

MRI-PLANNED STEREOTACTIC BODY RADIOTHERAPY FOR ORGAN-CONFINED PROSTATE CANCER: FEASIBILITY AND EARLY RESULTS

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INTRODUCTION

Stereotactic body radiotherapy (SBRT) offers theoretical advantages for treating prostate cancer. The purported low a/b ratio of prostate cancer¹⁻⁷ favors hypofractionated dose schedules. Conformal dose delivery should minimize dose to radiosensitive normal tissues adjacent the prostate. Delivering high radiation doses to the prostate requires correction for intrafractional prostate motion, which can be significant⁸⁻¹⁰. Thus real-time image guidance is required. Finally, precise treatment delivery implies accurate prostate localization, which is best achieved using MR imaging¹¹⁻¹².

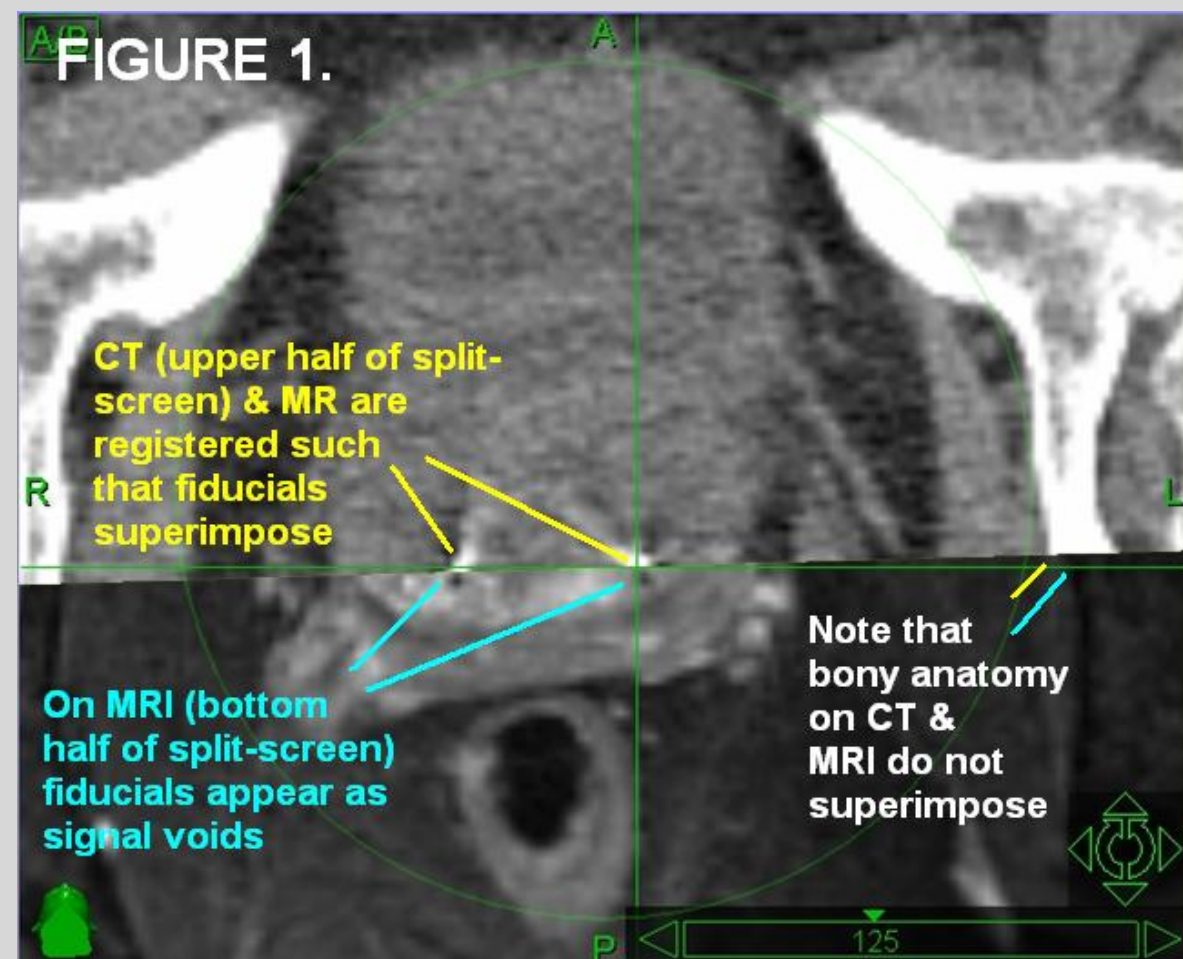
The CyberKnife SBRT platform can deliver dose with brachytherapy-like conformality¹³. Evaluations of actual treatment delivery confirm that its real-time image guidance system can treat with approximately 1mm accuracy¹⁴. We thus employed the CyberKnife with fused CT and MRI planning in a prospective study of SBRT for organ-confined prostate cancer. Feasibility, early toxicity and PSA responses are reported.

