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PHASE IV TRIAL EVALUATING THE USE OF STEREOTACTIC BODY RADIOTHERAPY FOR THE TREATMENT OF PROSTATE CANCER

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Index

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SCHEMA

R

E Stereotactic Body Radiotherapy (SBRT)

G

I Patient Groups: Prostate Cancer

S Dose-Fractionation:

As monotherapy (No pelvic radiotherapy):

T 30 – 40 Gy / 4 – 5 fractions

E After standard pelvic radiotherapy (45 Gy) for higher risk disease:

19 – 21 Gy / 2 – 3 fractions

R

Pelvic Radiotherapy
Conventionally fractionated external beam pelvic radiotherapy to a dose of 45 Gy in 25 fractions may be given at the discretion of the treating radiation oncologist based on high risk features (i.e. PSA > 20, Gleason score ≥ 7, T3 disease) or high intermediate risk features (i.e. Gleason Score 4 + 3= 7, PSA > 15).

Integrated Boost
At the discretion of the treating radiation oncologist, an integrated boost of ~ 1 Gy per fraction may be directed at the MR abnormality.

Hormone Therapy
Hormone therapy may be given at the discretion of the patient's urologist and/or radiation oncologist based on high risk features. All forms of androgen suppression including neoadjuvant, concurrent, and adjuvant hormone therapy may be recommended.

Radioprotectant
Rectal amifostine is encouraged but not required and may be given at the discretion of the treating radiation oncologist prior to each fraction. (See 8.1.6)

Eligibility
- Patient age ≥ 18 years
- Zubrod performance status of 0-3
- Biopsy-proven prostatic adenocarcinoma, clinical stage T1-3N0M0
- Prostate volume ≤ 100 cc
- No prior prostatectomy
- No prior central pelvis radiotherapy except as part of combination therapy for prostate cancer
- No history of scleroderma
- Signed study-specific consent form

1.0 Introduction

Prostate cancer is the most common cancer among American men. The American Cancer Society estimated about 192,280 new cases of prostate cancer in the United States in 2009. Prostate cancer is the second most common cause of cancer-related death with an estimated 27,360 men dying of prostate cancer in 2009. This accounts for 10% of all cancer-related deaths in men. However, with more than 2 million survivors of prostate cancer alive today in the United States, much of the current research focuses not only on improvements in tumor control but also in convenience of treatment delivery and quality of life after treatment. (www.cancer.org)

Due to a better understanding of the radiobiology of prostate cancer and the recent advances in precise delivery of radiation therapy, stereotactic hypofractionated radiotherapy is emerging as a new treatment modality with the potential to control organ confined prostate cancer while limiting treatment-related toxicity. The survival of a mammalian cell to radiation damage is classically described by a formalism known as the linear quadratic equation. This mathematical model suggests that the survival rate of an irradiated cell depends on the total radiation dose, the dose per fraction and the overall treatment time. The dose-response of a cell to fractionated radiation is described by the alpha-beta ratio (α/β). A recent review of 17 articles estimated the α/β ratio for prostate cancer cells to be 1.85 Gy which suggests that prostate cancer cells have a high sensitivity to fractionation, where higher doses of radiation delivered in fewer fractions would theoretically be advantageous.(1) Stereotactic body radiation therapy (SBRT) is a radiation delivery technique that employs state-of-the-art equipment to position a patient and precisely deliver a high dose of radiation to the treatment volume in a limited number of fractions (usually 5 or less).

Historically, hypofractionated radiation therapy has been reported as early as the 1960's in attempts at the time to improve allocation of resources. Results from a retrospective review of a United Kingdom regimen of hypofractionated radiation therapy using 6 fractions of 6 Gy to a total dose of 36 Gy were found to be comparable to other published outcome data in terms of local tumor control and survival. Early and late toxicity were reportedly within normal limits. (3) Hypofractionation for prostate cancer has more recently moved into several radiation therapy arenas, including external beam radiotherapy, high dose rate brachytherapy and stereotactic radiotherapy. The Radiation Therapy Oncology Group (RTOG) currently has a phase III protocol open to patient accrual comparing conventionally fractionated conformal radiation therapy in 41 fractions of 1.8 Gy (73.8 Gy total) to hypofractionated conformal radiation therapy in 28 fractions of 2.5 Gy (70 Gy total). Other studies have used fraction sizes ranging from 2.5 to 3.1 Gy. (4-7) High dose rate brachytherapy has been used to deliver 5.5 to 11.5 Gy fraction sizes. (8-9).

Recent technological advances have made it possible to deliver high doses of radiation therapy with high precision over just a few days while preserving function of surrounding critical structures. This treatment modality, termed stereotactic body radiotherapy (SBRT), is emerging as an expedient, safe, and effective radiation modality for a variety of malignancies. SBRT was recently defined by the American Society for Therapeutic Radiology and Oncology (ASTRO) as a "treatment method to deliver a high dose of radiation to the target, utilizing either a single dose or a small number of fractions with a high degree of precision within the body" (2). Stereotactic radiotherapy is a well-established treatment for intracranial metastases with local control rates of 80-90%.

Effective biochemical control with low rectal and bladder toxicity has been seen in several recently published clinical studies investigating stereotactic radiation therapy, mainly focusing on the feasibility of using SBRT to treat low-risk prostate cancer. New studies are also emerging that show safety and efficacy in using SBRT in intermediate and high risk prostate cancer patients as a boost after initial conventionally fractionated pelvic irradiation.

The early results of a Canadian phase I/II study (pHART3) using a five-fraction hypofractionated accelerated radiotherapy treatment (35 Gy in five daily fractions) for low risk organ confined prostate cancer were reported by Tang et al. After 6 months of follow up, there was no grade 3 toxicity; however, longer term follow-up is required to assess efficacy and toxicity. (10) Madsen et al. reported on 40 patients treated with SBRT for low risk prostate cancer. They all received 33.5 Gy in five fractions, which is equivalent to 78 Gy in 2 Gy fractions based on alpha/beta ratio of 1.5. The actuarial 4-year biochemical progression-free survival was 90% with a median follow-up of 41 months. There were only two cases of grade 3 acute urinary toxicity. No late toxicity more than grade 3 was reported. (11) King et al. recently reported the Stanford experience of treating 41 low-risk prostate cancer patients with 5 fractions of 7.25 Gy (36.25 Gy) using image-guided SBRT. After a median follow-up of 33 months, they reported no biochemical failure with early and late toxicity profiles no worse than conventional EBRT. In fact, they reported no patients with grade 4 or higher toxicities, only two patients with grade 3 late urinary toxicity and no grade 3 late rectal toxicity. In a separate report, they used the Expanded Prostate Cancer Index Composite (EPIC)-validated quality of life questionnaire to survey 32 consecutive patients treated with SBRT. The mean EPIC sexual domain summary score, sexual function score, and sexual bother score decreased by 45%, 49% ,and 25% respectively after 50 months of follow-up. The radiation dose to the penile bulb was not associated with erectile dysfunction. The investigators concluded that the rates of erectile dysfunction appeared comparable to those reported for other modalities of radiotherapy. (12-14)

