Preliminary Analysis of 3DCRT vs IMRT on the High Dose Arm of the RTOG 0126 Prostate Cancer Trial: Toxicity Report

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Purpose/Objective(s): A preliminary analysis of clinical & treatment characteristics associated with acute & late toxicity in men receiving high dose RT on a phase III RTOG dose escalation trial.

Materials/Methods: The trial started with 3DCRT and amended after 1 year to allow IMRT. Patients (pts) treated with 3DCRT received 55.8Gy to a PTV that included the prostate & proximal seminal vesicles (P+pSV) followed by a 23.4Gy to prostate only. IMRT pts were treated to the P+pSV to 79.2Gy. CTC v 2.0 & the RTOG/EORTC late morbidity scores were used for acute & late effects. Univariate & multivariate comparisons for acute effects were done with chi-squared & logistic regression; time to late effects with Gray's test and the Fine-Gray method.

Results: 748 of 763 pts randomized to the 79.2 Gy arm of RTOG 0126 were eligible & evaluable. 491 & 257 were treated with 3DCRT & IMRT, respectively. Median follow-up was 4.6y & 3.5y for 3DCRT & IMRT pts. Median D98 delivered to the PTV7920 was 80Gy for 3DCRT & 79.2Gy for IMRT. The median % of the bladder receiving at least xGy (pVx) for pV65, pV70 and pV75 were 25.3%, 22.2%, and 17.7% for 3DCRT and 19.7%, 16.6% and 13.1% for IMRT. The median rectum pV65, pV70 & pV75 were 27.4%, 21.7%, & 15.8% for 3DCRT and 23.0%, 18.2% & 13.0% for IMRT. For both bladder and rectum, the pVx was significantly lower with IMRT for 65, 70, and 75Gy (all $p<0.0001$). Acute toxicity; there are 16.9% Grade (G2), 2.5% G 3 and no G 4 or 5 in the 3D-CRT group; there are 13.9% G 2, 2.4% G 3, 0.4% G 4, and no G 5 in the IMRT group. Late toxicity; there are 23.6% G 2, 8.9% G 3, 0.4% G 4, and 0.2% G 5 (1 death) with 3D-CRT group; there are 19.9% G2, 4.7% G 3, 0.4% G 4, and no G 5 with IMRT. For G 2+ acute GI/GU toxicity, both univariate and multivariate analyses, show a statistically significant decrease in G 2+ acute collective GI/GU toxicity for IMRT. There are no significant differences with 3DCRT or IMRT for acute or late, G 2+ or 3+ GU toxicities. Despite a small number of events, univariate analysis shows a statistically significant decrease in late G 2+ GI toxicity for IMRT ($p=0.039$). On multivariate analysis, IMRT shows a trend for a 26% reduction in G 2+ late GI toxicity ($p=0.099$). Acute G 3+ toxicity was significantly associated with late G 3+ toxicity. With DVH data in the multivariate analysis, RT modality is not significant whereas white race & a % rectal V70 >=15% are significantly associated with G 2+ rectal toxicity.

Conclusions: IMRT is associated with a statistically significant reduction in acute G 2+ GI/GU toxicity. There is a trend for a clinically meaningful reduction in late G 2+ GI toxicity with IMRT. The occurrence of acute GI toxicity and large (>15%) volumes of rectum exceeding 70Gy are associated with late rectal toxicity.

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