Focal Prostate Radio-Frequency Ablation for the Treatment of Prostate Cancer

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Focal Prostate Radio-Frequency Ablation for the Treatment of Prostate Cancer

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INTRODUCTION:

Men diagnosed with non-palpable, unilateral, low-intermediate risk localized prostate cancer (defined as clinical stage T2a, PSA<10ng/ml, Gleason score <=7, in only one side of the prostate) and multi-parametric endo-rectal MRI with no lesions or lesions less than 1cm. in diameter and only on one side of the prostate are eligible for this study. Initial biopsy would need to have a minimum of 10 cores.

After enrollment, patients will undergo endo-rectal, multi-parametric 1.5 Tesla MRI with Dynamic contrast enhancement and Diffusion Weighted images. Areas on MRI that have a high level of suspicion for prostate cancer will be identified (right or left, Central or peripheral gland) and categorized from 1 Negative to 5 highly suspicious.

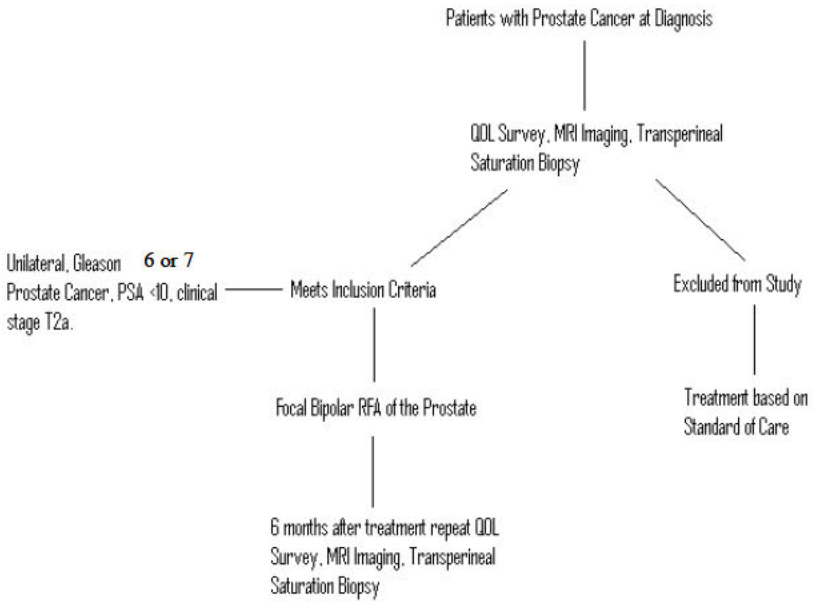
For study purposes, the prostate is divided into four regions: RIGHT CENTRAL, RIGHT PERIPHERAL, LEFT CENTRAL and LEFT PERIPHERAL. Patients must meet the original entry criteria on this repeat mapping biopsy and have unilateral prostate cancer. If the patients meet the mapping-biopsy enrollment criteria, they are treated with **focal bipolar radiofrequency ablation (RFA)** meaning RFA of the sites where the biopsies were positive but no more than one prostate side. Efficacy is defined as negative biopsy cores at the sites of the focal ablation on repeat extended biopsies at 6 months after RFA. A second MRI will be performed just prior to the 6 month repeat saturation biopsy performed identical to the original pre-treatment biopsy.

At baseline (prior to pre-treatment biopsy) and at 6 months (prior to the repeat biopsy used to define efficacy) the patient will complete an American Urologic Association lower urinary tract symptom score assessment (AUA score), Rectal Assessment Scale (RAS), International Index of Erectile Function (IIEF-5), and the EPIC quality of life questionnaires.

Following completion of the focal prostate radio-frequency ablation study at 6 months from treatment, patients will undergo standard/routine care including serum PSA level every 6 months and as needed digital rectal examinations; any future prostate biopsies will be performed at the discretion of the treating physician.

Patients will also be required to complete a medical resource utilization (MRU) form to capture resource utilization between study visits, which can be used to estimate costs associated with procedure related complications and health care visits. Patients will requested to complete a weekly diary of medical resource utilization to limit recall bias that may occur between study visits.

SCHEMA


Patients with Prostate Cancer at Diagnosis
QOL Survey, MRI Imaging, Transperineal Saturation Biopsy
Unilateral, Gleason 6 or 7 Prostate Cancer, PSA <10, clinical stage T2a.
Meets Inclusion Criteria
Excluded from Study
Focal Bipolar RFA of the Prostate
Treatment based on Standard of Care
6 months after treatment repeat QOL Survey, MRI Imaging, Transperineal Saturation Biopsy

SCHEDULE OF EVALUATIONS / STUDY CALENDAR

Parameter	Prestudy	Week 0	Week 6	3 months	6 months	End of Study Visit
History	X					
Physical examination including DRE	X		X	X	X	
QOL questionnaires (EPIC,IIEF,AUA,RAS)	X				X	
MRU (Recording weekly by patients; collected at the following visits by study coordinator)			X	X	X	
Toxicity assessment			X	X	X	
ECOG Performance Status	X				X	
Laboratory Investigations						
PSA	X		X	X	X	
CBC, differential, platelet count	X				X	
Serum Chemistries (must include, bilirubin, Alk Phos, ALT and AST)	X				X	
Glucose and Electrolytes (Na, K, C1, CO_2), BUN, Creatinine	X				X	
PT /PTT /INR	X				X	
U/A	X				X	
EKG	X				X	
Imaging Studies						
Chest X-Ray	X				X	
MRI and Mapping Biopsy	X				X	
Procedures						
RFA		X				
Discussion of final biopsy result and assessment of AEs						X

1.0 OBJECTIVES AND SCIENTIFIC AIMS

Primary Objective: To assess the local oncologic efficacy of focal RFA in men with unilateral, clinically localized prostate cancer as measured by the ability to obtain all negative biopsy cores at the sites of focal ablation of the cancer, “all negative” means no prostate cancer; if the biopsy contains inflammation, or pre-cancerous changes (high-grade prostatic intraepithelial neoplasia and /or atypical small acinar proliferation it will be considered negative for study purposes).

Secondary Objective: To evaluate the safety of the procedure and change in quality-of-life indicators from baseline to 6 months following focal RFA in patients with localized

prostate cancer. To understand and evaluate imaging characteristics of treated prostate cancer by bipolar RFA.

Tertiary Objective: To assess the potential health economic impact of focal RFA based on medical resource utilization data.

