

Re: Adjuvant Radiotherapy Following Radical Prostatectomy for Prostate Cancer

Daly T, Hickey BE, Lehman M, Francis DP, See AM

Cochrane Database Syst Rev 2011:CD007234

Experts' summary:

The authors report the results of a meta-analysis of three randomized clinical trials (ARO 96-02/AOU AP 09/95; European Organization for Research and Treatment of Cancer [EORTC] 22911; Southwest Oncology Group [SWOG] 8794) comparing radical prostatectomy alone to radical prostatectomy plus adjuvant radiation therapy for the treatment of men with prostate cancer and at least one of the following adverse pathologic features: extracapsular tumor extension, positive surgical margins, or seminal vesicle invasion. In total, 1815 men were studied (385 from ARO, 1005 from EORTC, and 425 from SWOG). Analysis of oncologic outcomes was performed at 5- and 10-yr time points. Notably, 5-yr data were derived from all three trials, whereas 10-yr data were from only the SWOG trial.

The analysis found that adjuvant radiation therapy improved biochemical progression-free survival at 5 and 10 yr with risk differences (RDs) of -0.16 (95% confidence interval [CI], -0.21 to -0.11) and -0.29 (95% CI, -0.39 to -0.19), respectively. Furthermore, at 10 yr, adjuvant radiation improved overall survival (RD: -0.11 ; 95% CI, -0.20 to -0.02) and reduced the risk of metastatic disease (RD: -0.11 ; 95% CI, -0.20 to -0.01). These results were not observed at 5 yr.

Experts' comments:

Approximately 20–40% of men with a positive surgical margin will recur following a radical prostatectomy [1,2]. Therefore, adjuvant radiation therapy for all men with a positive margin will result in overtreatment in the majority of patients in whom this is their sole adverse pathologic feature. This is of critical importance, as a significant percentage of men undergoing adjuvant radiation will suffer a serious side effect of treatment. For example, in the SWOG trial, 24% of men experienced a complication of radiation therapy, including proctitis, urethral stricture, and/or urinary incontinence [3]. Furthermore, one long-term complication of radiation therapy not captured in these trials is secondary malignancies. Our group has reported that men who undergo radiation for the treatment of prostate cancer are at an increased risk of developing bladder cancer [4]. Is it really worth subjecting all men with a positive surgical margin to the side effects of radiation therapy?

The benefits of adjuvant radiation therapy have long been established for cancers of the brain, breast, head and neck, stomach, and rectum. Adjuvant radiation for these tumors represents the only likely means for cure prior to metastatic spread, as there are currently no serum markers for the early detection of tumor recurrence. In contrast, prostate cancer is unique given our ability to accurately detect local recurrence with prostate-specific antigen testing. Thus, prostate cancer

is amenable to *early* salvage treatment with radiation therapy. This point has been demonstrated by a handful of nonrandomized studies, which have demonstrated durable oncologic outcomes with this management strategy [5–7]. In light of these data and the side effects associated with radiation therapy, we feel that initial monitoring with prompt salvage radiation is preferable to adjuvant treatment for men whose only adverse pathologic feature is a positive surgical margin. To date there exists no completed randomized trial comparing these two approaches for any combination of adverse pathologic features. We look forward to the results of three ongoing randomized trials designed to compare adjuvant to salvage radiation therapy: Triptorelin and Radiation Therapy in Treating Patients Who Have Undergone Surgery for Intermediate-Risk Stage III or Stage IV Prostate Cancer (ClinicalTrials.gov identifier NCT00667069), Radiotherapy and Androgen Deprivation In Combination After Local Surgery (RADICALS), and Radiotherapy Adjuvant Versus Early Salvage (RAVES).

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Simon MA, Kim S, Soloway MS. Prostate specific antigen recurrence rates are low after radical retropubic prostatectomy and positive margins. *J Urol* 2006;175:140–4.
- [2] Stephenson AJ, Wood DP, Kattan MW, et al. Location, extent and number of positive surgical margins do not improve accuracy of predicting prostate cancer recurrence after radical prostatectomy. *J Urol* 2009;182:1357–63.
- [3] Thompson Jr IM, Tangen CM, Paradelo J, et al. Adjuvant radiotherapy for pathologically advanced prostate cancer: a randomized clinical trial. *JAMA* 2006;296:2329–35.
- [4] Nieder AM, Porter MP, Soloway MS. Radiation therapy for prostate cancer increases subsequent risk of bladder and rectal cancer: a population based cohort study. *J Urol* 2008;180:2005–9.
- [5] Stephenson AJ, Scardino PT, Kattan MW, et al. Predicting the outcome of salvage radiation therapy for recurrent prostate cancer after radical prostatectomy. *J Clin Oncol* 2007;25:2035–41.
- [6] Trock BJ, Han M, Freedland SJ, et al. Prostate cancer-specific survival following salvage radiotherapy vs observation in men with biochemical recurrence after radical prostatectomy. *JAMA* 2008;299:2760–9.
- [7] Cotter SE, Chen MH, Moul JW, et al. Salvage radiation in men after prostate-specific antigen failure and the risk of death. *Cancer* 2011; 117:3925–32.

Mark S. Soloway*, Michael A. Gorin
Department of Urology, University of Miami Miller School of Medicine,
Miami, FL, USA

*Corresponding author. Department of Urology,
University of Miami Miller School of Medicine,
PO Box 016960 (M-814), Miami, FL 33101, USA.
E-mail address: msoloway@med.miami.edu (M.S. Soloway)

DOI: 10.1016/j.eururo.2012.02.013