

The abstract of this paper is given below:

## Long-Term Outcomes from a Prospective Trial of Stereotactic Body Radiotherapy for Low-risk Prostate Cancer

Christopher R. King, PhD, MD<sup>1</sup>, James D. Brooks, MD<sup>2</sup>, Harcharan Gill, MD<sup>2</sup>, and Joseph C. Presti Jr, MD<sup>2</sup>

<sup>1</sup>Department of Radiation Oncology & Urology  
UCLA School of Medicine, Los Angeles, CA

<sup>2</sup>Department of Urology  
Stanford University School of Medicine, Stanford, CA

### ABSTRACT

**PURPOSE:** Hypo-fractionated radiotherapy has an intrinsically different normal tissue and tumor radiobiology. The results of a prospective trial of stereotactic body radiotherapy (SBRT) for prostate cancer with long-term patient-reported toxicity and tumor control rates are presented.

**METHODS & MATERIALS:** From 2003-2009, 67 patients with clinically localized low-risk prostate cancer were enrolled. Treatment consisted of 36.25Gy in 5 fractions using SBRT with the CyberKnife as the delivery technology. No patient received hormone therapy. Patient self-reported bladder and rectal toxicities were graded on the RTOG scale.

**RESULTS:** Median follow-up was 2.7 years. There were no grade 4 toxicities. RTOG grade 3, 2 and 1 bladder toxicities were seen in 3% (2 pts), 5% (3 pts) and 23% (13 pts) respectively. Dysuria exacerbated by urologic instrumentation accounted for both patients with grade 3 toxicity. Urinary incontinence, complete obstruction or persistent hematuria was not observed. Rectal grade 3, 2 and 1 toxicities were seen in 0, 2% (1 pt) and 12.5% (7 pts) respectively. Persistent rectal bleeding was not observed. Low grade toxicities were substantially less frequent with QOD vs. QD dose regimen ( $p=0.001$  for GI and  $p=0.007$  for GU). There were 2 PSA, biopsy-proven failures with negative metastatic workup. Median PSA at follow-up was  $0.5\pm 0.72$ ng/mL. The 5-year Kaplan-Meier PSA relapse-free survival was 94% (95% CI: 85-102%).

**CONCLUSION:** Significant late bladder and rectal toxicities from SBRT for prostate cancer are infrequent. PSA relapse-free survival at 5-years compares favorably with other definitive treatments. Patient accrual and careful follow-up on clinical trial is indicated.

UCLA Website: Stereotactic Body Radiotherapy (SBRT) for Prostate Cancer

### Table Side Effects

Comparison of late urinary (GU) and rectal (GI) toxicity on the RTOG scale from the dose-escalation arm of randomized trials and the current study of prostate SBRT (King CR et al. 2010, see publications). No severe grade 4 side effects were observed. Mild (grade 2) and moderate (grade 3) side effects are less than that observed with published standard radiotherapy.

Series	n	FU median	GI gr. 2	GI gr. 3	GU gr. 2	GU gr. 3
Dutch (a)	333	4.2 yrs	27%	5%	26%	13%
MDA (b)	151	8.7 yrs	19%	7%	7%	3%
MGH (c)	196	8.9 yrs	24%	1%	27%	2%
RT01 (d)	422	5.2 yrs	20%	6%	4%	4%
SBRT (e)	67	2.7 yrs	2%	0%	5%	3.5%

a : Dutch Multicenter Dose Escalation Trial (16), 78Gy 3DCRT (90% of patients treated with 3-field technique)

b : M.D. Anderson Dose Escalation Trial (17), 78Gy 3DCRT (4-field technique 46Gy followed by 6-field technique for boost dose)

c : Proton Radiation Oncology Group (18), 79.2 CGE (50.4Gy 3DCRT with 4-field technique + 28.8 Gy with 1- or 2-field technique for proton boost)

d : UK MRC RT01 Dose Escalation Trial (19), 74Gy 3DCRT (4-field technique)