MATERIALS AND METHODS

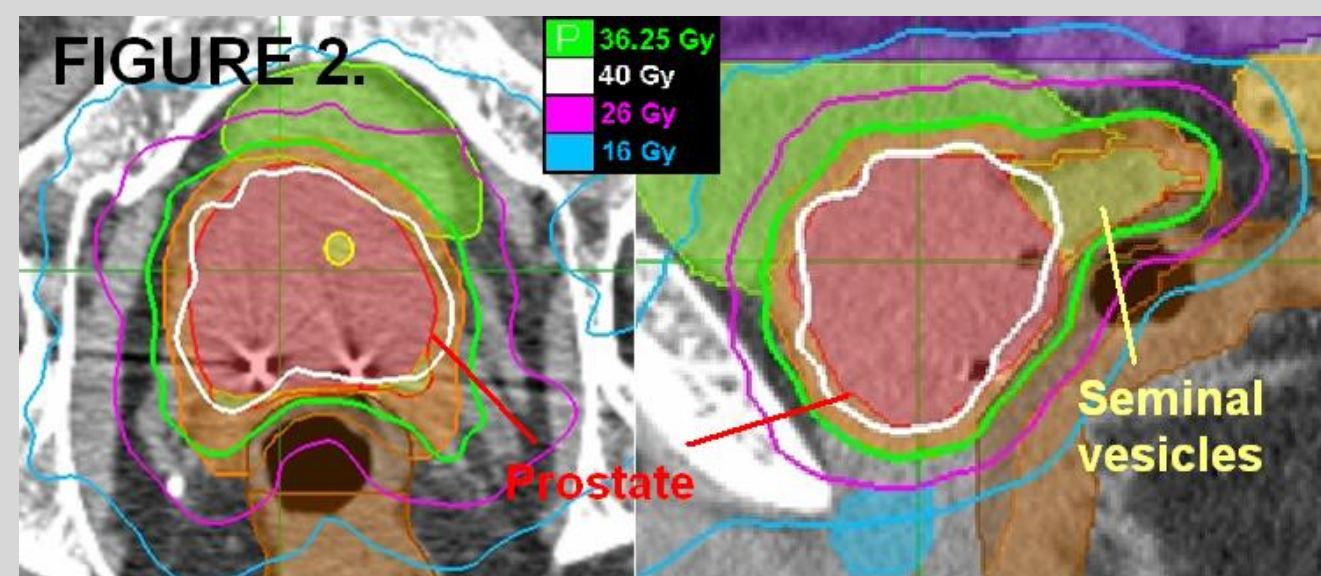
We report on the first 35 low- and intermediate-risk prostate cancer patients received SBRT using the CyberKnife. No supplemental external beam radiotherapy was administered. No patient received hormone therapy during or following treatment; six patients had received antiandrogen therapy prior to treatment. Twenty-one patients were part of a pilot study, and 14 patients were enrolled in an industry-sponsored multi-institutional trial¹⁵. Twenty low-risk patients had pre-treatment clinical characteristics defined by D'Amico: clinical stage T1b-T2a, Gleason ≤ 6 , and PSA < 10 ng/ml. The remaining 15 intermediate-risk patients were defined according to inclusion criteria for RTOG 0232: clinical stage T1c-T2b, with either Gleason = 7 and PSA < 10 ng/ml, or Gleason < 7 and PSA 10-20ng/ml. Patient characteristics are described in table 1.

