

AbstractID: 13983 Title: An In vivo Study on the Enhancement of Gene Therapy with MR-Guided Focused Ultrasound (MRgFUS)

Purpose: The purpose of this study is to investigate the feasibility of increasing the cellular uptake of AS-MDM2 for prostate cancer with image-guided focused ultrasound (MRgFUS).

Materials and Method: A GE/InSightec MRgFUS system was used in this experimental study. Human prostate cancer cells LNCaP (5×10^5) were grown orthotopically in the prostates of 28 nude mice. Animals were divided randomly into 4 Groups (n=7/group): Group 1: MRgFUS+AS-MDM2; Group 2: MRgFUS only; Group 3: AS-MDM2 i.v injection only; Group 4: control. For group one the tumors were treated using MRgFUS with the acoustic power of 4 W, pulse width of 0.1 sec and 300 pulses in one sonication. The focal peak was set within the target under MR guidance. Multiple sonications were used to cover the whole tumor. Immediately after the ultrasound treatment 0.1 ml of AS-MDM2, dissolved in PBS, was given by tail vein injection at 25 mg/kg. For group 2 animals were treated with the same as for group one except for AS-MDM2 injection. Animals in group 3 were treated with AS-MDM2 injection only and group 4 used as control. Mice were sacrificed 6 and 24 hr after treatment. The tumors were removed and processed for assessment of protein expression by immunohistochemical staining. The expression levels of MDM2, p53 and p21 proteins were quantified using an image-analysis system.

Results: We observed blood cell extravasations on H&E staining in the MRgFUS treated tumors, as compared to the other groups. There are no significant differences between groups with and without MRgFUS treated groups both 6 hours and 24 hours after treatment.

Conclusions: One single AS-MDM injection did not knock down MDM2 or result in increases in p53 and p21. The effect of multiple MRgFUS and AS-MDM2 treatments on the LNCaP tumor growth is warranted in future studies.