BACKGROUND AND RATIONALE

Epidemiological data demonstrate a marked increase in the number of men diagnosed with prostate cancer, and a profound migration towards earlier stage disease at the time of diagnosis. Implementation of large-scale serum prostate-specific antigen (PSA) screening programs and more extensive biopsy strategies are largely responsible for the increase in diagnosis. An analysis of the control group in the Prostate Cancer Prevention Trial illustrates the potential for extensive biopsy to result in over –diagnosis, of prostate cancer (Thompson et al.2004). Among 2,950 men with negative digital rectal examination (DRE) and PSA levels <4.0ng/ml, 15.2% harbored prostate cancer by biopsy, as did 6.2% of men with PSA levels<1.5ng/ml. In an era of increasing prostate cancer incidence and stage migration towards earlier disease, appropriate management of the disease requires assessment of risk; how likely is a given man's cancer to progress or metastasize over his remaining lifetime? What is the probability of success with treatment? What are the risks of side effects and complications with each treatment?
Prostate cancer is relatively slow growing, with doubling times for local tumors estimated at 2 to 4 years. Some prostate cancers prove to be so small, low-grade, and noninvasive that they appear to pose little risk to the life or health of the host. A recent review of radical prostatectomy series suggest that 25-30% of men undergoing radical prostatectomy have pathologic features in the radical prostatectomy specimen consistent with an insignificant or "indolent" cancer that posed little threat to life or health (organ-confined cancer < 0.5cc, no Gleason grade 4 or 5 component). However, the biological potential of histologically detectable cancers is difficult to characterize with certainty, and a traditional 10 to 12 core transrectal prostate biopsy may underestimate the extent of cancer in the prostate in up to 50% of men with low-risk cancer. With alternative risk-assessment strategies (including extended or mapping prostate biopsies) some men have focal cancers that would not warrant complete gland treatment with radical prostatectomy, brachytherapy or external beam radiation therapy. While deferring definitive therapy (active surveillance) until progression of disease is an option in patients with low-risk and some with intermediate cancer, some men with a diagnosis of "cancer" do not accept this approach, As such there appears to be a role for therapy solely targeting the cancer (focal therapy; the male "lumpectomy"). This has the theoretical advantage of treating/curing the cancer while at the same time having fewer side effects than traditional whole-gland treatments.

The mechanism of action of bipolar RFA is complex. It has been proposed that RFA exerts its efficacious effect by: (1) the induction of protein denaturation by thermocoagulation (2) the rupture of cell membranes from heating, (3) the transfer of water from intracellular to extracellular spaces, (4) vascular stasis, and (5) the induced apoptosis. The introduction of ultrasound guidance and the bi-polar design of the probe, allowed the heating process to be controlled and monitored in real time.

PRIMARY OBJECTIVE

This protocol will investigate the role of focal bipolar RFA in a defined prostate cancer population examining treatment efficacy (elimination of the cancer) based on repeat biopsy at six months from treatment.

SECONDARY OBJECTIVES

1. Changes from baseline in quality-of-life.
2. Image characteristics of treated prostate cancer by bipolar RFA
3. To evaluate the safety of the procedure

TERTIARY OBJECTIVE: Evaluate the health economic impact of focal RFA.

OVERVIEW OF STUDY DESIGN/INTERVENTION

1.1 Design

This is a pilot study examining the efficacy (primary endpoint) and quality-of-life changes, safety, and image characteristics by MRI (secondary endpoint) in men with unilateral prostate cancer treated with focal RFA. In addition, the study will collect medical resource utilization data to assess the health economic impact of focal RFA (tertiary endpoint). We estimated the negative biopsy rate at 6 months after focal bipolar RFA is greater than or equal to 90%.

1.2 Intervention

Before any study procedures are performed (which includes all screening procedures, pre-treatment, treatment/intervention procedures, etc.), all patients will be asked to sign an informed consent form.

Eligible patients will have been diagnosed with unilateral prostate cancer, with PSA <10, Gleason score 6 or 7, up to clinical stage T2a, and prostate volume<60 cc. At enrollment, patients will undergo 1.5T MRI with DCE and DWI imaging. The prostate is divided into four regions: RIGHT CENTRAL, RIGHT PERIPHERAL, LEFT CENTRAL and LEFT PERIPHERAL. Then they will undergo a pre-treatment transrectal mapping prostate biopsy as currently performed at our institution. This procedure is performed under general anesthesia as an outpatient procedure. For study purposes, the prostate biopsy cores will be obtained from four regions: RIGHT CENTRAL, RIGHT PERIPHERAL, LEFT CENTRAL and LEFT PERIPHERAL. For patients to be eligible for treatment with focal bipolar RFA under this protocol they must meet the original entry criteria on this pre-treatment mapping biopsy.

Those men meeting the mapping-biopsy criteria will subsequently be treated with focal bipolar RFA. Treatment is performed under general anesthesia and will include the regions of the prostate containing cancer based on the mapping biopsy. If there are multiple unilateral areas of the prostate involved with cancer, a hemi-ablation will be

performed. This is an outpatient procedure, that takes between 1 and 2 hours, with the patient arriving 1-2 hours prior to the procedure and remaining in the recovery room for 1-2 hours after the procedure. The patient is given a voiding trial. If the patient fails same day voiding trial a Foley catheter will be placed with a second trial performed approximately one week after treatment. Clinical follow-up visits will be scheduled at 6 weeks, 3 months, and 6 months after focal bipolar RFA at which time a digital rectal examination and PSA test will be performed. These follow-up visits and procedures are part of this study protocol.

The primary endpoint of the trial is assessed at 6 months after focal bipolar RFA by repeat MRI imaging and post treatment mapping biopsy performed the same as pre-treatment. Treatment efficacy, defined as all negative biopsy cores at the site of the focal ablation, will be determined by the results of this mapping biopsy that will include complete biopsy of all regions of the prostate. Secondary endpoints will be evaluated through the standard quality-of-life questionnaires. For those patients not enrolled on this study protocol, their data from completion of the quality-of-life questionnaires will not be included in this investigation. Any adverse events that occur as a result of this study will be recorded and reported to the regulatory committees at Moffitt and IRB.

If after the mapping biopsy the patient does not meet the criteria for focal RFA, he will be excluded from this study protocol but considered and offered other management options for prostate cancer including active surveillance, radical prostatectomy or radiation therapy.

Stopping rules:

Criteria for stopping the Study:

1. If at the second mapping biopsy done at 6 months, more than 4 patients have a positive biopsy in the ablated area, the study will be stopped. This is based on the current treatment failure rate of 20% for radical prostatectomy.
2. If even one patient develops hematuria after the procedure requiring a second procedure to be performed, the study will be terminated.
3. If even one patient requires a Foley catheter for greater than 2 weeks following the procedure, the study will be terminated.
4. If even one patient develops an infection requiring inpatient hospitalization, the study will be terminated.
5. If even one patient develops a rectal fistula the study will be terminated.

3.0 THERAPEUTIC/DIAGNOSTIC AGENTS

Before any study procedures are performed (which includes all screening procedures, pre-treatment, treatment/intervention procedures, etc.), all patients will be asked to sign an informed consent form.

