Focal Laser Ablation of Prostate Cancer: Phase I Clinical Trial

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Abbreviations and Acronyms

3-D = 3-dimensional
CaP = prostate cancer
DCE = dynamic contrast enhancement
FLA = focal laser ablation
GS = Gleason score
HIFU = high intensity focused ultrasound
I-PSS = International Prostate Symptom Score
mp = multiparametric
MR = magnetic resonance
MRI = magnetic resonance imaging
MRT = magnetic resonance thermometry
PSA = prostate specific antigen
PV = prostate volume
ROI = region of interest
SHIM = Sexual Health Inventory for Men
US = ultrasound

Purpose: Focal laser ablation is an investigational technique to treat prostate cancer in a region confined manner via coagulative necrosis. This phase I trial primarily examines the safety of transrectal magnetic resonance imaging guided (in-bore) focal laser ablation in men with intermediate risk prostate cancer. An exploratory end point is cancer control after 6 months.

Materials and Methods: In an institutional review board approved trial we studied focal laser ablation in 8 men with intermediate risk prostate cancer diagnosed using magnetic resonance-ultrasound fusion. Focal laser ablation was performed by inserting a cylindrically diffusing, water cooled laser fiber into magnetic resonance visible regions of interest, followed by interstitial heating at 10 to 15 W for up to 3 minutes. Secondary safety monitors (thermal probes) were inserted to assess the accuracy of magnetic resonance thermometry. Comprehensive magnetic resonance-ultrasound fusion biopsy was performed after 6 months. Adverse events and health related quality of life questionnaires were recorded.

Results: Focal laser ablation was successfully performed in all 8 subjects. No grade 3 or greater adverse events occurred and no changes in International Prostate Symptom Score or International Index of Erectile Function 5 were observed. Ablation zones, as measured by posttreatment magnetic resonance imaging, had a median volume of 3 cc or 7.7% of prostate volume. Prostate specific antigen decreased in 7 men ($p < 0.01$). At followup magnetic resonance-ultrasound fusion biopsy cancer was not detected in the ablation zone in 5 men but was present outside the treatment margin in 6 men.

Conclusions: Focal laser ablation of the prostate is feasible and safe in men with intermediate risk prostate cancer without serious adverse events or changes in urinary or sexual function at 6 months. Comprehensive biopsy followup indicates that larger treatment margins than previously thought necessary may be required for complete tumor ablation.

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THE advent of multiparametric MRI for the localization of prostate cancer and targeted biopsy has provided a scientific basis for focal therapy research.[1–4] Theoretically focal therapy offers the possibility of cancer control with little treatment related morbidity[5] but only a few clinical trials have been performed. Ahmed et al used HIFU to treat MRI identified lesions in 42 men.[6] Oto et al used focal laser ablation to treat MRI identified lesions in 8 men.[4] van den Bos et al recently reported the use of irreversible electroporation to focally treat lesions that were visualized with MRI and contrast enhanced ultrasound.[2]

Focal laser ablation, or laser interstitial thermal therapy, relies on localized heating of the prostate via a fiber coupled infrared laser.[7] Unlike HIFU, FLA relies on coagulative necrosis to remove tissue, while avoiding cavitation, carbonization or vaporization.[8] Unlike HIFU or irreversible electroporation, FLA provides the opportunity for treatment without the use of general anesthesia.

In this trial we gathered safety and feasibility data and explored the potential to simplify FLA. The primary end point in this phase I trial was the absence of any grade 3 adverse event (CTCAE, v4.03). Exploratory end points were changes in sexual and urinary function compared to baseline, as well as radiologic and histological changes. To date, FLA has almost exclusively been performed in a MRI tube (in-bore) because of direct image guidance and the potential usefulness of MRT for intraprostatic temperature monitoring. In the present study MR compatible thermal probes were placed at various locations in the prostate before FLA. Thus, the study design allowed simultaneous comparison of MR thermometry and direct thermal recordings during FLA.[4]

We reasoned that if direct temperature recording could replace MR thermometry, then perhaps FLA could be performed in a clinic setting under MR-US fusion guidance. The early success of FLA,[3,4] the simplicity of thermal probes[9] and a large in-house experience with MR-US fusion biopsy[10] lent further impetus to the present work.

MATERIALS AND METHODS

Patients

The patients in this trial were 8 men age 58 to 72 years with clinical stage T2b or less CaP and Gleason score 3+4=7 or less. All 8 were diagnosed by MR-US fusion biopsy, incorporating targeted and systematic sampling,[11] which showed CaP within a single MR visible lesion and no GS greater than 6 elsewhere in the prostate. The men were selected per entry criteria from those undergoing fusion biopsy in a cohort described elsewhere.[11] Complete inclusion and exclusion criteria are listed elsewhere (NCT02224911). 3T MRI using a body coil was acquired and interpreted using PI-RADS (Prostate Imaging Reporting and Data System) and a 5-point grading system devised in-house.[11] FLA was performed within 6 months of diagnosis in the 4th quarter of 2014. MRI studies and FLA were performed in the radiology department at UCLA Ronald Reagan Hospital with institutional review board approval and oversight by a data safety monitoring board from Jonsson Cancer Center. Patient characteristics are shown in table 1.

Procedure Planning

MR enhancing index ROIs with biopsy confirmed cancer were targeted using FLA. ROI characteristics were determined by 3-D segmentation of the MRI. Fiber locations and desired margins were planned in advance using custom software developed using MATLAB 2014b and C++, according to each patient's ROI geometry and location in the prostate. Prior work with MRI-histopathology correlation indicates that MRI systematically underestimates true tumor volume by up to 1.5 cm.[12] This margin was then further refined by using prior biopsy information, ie 3-D locations of positive and negative cores. Based on preliminary data obtained during a sizeable in-bore experience (courtesy of John Feller, MD, Desert Medical Imaging, Palm Desert, California), we estimated that a 3-minute laser activation at 12 to 15 W would create a zone of coagulation necrosis extending radially approximately 1 cm around the laser tip.

Table 1. *Baseline characteristics of men enrolled in FLA trial*

Pt No.—Age		PSA (ng/ml)	PV (MRI, cc)	Max ROI Diameter (MRI, mm)	Lesion Location	MRI Grade*	GS	Max Ca Core Length (mm)
1—72		20.3	46	17	Transition zone	3	7	1
2—67		8.9	33	10	Peripheral zone	3	7	5.5
3—61		6	66	9	Peripheral zone	4	7	9
4—63		2.8	37	13	Peripheral zone	4	7	2.5
5—66		5.8	45	18	Transition zone	5	6	6
6—54		11.7	30	7	Transition zone	3	7	5
7—63		4.8	29	6	Transition zone	4	7	2.1
8—58		17.7	34	26	Peripheral zone	5	7	3
Median	63	7.45	35.5	11.5	—	4	7	4

At baseline at least 10 systematic biopsy cores were obtained to exclude multifocality and at least 2 cores were obtained from the MR visible ROI, ie the lesion to be treated.
*UCLA grading system.[15]