The results of a phase I dose escalation trial conducted by the University of Texas Southwestern Medical Center were presented at the American Society of Clinical Oncology 2010 Genitourinary Cancers Symposium. Forty-five patients with low to intermediate risk prostate cancer were treated with a 5 fraction SBRT regimen using image guidance, intensity modulation, and a rectal balloon with pretreatment enema. The starting radiation dose was 45 Gy in 5 fractions with subsequent dose escalation to 47.5 Gy and 50 Gy. Patients were followed for toxicity using CTCAE (Common Terminology Criteria for Adverse Events) v3 scoring, as well as AUA (American Urological Association) and EPIC questionnaires. After a median follow-up of 12 months, the investigators observed no grade 3 gastrointestinal toxicities and only one patient with grade 3 genitourinary toxicity. Mean AUA score before SBRT was 5 and during follow-up increased to 8-9. EPIC rectal mean scores were decreased at 6 weeks to 12 months but returned to baseline at 18 months. PSA control was 95% using the nadir-plus-2 definition and 100% using the 3-consecutive-rises definition. Currently, the phase II study that is being conducted utilizes 50 Gy in 5 fractions. (15)

Katz et al. (16) also recently published their results with SBRT for localized prostate cancer. Three hundred and four patients were treated as follows: 50 received 5 fractions of 7 Gy (total dose 35 Gy) and 254 received 5 fractions of 7.25 Gy (total dose 36.25 Gy). Two low risk patients and two high risk patients failed biochemically. However, biopsy revealed both of the low risk patients and one of the high risk patients to be disease free in the prostate gland. In this study, rectal administration of amifostine was given prior to each treatment which likely assisted in keeping toxicity low. In fact, despite higher therapeutic doses based on biological equivalent dose (BED) calculations, the observed rate of acute urinary and rectal toxicity was low, with less than 5% of patients experiencing any acute grade II urinary or rectal toxicity and none experiencing any higher grade toxicity. Late toxicity was also less in the recent study using rectal amifostine when compared to previously published studies. For instance, King et al. reported late grade II urinary toxicity in 24% of patients (33-month follow-up) compared to 2% for the 35 Gy dose level (30-month follow-up) and 5.8% for the 36.25 Gy dose level (11-month follow-up). Regarding late bowel effects, King et al. observed 15% grade II toxicity at 33 month median follow-up. Katz et al. observed a late bowel toxicity rate of 4.2% for grade I toxicity and no higher grade toxicity for the 35 Gy dose level with 30 months of follow-up. They attribute their low bowel toxicity rate to the rectal administration of amifostine prior to SBRT delivery. (12, 16) Amifostine has been reported to significantly reduce the incidence of radiation-induced toxicity in multiple studies and when administered rectally has no related toxicity as opposed to intravenous administration which can cause significant

nausea. In both of these studies, late toxicity rates may increase with more follow-up, but what has been reported thus far is encouraging.

Katz and colleagues also recently reported their preliminary experience with SBRT as a boost for 73 intermediate and high risk prostate cancer patients after initial treatment with 45 Gy conventionally fractionated pelvic irradiation. The 3-fraction SBRT boost dose was escalated from 18 Gy to 19.5 Gy to 21 Gy. After a median follow-up of 33 months, there were less than 7% grade 2 and no higher grade acute toxicities; one grade 3 late toxicity and no grade 4 late toxicities. Of the 97% of patients that had at least 2 years of follow-up, 71.8% achieved a PSA nadir of 0.5 ng/mL. Three-year actuarial biochemical control rates were 89.5% and 77.7% for intermediate and high risk patients, respectively – 3 intermediate risk and 7 high risk patients with biochemical failures. (17)

The University of San Francisco (UCSF) recently published their results with SBRT both as monotherapy and as a boost treatment for prostate cancer. At the time of the study, 38 patients had been treated with a minimum follow-up of 12 months – 20 as monotherapy (9.5 Gy x 4 fractions) and 18 as a boost (9.5 Gy x 2 fractions) after external beam radiotherapy and androgen deprivation therapy. With a median follow-up of 18.3 months, 42% and 11% had acute grade 2 genitourinary and gastrointestinal toxicity, respectively, with no grade 3 or higher acute toxicity. Two patients experienced late grade 3 genitourinary toxicity. All patients were free of biochemical or clinical recurrence at the time of follow-up with a median PSA nadir of 0.35 ng/mL. (18)

The UCSF authors drew upon their experience with high dose rate (HDR) brachytherapy in which they were able to achieve similar dosimetry when compared with SBRT. Hypofractionation with HDR brachytherapy has demonstrated excellent efficacy and toxicity profiles as both monotherapy and after external beam radiotherapy as a boost for organ confined prostate cancer. The UCSF has recently reported its experience with HDR brachytherapy boost in mostly intermediate and high risk disease in which they achieved 5-year bNED (biochemical no evidence of disease) rates of 93% with minimal toxicity. (19) Superior bNED rates have also been reported in a randomized Phase III trial of HDR brachytherapy boost compared with external beam radiotherapy (EBRT) alone. (20) In addition, a systematic review of the literature recently concluded that the combination of EBRT and HDR brachytherapy results in superior bNED rates and overall survival when compared with EBRT alone or EBRT with a permanent prostate seed implant boost. (21) Grills and colleagues at William Beaumont Hospital have reported their HDR brachytherapy experience. Compared with permanent prostate seed implant with low dose rate palladium seeds, HDR brachytherapy was not only able to achieve equivalent biochemical control, but was also associated with decreased rates of acute and late toxicity and improved quality of life measures. (22) Using the HDR brachytherapy dose and fractionation, SBRT could theoretically achieve the excellent therapeutic profile of HDR brachytherapy while avoiding the risks of an invasive procedure and its inherent logistical challenges.

SBRT for prostate cancer appears to be effective in controlling disease with acceptable toxicity. However, more studies are needed with longer term follow-up. St. John's Mercy has installed an Elekta Synergy-S® linear accelerator at the David C. Pratt Cancer Center that is specifically designed to deliver highly-precise SBRT treatments. It has a tightened isocenter accuracy calibrated to a precision of within 1.5 mm diameter, a micro-MLC for treatment of small radiation ports, a specially designed Hexapod® table top that can correct for patient misalignment in both translational and rotational directions, an onboard cone-beam kV CT for precise tumor localization immediately prior to treatment, and four-dimensional CT (4D-CT) which together allow for accurate monitoring of and compensation for tumor motion during respiration, active breathing control for respiratory gating, and real-time continuous fluoroscopic capability for visual confirmation that the target remains in the treatment field.

2.0 Objectives

This study will evaluate the local control rate as well as acute and late toxicity rates of stereotactic body radiotherapy (SBRT) for the treatment of organ confined prostate cancer.

2.1 Hypothesis

2.1.1 For selected patients with localized prostate cancer (clinical stage T1-2N0M0), stereotactic body radiotherapy (SBRT) is technically feasible with acceptable complication rates.

