AbstractID: 7115 Title: MR Guided Focused Ultrasound (MRgFU) For The Treatmentment of Prostate Cancer: A Feasibility Study of Increasing Cellular Uptake of AS-MDM2 in vivo

Purpose: MDM2 is an oncogene and overexpressed in 30-40% of prostate cancer. Antisense MDM2 oligonucleotide (AS-MDM2) inhibits MDM2 expression, and enhances the effects of radiation and chemotherapy on prostate cancer. The purpose of this study is to investigate the feasibility of increasing the cellular uptake of AS-MDM2 using MR guided High Intensity Focused Ultrasound (MRgFU).

Materials and Methods: A HIFU system (InSightec ExAblate 2000) and a 1.5T MR scanner (GE) were used for this study. Human prostate cancer cells LNCaP 10^5, were grown orthotopically in the prostates of 11 nude mice. Extensive experiments were performed to determine the optimal MR parameters for target delineation and the optimal ultrasound parameters for animal treatment studies using an acoustic phantom. The mice bearing implanted prostate tumors ($61\pm22 mm^3$) were treated under general anesthesia using pulsed focused ultrasound with the output acoustic power of 4W, pulse width of 100msec and either 300 or 900 pulses in one sonication. The focal region is cigar shaped, about 2mm in diameter and 10mm in focal length. The focal peak was set within the target under the MR guidance. Two to four sonications were used to cover the whole tumor. Immediately after the treatment 0.1ml of AS-MDM2, dissolved in PBS, was given by tail vein injection at doses 25mg/kg. After 24hr, the animals were sacrificed and tumors were removed. The expression levels of p53 proteins were analyzed by immunohistochemical staining.

Results: Our preliminary results showed that the animals tolerated well the HIFU treatment. With 300 pulses per site in each sonication blood cell extravasation on H&E staining and an increase in p53 expression ($5.0\pm2.4\%$) in the treated tumor bearing LNCaP cells were observed as compared to the control group ($1.3 \pm 0.5\%$).

Conclusion: MRgFU can be used an alternative treatment modality for prostate cancer treatment.