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GENERATION OF VOLUMETRIC BOILING HISTOTRIPSY LESIONS IN TISSUE USING A MULTI-ELEMENT ARRAY OF A CLINICAL HIFU SYSTEM

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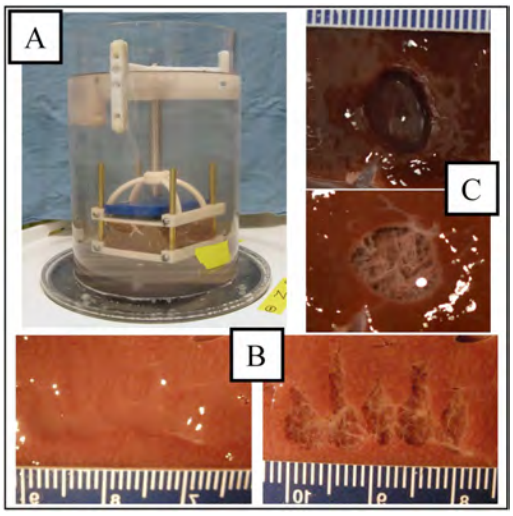
In most high intensity focused ultrasound (HIFU) applications, tissue is thermally ablated due to heating caused by ultrasound energy absorption. Recently, a new method named boiling histotripsy was developed at the UW/MSU to mechanically fractionate tissue. The method applies MHz-frequency millisecond-long pulses with shocks to cause boiling in tissue by shock wave heating and interaction of shocks with the resulting vapor cavity. A typical treatment to generate a single lesion lasts around 30 s, requiring about 30 pulses with a pulse repetition frequency (PRF) of about 1 Hz. The dimensions of the resulting lesion are about 5 mm by 3 mm. Clinically relevant tissue volumes to be ablated may be up to several cubic centimeters; therefore, multiple lesions should be generated to cover the entire targeted region. The goal of this study was to test if a clinical HIFU system is capable of generating volumetric BH lesions and to develop exposure protocols for such treatments. A boiling histotripsy pulsing scheme was combined here with the electronic steering of a multi-element 1.2 MHz HIFU phased array (Sonalleve, Philips Healthcare, Vantaa, Finland) to generate large, mechanically fractionated lesions in polyacrylamide gel samples and in ex vivo bovine tissue. Sonications were performed at a tissue depth of 2 cm with 10 ms-long pulses, PRFs 1 – 10 Hz, and 250 W acoustic power, which corresponded to about 65 MPa in situ shock amplitude. Using electronic steering transverse to the axis of the transducer, two different spatial patterns of focal locations were tested: lines of single lesions separated by 2 mm and circles of single lesions with a similar spacing along each circular arc. Circles with radii of 2, 4, 6, and 8 mm were tested. Each single lesion in a pattern was generated with either a sequential treatment plan (by sending the required number of pulses to each location and then proceeding to the next location in a raster-like fashion), or a non-sequential treatment plan with consecutive HIFU pulses sent to different target locations. Strategies for non-sequential treatments included both raster-like scan patterns for consecutive pulses and patterns that maximized the distance between consecutive pulses to diminish heat accumulation and thermal effects. For all treatments, each point received 30 pulses. Final lesions were examined in a small MRI coil, then analyzed grossly and histologically. Sonications with a 1 Hz PRF produced purely mechanical lesions while increasing thermal effects were observed for sonications at repetition rates of 3 – 10 Hz. For purely mechanical lesions separated by 2 mm, adjacent lesions merged to produce uniform volumes of fractionated tissue. BH lesions produced with electronic steering up to 8 mm off axis were similar to those generated on-axis, even though full power compensation for off-axis sites was not used. Moreover, lesions appeared to be the same for both sequential and non-sequential treatment plans. Finally, it was observed in some lesions that larger vessels could be spared while surrounding liver tissue was effectively fractionated. It was shown that a clinical HIFU system is capable of producing volumetric lesions of mechanically fractionated tissue using a boiling histotripsy method in conjunction with electronic steering of the focal beam. Successful sonications performed at 2 cm depth in tissue required less than 25% of the maximum system power, thus permitting implementation of this approach under clinically relevant conditions with greater attenuation. Work supported by NIH EB7643, K01 EB 015745, T32 DK007779, and RFBR 13-02-00183.



Photographs of the experimental setup (A) and mechanically fractionated lesions arranged in either a line (B) or circles (C). In (B) there are 5 single lesions with 4 mm separation with (left) and without (right) fractionated content; in (C) a volumetric lesion formed by generating a central lesion and two circles of lesions separated by 2 mm radially with (top) and without (bottom) fractionated content.