2.1.2 Biochemical control with stereotactic body radiotherapy (SBRT) will be at least as good as standard fractionation radiation therapy

2.2 Study Design

2.2.1 Single site, non-randomized, prospective, phase IV trial

2.2.2 Study group will include organ confined prostate cancer

2.2.3 Data collected will include patient demographics, pathology data, tumor stage, SBRT dose fractionation scheme, dose received by adjacent critical normal tissues, tumor recurrence data, and acute and late toxicities.

2.2.4 Follow up data will be collected during the patient's standard office visits. The anticipated duration of this study is 5 years

2.3 End Points

2.3.1 Primary endpoints will be biochemical control rate

- Serial blood tests for prostate specific antigen (PSA) levels will be obtained at regular intervals
- The "Phoenix definition" for biochemical recurrence (nadir + 2 ng/ml) will be used

2.3.2 Secondary endpoint will be late toxicity rate.

- Grading of acute and late complications is defined in Section 12.3 (Appendix III)

3.0 Patient Selection

3.1 Eligibility Criteria

3.1.1 Patient age of at least 18 years

3.1.2 Zubrod performance status of 0-3

3.1.3 T1-3N0M0 adenocarcinoma of the prostate

3.1.4 Prostate volume $\leq$ 100 cc

3.1.5 No prior pelvic radiotherapy except as part of combination therapy for prostate cancer

3.1.6 Signed study-specific consent form

3.2 Exclusion Criteria

3.2.1 Extension of local tumor to involve adjacent organs other than seminal vesicles (T4)

3.2.2 Prostate volume > 100 cc

3.2.3 Nodal involvement

3.2.4 Metastatic disease

3.2.5 Prior central pelvis radiotherapy except as part of combination therapy for prostate cancer

3.2.6 History of scleroderma

3.2.7 Patients with psychiatric or addictive disorder that would preclude obtaining informed consent

4.0 Pretreatment Evaluation

- **4.1** Patient history, including prior radiation and chemotherapy treatments
- **4.2** Physical examination including digital rectal examination
- **4.3** Tissue biopsy confirming a diagnosis of malignancy
- **4.4** Abdominopelvic CT scan or MRI as clinically indicated
- **4.5** Bone scan and chest x-ray as clinically indicated
- **4.6** CBC, platelets, bilirubin, albumin, AST, ALT, PT, PTT as clinically indicated

5.0 Fiducial Placement

- **5.1** Three gold fiducials will be placed within the prostate gland under ultrasound guidance in different locations
- **5.2** Fiducials should be placed at least 7 days prior to simulation because of the possibility of migration

6.0 Simulation

- **6.1** Bowel Prep on the morning of simulation including Dulcolax® laxative and a Fleet Enema.
- **6.2** Balloon catheter with 60 cc diluted barium contrast positioned in the rectum to stabilize pelvic anatomy
- **6.3** Custom body immobilization with the BodyFix system
- **6.4** CT simulation without IV contrast with 1-2 mm slice thickness, including at least 5 cm above and below the treatment volume.
- **6.5** 3-point leveling tattoos
- **6.6** Contrast enhanced MRI of the pelvis with 1-3 mm slice thickness (saline-filled 60 cc rectal balloon in place); CT-MRI fusion for target volume and normal tissue delineation

7.0 Radiation Treatment Planning

7.1 Target Definition

- **7.1.1** Gross tumor volume (GTV) is contoured on the planning CT scan. MRI images will be registered to the planning CT dataset to assist in constructing the GTV and normal structure volumes. GTV will include the entire prostate gland. The proximal seminal vesicles may be included in the GTV at the discretion of the treating radiation oncologist based on high risk features (e.g. Gleason score > 6 and PSA > 15 ng/ml). GTV_{MR} may be contoured to delineate the visible MR abnormality and may be targeted for an integrated boost at the discretion of the treating physician.
- **7.1.2** Clinical target volume (CTV) will be equal to the GTV
- **7.1.3** Planning target volume (PTV) will be defined as the CTV plus a 3-5 mm expansion margin throughout except posteriorly by the rectum where a 2-3 mm margin will be used. For high risk patients with organ confined disease (e.g. Gleason score 8-10 and/or PSA > 20 ng/ml), the PTV will also include a 5-8 mm margin on the involved side of the prostate.

7.2 Dose-Specification

- **7.2.1** The total prescription dose for SBRT will be 30 – 40 Gy in 4 – 5 fractions delivered 2 to 3 times per week. The total prescription dose for SBRT as a boost after prior conventionally fractionated external beam pelvic radiotherapy (45 Gy in 25 fractions) will be 19 – 21 Gy in 2 – 3 fractions delivered 2 to 3 times per week. At the discretion of the treating radiation oncologist, an integrated boost of ~ 1 Gy per fraction may be directed at the MR abnormality.

7.2.2 Radiation beams will conform to the PTV outline without additional margin and the dose will be prescribed to the isodose line (IDL) that covers at least 95% of the PTV. The 105% IDL should be confined to the PTV.

7.2.3 Conformality index (CI) = Prescription IDL volume / PTV volume
Goal = CI $\leq$ 1.2

7.2.4 Gradient index (GI) = 50% Prescription IDL volume / Prescription IDL volume
Goal = GI $\leq$ 3

7.3 Normal Tissue Dose Constraints

7.3.1 The normal structures that will be contoured using the planning CT/MR fusion are listed below with their respective dose constraints (five fractions) as derived from the available literature:

STRUCTURE	VOLUME	DOSE
Spinal Cord	D_{max}	22.5 Gy
	< 10 cc	20 Gy
Cauda Equina	D_{max}	27.5 Gy
	< 10 cc	25 Gy
Sacral Plexus	D_{max}	30 Gy
	< 10 cc	27.5 Gy
Anterior Rectal Wall	D_{max}	No more than 105% Rx
Posterior Rectal Wall	D_{max}	20 Gy
Lateral Rectal Wall	D_{max}	No more than 100% Rx
	< 3 cc cumulative (both sides)	50 Gy
Rectum superior to prostate	D_{max}	30 Gy
	< 10 cc	25 Gy
Small Intestine	D_{max}	30 Gy
	< 10 cc	25 Gy
Prostatic Urethra	D_{max}	No more than 105% Rx
Bladder	D_{max}	No more than 105% Rx
	< 10 cc	20 Gy
Penile Bulb	D_{max}	No more than 105% Rx
	< 3 cc	30 Gy
Femoral Heads	< 10 cc cumulative (both sides)	30 Gy
Skin not within fold	D_{max}	25 Gy
Skin within fold (e.g. gluteal fold)	D_{max}	20 Gy

8.0 Stereotactic Body Radiotherapy Treatment Delivery

8.1 Premedication

The decision to premedicate a patient prior to prostate SBRT is at the discretion of the treating radiation oncologist. While there is no universal agreement, the following are a list of agents that have been suggested by some investigators to potentially reduce patient discomfort and possibly prevent acute and/or late toxicity if used as premedication prior to prostatic SBRT.

8.1.1 Corticosteroids (Decadron 4-10 mg PO or equivalent) 15-60 minutes prior to each fraction for the intended purpose of modulating immediate inflammatory effects.

