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New Methods and Transducer Designs for Ultrasonic Diagnostics and Therapy

Rybyanets A.N., [a]* Naumenko A.A. [a], Sapozhnikov O.A. [b], Khokhlova V.A. [b]

[a] *Institute of Physics, Southern Federal University,194 Stachky Ave., 344090 Rostov on Don, Russia*
[b] *Physics Faculty, Moscow State University, Leninskie Gory, 119991 Moscow, Russian Federation*

Abstract

Recent advances in the field of physical acoustics, imaging technologies, piezoelectric materials, and ultrasonic transducer design have led to emerging of novel methods and apparatus for ultrasonic diagnostics, therapy and body aesthetics. The paper presents the results on development and experimental study of different high intensity focused ultrasound (HIFU) transducers. Technological peculiarities of the HIFU transducer design as well as theoretical and numerical models of such transducers and the corresponding HIFU fields are discussed. Several HIFU transducers of different design have been fabricated using different advanced piezoelectric materials. Acoustic field measurements for those transducers have been performed using a calibrated fiber optic hydrophone and an ultrasonic measurement system (UMS). The results of *ex vivo* experiments with different tissues as well as *in vivo* experiments with blood vessels are presented that prove the efficacy, safety and selectivity of the developed HIFU transducers and methods.

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Keywords: elastic losses; scattering; dispersion; ceramic matrix piezocomposites; complex impedance.

1. Introduction

Ultrasound has found usage in all aspects of the medical field, including diagnostic, therapeutic, and surgical applications. The use of ultrasound as a valuable diagnostic and therapeutic tool in several fields of clinical medicine is now so well established that it can be considered essential for good patient care (Hill *et al.*, 2004). However, remarkable advances in ultrasound imaging technology over last decade have permitted us now to envision the combined use of ultrasound both for imaging/diagnostics and for therapy. Traditional therapeutic applications of

* Corresponding author. Tel.: +7-863-2434122; fax: +7-863-243-4122.
E-mail address: arybyanets@gmail.com

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ultrasound include the treatment of soft tissue and bone injuries, wound healing, hyperthermic cancer treatment, focused ultrasound surgery of Parkinson's disease, glaucoma and retinal detachment and for sealing traumatic capsular tears, benign prostatic hyperplasia, the liver, the kidney, prostate and bladder tumours, vascular occlusion therapy, and tool surgery (Hill *et al.*, 2004; Ter Haar, 2007).

Therapeutic transducers are usually made of low loss lead zirconate-titanate (PZT) or recently from 1-3 connectivity type piezocomposites (Rybyanets, 2012). They are mounted in a light-weight, hand-held waterproof housing, and are typically air-backed. In the past decade, with the advent of faster processing, specialized contrast agents, understanding of nonlinear wave propagation, novel real-time signal and image processing as well as new piezoelectric materials, processing technologies and ultrasound transducer designs and manufacturing, ultrasound imaging and therapy have enjoyed a multitude of new features and clinical applications (Hill *et al.*, 2004; Rybyanets, 2011).

The paper presents the results on development and experimental study of different high intensity focused ultrasound (HIFU) transducers. Technological peculiarities of the HIFU transducer design as well as theoretical and numerical models of such transducers and the corresponding HIFU fields are discussed. Several HIFU transducers of different design have been fabricated using different advanced piezoelectric materials. Acoustic field measurements for those transducers have been performed using a calibrated fiber optic hydrophone and an ultrasonic measurement system (UMS). The results of *ex vivo* experiments with different tissues as well as *in vivo* experiments with blood vessels are presented that prove the efficacy, safety and selectivity of the developed HIFU transducers and methods.

