude at the focus
Transducers with different angular aperture

\[ f_0 = 1.5 \text{ MHz}, \ a_0 = 4 \text{ cm}, \ F_{1,2,3} = 8; 12; 16 \text{ cm} \]
\[ F\text{-number} = 1; 1.5; 2 \]

Hypothesis: shock amplitude at the focus is determined by the angular aperture \((F\text{-number})\) of the transducer
Numerical methods:

- Most accurate 3D Westervelt equation with holography boundary condition for detail field analysis
- Equivalent source model to correlate KZK results with realistic transducer parameters
- Axially symmetric KZK equation for solving an inverse problem
Nonlinear propagation model: 3D full diffraction

Westervelt equation:

\[
\frac{\partial^2 p}{\partial \tau \partial z} = \frac{c_0}{2} \left( \frac{\partial^2 p}{\partial x^2} + \frac{\partial^2 p}{\partial y^2} + \frac{\partial^2 p}{\partial z^2} \right) + \frac{\beta}{2\rho_0 c_0^3} \frac{\partial^2 p^2}{\partial \tau^2} + \frac{\delta}{2c_0^3} \frac{\partial^3 p}{\partial \tau^3}
\]

\[\tau = t - \frac{z}{c_0}\]

3D full wave nonlinear models can accurately simulate the entire field of HIFU sources at high outputs in water and in tissue, but they are very intensive computationally.


Nonlinear propagation model: **numerically efficient**

**Axially symmetric KZK equation (reduced diffraction):**

\[
\frac{\partial^2 p}{\partial \tau \partial z} = \frac{c_0}{2} \left( \frac{\partial^2 p}{\partial x^2} + \frac{\partial^2 p}{\partial y^2} \right) + \frac{\beta}{2 \rho_0 c_0^3} \frac{\partial^2 p^2}{\partial \tau^2} + \frac{\delta}{2 c_0^3} \frac{\partial^3 p}{\partial \tau^3}
\]

\[\tau = t - z / c_0\]

**boundary condition in the plane** \(z = 0\)


**Axially symmetric KZK model** is much less extensive numerically than 3D Westervelt modeling: about 1000 times less memory requirements; computational time for modeling shock waves: from tens of hours to minutes
Equivalent source model
relates boundary condition to the KZK equation
to parameters of the designed transducer

\[ p(z = 0, r, \tau) = p_0^e \sin \left[ \omega_0 \left( \tau + \frac{r^2}{2c_0 F_e} \right) \right], \quad r \leq a_e \]


Parameters of the equivalent source boundary condition to the KZK model \( p_0^e, a_e, F_e \)
are related to those of the HIFU transducer to achieve the best fit of the pressure
distributions on the beam axis measured or modeled at low output level.
Example: 1 MHz, 7-element array
equivalent-source modeling (linear field)

\[ a = 7.4 \text{ cm}, \quad F = 14 \text{ cm} \]

Holographic boundary condition for full diffraction modeling

O.A. Sapozhnikov et al. JASA 2015
138(3), 1515-1532.

Measurements, Rayleigh, and parabolic equivalent-source modeling

Pressure amplitude at the beam axis and in the focal plane

Measurements, parabolic (KZK) and full diffraction modeling agree well in the focal lobe of the linear beam
Example: Validation of nonlinear simulation results for equivalent-source modeling *versus* experiment measurements, *full diffraction (3D Westervelt)*, *parabolic (2D KZK) modeling*

Nonlinear pressure waveforms, measured at the focus agree well with those simulated based on the KZK and Westervelt equations.

Peal positive and peak negative pressures at the focus *versus* transducer output

![Graph showing peak positive and negative pressures versus transducer output](image)

Pressure waveforms at the focus

![Waveform plots](image)
Solution to the inverse problem:

• Find multiparametric solutions to the KZK equation

• Consider three characteristic nonlinear regimes of focusing:
  - quasilinear
  - developed shock fronts
  - saturation

• Determine transducer focusing angle, aperture, and intensity to achieve chosen regime at specific pressure levels
**Multi-parametric solution to the KZK equation**

KZK equation in dimensionless variables only 2 parameters

\[
\frac{\partial}{\partial \theta}\left[ \frac{\partial P}{\partial \sigma} - NP \frac{\partial P}{\partial \theta} - A \frac{\partial P^2}{\partial \theta^2} \right] = \frac{1}{4G} \Delta_{\perp} P
\]

- **Nonlinearity**
- **Absorption**
- **Diffraction**
- **Source amplitude**
- **Linear focusing gain**

