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Physics Procedia

Physics Procedia 87 (2016) 132 - 138

## 44th Annual Symposium of the Ultrasonic Industry Association, UIA 44th Symposium, 20-22 April 2015, Washington, DC, USA and of the 45th Annual Symposium of the Ultrasonic Industry Association, UIA 45th Symposium, 4-6 April 2016, Seattle, WA, USA

## Design of HIFU transducers to generate specific nonlinear ultrasound fields

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## Abstract

Various clinical applications of high intensity focused ultrasound (HIFU) have different requirements on the pressure level and degree of nonlinear waveform distortion at the focus. Applications that utilize nonlinear waves with developed shocks are of growing interest, for example, for mechanical disintegration as well as for accelerated thermal ablation of tissue. In this work, an inverse problem of determining transducer parameters to enable formation of shocks with desired amplitude at the focus is solved. The solution was obtained by performing multiple direct simulations of the parabolic Khokhlov–Zabolotskaya–Kuznetsov (KZK) equation for various parameters of the source. It is shown that results obtained within the parabolic approximation can be used to describe the focal region of single element spherical sources as well as complex transducer arrays. It is also demonstrated that the focal pressure level at which fully developed shocks are formed mainly depends on the focusing angle of the source and only slightly depends on its aperture and operating frequency. Using the simulation results, a 256-element HIFU array operating at 1.5 MHz frequency was designed for a specific application of boiling-histotripsy that relies on the presence of 90-100 MPa shocks at the focus. The size of the array elements and focusing angle of the array were chosen to satisfy technical limitations on the intensity at the array elements and desired shock amplitudes in the focal waveform. Focus steering capabilities of the array were analysed using an open-source T-Array software developed at Moscow State University.

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Keywords: HIFU, nonlinear waves, shocks, transducer design, boiling histotripsy

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High Intensity Focused Ultrasound (HIFU) is an emerging medical technology developed for noninvasive surgery applications. The method utilizes focused ultrasound waves that propagate from the external transducer through the skin to the targeted location to either thermally or mechanically ablate an unwanted tissue within the patient body. In conventional HIFU treatments that operate at moderate in situ intensity levels of about several hundred W/cm<sup>2</sup>, ultrasound waves of nearly harmonic shape (Fig. 1(a)) generate purely thermal lesions at the focus (Fig. 1(c)). Higher intensities, up to several kW/cm<sup>2</sup>, can be used to accelerate treatments. At increased intensities, nonlinear propagation effects accumulate on the way from the transducer leading to formation of high-amplitude shocks in the ultrasound waveform at the focus (Fig 1(b)). When shocks are present, tissue heating is significantly stronger than heating by harmonic waves of the same pressure magnitude; boiling temperatures can be reached at the focus in milliseconds (Canney et al., 2008). Thermal lesions with a vaporized core can be rapidly generated when shockinduced boiling occurs (Fig. 1(d)). Short ultrasound pulses with shocks can be also used to generate purely mechanical liquefaction of tissue (histotripsy) (Fig 1(e)) (Hoogenboom et al., 2015, Khokhlova V. et al., 2015). Recently, two histotripsy methods have been developed. Both methods use a pulse-periodic irradiation protocol with a low duty factor of <1% to avoid accumulation of heating in tissue. Cavitation cloud histotripsy uses microsecond long pulses that generate a cavitation cloud in the focal region (Parsons et al., 2006), and boiling histotripsy (BH) uses millisecond-long pulses that induce localized boiling of tissue within each pulse (Khokhlova T. et al., 2011). Different methods of histotripsy require specific pressure levels and shock amplitudes at the focus. In general, higher peak pressures and therefore shock amplitudes are required for the cavitation cloud histotripsy method as compared to boiling histotripsy (Maxwell et al., 2012). To evaluate nonlinear ultrasound fields of existing transducers or to develop transducers optimized for specific shock-based applications, an inverse problem to determine transducer parameters capable of generating a desired shock amplitude or peak pressures at the focus should be solved.

In this work, multi-parametric calculations based on the KZK equation are performed to solve this problem for the case of a single-element spherically-shaped source. The modelling results were applied for designing a multielement phased array for boiling histotripsy applications. Geometric parameters of the array that provide developed shock fronts of 90-100 MPa amplitude at the focus were determined. Focus steering capabilities of the array were analysed using an open-source T-Array software developed at Moscow State University.



Fig. 1. One cycle of a typical linear waveform (a), and nonlinearly distorted waveform with a shock (b) at the focus used in HIFU to generate a (c) purely thermal lesion, (d) thermal lesion with boiling, and (e) mechanical lesion in tissue.

## 2. Method

The hypothesis of the study was the fact that pressure levels in the focal waveform at which shocks are developed are mainly determined by the transducer focusing angle characterized by its  $F_{number} = F / 2a_0$ , where F – is the focal length of the source and  $a_0$  – is its radius. For transducers of different aperture but same  $F_{number}$ , the shape and the length of the main focal lobe on the beam axis in case of linear focusing are very close to each other (Fig. 2(a)). For transducers with different  $F_{number}$ , i.e. different focusing angles, the length of their focal lobes are significantly

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