**A Twenty-Year Update on the Outcomes of a Randomized Dose-Escalation Trial for Prostate Cancer**

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**Purpose/Objective(s):** Given the indolent nature of prostate cancer and prolonged time to progression, we sought to report the long-term results of a randomized radiation therapy dose escalation trial.

**Materials/Methods:** From 1993-1998, a total of 301 low to high risk prostate cancer patients were randomized to external beam radiation using 70 Gy vs. 78 Gy without planned neoadjuvant or adjuvant hormone therapy. Recurrences were defined as follows: Biochemical failure as per the Phoenix criteria; local failure as palpable disease confirmed via biopsy or biopsy done due to rising PSA; regional nodal failure diagnosed with a CT scan and/or biopsy; and distant metastasis diagnosed by a bone scan. Death was confirmed through chart review, Social Security Death Index, and/or family contact. Kaplan-Meier analysis was used to determine rates of freedom from biochemical or clinical failure (FFF), disease-specific survival, and overall survival. A Cox proportional hazards model was used for multivariate analysis.

**Results:** Median follow-up was 14.3 years. There was no treatment arm difference in age, ethnicity, PSA, Gleason score, or NCCN risk stratification. Of the 301 patients, 214 were deceased as of December 2017. Of the living patients, 22 requested to stop contact and/or were lost to follow-up. Median time since last contact among all living patients was 24 months (range: 0 - 231). Comparing the 70 Gy vs. 78 Gy arms, FFF at 20 years was 53.8% vs. 74.3%, respectively (p=0.0018), largely driven by improvements in both biochemical failure (24.4% vs. 13.5%, respectively; p=0.05) and distant failure (17.4% vs. 5.3%, respectively; p=0.020). FFF was significantly higher in the 78 Gy arm for low (p=0.035) and intermediate (p=0.020) NCCN risk groups. Multivariate factors that predict for FFF include pre-treatment PSA >10 ng/ml, Gleason score, and tumor stage. Out of 107 failures, 91 received salvage treatment at a median of 57.7 months from protocol treatment (range: 7.7 – 257.5; p=0.553). There was no significant difference in overall or disease-specific survival, although, at 20 years after treatment, the latter was 68.4% vs. 82.3% favoring dose escalation (HR: 0.57, CI 0.31-1.06; p=0.074). A total of 7 patients (2.3%) had secondary malignancies, possibly radiation-related: 1 rectal and 6 bladder, without a difference between treatment arms.

**Conclusion:** With 20 years follow up, dose escalation continues to confer significantly improved freedom from biochemical and distant metastatic failure in patients with localized prostate cancer. Death from prostate cancer was trending toward significance and was nearly halved by dose escalation. Among all patients, long-term secondary malignancy rates are well within the range of studies with shorter follow-up. This group of patients offers unique insight into the impact of increased radiation dose.