2. Theoretical Calculations and Numerical Modeling of HIFU

The characterization of medical acoustic devices that operate at high output levels has been a research topic and an issue of practical concern for several decades (Dyson *et al.*, 1983). The importance of nonlinear effects has been considered and addressed even at diagnostic levels of ultrasound (Khokhlova *et al.*, 2006). Numerical modeling has been used to predict high amplitude acoustic fields from medical devices. One advantage of modeling is that it can be used to determine the acoustic field in both water and tissue. Numerical algorithms, most commonly based on the nonlinear parabolic Khokhlov-Zabolotskaya-Kuznetsov (KZK) equation, have been developed and applied to the nonlinear fields of lithotripters, unfocused ultrasonic piston sources, diagnostic ultrasonic transducers operating in tissue harmonic imaging mode, focused ultrasound sources, and HIFU sources. For strongly focused fields non-linear models such as Westervelt equation can be used, which is a generalization of the classical wave equation to the nonlinear case in the approximation of the absence of back propagating waves. Even more complex models based on the solution of the full nonlinear wave equation have been developed (Khokhlova *et al.*, 2001). However, these approaches require large computing power and time-consuming calculations (up to several days) on supercomputers, i.e. practically inapplicable to practical problems. This difficulty can be significantly reduced by using the evolution equation for the quasi-plane wave. The corresponding equation in nonlinear acoustics equation is known as the KZK equation (Khokhlova *et al.*, 2006; Khokhlova *et al.*, 2001).

3. Applications of HIFU for Hemostasis

Acoustic hemostasis may provide an effective method in surgery and prehospital settings for treating trauma and elective surgery patients. Application of HIFU therapy to hemostasis was primarily initiated in an attempt to control battlefield injuries on the spot. High-intensity ultrasound (ISA = 500-3000 W/cm2) is usually adopted for hemostasis. Many studies on animal models have been successful for both solid organ and vascular injuries. The thermal effect has a major role in hemostasis. The proposed mechanisms of its action are as follows. Structural deformation of the parenchyma of a solid organ due to high temperature induces a collapse of small vessels and sinusoids or sinusoid-like structures. Heat also causes coagulation of the adventitia of vessels, and subsequently, fibrin-plug formation. The mechanical effect of acoustic cavitation also appears to play a minor role in hemostasis. Microstreaming induces very fine structural disruption of the parenchyma to form a tissue homogenate that acts as a seal and induces the release of coagulation factors . No statistically significant hemolysis or changes in the number of white blood cells and platelets have been observed when blood is exposed to HIFU with intensities up to 2000 W/cm^2 Rybyanets, 2011). The main drawback of the hemostasis applications is low ultrasound absorption ability of blood and, as a result, low heating and coagulation rate at real blood flow. In this section, HIFU transducer design, onlinear acoustic field calculations and in-vivo experiments on blood vessels confirming enhanced hemostasis are described.

3.1. HIFU transducers design

HIFU transducer comprised 1,6 MHz spherical element made from porous piezoceramics (Rybyanets, 2011; Rybyanets, 2012) with 80 mm aperture and 40 mm centre hole having radius of curvature 54 mm. The piezoelement was sealed in custom-designed cylindrical housing filled with the mineral oil providing acoustic contact and cooling of the element. The housing had an acoustic window made of very thin (0.15 mm) PVC membrane. Centre opening was reserved for ultrasonic imaging transducer (Figure 1).

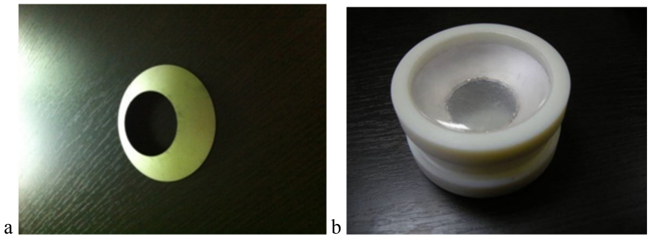

Fig 1. Focusing piezoelement (a) and assembled HIFU ultrasonic transducer (b).

3.2. Acoustic Field Calculations

Calculations of acoustic fields of HIFU transducers were made using the models and algorithms described above. Figure 2 shows two-dimensional distributions of heat sources power in HIFU transducer's acoustic axis plane. Power density levels are represented in absolute values (kW/cm^3).

