

The Optimal Timing of Salvage Radiotherapy following Radical Prostatectomy. A Meta-Analysis

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Purpose/Objective(s): Salvage radiotherapy (SRT) following radical prostatectomy can potentially eradicate residual microscopic disease. Defining the optimal patient and treatment factors is essential and is particularly relevant within the context of adjuvant vs. early vs. delayed post-op RT.

Materials/Methods: A meta-analysis of all indexed peer-reviewed published SRT studies from 1996 to 2010 was performed to identify the pathologic factors (Gleason grade, extracapsular extension, seminal vesicle involvement, margin status), the clinical factor (PSA level prior to SRT) and the treatment factors (RT dose, concurrent use of androgen deprivation) associated with relapse-free survival (RFS) after SRT. RFS was uniformly defined as a PSA > 0.2 ng/mL following SRT. Only studies reporting Kaplan-Meier RFS at a minimum of 3 years were included. Radio-biological interpretation of biochemical tumor control is used to provide the framework for the observed relationships.

Results: A total of 42 studies encompassing 6098 patients satisfied the meta-analysis entry criteria. Median follow-up was on average 47 +/- 22 months. Only PSA level prior to SRT ($p = 0.0002$) and RT dose ($p = 0.0060$) had a significant and independent association with RFS. There was an average 2.5% loss in RFS for each incremental 0.1 ng/mL PSA at the time of SRT. With a PSA level of < 0.2 ng/mL prior to SRT, the RFS approached 63%. The RFS vs. pre-SRT PSA level relationship is well fit by an exponential curve ($p = 0.0001$), is consistent with the Poisson model of tumor control, and is indicative that post-op PSA level is an accurate measure of the burden of microscopic disease. Dose-response is well fit by a sigmoidal curve ($p = 0.0017$) with a The TCD50 of 67.8 Gy. Dose for salvage RT in the range of 60 to 70 Gy appears to be on the middle steep part of the sigmoidal dose response curve, with a dose of 70 Gy achieving 55% RFS as compared to only 35% for 60 Gy. There was a 2.2% (95% CI, 1.0-3.4) improvement in RFS for each additional Gy.

Conclusions: This study provides level 2a evidence for initiating SRT at the lowest possible PSA and with escalated RT dose above 70 Gy. Progressively better tumor control rates with SRT after radical prostatectomy are achieved with a lower PSA at initiation and with a higher RT dose. Based on a comparison of RFS rates, the evidence supports early SRT as an alternative strategy to immediate adjuvant RT.