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DESIGN OF A TRANSRECTAL PROBE FOR BOILING HISTOTRIPSY ABLATION OF PROSTATE

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OBJECTIVES Thermal ablation of prostate tissue with high intensity focused ultrasound (HIFU) has recently received FDA approval as a non-invasive treatment alternative to first-line prostate cancer treatment options. However, current clinical transrectal HIFU systems have several limitations including the potential for collateral damage due to heat diffusion and minimal real-time ability to monitor treatment efficacy. These limitations are potentially ameliorated by our HIFU boiling histotripsy (BH) approach, which delivers milliseconds duration HIFU pulses with shock fronts to the focus. Interaction between the shocks and the ensuing vapor bubble produces precise mechanical tissue ablation. The presence of hyperechoic bubbles generated by BH and the resulting hypoechogenicity of fractionated tissue allow for reliable real-time targeting and monitoring the treatment with B-mode ultrasound. Owing to the rapidity of tissue bioeffects (milliseconds) and the mechanical mode of action, BH minimizes heat-sink effects and thermal spread that complicate thermal treatments. Current clinically available transrectal HIFU transducers have stringent anatomic requirements to their size and shape. The goal of this study was to demonstrate the ability of transducers with such small form-factor and technical limitations on the intensity levels at their surface to achieve acoustic pressures necessary for BH treatment at clinically relevant depths in tissue.

METHODS Multi-parametric numerical simulations of nonlinear HIFU fields generated by probes of different frequencies and geometries were conducted to design a transducer capable of operating in shock-forming conditions relevant to BH. Parameters of an FDA-approved HIFU device (e.g. Ablatherm) were used as a starting point to meet clinical constraints for transrectal use. Two sets of simulation approaches were employed. First, a less computationally intensive approach based on the equivalent source method and axially symmetric KZK equation was used to determine a range of possible design specifications. While the feasibility of reaching BH exposure parameters was shown within the frequency range of 2 – 3 MHz, the lowest value of 2 MHz was chosen for the initial transducer design to enable larger lesions in tissue and to minimize nearfield-heating effects. Second, more computationally intensive simulations of a full 3D acoustic field were conducted for this frequency based on the Westervelt equation to determine the most appropriate parameters for fabricating a pre-clinical prototype of a transrectal BH transducer. Simulations were performed in water at increasing power outputs assuming that shock-forming conditions necessary for BH should be reached at the focus at the source intensity of less than 10 W/cm^2. This limitation was chosen based on the current limitations of about 40 W/cm^2 for the safety of the transducer, approximate four fold power losses in tissue at 2 MHz with attenuation of 1 dB/cm/MHz, and focusing at up to 3 cm depth in tissue relevant to the conditions of future pre-clinical studies in dogs.

RESULTS A sketch of the proposed preliminary design of a 2 MHz BH probe is shown in Fig. 1 and its linear field pattern is illustrated in Fig. 2. The transducer has 50 mm length, 35 mm width, 20 mm diameter of the central opening, and 40 mm focal distance. Simulated pressure waveforms at the focus at increasing transducer output are presented in Fig.3a. Corresponding shock amplitudes, peak positive, and peak negative pressures in the focal waveform are shown in red color in Fig. 3b. The results demonstrate that shock amplitude of 110 MPa is achieved at the focus for the transducer intensity of 10 W/cm^2. Such shock amplitude is compatible with BH bubble activity confirming the feasibility of using the

probe for pre-clinical BH studies. If the width of the probe is decreased by 5 mm (results shown in blue color in Fig. 3b), the shock amplitude generated at 10 W/cm^2 transducer intensity, would be 95 MPa, which is still acceptable for BH. However, a wider form factor leading to higher shock amplitudes would allow more rapid tisue boiling and shorter pulse duration.

CONCLUSIONS In this simulation study, we demonstrated that BH exposure parameters could be reached at the focus of a miniature transducer with dimensions not exceeding those currently used clinically for transrectal thermal HIFU treatments. It was shown that shock amplitudes up to 100 MPa in the focal waveform sufficient for BH are achievable at up to 3 cm focal depth in tissue at 2 MHz HIFU frequency assuming attenuation in tissue of 1 dB/cm/MHz and intensity limitation at the transducer surface of 40 W/cm^2. Further minimization of the transducer form-factor may still be possible while maintaining clinically relevant shock generation conditions at the focus. Work supported by RFBR 17-54-33034, NIH R21CA219793, and RO1EB007643.