e : current series

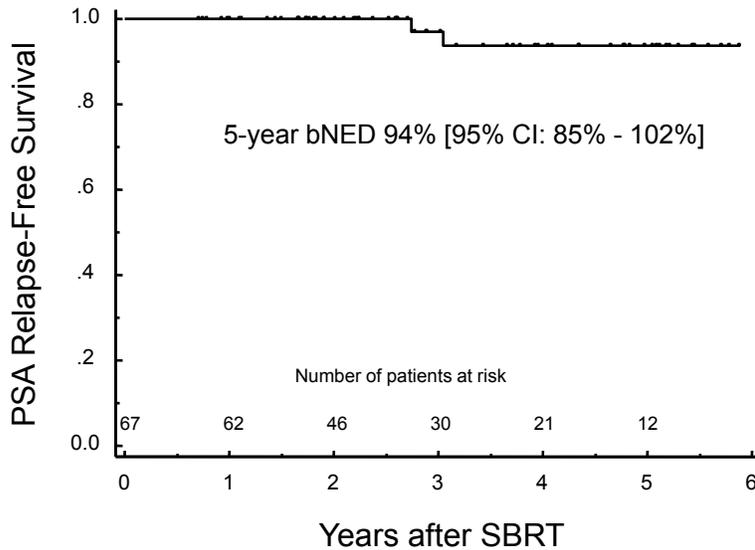
3DCRT: 3-dimensional conformal radiotherapy

CGE: cobalt gray equivalent (dose equivalent to Gy)

### Figure Prostate Cancer Control Rates with SBRT

The cancer control rates (PSA relapse-free survival) at 5-years after prostate SBRT is 94%. This very high cure rate is equal to that observed with either surgery, standard external beam radiotherapy, or brachytherapy. (King CR, et al. 2010, see Publications)

Figure 1



## SBRT Treatment Planning

There are three simple steps in the planning process before treatment can begin:

- Placement of three gold seeds markers (fiducials) as described above
- CT scan (typically same day after placement of fiducials)
- MRI (typically right after the CT scan)

### CT Simulation

A CT scan is used in order to plan the course of radiotherapy. This scan is used to calculate exact doses of radiation given a patient's individual anatomy. The CT scan will be obtained after the placement of the three gold markers. For this CT scan, as well as for the daily treatments, you will be asked to have a comfortably full bladder (this is usually achieved by drinking 2-3, 8-oz glasses of fluids within the hour before the scheduled time for the scan). The intent of a full bladder is to expand more bladder away from the volume that receives higher doses of radiation.

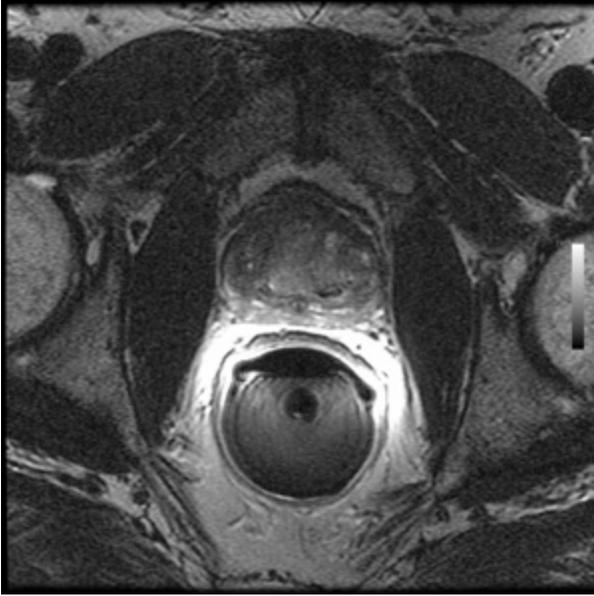
**Figure CT simulator:** The CT scan simulator is just like a regular CT scan in every respect. It is called a 'simulator' because it is integrated with our radiotherapy treatment planning software and allows us to simulate, or reproduce, the treatment delivery in the same anatomical position you are in during the CT scan. It takes 3-dimensional images of your internal anatomy in order to identify the prostate and all other pelvic organs. A mid-prostate axial slice is shown, with the prostate outlined with a thin red line, part of the bladder in thin yellow line. One of the gold fiducial markers can be seen and causes a streak artifact in the image. The femoral heads are also outlined in solid color.



