AbstractID: 13135 Title: Non-thermal cell damage and therapeutic potential of MR guided high-intensity focused ultrasound

Purpose: High-intensity focused ultrasound (HIFU) has garnered increasing interest in therapeutic applications for occlusion of blood flow, sealing of bleeding vessels, sonothrombolysis, myocardium revascularization channel creation, opening of the blood brain barrier and transdermal drug delivery. In this work, we investigate the non-thermal cell damage and therapeutic potential of HIFU for treating non-operable, radiation- and chemo-resistant cancers.

Method and Materials: An InSightec ExAblate 2000 with a 1.5T GE MR scanner was used in this study. MR thermometry was used to monitor the temperature elevation in real time to ensure non-thermal (below 42°C) sonication. LNCaP and PC3 cells were placed in thin plastic vessels and inserted in an ultrasound gel phantom with the ultrasound beam focused on the tumor cells. Cells were exposed to pulsed ultrasound (1MHz; 6W and 10W acoustic power; 5Hz frequency; 0.5duty cycle: 0.1s power on, 0.1s power off) for 60sec. Cell viability was assessed by trypan blue dye exclusion and clonogenic assay.

Results: Non-thermal cell damage by HIFU exposure was observed for both LNCaP and PC3 cells. At 6W acoustic power, the cell-death rate was 23.3+1.7% and at 10W it was 46.3+1.9% for the LNCaP cells (see table below). The control group has a 12.7+0.3% death rate. For PC3 cells, the cell-death rate was 18.7+0.7% for the treated group and 9.0+0.6% for the control cells at 6W. The clonogenic assay results were consistent with the trypan blue dye analysis.

Conclusions: Our in vitro experiments confirmed the non-thermal effect of HIFU on prostate tumor cells. The exact mechanism for non-thermal cell damage needs to be investigated. Further in vivo experiments are warranted to derive optimal ultrasound parameters for HIFU cancer therapy and to provide preclinical toxicity data. This work is supported by Focused Ultrasound Surgery Foundation, DOD PC073127 and Varian Medical Systems. Technical support from InSightec is acknowledged.