8.1.2 Analgesic medication for patient comfort during long treatment duration.

8.1.3 Anti-anxiety medication for patient comfort during long treatment duration.

8.1.4 Tamsulosin (Flomax) starting on the first day of treatment and continuing for at least 3 months

8.1.5 Bowel Prep on the morning of each treatment, including Dulcolax® laxative formula and a Fleet Enema. The patient may also be asked to start a bowel regimen 3 days

prior to the simulation with Milk of Magnesia and Gas-X and continue throughout the course of treatment.

8.1.6 Amifostine 1500 mg mixed in saline and instilled into the rectum 20 minutes prior to each treatment

8.2 Treatment

8.2.1 The medical physics staff will perform routine quality assurance checks on the treatment machine to ensure that the mechanical isocenter stability is within specification (ie. diameter $\leq$ 1.5 mm).

8.2.2 The medical physics staff will perform patient-specific quality assurance measurements to ensure that the treatment plan is deliverable and that the dose distribution is accurate.

8.2.3 The patient will be positioned in the custom immobilization device on the Hexapod® treatment couch and the rectal balloon will be inserted and filled with 60 cc of barium contrast. He will then be aligned to 3-point setup points with the in-room lasers.

8.2.4 Daily CT localization of the GTV isocenter is required prior to each fraction. Once the patient is properly positioned, a cone-beam CT of the treatment area will be acquired, fused, and aligned to the treatment planning CT utilizing the patient's internal anatomy, fiducial markers, and contrast-filled rectal balloon. Translational and rotational adjustments of patient positioning are performed as indicated. If adjustments are required, an orthogonal (ex. AP and LATERAL) set of electron portal images or a second cone-beam CT is then obtained prior to treatment to confirm proper alignment of the isocenter.

8.2.5 Either multiple coplanar or noncoplanar static gantry angle intensity-modulated fields or rotational arcs will be utilized.

8.2.6 Only photon (x-ray) beams will be used, preferably in energies of 6-18 MV.

9.0 Drug Therapy

9.1 The use of hormone therapy is left to the discretion of the treating radiation oncologist and the patient's urologist.

9.2 All forms of androgen suppression including neoadjuvant, concurrent, and adjuvant hormone therapy may be recommended.

9.3 Chemotherapy is rarely if ever used for localized prostate cancer but is left to the discretion of the medical oncologist. Chemotherapy is not allowed during SBRT. Ideally, chemotherapy should not have been given within 30 days of starting radiation and should not resume until at least 2 weeks after completing radiation. In addition, it is not recommended to perform SBRT when targeted anti-angiogenesis therapy is planned within 2 months of the procedure.

10.0 Patient Assessment

10.1 Study Parameters

The following are suggested patient follow-up intervals and evaluations that may be performed to either assess for treatment toxicity or tumor response to SBRT:

Assessment	Pre-Rx	Post-Rx 6 wk	Post-Rx 3 mo	Post-Rx 6 mo	Post-Rx 9 mo	Post-Rx 1 yr
H&P / Weight	X	X	X	X	X	X[b]
Disease status	X	X	X	X	X	X[b]
AUA/EPIC Questionnaire	X	X	X	X	X	X
Toxicity Assessment		X	X	X	X	X[b]
PSA	X	X	X	X	X	X

AST / ALT / Alk Phos	X[a]					
Total Bilirubin	X[a]					
PT / PTT	X[a]					
Creatinine	X[a]					
CBC with Platelets	X					
Bone scan	X[a]					
CT/MR abdomen/pelvis	X					X[b]

a. if clinically appropriate
b. at the discretion of the treating radiation oncologist

10.2 Response Evaluation

10.2.1 Prostate Specific Antigen (PSA)

- Will be obtained every 3 months for the first 2 years, then as indicated at the discretion of the treating physician.
- Biochemical failure defined as nadir + 2 ng/ml
- Repeat imaging including abdominopelvic CT scan, MRI, or bone scan as clinically indicated.

10.3 Toxicity

10.3.1 The patient will fill out the American Urological Association (AUA) Symptom Score Sheet and Expanded Prostate Cancer Index Composite (EPIC) questionnaire for gastrointestinal, urinary and sexual quality of life. (14) (Appendix IV and Appendix V, respectively)

10.3.2 The investigator will report and record all serious adverse events that occur. Adverse events should be reported using the CTC grading system (Appendix III).

10.3.2 Examples of anticipated acute adverse events include:

- General malaise
- Urinary irritative or obstructive symptoms – dysuria, increased urinary frequency, nocturia, weak stream, hesitancy, and possible urinary retention
- Rectal irritation – loose stools, cramping, straining, hemorrhoidal inflammation
- Radiation dermatitis – dryness, tanning, redness, itching
- Localized hair loss
- Musculoskeletal pain

10.3.3 Examples of anticipated late adverse events include:

- Bleeding, ulceration and/or perforation of the bladder, rectum, or small bowel
- Neurologic changes including motor weakness, numbness, paresthesias, and/or bowel or bladder dysfunction
- Persistent changes in bowel or bladder habits
- Small bowel obstruction
- Urethral stricture resulting in urinary retention
- Localized skin fibrosis, edema, and/or ulceration
- Erectile dysfunction
- Radiation-induced secondary malignancy

10.3.4 Reporting of unanticipated or serious adverse events will be reported according to the institutions IRB policy. An unanticipated adverse event is defined as follows:

> Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, stereotactic body radiotherapy, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or

any other unanticipated serious problem associated with a treatment that relates to the rights, safety, or welfare of subjects.

10.4 Patient Withdrawal from Study

During the course of the study, it is possible that patients may withdraw or be withdrawn from the study. Factors that may lead to a withdrawal from the study may include, but are not limited to the following:

Patient Withdrawal……At any time a patient may voluntarily withdraw from the study. This withdrawal will not affect their future medical treatment or benefits.

Patient Lost to Follow-Up…….Should a patient be classified as lost to follow-up, efforts to contact the patient should be made.

Physician Decision……Should a physician decide that continuing in the study is detrimental to the health and welfare of the patient, the patient may be withdrawn from the study.

Medical Reason…….Should the patient condition deteriorate the patient may be withdrawn from the study to allow for proper medical care.

11.0 Risk/Benefit Analysis

11.1 Risk associated with SBRT for organ confined prostate cancer

11.1.1 Acute toxicities reported to occur as a result of SBRT for prostate cancer include, but are not limited to: general malaise, bowel/bladder irritation, local hair loss, and/or local musculoskeletal pain

11.1.2 Late toxicities reported to occur as a result of SBRT for prostate cancer are primarily gastrointestinal including bleeding, ulceration, perforation, stenosis, and/or fistula and genitourinary including urethral stricture, bleeding, ulceration, and erectile dysfunction.

