Salvage radiotherapy following biochemical relapse after radical prostatectomy: proceedings of the Genito-Urinary Radiation Oncologists of Canada consensus meeting

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Abstract

For patients with recurrent prostate cancer after radical prostatectomy, salvage radiotherapy is the only potentially curative treatment option. However, until recently there has been a paucity of data on the effectiveness of this approach. In light of recently published studies, the Genito-Urinary Radiation Oncologists of Canada (GUROC) met and crafted a consensus statement regarding the current place of salvage radiotherapy. GUROC also identified gaps in current knowledge and identified ongoing study protocols that will advance our knowledge in this area.

This report summarizes the main conclusions of the meeting and the commentary provided during the consensus-building process, and outlines the consensus statement that was subsequently adopted.

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Introduction

For patients with recurrent prostate cancer after radical prostatectomy, salvage radiotherapy is the only potentially curative treatment option. However, less than 50% of patients who receive secondary treatment for prostate cancer after radical prostatectomy undergo salvage radiotherapy — the majority are managed with androgen deprivation therapy, which offers a limited possibility of long-term disease control.[1] Because of concern among urologists that many patients with biochemical failure after surgery have occult metastatic disease, local salvage therapy is often not considered.

In light of new evidence on the role of adjuvant and salvage radiotherapy after radical prostatectomy, the Genito-Urinary Radiation Oncologists of Canada (GUROC) held a meeting in Toronto, Ont., in January 2007 to develop a consensus on the role of adjuvant and salvage radiotherapy following radical prostatectomy. This meeting brought together radiation oncologists from across Canada along with respected opinion leaders in prostate cancer treatment (Dr. Andrew Stephenson and Dr. Anthony Zietman). The format of the meeting included presentations, workshops and discussion sessions to provide an environment that facilitated the sharing of knowledge to aid in consensus development.

This paper highlights the treatment issues related to the use of salvage radiotherapy following radical prostatectomy and summarizes the recommendations put forth by the group. The consensus document on the role of adjuvant radiotherapy was reported in a separate article.[2]

Background

Radical prostatectomy is a well-established treatment modality that provides excellent control in localized prostate cancer. However, a significant proportion (about 15%–40%) of patients will develop biochemical recurrence following surgery depending on the selection criteria used at the time of surgery.[3–5] Although the possibility of a benign cause of persistent elevation of serum prostate-specific antigen (PSA) levels following prostatectomy should be considered (e.g., benign retained glands), a rising serum PSA level on repeat testing indicates persistent and (or) recurrent disease.[6]

The lack of data from randomized control trials in the area of biochemical failure following prostatectomy has led to a lack of agreement in the uro-oncological community regarding the optimal management of these patients.[7–9] In a survey of 4467 American Urological Association members, only 13% of respondents recommended radiotherapy for PSA-only relapse after surgery (site of failure undetermined).[7] This contrasts with a recommendation for salvage radiotherapy in this

setting by 59% of respondents in a broad-based Australian survey of practice and a 93% recommendation for radiotherapy in a British survey.[8,9] Over the past 10 years there have been multiple case series documenting the outcome of patients treated with salvage radiotherapy from individual institutions (Table 1).[10–35] However, the small patient numbers in most of these studies and resulting low statistical power have limited clinicians' ability to understand the outcome of treatment and to detect prognostic factors for treatment failure. Therefore, a multicentre international study of the outcome of salvage radiotherapy in a cohort of patients was performed and the results were presented by Dr. Andrew Stephenson, principal investigator for this project.

Outcome and prognostic factors for relapse after salvage radiotherapy in a multicentre study

A multi-institutional, retrospective cohort of 501 consecutive patients was assembled from 5 North American tertiary care referral centres who received salvage radiotherapy for PSA recurrence after radiotherapy between 1987 and 2002.[36] All patients had documented biochemical failure with rising serum PSA levels and received radiotherapy to the prostate bed (median dose 64.8 Gy). After radiotherapy, patients were monitored for disease recurrence using serial serum PSA level measurements and imaging studies where indicated. With a median follow-up of 45 months, the 4-year progression-free probability was 45%. A number of prognostic factors for disease progression were identified, including an elevated Gleason score, a short serum PSA level doubling time, a preradiotherapy serum PSA level of greater than 2.0 μg/L, and histopathological factors at the time of radical prostatectomy (i.e., negative surgical margins, seminal vesicle involvement). However, even in the unfavourable group with a Gleason score of 8–10 and negative surgical margins, the 4-year actuarial progression-free probability after salvage radiotherapy was a remarkable 18% provided that the serum PSA level was less than 2.0 μg/L (Fig. 1). In the most favourable subgroup of patients (Gleason score < 8, serum PSA level doubling time > 10 mo, positive surgical margins and serum PSA level < 2.0 μg/L) the 4-year actuarial progression-free probability after salvage radiotherapy was 77%.