From this scan your radiation oncologist will outline all of the internal anatomy, including the prostate, penile bulb, seminal vesicles (SVs), bladder, rectum, femoral heads, bowel, and lymph nodes. After that, the radiation physicist and the radiation oncologist work together in order to develop a treatment plan, one that can deliver the dose intended yet at the same time spare normal tissues and organs. Once the treatment plan is optimized, it is transferred to a computerized delivery system. Treatments generally can begin about 1-2 weeks after the CT scan has been obtained.

**Figure MRI Scanner:** The MRI scan is used to obtain a high resolution image of the prostate and pelvic organs. An image through the middle of the prostate gland is shown (the round doughnut shaped object near the bottom of the picture represents the rectal probe used to obtain this high resolution image, the prostate is located above that). The MRI can better evaluate where the cancer is within the prostate gland and confirm that the cancer has not extended beyond the capsule. This image is then fused with the CT scan image to plan with high precision the delivery of image-guided stereotactic radiotherapy.





Treatment typically takes about 15 minutes in total, including the set up time, and taking the setup x-rays. During the treatments you will meet with your UCLA radiation oncologist to review side effects and have an opportunity to ask further questions as well. You will be given a treatment schedule calendar. Treatments are done on an outpatient basis, and you will be able to drive to and from the treatment each day. There are in general no restrictions during the treatment course, and you can expect to be fully active.

## Radiotherapy Side Effects

Your doctors at UCLA will review with you the expected side effects. There are two organs that receive small doses of radiation due to their close proximity to the prostate, namely the bladder and the rectum. These temporary side effects appear gradually during the course of treatment and generally gradually resolve within 1-2 months after treatment. Your UCLA radiation oncologist will review with you how diet can be used to help minimize these side effects.

Transient bladder side effects of SBRT consist of irritative symptoms of frequency, urgency and possible very mild burning. When the bladder symptoms occur, your doctor will discuss with you ways to reduce them, primarily by reducing fluids and caffeine. Your radiation oncologist will determine whether you should be on a prescription medication to help with these side effects. The most common medication

prescribed is Flomax. Urinary incontinence or obstruction requiring a catheter has not been observed. Bleeding is also very rare but can occur especially when patients are taking blood thinners (such as aspirin, Plavix or Coumadin). Even when bleeding occurs, it will resolve by itself within a few weeks after treatments are completed.

Transient rectal or bowel side effects consist of the development of more frequent and looser bowel movements, and possibly more gas, but not diarrhea. These are generally very manageable with a dietary restriction from salads, fruits and vegetables. Occasionally, medication such as Imodium, will be prescribed to control bowel movement frequency. Bleeding with bowel movements is quite rare, and sometimes associated with taking blood thinners such as aspirin, Plavix or Coumadin, or among patients with hemorrhoids. As with urinary bleeding, this usually consists of only tiny amounts of blood, and for the majority of patients resolves by itself within a few weeks of completing treatment.

Erectile dysfunction (ED) is a long-term potential consequence of any treatment for prostate cancer, and depends on many factors unrelated to treatment (such as smoking history, current medications, diabetes, age). For SBRT the risk of developing ED is roughly 30-50% at 5 years after treatment. Medications such as Viagra, Cialis or Levitra are often still effective nevertheless.

Aside from these side effects, you will not experience skin burns, nausea, hair loss, or pain. Fatigue is usually not a side effect of the radiation itself or at most would be very mild.

## Follow up care after SBRT

Your UCLA doctors will establish a follow up schedule after you have completed your course. These follow up visits will be at regular time intervals, about every 3-4 month during the first 2 years, then every 6 months up to 5 years, and yearly thereafter.

The primary purpose of these follow ups is to monitor both side effects and tumor response. PSA will be obtained at each follow up. It is expected that PSA will fall to low levels, and reach a low point (called nadir) typically within less than 1 year. This low point is commonly below a level of 1.0 ng/mL. Unlike surgery, where PSA must reach undetectable levels after the removal of the prostate gland, PSA never reaches undetectable levels after any form of radiotherapy. The reason is that a small proportion of normal prostate gland will survive radiation and will produce low levels of background PSA.