11.2 Minimization of Risks

Although the risks outlined in Section 10.3 may occur, the likelihood of serious events occurring is considered uncommon as long as certain precautions are taken. The potential risks have been minimized by:

- Premedication as described in Section 8.1, (e.g. rectal amifostine)
- Improved rectal dose profile with rectal balloon
- Strict compliance with normal tissue dose constraints as described in Sections 7.3

11.3 Potential Patient Benefits

11.3.1 Ability to offer effective and expedient local therapy

11.3.2 Reduction in amount of radiation delivered to adjacent normal structures compared to standard-fractionation radiation therapy

11.3.3 Significantly reduced treatment duration compared to standard-fractionation radiation therapy

11.4 Justification of the Study

For men diagnosed with localized prostate cancer, choosing between the various treatment options can be confusing and sometimes frustrating. For those who wish to avoid an invasive procedure, external beam radiotherapy which is fractionated daily over about two months has been the only alternative. Recent technological advances in stereotactic positioning of a patient for precise radiation delivery with online image guidance have led to a trend in radiation oncology of hypofractionation, which for the patient equals shorter treatment duration with the potential of equivalent or better tumor control

and toxicity rates. The use of hypofractionation in prostate cancer in particular is supported by its radiobiology; however, the proximity of adjacent organs at risk including the bladder and rectum has previously precluded its widespread adoption. When carefully administered, SBRT offers the potential to deliver the high doses necessary to control prostate cancer while sparing the adjacent structures in just five fractions.

11.5 Statistical Analysis

11.5.1 The overall survival and biochemical control rates will be analyzed.

11.5.2 The incidence rate for any serious adverse events will be calculated.

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13.0 Appendices

13.1 Appendix I

St. John's Mercy Medical Center
Informed Consent for a Clinical Research Study

STUDY TITLE: PHASE II TRIAL EVALUATING THE USE OF STEREOTACTIC BODY RADIOTHERAPY FOR THE TREATMENT OF PROSTATE CANCER

This is a clinical trial (type of research study). Clinical trials include only patients who choose to take part. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family and friends before making your decision.

WHAT SHOULD YOU KNOW ABOUT THE RESEARCH DOCTOR?

You should know that your relationship with a research doctor is different from your relationship with your personal doctor. Your personal doctor is treating your specific problem with the hope of a benefit for you. When a doctor is your research doctor, he/she is treating all subjects under a specific protocol to learn about the results of a treatment, and with the understanding that you may or may not benefit from your participation in the study. Be sure to ask questions of the study doctor if you want more information about this relationship.

The Radiation Oncologists of this study are part owner of the radiosurgery treatment equipment. The Radiation Oncologists will receive financial compensation when the equipment is used in addition to the professional fee normally charged.

WHY IS THIS STUDY BEING PERFORMED?

For men diagnosed with prostate cancer, choosing between the various treatment options can be confusing and sometimes frustrating. Some men wish to avoid an invasive procedure such as surgical removal of the prostate or implantation of radioactive seeds. In that case, external beam radiotherapy which is administered daily over about two months has been the only alternative. Recent technological advances in positioning the patient for precise radiation delivery using sophisticated computers have led to a new concept of **hypofractionation**, or fewer radiation treatments given at a higher dose per day. This new technique is called **stereotactic body radiotherapy (SBRT)**, which means the precise delivery of high-dose radiation in 5 or fewer treatments. SBRT allows shorter overall treatment duration with the potential of equivalent or better tumor control and side effects compared to standard fractionation. The use of SBRT in prostate cancer in particular is supported by its sensitivity to radiation; however, the risk of damaging nearby organs including the bladder and rectum has previously prevented its widespread use. When carefully administered, SBRT offers the potential to deliver the high doses necessary to control prostate cancer while sparing the nearby structures in just five fractions. The purpose of this study is to collect additional data on the effectiveness of stereotactic body radiotherapy for prostate cancer.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 100 people are expected to participate in this clinical study.

WHAT IS INVOLVED IN THE STUDY?

If you wish to take part in this study, a series of tests will be performed to determine if you qualify for participation in the clinical study. Your physician will ask you a series of questions regarding your medical history and a standard physical exam will be performed.

If you qualify for the study, you may first have at least 3 gold markers placed into the prostate by a diagnostic radiologist to help locate your tumor during radiation treatment. Next, you will undergo a radiation treatment planning session called a simulation. At this visit, a custom rigid foam device will be fabricated to immobilize your body in the correct position for treatment. A deflated rectal balloon catheter will be inserted into the rectum and inflated. A CT scan and an MRI scan of your pelvis will be obtained to plan your treatment. Permanent small tattoos may be applied to your skin to aid in positioning your body on the treatment table.

There may be several days between the simulation and the day you begin radiation. During this time, complex radiation treatment planning will be performed by your radiation oncologist and their medical physics staff. If your radiation oncologist recommends SBRT alone, you will receive 4 or 5 radiation treatments. Based on an assessment of high risk features, your physician may recommend a 5 week course of daily radiation therapy directed at your pelvis prior to administering 2 or 3 SBRT treatments directed at the prostate. Your physician will explain your treatment in more detail. Each radiation session may take an hour or longer to complete. After the entire radiation course is complete, you will be given follow-up instructions. You will be asked to fill out a confidential questionnaire at various time points after your treatment. Your honest answers to these questions will help the investigators to better understand the changes to your quality of life from this treatment.

HOW LONG WILL I BE IN THE STUDY?

We anticipate that you will remain in the study for approximately 5 years. After treatment is completed routine follow-up visits will be conducted, typically at 3 month intervals for the first 2 years, then less frequently.

Your physician may decide stop your treatment if: 1) your disease becomes worse, or 2) side effects become very severe, or 3) new scientific developments occur that indicate the treatment is not in your best interest, or 4) your physician believes that this treatment is no longer in your best interest. If your treatment is stopped, your doctor will discuss further treatment options with you.

WHAT ARE THE RISKS OF THE STUDY?

By participating in this study, you are at risk for several possible expected and unexpected side effects associated with stereotactic radiotherapy to the prostate. Some of these are described below; however, there also may be other side effects that we cannot predict. Most side effects go away shortly after the radiation therapy is stopped, but in some cases side effects can be serious, long-lasting, or permanent.

Risks arising from the delivery of stereotactic radiotherapy to the prostate which may occur shortly after completing treatment may include, but are not limited to:

- Generalized fatigue
- Diarrhea
- Rectal irritation
- Bladder irritation – urinary frequency, urgency, burning, slow stream
- Hair loss over the treatment area
- Skin irritation – redness, tanning, dryness, peeling, soreness, itchiness over the treatment area

- Temporary decrease in sperm count and gene mutation – take precautions not to conceive children during course of radiation treatment and for at least 12 months after completing therapy
- Muscular pain over the treatment area

Risks arising from the delivery of stereotactic radiotherapy to the prostate which may develop several months to years after completing treatment may include, but are not limited to:

- Bleeding ulceration and/or perforation (hole) in the bladder, rectum, and/or small bowel
- Chronic changes in bowel or bladder habits
- Erectile dysfunction
- Sterility
- Urethral stricture – possibly causing urinary retention which may require temporary placement of a catheter
- Injury to bones in the pelvis
- Radiation-induced cancer

I understand that all these side effects are possible. I may experience no side effects, some of them, or most of them. Although I will be closely monitored, not all side effects can be predicated and unforeseen problems can arise. I understand that there may be some unknown or unanticipated risks or discomforts in addition to those specified here.