3.1 Imaging

After the informed consent is signed, the patient will be scheduled for an MRI (dynamic contrast enhanced and diffusion weighted imaging using a 1.5 Tesla endorectal MRI. The regions where both imaging sets indicate the potential for disease will be identified and categorized to one or more of 4 possible regions of the prostate as defined below.

3.2 Mapping Prostate Biopsy

Transrectal ultrasound-guided prostate biopsies will be performed to determine study eligibility as well as to assess treatment efficacy. The two biopsy sessions (one pre-treatment and the other 6 months after focal RFA) will follow the same method. The rational for a complete mapping biopsy after RFA, rather than just sampling of the regions that were treated, is to identify cancer lesions not found in initial MRI/biopsy (thus, not treated) or cancer that may have developed after RF treatment.

Preparation/anesthesia: The patient will be given a Fleet enema prior to the procedure and administered prophylactic antibiotics. With the patient in the lithotomy position and under general anesthesia, transperineal saturation biopsies are obtained and separated in four sections: RIGHT CENTRAL, RIGHT PERIPHERAL, LEFT CENTRAL and LEFT PERIPHERAL.

3.3 Focal RFA of the Prostate

The equipment for whole-gland RFA of the prostate is FDA cleared for clinically localized prostate cancer, and the focal RFA equipment is also commercially available. The focal RFA equipment used in this study is cleared for radiofrequency soft tissue ablation by the FDA.

Description of procedure use for the Focal RFA of the Prostate:
The patient is given a Fleets enema prior to the procedure and administered prophylactic antibiotics. The procedure is performed on an outpatient basis under general. With the patient in the lithotomy position a Foley catheter is inserted into the bladder and the scrotum is elevated toward the abdomen either by taping or with a rolled towel. Perineal shave is optional. The rectum is irrigated with normal saline to ensure adequate bowel preparation. The perineum is prepared sterilely.

The bipolar RFA procedure is performed under transrectal ultrasound guidance. Transrectal ultrasound probe is inserted into the rectum. The probe is then connected to a stepper stabilizer and the pelvis is visualized at 5mm stepping increments so that the

prostate, urethra, bladder, seminal vesicles, and anterior rectal wall can all be appropriately visualized. The ultrasound images and probe driving mechanism template are mated to allow accurate position of the probe so as to precisely target the regions of the prostate that were mapped during the biopsy. The desired target will be defined by which of the previously defined four regions of the prostate had positive biopsies as described above. An appropriate insertion location of the bipolar RFA probes are designed in the planning process to target the regions of the prostate to be ablated (the number of probes will depend upon the size/shape of the prostate and the location of the lesions to be ablated.

Designated regions of the prostate will be ablated via the ENCAGE™ (Trod Medical® Bradenton, FL) RFA system. ENCAGE™ has FDA clearance for percutaneous RF soft tissue / tumor ablation. The system consists of percutaneous probes connected to a RF bipolar generator which precisely controls the ablation. Once the target areas for ablation have been identified on TRUS the ENCAGE™ RFA probe will be inserted percutaneously through the skin of the perineum into the prostate under ultrasound guidance. Once the probe is positioned containing the prostate region designated for ablation, ablation will be initiated. RFA will occur at 0.5 cm increments along the longitudinal axis of the prostate under ultrasound guidance initiating cranially towards the prostate base and moving caudally towards the apex. The number of probes inserted percutaneously into the prostate will be predefined based on the target size and shape. Only one probe will be inserted at any time with prior probes removed before inserting the next. Once ablation has been completed the prostate and bladder neck will be surveyed with the TRUS. The TRUS probe will then be removed from the rectum and the Foley catheter will be deflated and removed from the bladder.

3.4 Assessment of Quality-of-Life

Assessment of quality of life (via completion of the questionnaires) will correlate with AUA symptom score, RAS, IIEF-15, and EPIC QOL.

Medical Resource Utilization

Medical resource utilization (MRU) will be recorded weekly through patient self-report using a patient MRU diary. These MRU data will allow for a health economic evaluation of the ENCAGE™ technology.

4.0 CRITERIA FOR SUBJECT ELIGIBILITY

4.1 Subject Inclusion Criteria

Subject Population:

- Men 18 years of age or older
- Diagnosis of adenocarcinoma of the prostate, confirmed by H.L. Moffitt Cancer Center review
- No prior treatment for prostate cancer
- ECOG performance status of 0 or1
- Prostate Cancer Clinical Stage T2a and below

- PSA <10 ng/ml (this will be the PSA level prompting the initial prostate biopsy)
- Prostate size <60 cc on transrectal ultrasound

Pre-enrollment biopsy parameters (as per H.L. Moffitt C.C. review)

- Minimum of 10 biopsy cores
- Gleason score 6 or 7
- Unilateral cancer (only right-sided or left-sided, not bilateral)

4.2 Subject Exclusion Criteria

- Men less than 18 years of age
- Medically unfit for anesthesia
- Histology other than adenocarcinoma
- Biopsy does not meet inclusion criteria
- Men who have received any hormonal manipulation (antiandrogens; LHRH agonist; 5-alpha-reductase inhibitors) within the previous 6 months

4.3 Inclusion of Women and Minorities**:** All participants will be men without previous treatment for prostate cancer. Men of all ethnic groups and races are eligible for the study. Thus women will not be included in this study.

4.4 Recruitment Plan

Potential research subjects will be identified by a member of the patient's treatment team, the protocol investigator, or research team at H. L. Moffitt Cancer Center. If the investigator is a member of the treatment team, he/she will screen their patient's medical records for suitable research study participants and discuss the study and their potential for enrolling in the research study. Potential subjects contacted by their treating physician will be referred to the investigator/research staff of the study.

The principal investigator may also screen the medical records of patients with whom they do not have a treatment relationship with, for the limited purpose of identifying patients who are eligible to enroll in the study and to record appropriate contact information in order to approach these patients regarding the possibility of enrolling in the study.

During the initial conversation between the investigator/research staff and the patient, the patient may be asked to provide certain health information that is necessary to the recruitment and enrollment process. The investigator/research staff may also review portions of their medical records at H. L. Moffitt Cancer Center in order to further assess eligibility. They will use the information provided by the patient and /or medical record to confirm that the patient is eligible and to contact the patient regarding study enrollment. If the patient turns out to be ineligible for the research study, the research staff will destroy all information collected on the patient during the initial conversation

and medical review, except for any information that must be maintained for screening log purposes.

In most cases, the initial contact with the prospective subject will be conducted either by the treatment team, investigator or the research staff working in consultation with the treatment team. The recruitment process outlined presents no more than minimal risk to the privacy of the patients who are screened and minimal patient health information (PHI) will be maintained as part of a screening log.