Tumor is believed to be controlled when the PSA level remains low and steady. Sometimes, PSA will 'bounce' up and down by as much as 1-2 points during the first couple of years after treatment, and this is normal. Your doctors will discuss with you at each follow up the PSA where you stand.

## Contact Us for Prostate SBRT

The prostate treatment program at UCLA is open for eligible patients who fit the criteria for low to intermediate risk group (as outlined above). Your UCLA doctors will discuss with you whether you are a good candidate for this and answer all of the questions you might have regarding this unique clinical program. If you would like to set up an appointment with our physicians, or speak with our Nurse Coordinator, please call:

Anne Wagner, RN  
(310) xxx-xxxx

## Websites

As you can imagine, there are countless websites for cancer patients. The websites suggested are far from being an exhaustive list, but are very informative and have the advantage of not being sponsored by any industry, and therefore present fair, balanced and unbiased information.

US Prostate Cancer Charity  
[ustoo.org](http://ustoo.org)

US National Cancer Institute  
[cancernet.NCI.nih.gov](http://cancernet.NCI.nih.gov)

American Cancer Society  
[www.Cancer.org](http://www.Cancer.org)

---

## Terminology

PSA: prostate specific antigen

DRE: digital rectal examination

Gleason grade: cancer aggressiveness on a scale that bears the name of the pathologist, Dr. Gleason

T-stage: tumor stage, representing whether or not a nodule can be felt

CT: computer tomography

MRI: magnetic resonance imaging

SBRT: stereotactic body radiotherapy

Brachytherapy: surgical procedure whereby catheters and radioactive seeds are placed

LINAC: linear accelerator

Fiducials: reference gold markers

Gray: unit of radiation dose (1 Gray = 100 'rads')

## Peer Reviewed References for Prostate SBRT

King CR, Brooks JD, Gill H, Presti JC Jr.

Long-term outcomes of Stereotactic Body Radiotherapy for Localized Prostate Cancer: Results of a Prospective trial.

Int J Radiat Oncol Biol Phys. 2010 in press

King CR, Brooks JD, Gill H, Pawlicki T, Cotrutz C, Presti JC Jr.

Stereotactic body radiotherapy for localized prostate cancer: interim results of a prospective phase II clinical trial.

Int J Radiat Oncol Biol Phys. 2009 Mar 15;73(4):1043-8.

King CR, Lehmann J, Adler JR, Hai J.

CyberKnife radiotherapy for localized prostate cancer: rationale and technical feasibility.

Technol Cancer Res Treat. 2003 Feb;2(1):25-30.

Wiegner EA, King CR.

Sexual Function after Stereotactic Body Radiotherapy for Prostate Cancer: Results of a Prospective Clinical Trial.

Int J Radiat Oncol Biol Phys. 2010;

Friedland JL, Freeman DE, Masterson-McGary ME, Spellberg DM.

Stereotactic body radiotherapy: an emerging treatment approach for localized prostate cancer.

Technol Cancer Res Treat. 2009 Oct;8(5):387-92.

Townsend NC, Huth BJ, Ding W, Garber B, Mooreville M, Arrigo S, Lamond J, Brady LW.

Acute Toxicity after CyberKnife-Delivered Hypofractionated Radiotherapy for Treatment of Prostate Cancer.

Am J Clin Oncol. 2010;

Katz AJ, Santoro M, Ashley R, Diblasio F, Witten M.

Stereotactic body radiotherapy for organ-confined prostate cancer.

BMC Urol. 2010 Feb 1;10:1.

Madsen BL, Hsi RA, Pham HT, Fowler JF, Esagui L, Corman J.

Stereotactic hypofractionated accurate radiotherapy of the prostate (SHARP), 33.5 Gy in five fractions for localized disease: first clinical trial results.

Int J Radiat Oncol Biol Phys. 2007 Mar 15;67(4):1099-105.

Katz AJ.

CyberKnife radiosurgery for prostate cancer (review article).

Technol Cancer Res Treat. 2010 Oct;9(5):463-72.

UCLA Website: Stereotactic Body Radiotherapy (SBRT) for Prostate Cancer