Reproductive risks:
You should not father a baby during radiation and for 6 months after completing your radiation treatments, because the radiation can affect an unborn baby. It is important that you understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Ask about counseling and more information about preventing pregnancy.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be a direct medical benefit to you. However, there have been several trials completed at other institutions that have shown similar control rates after stereotactic body radiotherapy as that found with standard treatment for prostate cancer. It is also convenient, requiring only 5 radiation sessions and no anesthesia or hospitalization. Toxicity risk has been reported to be fairly low.

WHAT OTHER OPTIONS ARE THERE?

Other treatment options may include surgery, standard-fractionation radiation therapy, permanent seed brachytherapy, or other investigational procedures. Your doctor can provide information about your disease and the benefits of the different treatments for you. You should feel free to talk with your doctor about your disease and expected outcomes. The doctor involved in your care will be available to answer any questions you have about this program. You are free to ask your doctor any questions concerning this program now or in the future.

You are free to seek care from a doctor of your choice at any time. If you do not take part in, or withdraw from, the study you will continue to receive alternate care.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. This Informed Consent and another document called an "Authorization to Use and

Disclose Health Information" control how your health information may be used and disclosed during and after this study. The results of this study may be published or presented at meetings but will not include your name or reveal your identity. To participate in this study, you must sign both the Informed Consent and the Authorization to Use and Disclose Health Information. Your personal information may be disclosed if required by law.

WHAT ARE THE COSTS?

Taking part in this study may lead to added costs to you or your insurance carrier. Specifically, you or your insurance carrier will be responsible for the costs of the baseline blood tests, diagnostic imaging studies, stereotactic radiotherapy planning and delivery, and follow-up visits which would otherwise be a standard part of your care. Please ask about any expected added costs or insurance problems. St. John's Mercy Medical Center has personnel that can assist you with this.

Every precaution will be taken to prevent any injury to you during the study. In the event that injury occurs as a result of this study, treatment will be available. You or your insurance carrier will be responsible for the costs of the treatment. No funds have been set aside for compensation in the event of a research related injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

You will not receive payment for participating in this study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Your participation is voluntary. You may choose not to take part or may leave the study at any time. Your choice will not affect your doctors from providing care to you. Choosing not to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled.

You will be told of any important new findings developed during the course of your participation in this study that may affect your willingness to continue in the study. The investigator may withdraw you from this study if issues occur that show that you should not continue to participate.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions or concerns regarding this study, or a research-related injury, you may contact one of the Principal Investigators, Dr. Jaymeson Stroud at 314-251-6844 or Dr. Bethany Sleckman at 314-251-5665.

For questions about your rights as a research participant, contact Dr. Donald York, Chairman of the St. John's Mercy Medical Center Institutional Review Board (which is a group of people who review the research to protect your rights), at 314-569-6453.

Your doctor understands the importance of your contribution to clinical studies that attempt to improve medical care. Your doctor will make every effort to minimize, control, and treat any problems that may happen as a result of your participation in this study. If you believe that you are injured solely as a result of the study, or if you have questions regarding the study, please contact the Principal Investigator.

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's Cancer Information Service at 1-800-422-6237 or TTY:1-800-322-8615

Visit the NCI's Web Sites:

- Cancer Trials: comprehensive clinical trials information
  http://cancertrials.nci.nih.gov
- CancerNet: accurate cancer information including PDQ
  http://cancernet.nci.nih.gov

SIGNATURES

I have read all the above, asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review or discussion. I willingly give my consent to participate in this study. Upon signing this form I will receive a copy. I may also request a copy of the protocol (full study plan).

Participant (sign) _____

Participant (written) _____

Date _____

Principal Investigator _____

Staff Member Performing Consent Process _____

Witness _____

IRB Stamp (This form is INVALID if the stamp is not present.)

13.2 Appendix II

KARNOFSKY PERFORMANCE SCALE

100	Normal; no complaints; no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or do active work
60	Requires occasional assistance, but is able to care for most personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated, although death not imminent
20	Very sick; hospitalization necessary; active support treatment is necessary
10	Moribund; fatal processes progressing rapidly
0	Dead

ZUBROD PERFORMANCE SCALE

0	Fully active, able to carry on all pre-disease activities without restriction (KPS 90-100)
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work (KPS 70-80)
2	Ambulatory and capable or all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours (KPS 50-60)
3	Capable of only limited self-care, confined to bed or chair 50% of more of waking hours (KPS 30-40)
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair (KPS 10-20)

13.3 Appendix III

Common Terminology Criteria for Adverse Events v3.0 (CTCAE)

	GRADE				
Toxicity	**1**	**2**	**3**	**4**	**5**
CONSTITUTIONAL					
Fatigue	Mild fatigue over baseline	Moderate or causing difficulty performing some ADL	Severe fatigue interfering with ADL	Disabling	-
Fever	100.4-102.2°F	102.3-104.0°F	> 104.0°F for ≤ 24 hr	> 104.0°F for > 24 hr	Death
Weight loss	5 - < 10% of baseline	10 - < 20% of baseline	≥ 20% of baseline; tube feeding or TPN indicated	-	-
PAIN					
Pain due to radiation	Mild pain not interfering with function	Moderate pain: pain or analgesics interfering with function, but not interfering with ADL	Severe pain: pain or analgesics severely interfering with ADL	Disabling	-
Myositis (inflammation or damage of muscle)	Mild pain not interfering with function	Pain interfering with function, but not interfering with ADL	Pain interfering with ADL	Disabling	Death
SKIN					
Radiation dermatitis	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation other that skin folds and creases; bleeding induced by minor trauma or abrasion	Skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site	
Telangiectasia	Few	Moderate number	Many and confluent	-	-
Ulceration	-	Superficial ulceration < 2 cm size; local wound care; medical intervention indicated	Ulceration ≥ 2 cm size; operative debridement, primary closure or other invasive intervention indicated (ex. Hyperbaric oxygen)	Life-threatening consequences; major invasive intervention (ex. Complete resection, tissue reconstruction, flap, grafting)	Death
Fibrosis	Increased density, "spongy" feel	Increased density with firmness or tethering	Increased density with fixation of tissue; operative intervention indicated; interfering with ADL	Life-threatening; disability; loss of limb; interfering with vital organ function	Death
Soft Tissue Necrosis	-	Local wound care; medical intervention indicated	Operative debridement or other invasive intervention indicated (ex. Hyperbaric oxygen)	Life-threatening consequences; major invasive intervention indicated (ex. Tissue reconstruction, flap, or grafting)	Death
NEUROLOGY					
Neuropathy: Motor	Asymptomatic, weakness on exam/testing only	Symptomatic weakness interfering with function, but not interfering with ADL	Weakness interfering with ADL; bracing or assistance to walk (e.g. cane or walker) indicated	Life-threatening; disabling (e.g. paralysis)	Death
Neuropathy: Sensory	Asymptomatic, lost deep tendon reflexes or paresthesia (including tingling), not interfering with function	Symptomatic alteration or paresthesia (including tingling), interfering with function, not interfering with ADL	Sensory alteration or paresthesia interfering with ADL	Disabling	Death

