

PP-24

Feasibility study to evaluate the safety and preliminary effectiveness of focal MR-guided focused ultrasound treatment of locally confined low-risk prostate cancer – Initial North American experience

S. Ghai, U. Lindner, T. van der Kwast, E. Hlasney, P. Spensieri, S. McCluskey, M. Haider, W. Kucharczyk, J. Trachtenberg

University Health Network, University of Toronto, Toronto, ON, Canada

Background/Introduction: Multi-parametric MRI (mp-MRI) imaging represents the state of the art imaging technique for detection, localization, staging and also characterization of tumor aggressiveness of prostate cancer. This advantage makes MRI the more suitable technique for targeting focal cancer lesions in the prostate. MRI also provides real-time MR thermometry, thereby allowing closed loop monitoring and controlling the treatment to ensure selective and adequate tumor ablation.

The ExAblate MRgFUS system (InSightec. Ltd, Haifa, Israel) combines standard 1.5/3T MRI scanner with HIFU (High Intensity Focused Ultrasound) energy that is transmitted from a phased array endorectal transducer of 990 elements embedded in a probe with circulating degassed water in a temperature of 14°C. The treatment is performed by macrosonications that are fan-like batches of nominal subsonications. Each subsonication itself is a column-like clustering of points to which energy is continuously targeted. During sonications the system acquires thermal imaging that is displayed to the user in terms of temperature and accumulated dose.

The goal of this study is developing preliminary data to evaluate the safety and preliminary effectiveness of focal MRgFUS treatment of low risk prostate cancer. A total of 8 patients will be treated in our institute under this Phase 1 study.

Methods: Four patients (age range 56 – 67 years), all with Gleason 6 (3+3) prostate cancer (PCa) in two or less cores on a prior biopsy were consented and enrolled in the study. Each patient was assessed for eligibility by mp-MRI followed by transrectal ultrasound guided extended mapping biopsy. Three MRI visible cancerous foci on mp-MRI were identified on 2 of the 4 patients. Two patients did not have visible cancerous foci on mp-MRI. Transrectal 16- core mapping biopsy plus additional sample from each MR target was performed as per protocol for prostate glands over 20 cc in volume. This included 4 samples from peri-urethral locations (2 on each side), to map the medial extent of the tumor. Proximal end of each biopsy sample was inked. Mapping biopsy results revealed Gleason 6 PCa in all the four patients without tumor upgrade. CT of the pelvis was performed in all patients to rule out calcification in the treatment beam path.

In two patients, 3 sites of tumor were visible on MRI and the treatment was targeted to the sites. Since the tumor was not visible on T2WI in the other two patients, the treatment target volume included the sectors from which the cores were positive. MRgFUS treatment was performed under general anaesthesia approximately one month after the biopsy in all patients. Foley's catheter was placed prior to treatment for continuous bladder drainage in 3 of the 4 patients. Suprapubic catheter was placed in one patient since the site of MRI visible target was directly anterior to the urethra. The suprapubic catheter was clamped following the treatment and was also discharged on a Foley catheter.

Results: Macrosonications (range 3 – 12) were used to treat the area of the tumor. Single nominal sonication was also used at the end to cover a marginal dose region at the lateral aspect of the region of treatment in 1 patient.

Median time for each patient in the magnet was 230 minutes (range 170 – 430mts), of which the median treatment time was approximately 72.5 minutes (range 30 – 170 minutes). The median number of treatment sonications per patient was 6 (range 3 – 12). The area of targeted thermal delivery was 3.7 cc per patient (range 0.4 – 4.1 cc). The final median non perfused volume (NPV) at the end of the treatment was 5.4cc (range 2.2 – 7.6cc). Foley's catheter was removed in one patient 2 hours after the procedure, and at one week in the other 3 patients. All patients were discharge from the hospital 3-4 hours post treatment. There was no immediate complication following the procedure and the patients had no adverse symptoms at time of discharge.

Efficacy will be assessed at 6 months post-treatment, using repeat Transrectal Mapping Biopsy of the prostate and by periodic PSA. Post-therapy changes from baseline to 6 months in patient's status secondary to his prostate treatment and satisfaction from the treatment will be assessed using the ICIQ-SF, SF-12, IPSS, and IIEF-15 questionnaires.

Up to date, 3 of the 4 treated patients have had 6 month follow-up MRI. There was an MRI visible PCa focus in 1 of these 3 patients, which was covered by the treatment on the follow-up post treatment scan. No MR visible PCa focus was seen in any of the 3 post treatment MRI's. Repeat transrectal mapping biopsy in one of these three patients thus far, revealed coagulative necrosis in the ablated area, though microfocus (<1mm) PCa was seen in 1 core at the margin of ablation zone and in 2 other cores at different sites in the gland. Two patients are scheduled for the 6 month biopsy in a week and the results would be available by the time of the symposium. Post treatment questionnaires at 1 week, 1 month and 6 months revealed no change from baseline in 3 patients. One patient has been moderately symptomatic with erectile dysfunction since treatment.

Conclusion: This study affirms the feasibility of safely performing this procedure in humans, though oncologic outcome is awaited. It has the ability to safely ablate the target area though further appropriate studies will be needed to confirm it as a valid option along with other techniques such as laser ablation, for focal treatment of localised or index site PCa.

Disclaimer: The study has been sponsored by InSightec.

The first 3 treated patients were presented at the 3rd International Symposium on Current and Future Applications of Focused Ultrasound 2012, Bethesda North Marriott Hotel and Conference Center, Bethesda, MD, USA, October 2012. Oncologic outcome was not available on any patient at that time.