5.0 PRE-TREATMENT EVALUATION AND IMAGING

The pre-enrollment clinical evaluation will include a complete medical history, physical examination including digital rectal examination, review of prostate biopsy information including Gleason score, review of any imaging studies, and clinical staging (TNM staging). Patients with up to clinical stage T2a prostate cancer meeting the aforementioned clinical and biopsy criteria are eligible for enrollment. If the patient had their diagnostic biopsy performed at an outside institution, these biopsy slides must be reviewed at our center prior to determining patient eligibility. If there is a discrepancy between the outside and H. L. Moffitt Cancer Center pathology reviews, we will rely on the H. L. Moffitt Cancer Center review to determine eligibility.

Baseline visit: determine patient eligibility. If patient's diagnostic prostate biopsy has not yet been reviewed at pathology, a request will be made to have pathology review the slides and provide a review for diagnosis. Once eligibility is confirmed and patient agrees to participate in the study an informed consent is signed. Pre-mapping imaging and biopsy assessment #1 (week 0 to 12): After the informed consent is signed, the patient will be scheduled for an MRI (DCE and DWI using a 1.5T MRI if possible with a Sentinal Endorectal coil). The regions where both imaging sets indicate the potential for disease will be identified. During the initial transrectal-guided mapping prostate biopsy, all acquired ultrasound images will be registered to the MRI images. Baseline laboratory studies including serum electrolytes, UA, PT/PTT/INR, CBC, electrocardiogram and chest xray will be performed on patients prior to the procedure. A consent (separate from the informed consent to participate in the study) for the biopsy procedure will be obtained per the Cancer Center's policy for any procedure conducted for treatment/diagnosis.

Patients will also be asked to complete an assessment (see appendixes A-D) of urinary, sexual and bowel functioning, as well as overall quality of life, at baseline. These assessments will be completed at the beginning of the study and at 6 months after the RFA procedure during their clinic visit.

6.0 TREATMENT/INTERVENTION PLAN

Before any study procedures are performed (which includes all screening procedures, pre-treatment, treatment/intervention procedures, etc.), all patients will be asked to sign an informed consent form.

Prior to the mapping prostate biopsy, patients will be required to have an EKG and Chest X-Ray. Eligible patients are evaluated with a transrectal-guided transperineal mapping

prostate biopsy. Patients meeting our definition of low-risk or intermediate prostate cancer (up to clinical stage T2a, PSA< 10ng/ml, Gleasons score 6 or 7), will undergo RFA of the regions containing cancer on the mapping biopsy (focal bipolar RFA). Six months following focal bipolar RFA the patient will undergo a second mapping biopsy.

7.0 EVALUATION DURING TREATMENT/INTERVENTION

Before any study procedures are performed (which includes all screening procedures, pre-treatment, treatment/intervention procedures, etc.), all patients will be asked to sign an informed consent form.

Focal bipolar RFA will be done (after 4 weeks and no more than 12 weeks of initial mapping biopsy): a separate informed consent for this procedure will be obtained (which is separate from the informed consent to participate in the study), per the Cancer Center's policy for any procedure conducted for treatment/diagnosis. If the laboratory studies obtained at the pre-mapping biopsy assessment are still valid (within 6 months), they will not be repeated.

Six weeks after focal bipolar RFA; DRE, PSA, assessment of toxicity will be done**.** Toxicity of transperineal prostate biopsy includes bleeding, infection, urinary retention. Toxicity of focal bipolar RFA includes bleeding, infection, urinary incontinence, urinary retention, erectile dysfunction, urinary urgency, urinary frequency and rectal fistula.

Three months after focal RFA; DRE, PSA, assessment of toxicity will be done as mentioned in the preceding paragraph.

Six months after focal bipolar RFA; DRE, PSA, QOL questionnaire, assessment of toxicity; obtain serum electrolytes, UA, EKG and chest x-ray in preparation for repeat mapping biopsy to be done. The patient will be scheduled for the second MRI imaging and transrectal-guided mapping prostate biopsy # 2 to be completed within 6-8 months after focal bipolar RFA. After a biopsy is requested we will have a patient follow up in 1-2 weeks for discussion of results and assessment of any adverse events (this will be the end of study visit).

Patients will record weekly medical resource utilization data to share with their study coordinator at routine scheduled visits.

8.0 Adverse Event Reporting and Safety Monitoring

The principal investigator will have the primary responsibility for data safety and monitoring. Input will be sought from members of the study protocol concerning data and safety issues. The PI of the study will have primary responsibility for ensuring that the protocol is conducted as approved by the SRC and IRB. The PI will ensure that the monitoring plan is followed, that all data required for oversight of monitoring are accurately reported to the DSMB and/or to the PMC and IRB as required, that all adverse events are reported according to the protocol guidelines, and that any adverse events reflecting patient safety concerns are appropriately reported.

Members of the study team will meet at least monthly. The following data will be reviewed:

1. Rate of accrual
2. Adverse events
3. Protocol deviations and/or violations

Interim analysis is due from the PI once 50% accrual of total patients/subjects has been reached or 10 patients enrolled. The monitor will work directly with the study team to ensure the safety and protocol adherence for each patient. If necessary, corrective action and/or educational programs will occur to ensure subject safety and data integrity. Reports to the SRC, PMC and IRB will be submitted as required.

Biomed Research, Inc. will be performing monitoring services for MCC protocol #17753 on behalf of Trod Medical LLC. Contact information for Biomed below.

8.0 Definitions:

8.0.1 Adverse Event: Any unfavorable and unintended sign, symptom or disease temporally associated with the use of a medical treatment, regardless of whether it is related to the medical treatment.

8.0.2 A serious adverse event (SAE) is defined as any adverse event that results in death, a life-threatening experience, inpatient hospitalization, prolongation of existing hospitalization, persistent disability, or congenital anomaly or birth defect.

8.0.3 Study therapy is the required treatment or procedure defined on the

protocol.

8.0.4 Non-protocol therapy is defined as any treatment or procedure not described in the protocol

8.1 Adverse event assessment:

8.11 The type of event using NCI Common Toxicity Criteria for Adverse Events (CTCAE) version 4.0 will be identified and graded for severity.

8.12 The relationship of the adverse event to the therapy or procedure will be determined as follows: Unrelated; Unlikely; Possible; Probable; Definite

8.13 For reporting purposes, an adverse event is considered unexpected when either the type of event or severity of the event is not listed in the study consent

8.2 Serious Adverse Events (SAEs):

8.2.1 All study-related, unexpected Grade 3 or 4 SAEs will be immediately reported to the IRB. These toxicities will be reviewed by the principal investigator and appropriate measures taken in terms of delaying, modifying or stopping therapy.

8.2.2 The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 will be utilized for adverse event reporting *(http://ctep.cancer.gov/reporting/ctc.html)*.