GI TRACT					
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration, or malnutrition; IV fluids indicated < 24 hr	Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated ≥ 24 hr	Life-threatening consequences	Death
Vomiting	1 episode in 24 hr	2-5 episodes in 24 hr; IV fluids indicated < 24 hr	≥ 6 episodes in 24 hr; IV fluids or TPN indicated ≥ 24 hr	Life-threatening consequences	Death
Diarrhea	Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4-6 stools per day over baseline; IV fluids indicated < 24 hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL	Increase of ≥ 7 stools per day over baseline; IV fluids indicated ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL	Life-threatening consequences (e.g., hemodynamic collapse)	Death
Enteritis	Asymptomatic, pathologic or radiographic findings only	Abdominal pain; mucous or blood in stool	Abdominal pain, fever, change in bowel habits with ileus; peritoneal signs	Life-threatening consequences (ex. Perforation, bleeding, ischemia, necrosis)	Death
Ulceration	Asymptomatic, radiographic or endoscopic findings only	Symptomatic; altered GI function (altered dietary habits, oral supplements); IV fluids indicated < 24 hr	Symptomatic and severely altered GI function (inadequate oral caloric or fluid intake); IV fluids, tube feedings, or TPN indicated ≥ 24 hr	Life-threatening consequences	Death
Bleeding	Mild, intervention (other than iron supplements) not indicated	Symptomatic and medical intervention or minor cauterization indicated	Transfusion, interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences; major urgent intervention indicated	Death
Perforation	Asymptomatic radiographic findings only	Medical intervention indicated; IV fluids indicated < 24 hr	IV fluids, tube feedings, or TPN indicated ≥ 24 hr; operative intervention indicated	Life-threatening consequences	Death
Stricture	Asymptomatic radiographic findings only	Symptomatic; altered GI function (altered dietary habits, vomiting, bleeding, diarrhea); IV fluids indicated < 24 hr	Symptomatic and severely altered GI function (altered dietary habits, diarrhea, or GI fluid loss); IV fluids, tube feedings, or TPN indicated ≥ 24 hr; operative intervention indicated	Life-threatening consequences; operative intervention requiring complete organ resection	Death
Fistula	Asymptomatic; radiographic findings only	Symptomatic; altered GI function (ex. Altered dietary habits, diarrhea, or GI fluid loss); IV fluids indicated < 24 hr	Symptomatic and severely altered GI function (ex. Altered dietary habits, diarrhea, or GI fluid loss); IV fluids, tube feedings, or TPN indicated ≥ 24 hr	Life-threatening consequences	Death
GENITOURINARY					
Bladder spasms	Symptomatic, intervention not indicated	Symptomatic, antispasmodics indicated	Narcotics indicated	Major surgical intervention indicated (e.g., cystectomy)	
Cystitis	Asymptomatic	Frequency with dysuria; macroscopic hematuria	Transfusion; IV pain medications; bladder irrigation indicated	Catastrophic bleeding; major non-elective intervention indicated	Death
Fistula	Asymptomatic; radiographic findings only	Symptomatic; noninvasive intervention indicated	Symptomatic interfering with ADL; invasive intervention indicated	Life-threatening consequences; operative intervention requiring partial or full organ resection; permanent urinary diversion	Death
Incontinence, urinary	Occasional (e.g.,	Spontaneous, pads	Interfering with ADL;	Operative intervention	-

	with coughing, sneezing, etc.), pads not indicated	indicated	intervention indicated (e.g., clamp, collagen injections)	indicated (e.g., cystectomy or permanent urinary diversion)	
Urinary frequency/urgency	Increase in frequency or nocturia up to 2 x normal; enuresis	Increase >2 x normal but <hourly	≥1 x/hr; urgency; catheter indicated	-	-
Urinary retention	Hesitancy or dribbling, no significant residual urine; retention occurring during the immediate postoperative period	Hesitancy requiring medication; or operative bladder atony requiring indwelling catheter beyond immediate postoperative period but for <6 weeks	More than daily catheterization indicated; urological intervention indicated (e.g., TURP, suprapubic tube, urethrotomy)	Life-threatening consequences; organ failure (e.g., bladder rupture); operative intervention requiring organ resection indicated	Death
Stricture, GU	Asymptomatic, radiographic or endoscopic findings only	Symptomatic but no hydronephrosis, sepsis or renal dysfunction; dilation or endoscopic repair or stent placement indicated	Symptomatic and altered organ function (e.g., sepsis or hydronephrosis, or renal dysfunction); operative intervention indicated	Life-threatening consequences; organ failure or operative intervention requiring organ resection indicated	Death
MUSCULOSKELETAL					
Fracture	Asymptomatic, radiographic findings only	Symptomatic but non-displaced; immobilization indicated	Symptomatic and displaced; operative intervention indicated	Disabling	Death
METABOLIC					
Albumin	3-4 g/dL	2-2.99 g/dL	< 2 g/dL		Death
Alkaline phosphatase	> nl – 2.5 x nl	> 2.5 – 5 x nl	> 5 – 20 x nl	> 20 x nl	-
ALT	> nl – 2.5 x nl	> 2.5 – 5 x nl	> 5 – 20 x nl	> 20 x nl	-
AST	> nl – 2.5 x nl	> 2.5 – 5 x nl	> 5 – 20 x nl	> 20 x nl	-
Bilirubin	> nl – 1.5 x nl	> 1.5 – 3 x nl	> 3 – 10 x nl	> 10 x nl	-
Creatinine	> nl – 1.5 x nl	> 1.5 – 3 x nl	> 3 – 6 x nl	> 6 x nl	Death
SECONDARY MALIGNANCY	-	-	Non-life-threatening basal or squamous cell carcinoma of the skin	Solid tumor, leukemia, or lymphoma	Death

13.4 Appendix IV ON-STUDY AUA SYMPTOM SCORE

PLEASE FILL OUT THIS SHORT QUESTIONNAIRE TO HELP US FIND OUT MORE ABOUT ANY URINARY PROBLEMS YOU MIGHT HAVE. CIRCLE A NUMBER IN EACH COLUMN THAT BEST DESCRIBES YOUR SITUATION. YOU MUST ANSWER ALL QUESTIONS.

	Not at all	**Less than one time in five**	**Less than half the time**	**About half the time**	**More than half the time**	**Almost always**
1. Over the past month 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**
2. Over the past month or so, how often have you had to urinate again, less than two hours after you finished urinating?	**0**	**1**	**2**	**3**	**4**	**5**
3. Over the past month or so, how often have you found you stopped and started again several times when you urinated?	**0**	**1**	**2**	**3**	**4**	**5**
4. How often do you find it difficult to postpone urination?	**0**	**1**	**2**	**3**	**4**	**5**
5. Over the past month or so, how often have you had a weak urinary stream?	**0**	**1**	**2**	**3**	**4**	**5**
6. Over the past month or so, how often have you had to push or strain to begin urination?	**0**	**1**	**2**	**3**	**4**	**5**
	Not at all	**Once every 8 hours**	**Once every 4 hours**	**Once every 3 hours**	**Once every 2 hours**	**At least once every hour**
7. Over the past month or so, how often did you most typically get up at night to urinate?	**0**	**1**	**2**	**3**	**4**	**5**

Total per column _____ _____ _____ _____ _____ _____

_____ _____ _____

Patient Name Patient Signature Date This Form was Completed

13.5 Appendix V

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

5. How many pads or adult diapers <u>per day</u> 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)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>
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

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

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 <u>any</u> 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!!

