ROBOTIC RADIOSURGERY FOR ORGAN-CONFINED PROSTATE CANCER: EARLY TOXICITY OUTCOMES FROM A MULTI-INSTITUTIONAL TRIAL

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INTRODUCTION
Stereotactic radiosurgery (SRS) is the precise delivery of an ablative radiation dose to a specific target from numerous converging Winston-radiosurgery beams. The low uGy ratio of prostate cancer favors the hypofractionated dose schedules inherent to SRS. Since prostate motion can be substantial[1-3], SRS of the prostate requires a targeting system to correct for intrafractional organ motion. The prostate is adjacent to radiosensitive organs, so the ablative radiation dose must conform closely to the targeted gland, and must rapidly decline at the bladder and rectum. A non-isocentric robotic radiosurgical platform (CyberKnife, Accuray, Inc.) appears ideal for prostate SRS, as it can localize and treat the moving prostate with high accuracy[4], and delivers dose with brachytherapy-like conformity[5].

Several single-institution reports[6-8] describe acceptable toxicity and favorable PSA responses in the treatment of prostate cancer with five fractions of 7-8 Gy using the CyberKnife. We designed a prospective multi-institution trial[9] employing SRS to treat organ-confined prostate cancer, with primary objectives to evaluate rates of toxicity and freedom from biochemical relapse. Early toxicity and PSA responses are reported, as well as quality of life (QOL) outcomes in patients with 1+ years of follow-up.

TREATMENT: All patients had at least three gold fiducials placed for target tracking. MR imaging was used to assist in target localization. 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-mm. The PTV was prescribed 36.25Gy in five fractions of 7.25Gy each. This protocol differed from earlier reports[6-9] in that the dose to the prostate was escalated using a simultaneous boost: the prostate D95% was prescribed 40Gy in five fractions of 8Gy each (see figure 2). Assuming an uGy ratio of 32uGy, this yields a BED(2) equivalent dose of 200.8Gy, comparable to that delivered with LDR brachytherapy. No supplemental external beam radiotherapy was administered.

The CyberKnife SRS system was used to treat all patients, correcting for both translational and rotational target motion in real time. 150-200 beams were typically employed (figure 3: light blue lines are active beams). A typical fraction was delivered in under one hour, and the 5-fraction course was completed in 5-11 days.

Toxicity was assessed using CTCAE v3 criteria. Rates of acute toxicities were reported for all patients with 3+ months follow-up. Late toxicities (occurring > 3 months after treatment) were reported for patients with ≥ 12-months follow-up. The AUA Symptom Index and the SHIM (Sexual Health Inventory for Men) were used to assess pre- and post-treatment urinary and sexual QOL. PSA responses were recorded, biochemical failures were reported using n+2 definition.

RESULTS
Since November 2007, 211 hormone-naive patients from 17 institutions were treated and followed 3+ months. Of these patients, 98 had ≥ 12-months follow-up. No grade 3 acute toxicities were reported. Grade 2 GU and GI toxicities occurred in 20% and 9% of patients, respectively. Three patients (1.4%) required temporary catheter placement for acute urinary retention. Grade 2 late GU and GI toxicities occurred in 5% and 14% of patients, respectively. One late Grade 3 toxicity (bladder neck necrosis 1 year after treatment) was reported. These incidences are illustrated in figure 4.

The most common acute toxicities (see figure 5) were frequency/urgency (59%), dysuria (48%), urinary retention (39%), diarrhea (29%), proctitis (12%), rectal bleeding (11%), and fatigue (20%). The most common late toxicities were frequency/urgency (12%), dysuria (10%), urinary retention (14%), and diarrhea (5%). Incidences of the various grades of late toxicities are illustrated in figure 6.

CONCLUSIONS
In a multi-institutional study evaluating CyberKnife SRS for patients with organ-confined prostate cancer, rates of serious acute and early late toxicities were modest. Urinary QOL was adversely affected by acute toxicity, but by 3 months had returned to near-normal. At one year follow-up, decrements in sexual QOL appeared to be within range of other radiotherapy modalities. Initial PSA responses are encouraging. We await longer follow-up to assess late toxicity and efficacy.

REFERENCES