8.2.3 SAEs must be followed until resolution or deemed irreversible.

8.3 Routine reporting:

8.3.1 Serious and/or unexpected adverse events will be reported to the IRB according to current IRB policy as well as Moffitt's Protocol Monitoring Committee (PMC) according to current PMC policy.

8.4 Potential Adverse Events that may occur as part of conducting this study include:

Transperineal prostate biopsy:

- Bleeding
- Infection
- Urinary retention

Focal Bipolar RFA

- Bleeding

- Infection
- Urinary Incontinence
- Urinary Retention
- Erectile Dysfunction
- Urinary Urgency
- Urinary Frequency
- Rectal Fistula

9.0 CRITERIA FOR THERAPEUTIC RESPONSE/OUTCOME ASSESSMENT

The primary endpoint of this study is a negative prostate biopsy in the region that was radio frequency ablated 6 months after treatment.

10.0 CRITERIA FOR REMOVAL/ WITHDRAWAL FROM STUDY

- The study will be terminated if a rectal fistula develops in any patient as a result of treatment.
- The patient may withdraw consent for the study at any time. If at any time the patient develops progressive disease he will be taken off the study and referred for alternative therapy.
- If the participant is not following the study procedures as outlined in the protocol/ informed consent, he may be removed from the study. If the participant is removed from the study, he will be referred for alternative therapy.
- If at any time the patient is found to be ineligible for the protocol as designated in the section on Criteria for Patient/Subject Eligibility (i.e., a change in diagnosis, etc.), the patient will be removed from the study.

11.0 BIOSTATISTICS

11.0 Statistical Consideration

11.1 Study Design/Endpoints

This is a prospective study. The primary endpoint is safety of the procedure negative prostate biopsy rate at six months. The secondary endpoint is quality of life and safety of the procedure.

11.2 Sample Size/Accrual Rate

This is a pilot study so the sample size justification is based on providing reasonable precision of the primary efficacy endpoint, the negative biopsy rate at 6 months after focal bipolar RFA. We estimated the negative biopsy rate at 6 months after focal bipolar RFA is greater than or equal to 90%. If the negative biopsy rate at the 6-month visit is 90%, a sample size of 20 patients provides a two-sided 95% confidence interval of 68.3-98.8%. If the negative biopsy rate at the 6-month visit is 95%, the 95% corresponding confidence interval is 75.1-99.9%. Thus, the total sample size for this study will be 20 patients. We estimate an accrual rate of 4 patients a month. We anticipate completion of this study over a one year time period.

11.3 Stratification Factors

No stratification factors will be applied.

11.4 Analysis of Primary Endpoint

Descriptive statistics will be used to summarize patients' demographic and clinical characteristics collected at each visit. Mean, standard deviation and range will be calculated for continuous variables, and frequency and percentage will be generated for categorical variables. The primary objective is to assess the local oncologic efficacy of focal RFA in men with low-risk prostate cancer. The primary efficacy endpoint is negative biopsy rate at 6 months after focal bipolar RFA. The point estimate and its 95% confidence interval will be calculated using the exact binominal method.

11.5 Analysis of Secondary Endpoints

The secondary objective is to evaluate the change from baseline in quality-of-life indicators following focal RFA in patients with low-risk localized prostate cancer. The patients will complete the EPIC, AUA, RAS, and IIEF-5 questionnaires at baseline, 3- and 6-month visit. The QOL will be primarily based on the EPIC, developed to measure health related quality of life among men with prostate cancer. The EPIC assesses the disease-specific aspects of prostate cancer and its therapies and comprises four summary domains (Urinary, Bowel, Sexual and Hormonal) [Wei et al, 2000]. The EPIC summary score and subscale characteristics at each time-point will be calculated based on its scoring instruction (http://roadrunner.cancer.med.umich.edu/epic/epicmain.html). The summary score of the AUA, RAS and IIEF-5 questionnaires will be also calculated. Descriptive statistics (mean, median, standard deviation and inter-quartile range) will be

applied to summarize the QOL scores at each time-point and the score change between the 3- or 6-month visit and baseline. The normal distribution assumption of these score changes will be evaluated. The QOL score change from baseline will be evaluated using either the paired t-test if the original or transformed data are normally distributed, or the Wilcoxon signed-rank test whenever the normality assumption cannot be justified.

For safety analyses, the definitions of adverse event and serious adverse event were listed in Section 8.0. adverse event will be summarized by worst NCI CTCAE version 4.0 grade and serious adverse event will be listed separately. Safety data, such as toxicity and laboratory test, will be summarized by time point of collection. Descriptive statistics will be calculated for quantitative safety data and frequency counts will be summarized for classifications of qualitative safety data.

The image characteristics will be summarized using descriptive statistics. Mean, standard deviation and range will be calculated for continuous variables, and frequency and percentage will be generated for categorical variables.

Analysis of Tertiary Endpoint

The tertiary objective is to assess the potential health economic impact of focal RFA through the collection of medical resource utilization (MRU) data. Patients will collect weekly data on health care visits including clinician seen, indication for visit and any procedures associated with the visit. Descriptive statistics will summarize the frequency of visits by indication and will consider both visits captured in the MRU form as well as data collected on the adverse event form.

Cost values will be assigned to health care visits based on the indication and procedures/evaluations completed as a part of the visit. These costs will be assigned throughout the 6 month duration of the study to estimate the average cost of MRU after focal RFA.

12.0 RESEARCH PARTICIPANT REGISTRATION

Confirm in the electronic medical record that the patient has received the Notice of Privacy Practice. This must be obtained before the eligibility confirmation and obtaining of the research informed consent.

- Confirm eligibility as defined in the section entitled Criteria for Patient/Subject Eligibility.
- Obtain written informed consent from each patient

13.0 DATA MANAGEMENT ISSUES

The clinical research nurse/study coordinator responsibilities include: project compliance, data collection, abstraction and entry, data reporting, regulatory monitoring, problem resolution and prioritization, and coordinate the activities of the protocol study team.

The data collected for this study will be entered into a secure database at Biomed. Source documentation will be available to support the computerized patient record.

13.1 Quality Assurance

Weekly registration reports will be generated to monitor patient accruals and completeness of registration data. Routine data quality reports will be generated to assess missing data and inconsistencies. Accrual rates and extent and accuracy of evaluations and follow-up will be monitored periodically throughout the study period and potential problems will be brought to the attention of the study team for discussion action. Random-sample data quality and protocol compliance audits will be conducted by the study team, at a minimum of two times per year, more frequently if indicated

Data collection and record keeping

13.2 Data monitoring and sponsor CRFs collection will be performed by Biomed Research. The clinical data for this protocol will be recorded on patient Case Report Forms (CRF's) printed on 3-part NCR and bound into individual patient booklets. Once all data queries are resolved for a given data form, the white copy will go to the sponsor (Trod), the yellow copy will go to MCC data management, and the pink copy will stay with the MCC clinical coordinator for study archiving. Biomed will monitor conformance to the protocol informed consent, AE's, etc. as well as verify random CRF's to source documents and work with MCC to resolve data queries. Biomed will be responsible to collect the sponsor's copy (white) of the completed/verified/signed CRF's, but Biomed will not retain sponsor CRF's.

