

1068 Defining the Optimal Hypofractionation Schedule: An Outcomes Nomogram for Multi-Fraction High-Dose-Rate Brachytherapy Boost (HDRBB) for Prostate Cancer Based on 1,934 Cases

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Purpose/Objective(s): To model multicentre HDRBB outcomes with particular regard to designing optimal fractionation schedules.

Materials/Methods: Data of 1,934 men treated with HDRBB implants from 1991–2003 for T1-3 clinically localized prostate cancer at 4 institutions were analysed. Combined external beam radiotherapy (EBRT) and HDRBB to the prostate was used, and 49% also had androgen deprivation therapy (ADT) given with treatment for a median of 6 months. HDRBB was performed prior to, during, or after EBRT in 32%, 21% and 47% of cases respectively, with the number of implant procedures being 1, 2 or 3 in 27%, 69% and 4% respectively. EBRT was delivered to the prostate only in 91% of cases. Follow-up was determined from the date of completing the last radiation treatment. The primary endpoint was nadir + 2 ng/mL “Phoenix definition” biochemical failure (bF) using raw PSA data (n = 19528), and outcome modelling was based on a proportional hazards analysis.

Results: Median biochemical follow-up was 52 months, with the median age, initial prostate-specific antigen (PSA) and biopsy Gleason score (GS) being 67 years, 9.1 ng/mL and 7 respectively, while 54% had stage T1-2a tumours and 12% T3. This equated to NCCN risk grouping numbers of: low risk 9%; intermediate risk 60%; high risk 31%. The EBRT dose was >44 Gy in 48% (median 46 Gy) and 36 Gy in 27%. Four fraction HDRBB (n = 1197) ranged from 4–6 Gy per fraction, the 3 fraction (n = 408) implants from 5.5–6.5 Gy per fraction, and the 2 fraction (n = 329) from 8.25–11.5 Gy. The commonest HDR schedules were 4 × 6 Gy fractions (n = 743), 3 × 6.5 Gy (n = 223), 3 × 6 Gy (n = 155), 4 × 5 Gy (n = 137), or 2 × 9.5 Gy (n = 107).

The freedom from bF (FFbF) for low, intermediate and high risk cases at 5 years was estimated at 85.5% (95% confidence interval [95% CI] 79.1–90.7%), 85.3% (95% CI 83.7–88.7%) and 72.9% (95% CI 68.6–76.9%) respectively. In multivariate analysis, increasing PSA, GS and stage were associated with a significantly worse FFbF ($p \leq 0.0001$ for all) as was a younger age ($p = 0.0006$). ADT use was also of significant benefit ($p = 0.029$), increasing the 5 year FFbF of the intermediate risk group from 84.1% (95% CI 80.9–87.2%) to 89.3% (95% CI 85.8–92.5%) for example. The dose of EBRT was not significant in determining outcome, nor the order of the HDRBB.

Both the dose per fraction and the number of fractions of HDRBB strongly predicted FFbF ($p < 0.0001$ for both). Non-parametric non-linear modelling of HDRBB fraction size showed a prominent dose response effect in 3 and 4 fraction implants. Two fraction implants were all associated with low failure hazards, despite not showing an obvious dose response. A nomogram to displaying these variables was developed with a bootstrap-corrected concordance index of 0.67.

Conclusions: This study shows HDRBB at current fraction sizes to be an effective treatment for localized prostate cancer, and a nomogram to aid treatment decision making is presented. Optimal HDRBB fractionation remains difficult to define and these data suggest that large studies with long-term follow-up will be required to demonstrate differences. The apparent small impact of neoadjuvant ADT in addition to HDRBB needs further definition.

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1069 The Influence of Age as a Predictor of Outcome in Prostate Cancer Patients Treated on RTOG Trials

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Purpose/Objective(s): Age is controversial as a predictor of prostate cancer outcome, with some investigators feeling that younger age portends a worse outcome, while others feel the opposite. In addition to the expected influence of age at diagnosis upon overall survival, we hypothesized that age would impact local failure and distant metastases in patients treated with radiation therapy.

Materials/Methods: Analyzable patients treated on five RTOG prostate trials (7506, 7706, 8531, 8610 and 9202) were included in this study. Overall survival was defined as death by any cause, local failure was defined as clinical evidence of local recurrence by palpation or imaging methods, or stable disease beyond 18 months, and distant metastases were defined by clinical or imaging evidence of distant disease. The Kaplan-Meier method is used to estimate the overall survival and the log-rank test is used to test significance; and the cumulative incidence method is used to estimate the local failure rate and distant metastasis rate and Gray’s test is used to test significance. The outcomes were modeled using multivariate Cox proportional hazards regression with the following covariates: Clinical T-stage, Gleason score, hormone therapy prescribed in protocol, study, and pre-enrollment surgery, and study number.

Results: 3939 patients were available for analysis, with mean follow-up of 9.1 years for patients under 70 and 7.7 years for patients above age 70. On multivariate analysis, age greater than 70 was associated with a hazard ratio of 1.49 for worse overall survival ($p < .0001$). There was no significant difference in local control between patients greater than 70 and patients less than 70 ($p = .92$). Patients less than 70 were at a higher risk of distant metastases with a hazard ratio of 1.24 (p -value = 0.0006).

Conclusions: There is no difference in local control between patients greater than 70 and patients less than 70 in a series of RTOG trials. Patients younger than 70 have a higher risk of distant metastases, even when controlling for known prognostic factors such as T stage, Gleason score and hormonal use.

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