Table 1. Patient Characteristics			# pts (% of risk grp)
Low Risk (20 pts)	PSA	< 10 ng/ml	20 (100%)
	Gleason Score	5	3 (15%)
		6	17 (85%)
	Clinical State	T1c	14 (70%)
Intermediate Risk (15 pts)	PSA	< 10 ng/ml	12 (80%)
		10 – 20 ng/ml	3 (20%)
	Gleason Score	3+3	3 (20%)
		3+4	8 (53%)
		4+3	4 (27%)
	Clinical State	T1c	7 (47%)
		T2a	4 (27%)
		T2b	4 (27%)

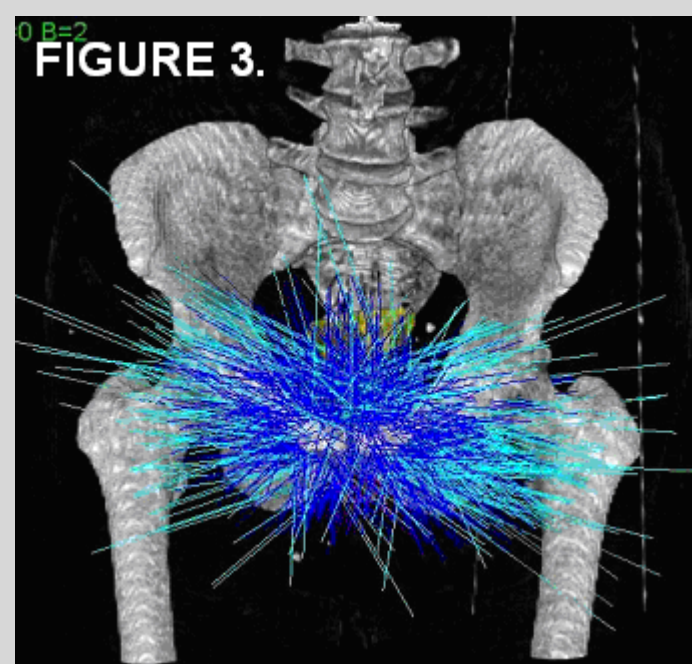
All patients had at least four gold fiducials placed for target tracking. MRI was used to assist in target localization in 34 patients; in one patient MR imaging was contraindicated. A T2-weighted fast spin echo sequence was employed in all patients. Since prostate position relative to bony anatomy varies with time, MRI/CT registration was performed using fiducials as landmarks (see figure 1).



Treatment: For low-risk patients, the PTV was defined as the prostate plus 3mm posteriorly, and 5mm in all other dimensions. For intermediate-risk patients, the PTV was defined as the prostate plus the proximal 2cm of seminal vesicles expanded 3-5mm. The PTV was prescribed 36.25Gy in five fractions of 7.25Gy each. This protocol differed from earlier reports^{16,17} in that the dose to the prostate was escalated using a simultaneous boost: the prostate (with no margin) D95% was prescribed 40Gy in five fractions of 8G each (see figure 2).



The CyberKnife radiosurgery system was used to treat all patients, correcting for both translational and rotational target motion. 150-200 beams were typically employed (figure 3: light blue lines are active beams), using one or two collimators. Treatment was delivered daily.