13.6 Appendix VI

DEMOGRAPHIC FORM – Page 1 of 1

1. Name _____(last) _____(first)

2. Date of Birth ____/____/_____

3. RT Number _____

4. Race: ☐ Asian ☐ Caucasian ☐ Black ☐ Other, specify_____

5. Zubrod PS: ☐ 0 ☐ 1 ☐ 2

6. Radiation oncologist: _____

7. Medical oncologist: _____

8. Surgeon: _____

9. Tumor category: ☐ Prostate Cancer, Low Risk
☐ Prostate Cancer, Intermediate Risk
☐ Prostate Cancer, High Risk

10. AJCC Staging Classification: ☐ T1__ ☐ T2__

11. Gleason Score: ☐ 6 or less ☐ 7 (3+4) ☐ 7 (4+3) ☐ 8-10

12. Presenting PSA: _____ ng/ml Date:_____

13. Baseline Labs (if clinically indicated): Total bilirubin _____
Serum albumin _____
Alkaline phosphatase _____ALT _____ AST _____
PT _____ PTT _____
Creatinine _____
WBC _____Hb _____ Platelets _____

14. Hormone Therapy: ☐ No
☐ Yes Start Date_____ Intended Duration_____

16. Fiducials: ☐ Date placed _____
Location 1._____2._____ 3._____

Person completing form : Signature _____

Print Name _____

13.7 Appendix VII

TREATMENT FORM – Page 1 of 1

1. Name _____(last) _____(first)

2. RT Number _____

3. MRI scan for planning: ☐ yes
   ☐ no

4. Tumor category: ☐ Prostate Cancer, Low Risk
   ☐ Prostate Cancer, Intermediate Risk
   ☐ Prostate Cancer, High Risk

5. Tumor Details:

Maximum Diameter (cm)	GTV Volume (cc)	PTV Margin (mm)						PTV Volume (cc)
		A	P	R	L	S	I	

6. Treatment Portal Design:
   - ☐ Static gantry angle (coplanar), specify number of fields _____
   - ☐ Static gantry angle (non-coplanar), specify number of fields _____
   - ☐ Dynamic arc (coplanar), specify number of arcs _____
   - ☐ Dynamic arc (non-coplanar), specify number of arcs _____

7. Premedication:
   - ☐ Flomax dose_____mg, start date_____
   - ☐ Amifostine, dose 1500 mg PR
   - ☐ Bowel Prep, Stool softener, specify drug_____, and Fleet enema
   - ☐ Anti-anxiety, specify drug _____, dose _____mg,
   - ☐ Decadron, specify dose _____ mg
   - ☐ Analgesics, specify drug _____, dose _____ mg

8. Dose-Fractionation Scheme:

Total Dose (Gy)	Dose per Fx (Gy)	# Fx	Prescription IDL (%)	D_{max} (Gy)
36.25	7.25	5		

9. Dose to Normal Tissues:

STRUCTURE	VOLUME	CONSTRAINT(Gy)	DOSE (Gy)
Spinal Cord	D_{max}	22.5	
	< 10 cc	20	
Cauda Equina	D_{max}	27.5	
	< 10 cc	25	
Sacral Plexus	D_{max}	30	
	< 10 cc	27.5	
Anterior Rectal Wall	D_{max}	38	
Posterior Rectal Wall	D_{max}	20	
Lateral Rectal Wall	D_{max}	36.25	
Cumulative (L & R)	< 3 cc	50	
Rectum superior to prostate	D_{max}	30	
	< 10 cc	25	
Small Intestine	D_{max}	30	
	< 10 cc	25	
Prostatic Urethra	D_{max}	38	
Bladder	D_{max}	38	
	< 10 cc	20	
Penile Bulb	D_{max}	38	
	< 3 cc	30	
Femoral Heads Cumulative (L & R)	< 10 cc	30	
Skin not within fold	D_{max}	25	
Skin within fold (e.g. gluteal fold)	D_{max}	20	

Person completing form : Signature _____

Print Name _____

13.8 Appendix VIII

FOLLOW-UP VISIT FORM – Page 1 of 2

1. Name _____(last) _____(first)

2. RT Number _____

3. Date of Visit: ____/____/_____

4. Blood work:

Lab		Date:		Date:		Date:	
Total Bilirubin							
Albumin							
Alkaline Phosphatase							
ALT	AST						
PT	PTT						
Creatinine							

4. Radiation Therapy related adverse events

Adverse Event	CTC V3.0 Grade	Timing	Treatment	Comments
ACUTE				
☐ Fatigue				
☐ Weight loss				
☐ Diarrhea				
☐ Urinary frequency/urgency				
☐ Dysuria				
☐ Alopecia				
☐ Radiation dermatitis				
☐ Musculoskeletal Pain				
☐ Neuropathy, Motor				
☐ Neuropathy, Sensory				
LATE				
☐ GI Bleeding				
☐ GI Ulceration				
☐ GI Perforation				
☐ GI Stricture				
☐ Fistula				
☐ GU Bleeding				
☐ GUUlceration				
☐ GU Perforation				

☐ GU Stricture				
☐ Sterility				
☐ Impotence				
☐ Pelvic bone injury				
☐ Neuropathy, Motor				
☐ Neuropathy, Sensory				

5. Serious adverse event? ☐ No ☐ Yes, submit report to HIC

6. Has systemic therapy been given? ☐ No ☐ Yes

If yes, list therapy

Agent(s)	Start Date	Stop Date
_____	____/____/_____	____/____/_____
_____	____/____/_____	____/____/_____
_____	____/____/_____	____/____/_____

7. PSA since last follow-up visit ☐ No ☐ Yes, date ____ / ____ / _____

Current Level_____ng/ml

Nadir Level_____ng/ml

8. Radiologic Imaging since last follow-up visit ☐ No ☐ Yes, date ____ / ____ / _____

☐ CT Scan Date____/____/_____

☐ Bone Scan Date____/____/_____

9. Disease Status

☐ No evidence of tumor

☐ Biochemical recurrence Date____/____/_____

☐ Local recurrence within the treatment volume Date____/____/_____

☐ Distant recurrence, specify site _____Date____/____/_____

10. Additional treatment for recurrent disease

Surgery ☐ Yes ☐ No Date of surgery ____/____/_____

Hormone therapy, agents _____☐ Yes ☐ No Start date ____/____/_____

Other, specify _____☐ Yes ☐ No Start date ____/____/_____

11. Death ☐ No ☐ Yes, date ____/____/_____ Cause _____

Person completing form : Signature _____

Print Name _____