

Dr. Izawa's rebuttal

There are proponents for adjuvant radiotherapy and the reasons for this are clearly outlined in this debate.

As my colleague correctly states, "the optimal management for patients at high risk of local recurrence after radical prostatectomy ... is still a contentious issue."¹ There is no level I evidence comparing adjuvant radiotherapy with contemporary salvage radiotherapy.

Although the Southwest Oncology Group (SWOG) study 8794 and the European Organization for Research and Treatment of Cancer (EORTC) study 22911 are randomized trials that favour adjuvant radiotherapy, the other arms to these studies did not provide patients with salvage radiotherapy at a time that is currently deemed to be appropriate with detectable serum prostate-specific antigen (PSA) levels less than 0.5–1.0 µg/L.^{2–4} Furthermore, there are many other factors that make these studies inadequate to definitively answer the question of whether contemporary salvage radiotherapy or adjuvant radiotherapy is superior for patients at risk of clinical local failure after radical prostatectomy. These factors may in fact have biased the studies in favour of adjuvant radiotherapy.

In the SWOG trial, these factors include the following:

- about 33% of patients had a detectable serum PSA level of 0.2 µg/L or greater after surgery;
- a significant number of patients did not undergo central pathological review;
- of the 211 men randomly assigned to observation only, 70 ultimately received salvage radiotherapy;
- more patients in the observation arm had higher Gleason grades of 7 to 10;
- of the men who received salvage radiotherapy, 37% of the treatments were for objective recurrences rather than for a detectable PSA;
- the serum PSA level for men receiving salvage radiotherapy for PSA failures alone was not reported.²

The factors that may have biased the results in favour of adjuvant radiotherapy in the EORTC study include the following:

- the postoperative serum PSA level remained greater than 0.2 µg/L in 10.7% of patients;
- salvage radiotherapy was used in the "wait and see" arm; however, it was for local recurrence rather than PSA recurrence.⁴

Both the SWOG and EORTC trials were also initiated in the pre-PSA era and conducted without the contemporary PSA follow-up patients undergo today to allow for what is currently deemed to be appropriate salvage radiotherapy.

Despite the differences in radiotherapy dosing in patients

undergoing adjuvant versus salvage radiotherapy, certainly the treatment-related toxicity is greater for patients undergoing adjuvant radiotherapy.^{2,4} Low-grade, nonurinary morbidity was significantly increased and grades 1–3 late effects were more frequent in the patients who received adjuvant radiotherapy. Also, the incidence of urethral stricture was significantly higher in the adjuvant radiotherapy group.

With regard to additional beneficial effects of adjuvant radiotherapy reducing the number of patients requiring hormonal therapy, if the trigger to initiate salvage radiotherapy had been appropriate, the increased use of hormonal therapy in the "wait and see" arm may not have occurred.

Lastly, if one does choose to look at other therapeutic paradigms in head and neck, colorectal and breast cancers and compare them to prostate cancer, we must be careful. Prostate cancer biology is unique with different treated natural histories than the other malignancies and the prognoses are very different among diseases that would be staged similarly.

In summary, the efficacy of salvage radiotherapy appears equivalent to adjuvant radiotherapy when applied for biochemical failure after surgery when serum PSA levels are 0.5 µg/L or less, which is very feasible in the current PSA era. Salvage radiotherapy strategies also avoid the administration of radiotherapy to those that are not destined to have local disease recurrence, and avoid unnecessary local therapy in those with occult metastases. Quality of life outcomes will likely also be superior in patients undergoing a surveillance strategy with appropriate salvage radiotherapy. Only through trials, such as RADICALS,⁵ is there hope to answer the question of whether contemporary salvage radiotherapy or adjuvant radiotherapy is better for patients.

This article has been peer reviewed.

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