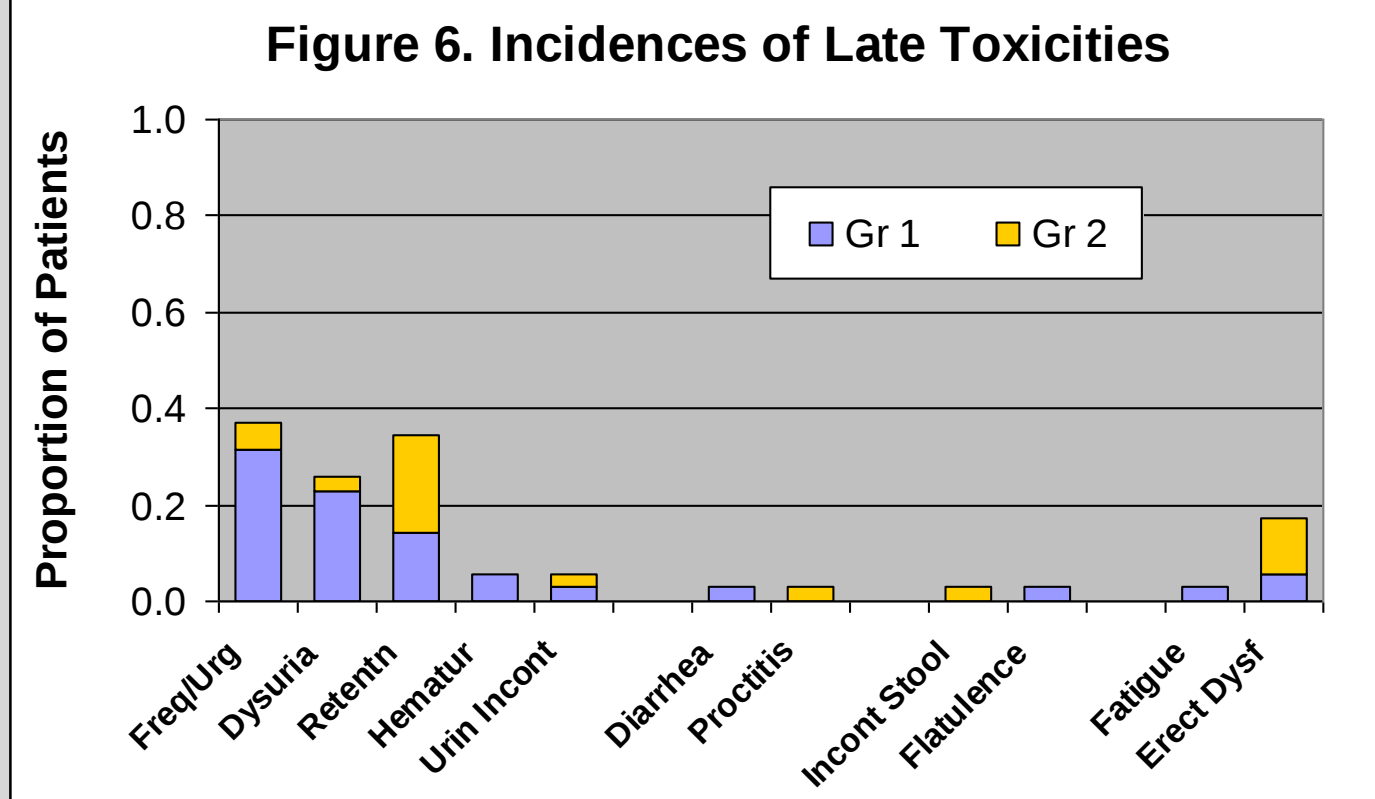
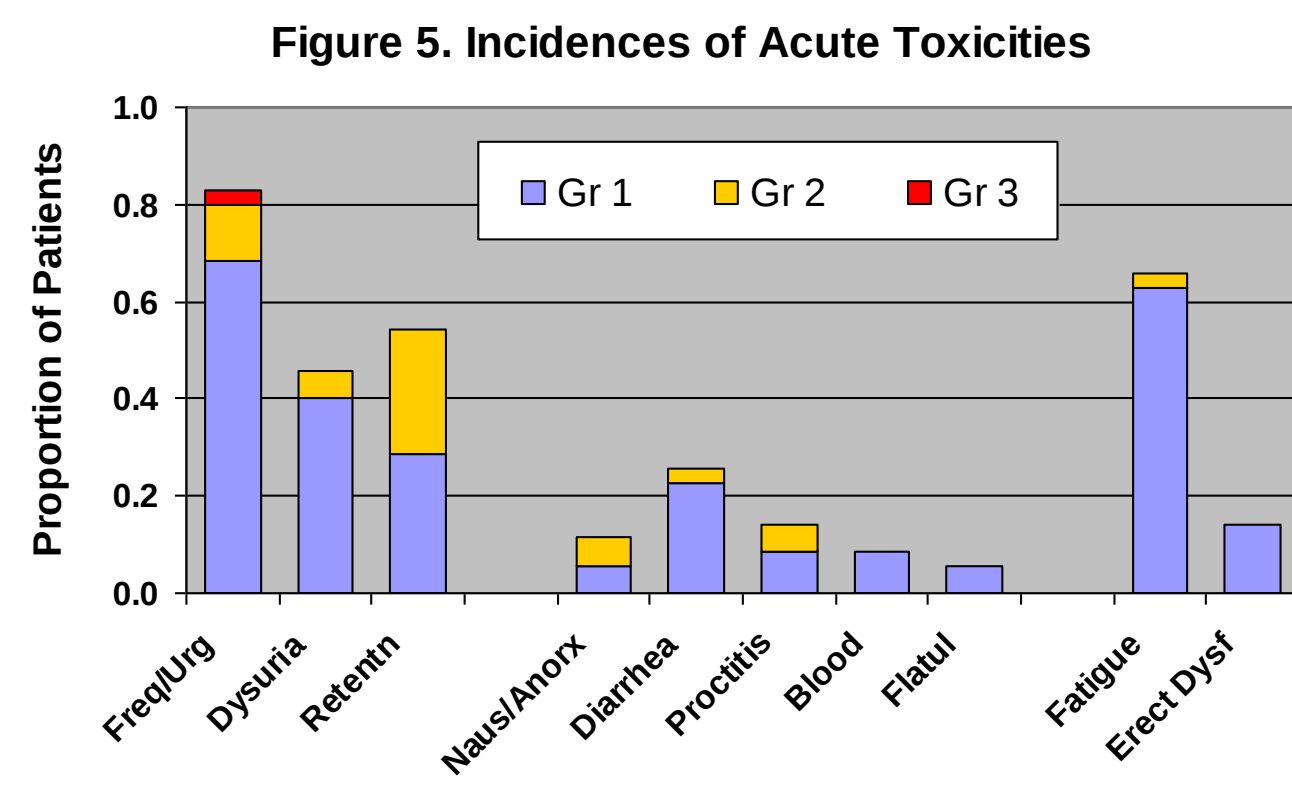