13.2.1 Identifying patient information will be kept confidential. CRF's will not contain the patient's MRN, name, etc. only, a "Subject Record ID No (3 digits)" and "Subject Initials" (F, M, L). The Clinical Research Nurse/Coordinator at Moffitt will maintain the "key" that links patients (with their name, MRN, etc.) to their "Subject Record No." The "key" will be destroyed upon completion of data analysis for this study. Identifying patient information will be kept confidential. All direct identifying (name, medial record number, etc.) will be destroyed and removed from the computer upon completion of data analysis for this study.

13.2.2 Representatives of the IRB, OHRP, Moffitt Committees and Center for Medicare and Medicaid Services (CMS) will have access to patient information as it pertains to the study.

13.2.3 Privacy and confidentiality of the information will be protected to the extent provided by the law.

13.2.4 The Principal Investigator and the Clinical Research Nurse/Coordinator assigned to the study protocol will be primarily responsible for maintaining all study related documents including the clinical research forms, as well as for providing the sponsor with its copy of each completed CRF. All data collection will be performed on hard-copy (3-part NCR) CRF's. The review of medical records (by the study team at Moffitt) within the Cancer Center's institutional database will be done in a manner to assure that patient confidentiality (PHI) is protected and maintained at all times.

14. ETHICS/ HUMAN SUBJECT'S PROTECTION

14.1 Patient Consent: Patients who are candidates for this study at Moffitt Cancer Center will be approached for this study. Patients meeting the eligibility criteria will be consented using the IRB approved consent form. The consent will be verbally explained to the participant by a member of the research team, describing the study procedures, risks, benefits, etc. Patients must be freely consenting adults. Patients who meet eligibility criteria and provide informed consent as documented by a signed consent form by the clinical note of the consenting investigator will be enrolled in this study. All subjects interested in participating in this study will be given a copy of the informed consent form to read and sign. Each subject who is interested in participating in this study will be asked to sign and date the IRB approved consent form. All discussions related to participating in this study and obtaining informed consent will take place in a private room in the clinic at Moffitt to ensure the privacy and confidentiality of each subject is protected. Only members of the research team will be involved in this process and have access to the signed consent forms. All signed consent forms will be stored in a locked file cabinet.

14.2 Regulatory Approval: The trial will be approved by both the H. Lee Moffitt Cancer Center and Research Institute's Scientific Review Committee (SRC) and the Institutional Review Board (IRB).

14.3 Protocol Modifications: No modifications will be made to the protocol and implemented without the agreement of the investigators and approval from the Moffitt Scientific Review Committee (SRC) and the Institutional Review Board (IRB). Changes that significantly affect the safety of the patients, the scope of the investigation, or the scientific quality of the study will require approval from the SRC and IRB prior to implementation, except where the modification is necessary to eliminate apparent immediate hazard to human subjects. Any departures from the protocol will be documented in the case report form and the source documentation and reported the SRC and IRB.

- **14.4 Potential Risks:** There are risks associating with having any type of surgery. The surgery team will explain these risks to the potential participants and inform them they will be asked to sign a separate consent form for the standard of care treatment and if they agree to participate, an informed consent to participate in this research study. These risks include bleeding, infection, urinary incontinence, risk of anesthesia related complications, urinary retention, erectile dysfunction, urinary urgency, frequency and rectal fistula. There are also psychological risks associated with completing the quality of life questionnaires.

As with any research study, there is always a potential risk of unintentional disclosure of protected personal health information (PHI); however, every precaution will be taken to ensure all PHI and data collected as part of this study is kept confidential. All data will be kept confidential.

14.5: Potential Benefits: Participants will not directly benefit for taking part in this study. We hope that the results of this study will someday benefit future patients with prostate cancer.

14.6: Payment and Costs:

14.6.1: Payment

Participants will not be paid to participate in this study.

14.6.2: Costs to Participate

There will be no extra cost to patients as a result of participating in this study. Costs of standard medical care for RFA, including all costs of the surgery, lab work, etc. will be charged to the patient and/or their insurance company.

Participants and/or their insurance company will be financially responsible for hospital inpatient, outpatient and follow-up visits that would normally or routinely occur in the management of their disease. Inpatient and outpatient visits could include charges for treatments, medications, physician visits, laboratory tests and procedures. Participants and /or their insurance company will be responsible for paying for the charges which are considered routine, since they would have received these services even if they were not participating in this study. Participants will be responsible for any costs not covered by their insurance company, including deductibles, co-payments and all out-of-pocket expenses. Participants and/or their insurance company will not be responsible for paying for the following testing and procedures that are specifically required for this research study and are not considered part of the routine management of their disease, if these procedures are performed at Moffitt Cancer Center.

- Procedure: Focal Bipolar Radiofrequency ablation of the Prostate.

- 6 Month Follow up Visit: PT, PTT - bleeding (clotting) tests, Chest x-ray - A chest x-ray is a radiology test that involves exposing the chest briefly to radiation to produce an image of the chest and the internal organs of the chest. Transperineal Mapping Prostate Biopsy- A method of detecting prostate cancer in men with elevated PSA. Electrocardiogram (EKG)-Measures the electrical function of your heart.

14.7: Confidentiality of Data: All data will be kept confidential. No names or identifying information will be included in any publications that result as conducting this study. Only data that does not include direct identifiers (such as name, MRN, etc.) will be shared with the company funding the study (Trod) or Biomed who will be monitoring this study on behalf of Trod. Although elements of dates will be shared with the sponsor, the sponsor will not be able to identify a specific subject/patient without access into Moffitt's computerized data systems.

15.0 FUNDING

[redacted]

Trod Medical will provide the funds and resources needed to carry out this study in accordance with MCC's internal processes and controls for investigator-initiated clinical/research studies.

16.0 REFERENCES

- Barzell WE, Melamed MR: Appropriate patient selection in the focal treatment of prostate cancer: the role of transperineal 3- dimensional pathologic mapping of the prostate- a four-year experience. Submitted manuscript 2007.

- Barzell WE, Whitmore WF: Transperineal template guided saturation biopsy of the prostate: rationale, indications and technique. Urology Times Vol. 31,No.5: 41-42 2003.

- Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, Minasian LM, Ford LG, Lippman SM, Crawford ED, Crowley JJ, Coltman CA, Jr.: *Prevalence of prostate cancer among men with a prostate-specific antigen level < or =4.0ng per millitier.* N Engl J Med 2004; 350:2239-2246

- Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG.Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer.Urology. 2000;56(6):899-905.