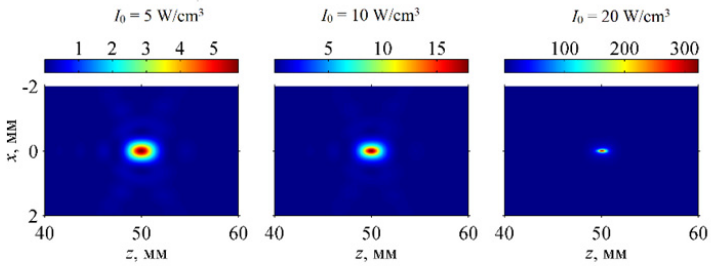

Fig. 2. Two-dimensional distributions of heat sources power in acoustic axis plane of HIFU transducer for 1,6 MHz frequency.

On Figure 3 acoustic pressure signals in the focus calculated at different initial intensities for 1,6 MHz frequency are shown. It is obvious that even at initial intensity level of 5 W/cm^2 non-linear effects lead to pressure profile asymmetry that transforms to a shock front in focus at initial intensity 20 W/cm^2 that give rise to extreme heating (Khokhlova *et al.*, 2006)

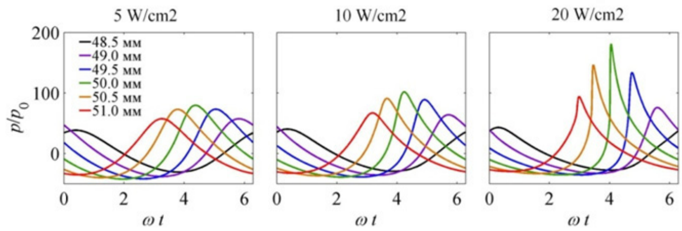

Fig. 3. Acoustic pressure signals in the focus calculated at different initial intensities for 1,6 MHz frequency.

3.3. In Vivo Experiments on Blood Vessels

The experiments were made on lamb's femoral artery at a standard protocol. During ultrasound exposure arterial blood flow was temporarily stopped using intravascular balloon. Ultrasonic transducer with 1,6 MHz frequency described in previous sections was used for experiments. All acoustic measurements were performed in 3D Scanning System (UMS3) using a fiber-optic hydrophone (FOPH 2000) from Precision Acoustics Ltd. Waveforms from the hydrophones and the driving voltage were recorded using a digital oscilloscope LeCroy. The transducer was driven by a function generator Agilent 33521B and a linear rf amplifier E&I model 2400L RF and operates in a CW mode. The acoustic intensity in the focal plane measured in water tank at 5000 W/cm2 (I_{SAL}) was kept for the object treatment. After sonication procedure and angiography study, the samples of femoral artery were extracted to confirm hemostasis and disclose vessel thrombus. The X-ray image of blood vessels obtained using contrast agents and photograph of dissected femoral artery are shown on Fig. 4.

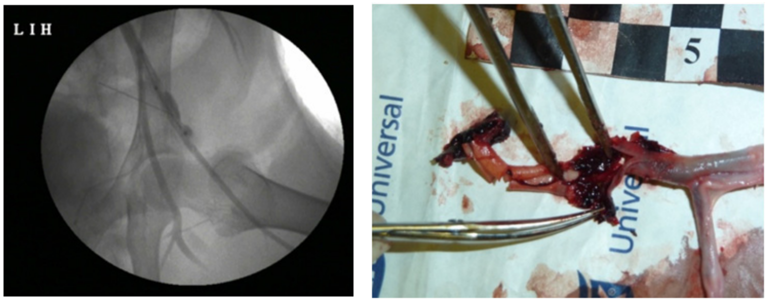

Fig. 4. Angiography image of blood vessels showing ultrasound hemostasis and photograph of vessel thrombus in dissected femoral artery.

4. Conclusions

The results of theoretical modeling and experimental study of different HIFU transducers were presented. *Ex vivo* experiments in tissues (fresh porcine adipose tissue, bovine liver) and *in vivo* experiments in lamb's femoral artery were carried out using different protocols. The results of theoretical modeling and tissue experiments prove the efficacy, safety, and selectivity of the developed HIFU transducers and methods enhancing the tissue lysis and hemostasis and can be used for various therapeutic, surgical and cosmetic applications.

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