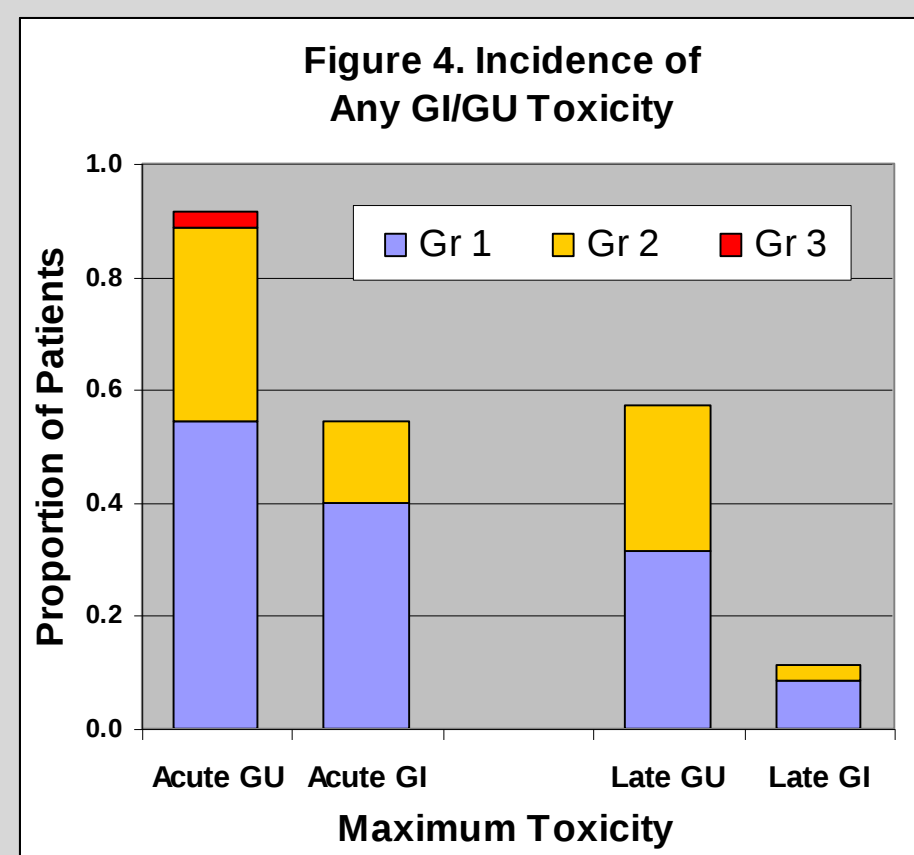