APPENDIX A

The International Index of Erectile Function (IIEF-5) Questionnaire

Over the past 6 months:					
1. How do you rate your **confidence** that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
2. When you had erections with sexual stimulation, **how often** were your erections hard enough for penetration?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
3. During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time)4	Almost always/always 5
4. During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
5. When you attempted sexual intercourse, **how often** was it satisfactory for you?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5

IIEF-5 scoring:

The IIEF-5 score is the sum of the ordinal responses to the 5 items.

22-25: No erectile dysfunction

17-21: Mild erectile dysfunction

12-16: Mild to moderate erectile dysfunction

8-11: Moderate erectile dysfunction

5-7: Severe erectile dysfunction

_____ _____

Signature of Patient or Legal Representative Date

_____ _____

Signature of Person Completing Form (if not patient) Relationship to Patient

APPENDIX B RECTAL ASSESSMENT SCALE –(RAS)

Date of Visit: _____ Total Score: _____

Please fill out this short questionnaire to help us find out more about any problems you may be having with diarrhea. Check the statement for each subject that best describes your situation during the past 7 days.

	0	1	2	3
Frequency of stools per day:	[ ] 0-1 Stools per day	[ ] 2 Stools per day	[ ] 3 Stools per day	[ ] 4 or more stools per day
Consistency of stools per day:	[ ] All stools formed	[ ] Stools formed and loose	[ ] Stools loose	[ ] Watery stools
Urgency of stools	[ ] No urgency	[ ] Somewhat urgent	[ ] Urgent	[ ] Very urgent
Abdominal discomfort:	[ ] No discomfort	[ ] Mild-moderate discomfort	[ ] Somewhat severe discomfort	[ ] Very severe discomfort
Hemorrhoid discomfort	[ ] No discomfort	[ ] Requires mild treatment (e.g. Tucks, sitz baths)	[ ] Requires topical medication (e.g. Preparation H., etc.)	[ ] Requires oral analgesics or narcotics for pain relief

Adapted from: RAS

_____ _____
Signature of Patient or Legal Representative Date

_____ _____
Signature of Person Completing Form (if not patient) Relationship to Patient

American Urological Association (AUA) Symptom Score

Please circle one number for each question.

	Not at All	Less Than 1 Time in 5	Less Than Half the Time	About Half the Time	More Than Half the Time	Almost Always
Over the past week or so, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
During the past week or so, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5
During the past week or so, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
How often have you found it difficult to postpone urination?	0	1	2	3	4	5
During the past week or so, how often have you had a weak urinary stream?	0	1	2	3	4	5
During the past week or so, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
During the last week, how many times did you most typically get up at night to urinate?	0	1 time	2 times	3 times	4 times	5 times

Total Score: _____

_____ _____
Signature of Patient or Legal Representative Date

_____ _____
Signature of Person Completing Form (if not patient) Relationship to Patient

MOFFITT CANCER CENTER 04/10
EMR: GU Patient Questionnaire / Radiation Oncology Questionnaire
Page 1 of 1

PATIENT NAME: _____
MR#: _____

EPIC

The Expanded Prostate Cancer Index Composite

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month_____Day_____Year_____

Name (optional): _____

Date of Birth (optional): Month_____Day_____Year_____

URINARY FUNCTION

This section is about your urinary habits. Please consider **ONLY THE LAST 4 WEEKS**.

1. Over the **past 4 weeks**, how often have you leaked urine?

   More than once a day..... 1
   About once a day..... 2
   More than once a week..... 3 (Circle one number)
   About once a week..... 4
   Rarely or never..... 5

2. Over the **past 4 weeks**, how often have you urinated blood?

   More than once a day..... 1
   About once a day..... 2
   More than once a week..... 3 (Circle one number)
   About once a week..... 4
   Rarely or never..... 5

3. Over the **past 4 weeks**, how often have you had pain or burning with urination?

   More than once a day..... 1
   About once a day..... 2
   More than once a week..... 3 (Circle one number)
   About once a week..... 4
   Rarely or never..... 5

4. Which of the following best describes your urinary control **during the last 4 weeks**?

   No urinary control whatsoever..... 1
   Frequent dribbling..... 2 (Circle one number)
   Occasional dribbling..... 3
   Total control..... 4

EPIC 2.2002

5. How many pads or adult diapers per day did you usually use to control leakage **during the last 4 weeks**?

None	0	
1 pad per day	1	
2 pads per day	2	(Circle one number)
3 or more pads per day	3	

6. How big a problem, if any, has each of the following been for you **during the last 4 weeks**?

(Circle one number on each line)

		No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a.	Dripping or leaking urine	0	1	2	3	4
b.	Pain or burning on urination	0	1	2	3	4
c.	Bleeding with urination	0	1	2	3	4
d.	Weak urine stream or incomplete emptying	0	1	2	3	4
e.	Waking up to urinate	0	1	2	3	4
f.	Need to urinate frequently during the day	0	1	2	3	4

7. Overall, how big a problem has your urinary function been for you **during the last 4 weeks**?

No problem	1	
Very small problem	2	
Small problem	3	(Circle one number)
Moderate problem	4	
Big problem	5	

BOWEL HABITS

The next section is about your bowel habits and abdominal pain.
Please consider **ONLY THE LAST 4 WEEKS**.

8. How often have you had rectal urgency (felt like I had to pass stool, but did not) **during the last 4 weeks**?

More than once a day	1	
About once a day	2	
More than once a week	3	(Circle one number)
About once a week	4	
Rarely or never	5	

9. How often have you had uncontrolled leakage of stool or feces?

More than once a day	1	
About once a day	2	
More than once a week	3	(Circle one number)
About once a week	4	
Rarely or never	5	

10. How often have you had stools (bowel movements) that were loose or liquid (no form, watery, mushy) **during the last 4 weeks**?

Never	1	
Rarely	2	
About half the time	3	(Circle one number)
Usually	4	
Always	5	

11. How often have you had bloody stools **during the last 4 weeks**?

Never	1	
Rarely	2	
About half the time	3	(Circle one number)
Usually	4	
Always	5	

EPIC 2.2002

12. How often have your bowel movements been painful **during the last 4 weeks**?

Never	1	
Rarely	2	
About half the time	3	(Circle one number)
Usually	4	
Always	5	

13. How many bowel movements have you had on a typical day **during the last 4 weeks**?

Two or less	1	
Three to four	2	(Circle one number)
Five or more	3	

14. How often have you had crampy pain in your abdomen, pelvis or rectum **during the last 4 weeks**?

More than once a day	1	
About once a day	2	
More than once a week	3	(Circle one number)
About once a week	4	
Rarely or never	5	

15. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Urgency to have a bowel movement	0	1	2	3	4
b. Increased frequency of bowel movements	0	1	2	3	4
c. Watery bowel movements	0	1	2	3	4
d. Losing control of your stools	0	1	2	3	4
e. Bloody stools	0	1	2	3	4
f. Abdominal/ Pelvic/Rectal pain	0	1	2	3	4

16. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks**?