**Boundary condition**

\[
P(\sigma = 0, R, \theta) = \begin{cases} \sin(\theta + GR^2), & R \leq 1 \\ 0, & R \geq 1 \end{cases}
\]

\[A \ll 1\]

Absorption is negligible when focusing in water

**KZK equation was solved for various values of** \( G \) **and** \( N \)

- \( 10 \leq G \leq 100 \) **20 points**
- For each \( G \): \( 0 < N \leq 1.5 \) **75 points**
- **19*75 = 1425 times**

**Water:**
- \( c_0 = 1500 \text{ m/s} \)
- \( \rho_0 = 1000 \text{ kg/m}^3 \)
- \( \varepsilon = 3.5 \)


**Solutions in 2D parameter space (\( N \) and \( G \)) were used to solve the inverse problem**
Three characteristic regimes of focusing

Focal peak positive pressure and shock amplitude versus source pressure

Definitions:
- **quasilinear focusing** – 10% of focal wave intensity is transferred to harmonics
- **developed shocks** - maximum ratio of shock amplitude to initial pressure
- **saturation** - steepness of the saturation curve $A_s(N)$ is 10% of that for developed shock regime
Example: regime of developed shock fronts at the focus

Shock front amplitude at the focus is related to the $F$-number of the transducer and its initial intensity, at which developed shock front forms.

Shock amplitude is determined by the focusing angle of the transducer and does not depend on its frequency and aperture.

Source aperture measured in wavelengths $ka = 126; 147; 168; 188$
Recipe
for designing a transducer with specific focal pressures and controlled degree of nonlinear effects (quasi-linear, developed shock, saturation)

- Decide on desired nonlinear regime of focusing
- Determine focusing angle for the KZK equivalent source
- Tune the angle and aperture of the transducer by matching axial distributions of the linear pressure field with equivalent-source model results.

[consider technical limitations on initial peak intensities]
Example: Design of a multi-element HIFU array for BH
developed shocks of 90 – 100 MPa

Predetermined parameters

- 256 elements – number of channels in US system
- 1.5 MHz frequency – from BH experiments
- 0.5 mm between elements – array safety
- 4 cm central hole – fits US imaging probe
- geometry of array location – compact spirals
- 30 W/cm² max intensity at the elements

Requirements to the nonlinear field at the focus

- developed shock front of 90-100 MPa
- achieved in water at $I_0 < 3.75 \text{ W/cm}^2$ at the elements (accounting for 9 dB losses for propagation in tissue)
Choosing focusing angle and diameter of elements

Developed shock front at the focus 90 - 100 MPa

KZK modeling

Focusing angle 58° equivalent source

Compare to spiral array

Focusing angle 74° of the array

Parameters of the array are determined to achieve developed shock amplitude of 90-100 MPa

Vary diameter of elements $D$

axial pressure in the linear beam array, equivalent source

$\frac{KZK modeling}{\text{equivalent source}}$

$\text{Focusing angle 58°}$

$\text{Focusing angle 74°}$

$\text{Compare to spiral array}$

$\text{Parameters of the array are determined to achieve developed shock amplitude of 90-100 MPa}$

$\text{Vary diameter of elements } D$

$\text{axial pressure in the linear beam array, equivalent source}$

$\text{Developed shock front at the focus 90 - 100 MPa}$
Evaluating electronic focusing capabilities of the array

Range of dynamic focusing is established by analyzing the quality of the array field: grating lobes of acceptable level, intensity in the main focus


**T-Array** is free, open-source software with a friendly GUI.

Current capabilities:

- analyze linear ultrasound fields generated by therapeutic phased arrays
- evaluate beam steering performance

[T-Array can be downloaded for free from](www.limu.msu.ru)
Final design of the array produced by Imasonic

Parameters of the array:

- 1.5 MHz
- 144 mm aperture
- 120 mm focal length
- 256 elements of 7 mm diameter
- Positioned with 0.5 mm gaps
- 16-arm spiral
- 40 mm central opening
Conclusions

Transducer design for generating nonlinear HIFU fields

• Method developed to relate transducer parameters to those of the equivalent source in the KZK model
• Accuracy of the method demonstrated
• Inverse problem solved using KZK model
  \[ \text{desired waveform} \leftrightarrow \text{nonlinear effects} \leftrightarrow \text{transducer parameters} \]

Application of the approach

• Multi-element HIFU array for BH applications designed using the proposed method
• T-Array software developed to analyze steering capabilities of HIFU arrays

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