Toxicities were assessed using CTCAE v.3 criteria. Domain-specific quality of life was assessed using validated instruments: International Prostate Symptom Score (IPSS), Expanded Prostate Cancer Index Composite Short Form (EPIC-26), and Sexual Health Inventory for Men (SHIM). QOL outcomes will be the subject of later reports. PSA responses were recorded; biochemical failures were reported using ASTRO and nadir+2 definitions.

RESULTS

Median follow-up was 18 months. Seven patients were followed three years or longer. One patient experienced CTCAE grade 3 acute (< 3 months after treatment) toxicity: urination more frequent than hourly (no need for catheter). This occurred one week after treatment, and improved after approximately one week. No grade 3 late (> 3 months after treatment) toxicities were observed. Grade 1-2 acute GU and GI toxicities were observed in 88% and 54% of patients, respectively (see figure 4).

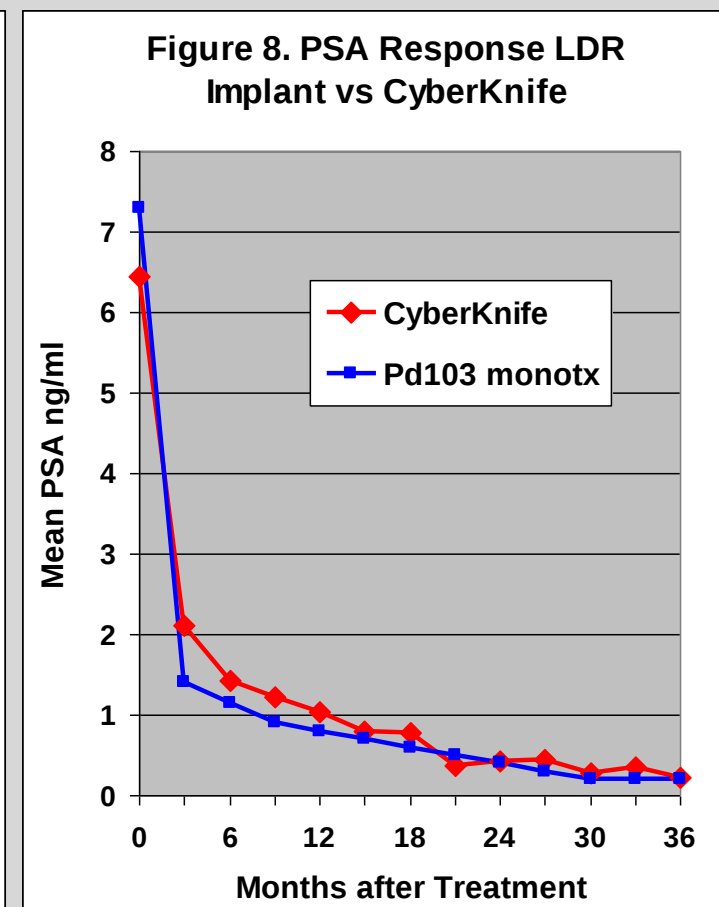
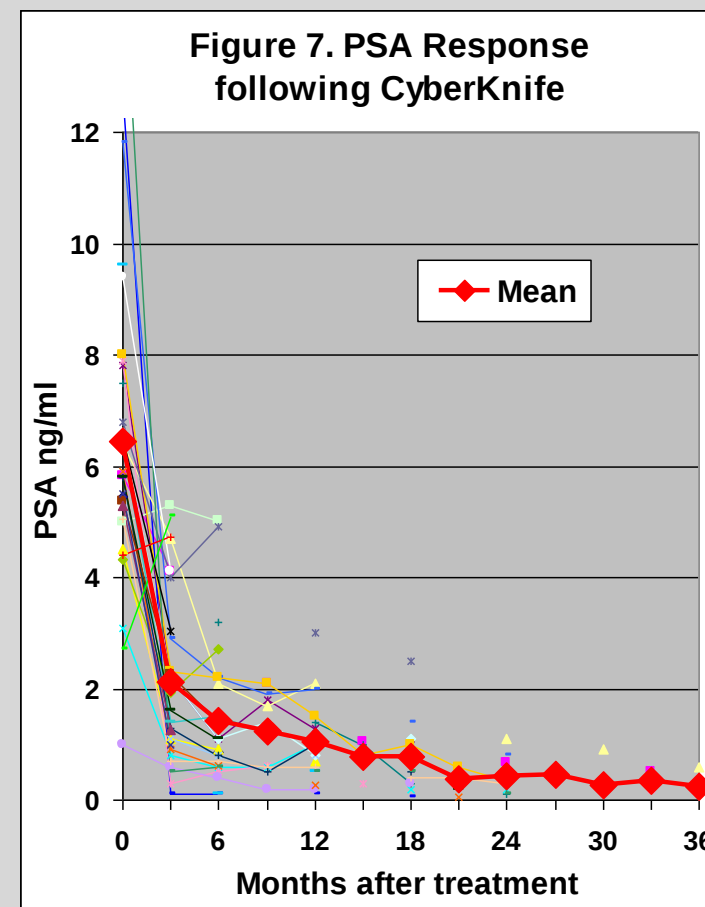
The most common acute toxicities (see figure 5) were frequency/urgency (83%), dysuria (46%), urinary retention (55%), frequent/loose stools (26%), and fatigue (66%). Grade 1-2 late GU and GI toxicities were reported in 57% and 12% of patients, respectively (figure 4).



The most common late toxicities were frequency/urgency (37%), dysuria (26%) and urinary retention (34%). Incidences of other late toxicities are illustrated in figure 6.

All grade 2 urinary retentions were due to medication use (typically an alpha blocker only); no patient required urinary catheterization.

PSA OUTCOMES: No patient demonstrated PSA failure by either ASTRO or nadir+2 definitions. For the 15 patients followed for more than 2 years, 12 had a PSA nadir of 0.5ng/ml or less; the mean 24-month PSA was 0.43ng/ml. Six of seven patients with 3+ years of follow-up have PSA values less than 0.3ng/ml, with a mean of 0.23ng/ml (see figure 7). This PSA response is similar to that seen following LDR brachytherapy¹⁸ (figure 8). One or more benign PSA rises were observed in 12 patients.



CONCLUSIONS

The feasibility of dose-escalated SBRT using fused MRI/CT planning, delivered with real-time image guidance on the CyberKnife was demonstrated in a small group of patients. Acute and early late toxicities were acceptable, and PSA responses appear favorable, within the limited follow-up period. We await further accrual on the multi-institutional protocol and longer follow-up to confirm acceptable toxicities, and to assess quality of life and biochemical outcomes.

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