No problem	1	
Very small problem	2	
Small problem	3	(Circle one number)
Moderate problem	4	
Big problem	5	

EPIC 2.2002

SEXUAL FUNCTION

The next section is about your **current** sexual function and sexual satisfaction. Many of the questions are very personal, but they will help us understand the important issues that you face every day. Remember, THIS SURVEY INFORMATION IS COMPLETELY CONFIDENTIAL. Please answer honestly about **THE LAST 4 WEEKS ONLY**.

17. How would you rate each of the following during the last 4 weeks? (Circle one number on each line)

	Very Poor to None	Poor	Fair	Good	Very Good
a. Your level of sexual desire?	1	2	3	4	5
b. Your ability to have an erection?	1	2	3	4	5
c. Your ability to reach orgasm (climax)?	1	2	3	4	5

18. How would you describe the usual QUALITY of your erections **during the last 4 weeks**?

None at all 1
Not firm enough for any sexual activity 2
Firm enough for masturbation and foreplay only ..... 3 (Circle one number)
Firm enough for intercourse 4

19. How would you describe the FREQUENCY of your erections **during the last 4 weeks**?

I NEVER had an erection when I wanted one 1
I had an erection LESS THAN HALF the time I wanted one 2
I had an erection ABOUT HALF the time I wanted one ..... 3 (Circle one number)
I had an erection MORE THAN HALF the time I wanted one 4
I had an erection WHENEVER I wanted one 5

20. How often have you awakened in the morning or night with an erection **during the last 4 weeks**?

Never 1
Less than once a week 2
About once a week ..... 3 (Circle one number)
Several times a week 4
Daily 5

21. **During the last 4 weeks**, how often did you have any sexual activity?

Not at all	1	
Less than once a week	2	
About once a week	3	(Circle one number)
Several times a week	4	
Daily	5	

22. **During the last 4 weeks**, how often did you have sexual intercourse?

Not at all	1	
Less than once a week	2	
About once a week	3	(Circle one number)
Several times a week	4	
Daily	5	

23. Overall, how would you rate your ability to function sexually **during the last 4 weeks**?

Very poor	1	
Poor	2	
Fair	3	(Circle one number)
Good	4	
Very good	5	

24. How big a problem **during the last 4 weeks**, if any, has each of the following been for you? (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Your level of sexual desire	0	1	2	3	4
b. Your ability to have an erection	0	1	2	3	4
c. Your ability to reach an orgasm	0	1	2	3	4

25. Overall, how big a problem has your sexual function or lack of sexual function been for you **during the last 4 weeks**?

No problem	1	
Very small problem	2	
Small problem	3	(Circle one number)
Moderate problem	4	
Big problem	5	

HORMONAL FUNCTION

The next section is about your hormonal function. Please consider **ONLY THE LAST 4 WEEKS**.

26. **Over the last 4 weeks,** how often have you experienced hot flashes?

More than once a day..... 1
About once a day..... 2
More than once a week..... 3 (Circle one number)
About once a week..... 4
Rarely or never..... 5

27. How often have you had breast tenderness **during the last 4 weeks**?

More than once a day..... 1
About once a day..... 2
More than once a week..... 3 (Circle one number)
About once a week..... 4
Rarely or never..... 5

28. **During the last 4 weeks,** how often have you felt depressed?

More than once a day..... 1
About once a day..... 2
More than once a week..... 3 (Circle one number)
About once a week..... 4
Rarely or never..... 5

29. **During the last 4 weeks,** how often have you felt a lack of energy?

More than once a day..... 1
About once a day..... 2
More than once a week..... 3 (Circle one number)
About once a week..... 4
Rarely or never..... 5

30. How much change in your weight have you experienced **during the last 4 weeks**, if any?

Gained 10 pounds or more.....1
Gained less than 10 pounds 2
No change in weight..... .....3 (Circle one number)
Lost less than 10 pounds 4
Lost 10 pounds or more.....5

31. How big a problem **during the last 4 weeks**, if any, has each of the following been for you? (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Hot flashes	0	1	2	3	4
b. Breast tenderness/enlargement	0	1	2	3	4
c. Loss of Body Hair	0	1	2	3	4
d. Feeling depressed	0	1	2	3	4
e. Lack of energy	0	1	2	3	4
f. Change in body weight	0	1	2	3	4

Overall Satisfaction

32. Overall, how satisfied are you with the treatment you received for your prostate cancer?

Extremely dissatisfied..... 1
Dissatisfied..... 2
Uncertain..... 3 (Circle one number)
Satisfied..... 4
Extremely satisfied..... 5

THANK YOU VERY MUCH!!

APPENDIX E

ID: ___ ___ - ___ ___ ___ **INITIALS: ___ ___ ___**

Site Subject **F M L**

Medical Resource Utilization Patient Diary

Patient Instructions:

Please complete the form below weekly by providing detail on non-study related health care visits. If there were multiple visits within a single week, please list out each individual visit.

Date	Did you have a health care visit this week (Y/N)?	If yes, *how many* healthcare visits did you have this week, and *where* did you visit?	For each of the visits, *who* did you see during this visit? (e.g., nurse, physician assistant, or physician)	What was the *primary reason* for this visit?	Did the healthcare personnel say the visit was *related to the RFA procedure*[1] (Y/N)?	What treatment did you receive during this visit, if any?
Week 1:						
Week 2:						
Week 3:						
Week 4:						
Week 5:						
Week 6:						
Week 7:						
Week 8:						
Week 9:						
Week 10:						
Week 11:						
Week 12:						

1. Note to MCC clinical coordinator: If the patient's response to this question is "Y" an AE form must also be completed.

ID: ___ ___ - ___ ___ ___ **INITIALS: ___ ___ ___**
Site Subject F M L

Medical Resource Utilization Patient Diary

Patient Instructions:
Please complete the form below weekly by providing detail on non-study related health care visits. If there were multiple visits within a single week, please list out each individual visit.

Date	Did you have a health care visit this week (Y/N)?	If yes, *how many* healthcare visits did you have this week, and *where* did you visit?	For each of the visits, *who* did you see during this visit? (e.g., nurse, physician assistant, or physician)	What was the *primary reason* for this visit?	Did the healthcare personnel say the visit was *related to the RFA procedure*[1] (Y/N)?	What *treatment* did you receive during this visit, if any?
Week 13:						
Week 14:						
Week 15:						
Week 16:						
Week 17:						
Week 18:						
Week 19:						
Week 20:						
Week 21:						
Week 22:						
Week 23:						
Week 24:						

1. Note to MCC clinical coordinator: If the patient's response to this question is "Y" an AE form must also be completed.