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 cancer[1-7] 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 significant[8-10]. Thus real-time image guidance is required. Finally, precise treatment delivery implies accurate prostate localization, which is best achieved using MR imaging[11-12].

The CyberKnife SBRT platform can deliver dose with brachytherapy-like conformality[13]. Evaluations of actual treatment delivery confirm that its real-time image guidance system can treat with approximately 1mm accuracy[14]. We thus employed the CyberKnife with fused CT and MRI planning in a prospective study of SBRT for organ-confined prostate cancer. Feasibility and early toxicity are reported.

MATERIALS AND METHODS

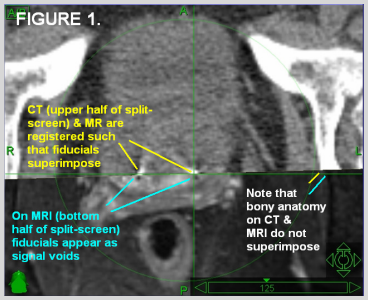
29 low- and intermediate-risk prostate cancer patients received SBRT monotherapy using the CyberKnife. Eighteen patients were part of a pilot study, and 11 patients were enrolled in an industry-sponsored multi-institutional trial[15]. Eighteen low-risk patients had pre-treatment clinical characteristics defined by D'Amico: clinical stage T1b-T2a, Gleason <=6, and PSA < 10ng/ml. The remaining nine intermediate-risk patients were defined according to inclusion criteria for RTOG 0232: clinical stage T1c-T2b, with either Gleason = 7 and PSA < 10ng/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 (18 pts)	PSA	< 10 ng/ml	18 (100%)
	Gleason Score	5	3 (17%)
		6	15 (83%)
	Clinical State	T1c	13 (72%)
		T2a	5 (28%)
Intermediate Risk (11 pts)	PSA	< 10 ng/ml	8 (73%)
		10 – 20 ng/ml	3 (27%)
	Gleason Score	3+3	3 (27%)
		3+4	5 (45%)
		4+3	3 (27%)
	Clinical State	T1c	5 (45%)
		T2a	3 (27%)
		T2b	3 (27%)

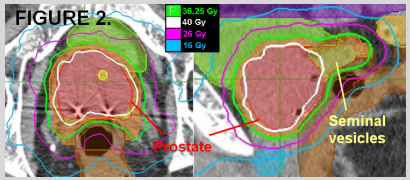
All patients had at least four gold fiducials placed for target tracking. MRI was used to assist in target localization in 28 patients; in one patient MR imaging was contraindicated. A T2-weighted fast spin echo sequence was employed in all patients. Since prostate position relative to bony anatomy varies with time, MRI/CT registration was performed using fiducials as landmarks (see figure 1).

FIGURE 1.



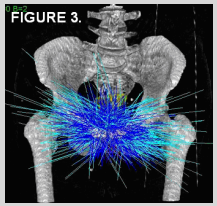
Treatment: For low-risk patients, the PTV was defined as the prostate plus 3mm posteriorly, and 5mm in all other dimensions. For intermediate-risk patients, the PTV was defined as the prostate plus the proximal 2cm of seminal vesicles expanded 3-5mm. At least 95% of the PTV received 36.25Gy in five fractions 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).

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.

FIGURE 3.



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. Four patients were followed for 30 months or longer. There were no CTCAE grade 3 or greater acute (< 3 months after treatment) or late (> 3 months after treatment) toxicities. Grade 1-2 acute GU and GI toxicities were observed in 96% and 48% of patients, respectively (see figure 4). Of patients reporting acute or late grade 2 GU toxicities, 80% were due to taking alpha-blockers only.

The most common acute toxicities (see figure 5) were frequency/urgency (88%), dysuria (40%), urinary retention (56%), frequent/loose stools (24%), and fatigue (64%). Grade 1-2 late GU and GI toxicities were reported in 39% and 4% patients, respectively (figure 4).

FIGURE 4. INCIDENCE OF ANY GI/GU TOXICITY: ACUTE & LATE

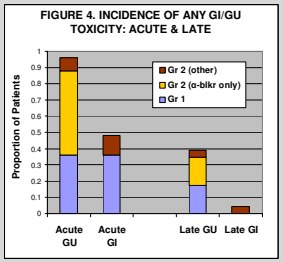
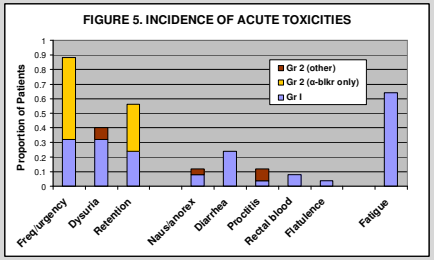
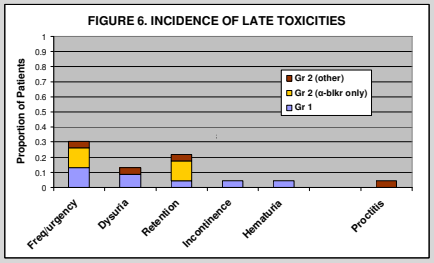


FIGURE 5. INCIDENCE OF ACUTE TOXICITIES



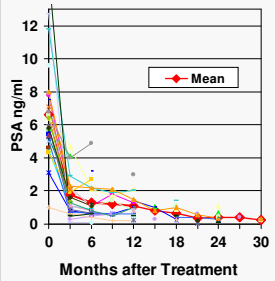
The most common late toxicities were frequency/urgency (30%) and urinary retention (22%). Incidences of other late toxicities are illustrated in figure 6.

FIGURE 6. INCIDENCE OF LATE TOXICITIES



PSA OUTCOMES: No patient demonstrated PSA failure by either ASTRO or nadir+2 definitions. For the 12 patients followed for more than 2 years, 10 had a PSA nadir of 0.5ng/ml or less; the mean 24-month PSA was 0.4ng/ml. All 4 patients with 30+ months of follow-up have PSA values less than 0.5ng/ml, with a mean of 0.2ng/ml (see figure 7). One or more benign PSA rises were observed in 11 patients.

FIGURE 7. PSA RESPONSE



CONCLUSIONS

The feasibility of dose-escalated SBRT using fused MRI/CT planning, delivered with near real-time image guidance on the CyberKnife radiosurgery platform was demonstrated in a small group of patients. Acute and early late toxicities were acceptable, and early 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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