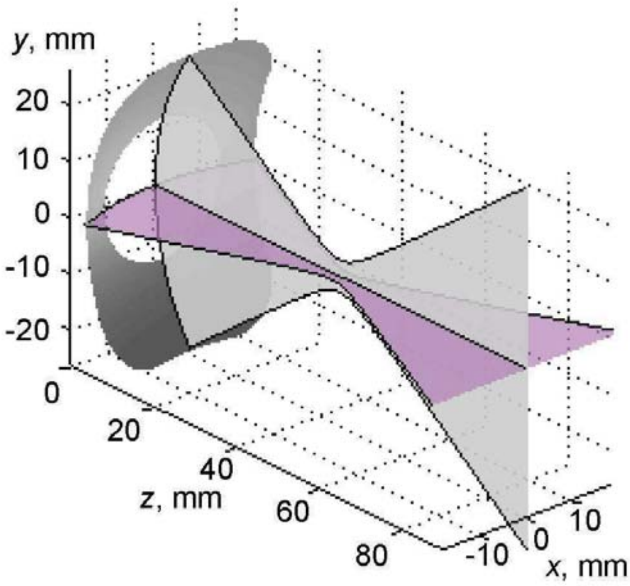

Figure1. Preliminary design of a HIFU transrectal transducer proposed for treating prostate tissue using boiling histotripsy (BH) method. A central opening is to hold a diagnostic array for targeting and real-time imaging of the treatment.

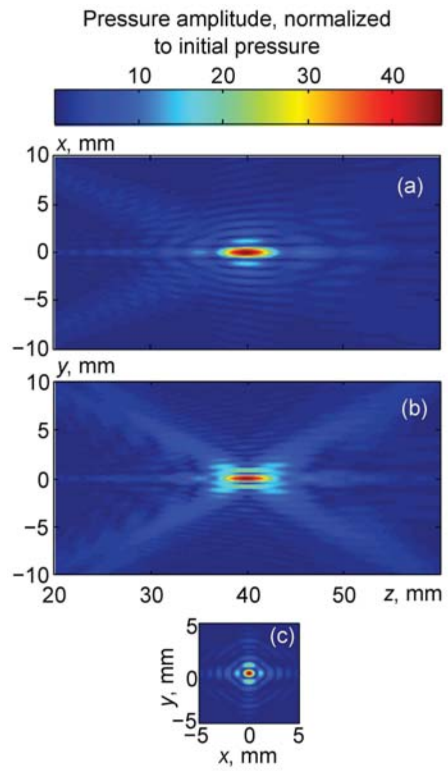

Figure 2. Distribution of the pressure magnitude (axial (a, b) and in the focal plane (c)) simulated linearly in water for a 2 MHz transducer with 50 mm length, 35 mm width, 40 mm radius of curvature, and 20 mm diameter of the central opening.

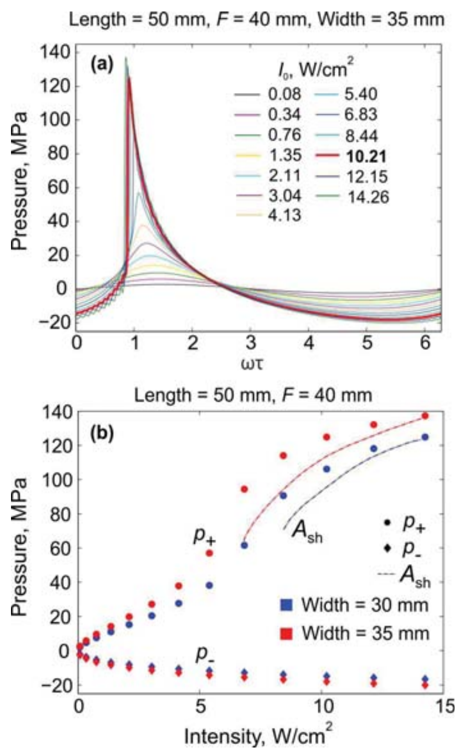

Figure 3. Focal waveforms generated at increasing intensity level at the surface of the transducer with 35 mm width (a). Peak pressures and shock amplitudes simulated at the focus in water using the Westervelt equation for the proposed transducers of 35 mm and 30 mm width (b).