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"Dynamic" active surveillance; a new strategy to follow patients with low and intermediate risk prostate cancer: Combined results of Phase I/II trial of MR imaging-guided focal laser ablation for low-to-intermediate risk prostate cancer

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Background & Purpose: Men diagnosed with localized low risk prostate cancer (PCa) and a significant life expectancy are usually offered the choice of two broad therapeutic options, either active treatment with surgery or irradiation with almost certain impairment in quality of life (i.e., sexual, genitourinary, or bowel dysfunction), or active surveillance (AS), with the low but real risk of disease progression and very long periods of careful clinical, biochemical, and histologic observation leading to significant burden to the patient and health care systems, as well as long-term psychological pressure.

Although prostate cancer is often multifocal, the volume of the largest, or index tumor has been felt to be the likely source of local and possibly distant spread of the tumor. Incidentally found, very low volume, low grade prostate cancer cells are probably indolent in nature, unlikely to spread, and likely contribute to the large disparity between the cumulative presence of prostate cancer and the mortality of the disease. The index lesion is usually demonstrated on multi-parametric MRI and most likely represents dense concentrations of moderate grade cells or lesser concentrations of high grade cells. The imageable nature of these sites creates a treatment target that if eliminated might decrease the risk of progression of the disease. Thus focal ablation of the index cancer, or the prostate section that harbors that cancer, could be very attractive for patients with low or low-intermediate-risk cancers who are uncomfortable with the risks associated with active surveillance or the side effects of radical therapy. The elimination of the MRI imageable index lesion is an opportunity to find the best balance between oncologic control and maintenance of quality of life.

Multi-parametric MRI (mp-MRI) imaging utilizing T2-weighted, diffusion weighted (DWI) and dynamic contrast enhanced MRI (DCE) represents the state of the art imaging technique for detection, localization, staging and also characterization of tumor aggressiveness of prostate cancer. Using its localizing strength, mp-MRI has increased opportunities in management of prostate cancer. Added advantage of MR thermometry allows real time closed loop monitoring and controlling the treatment to ensure selective and adequate tumor ablation as well as monitored preservation of sensitive surrounding tissue to minimize side effects.The goal of our study was to assess the safety and feasibility of focal laser ablation therapy in prostate cancer under MR guidance and predictors of its success.

Materials and Methods: Institutional review board approval was granted for prospective recruitment. Biopsy-proven low or intermediate risk PCa were included (NCCN risk). All patients underwent a pre-treatment diagnostic MRI, with target lesions outlined. The laser ablation treatment was performed as an outpatient procedure in the MR suite under deep sedation (IV Propofol). Initially, a modified MR-compatible template was used for the manual trans-perineal placement of translucent catheters to the site of the tumor. The final 20 treatments were performed with a semi-automated "trajectory alignment device" (robot) aided by custom software to ensure the safe, swift, and accurate placement of the catheters. When the catheter location was confirmed to be in the optimal location, a Visualase 980 nm water cooled fiber replaced the obturator within the catheter. Fibre illuminations were dependent on target volume. The zone of ablation, as well as surrounding tissue, was monitored simultaneously in real-time and in three dimensions by custom designed MRI thermography. Post-procedure coagulation volume was confirmed by contrast-enhanced T1-weighted imaging. Follow-up biopsy was performed 4 -6 months post ablation in 38/40 patients. The men were followed every six months thereafter.

Results: Treatment was successfully completed in all 40 patients. Two patients were lost to follow-up. Mean follow-up to date has been 671 days (range 150–1,157). None of the patients had any significant sustained side effects as a result of the treatments (no incontinence, bowel injury, or impotence). At 4 month or subsequent biopsy, 13/38 patients (34.2%) had evidence of

residual/recurrent cancer in the region treated, 25 patients (65.8%) had no recurrence. Between these groups there was no significant association between baseline Gleason-grade, PSA, risk category, number of positive biopsy cores or % core involvement, or tumor size/location/marginal extension. The likelihood of tumor on diagnostic MRI was significantly associated with recurrence (P=0.004). Complete lesion coverage by thermal ablation zone was significantly associated with no recurrence (P<0.0001). In the 13 patients with recurrent/residual disease, overall PSA doubling-time improved from mean of 1.46 years pre-treatment to 79.9 years post-treatment. Three of these patients reduced in risk category from intermediate to very low/low, 2 remained at intermediate risk, 3 patients post treatment biopsy results showed an increase from very low risk to low risk. Possible reasons for residual tumor likely include registration error at time of treatment, MR unrecognized sparse tumor at periphery of target, localization error, and deformation of the prostate at the 4 month biopsy such that new and not treated tumor was detected. Because, this protocol did not allow for retreatment, four patients underwent uncomplicated radical prostatectomy. All had intra-prostatic disease with negative margins and none has demonstrated biochemical recurrence.

Conclusions: Focal laser ablation is a feasible, safe, and possible effective therapy for patients with low-to-intermediate risk PCa. Predictors of successful therapy include biopsy confirmation of lesion presence on diagnostic MRI and full peri-procedural coverage of the target. Likely improvements in the procedure will include: enhanced localization of the tumor site with improved multi-modality imaging, real time tumor targeting, enhanced 3 dimensional thermograpy, and the ability to accurately localize and biopsy the treated site in the deformed prostate post therapy. The utility of these improvements to enhance the procedure in future studies will determine the true safety and oncologic efficacy of this form of "dynamic" surveillance and its true clinical benefit to patients.

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