A more extensive analysis by the same investigators was presented at the conference and recently published.[37] In this analysis, the study cohort was increased to 1540 patients from 17 centres with all patients treated between 1987 and 2005. With a median follow-up after completion of radiotherapy of 7.5 years, the 6-year progression-free probability was 32%, varying from 69% to 18% depending on pretreatment prognostic grouping (Fig. 2). This large study has allowed the identification of prognostic factors for relapse with a much greater degree of precision than the initial study and has led to the development of a nomogram to predict the outcome of salvage radiotherapy.[37] The impact of preradiotherapy serum PSA levels in the multi-institution study is shown in Figure 2 and demonstrates that progression-free probability is best when treatment is initiated when the serum PSA level is less than 0.5 μg/L.[37]

Neither disease-free interval (time from surgery to serum PSA level relapse) nor persistent serum PSA level elevation were found to be important in predicting failure after radiotherapy (and implicitly predicting isolated local failure) in this study by Stephenson and colleagues.[37] However, in other studies duration of the disease-free interval after radical prostatectomy has been shown to be important.[38]

Role of adjunctive hormonal therapy

There is a paucity of evidence to guide clinicians regarding the potential benefits, timing and optimal duration of hormonal therapy in conjunction with salvage radiotherapy following radical prostatectomy. The administration of preradiotherapy androgen deprivation therapy in Stephenson and colleagues' multicentre study appeared to improve the probability of remaining relapse-free on multivariable analysis.[37] However, less than 15% of patients in the study had hormonal therapy and the benefit of this approach remains unclear. The results of radiation treatment alone in patients with palpable local recurrence are poor and it would seem reasonable to consider the use of adjunctive hormonal therapy in these patients.

Radiation treatment toxicity

Salvage radiotherapy to the prostate bed is generally well tolerated with urinary frequency, diarrhea and fatigue as the most common acute side effects. Late grade 1–2 rectal and genitourinary toxicity is seen in about 5%–10% of patients — however, late grade 3 toxicity is reported in less than 4% of patients.[13–15,26,39] Postprostatectomy radiotherapy does not appear to significantly

Table 1. Literature summary of outcomes of salvage radiotherapy following radical prostatectomy*

Study	No. of study patients	Median (range) radiotherapy dose, Gy†	Median (range) follow-up time	Biochemical control, %; (follow-up time)†
Buskirk et al.[10]	368	64.8 (54.0–72.4)	5.0 (0.1–14.7) yr	46.0 (5.0 yr) 35.0 (8.0 yr)
Pazona et al.[11]	223	–	56.0 (0.0–188.0) mo	40.0 (5.0 yr) 25.0 (10.0 yr)
Ward et al.[12]	211	64.0 (55.0–72.0)	4.2 (0.1–15.0) yr	PSADT < 12.0 mo: 48.0 (5.0 yr), 34.0 (10.0 yr) PSADT ≥ 12.0 mo: 66.0 (5.0 yr) 37.0 (10.0 yr)
Maier et al.[13]	170‡	68.0 (photons) 78.0 (photons and neutons)	49.0 (1.0–37.0) mo	44.0 (7.0 yr)
Pisansky et al.[14]	166	64.0 (54.0–72.4)	52.0 (5.0–131.0) mo	46.0 (5.0 yr)
Katz et al.[15]	115	66.6 (37.8–75.6)	42.0 mo	46.0 (4.0 yr)
Brooks et al.[16]	114	64.0 (59.4–70.0)	6.3 (1.9–13.3) yr	50.0 (4.0 yr) 33.0 (6.0 yr)
MacDonald et al.[17]	102	66.0 (41.0–70.0)	4.2 yr (2.0 mo – 9.0 yr)	38.0 (5.0 yr)
Choo et al.[18]	98§	(60.0–66.0)	4.21 yr¶ 3.32 yr** 3.95 yr ††	26.0¶ 39.0** 14.0††
Anscher et al.[19]	89	66.0 (54.6–70.0)	48.0 mo	50.0 (4.0 yr)
Cadeddu et al.[20]	82	64.0 (50.0–75.0)	8.3 (1.0–13.0) yr	10.0 (5.0 yr)
Garg et al.[21]	78	66.0	25.0 mo	73.0
Song et al.[22]	73	66.6 (61.2–70.2)	36.0 (6.0–92.0) mo	39.0 (4.0 yr)
Nudell et al.[23]	69	(60.0–74.0)	37.0 mo	47.0 (4.0 yr)
Peyromaure et al.[24]	62	65.0 (58.0–69.0)	44.0 (3.0–140.0) mo	63.0
Do et al.[25]	60	64.8 (59.4–64.8)	36.0 (9.0–96.0) mo	50.0
Catton et al.[26]	59	60.0 (54.0–65.0)	43.0 (3.0–108.0) mo	30.0 (PSA < 2.0) 5.0 (PSA ≥ 2.0)
Chawla et al.[27]	54	64.8 (60.4–64.8)	45.0 mo	35.0 (5.0 yr)
Vanuystel et al.[28]	53	66.0	33.0 mo	46.0 (3.0 yr)
De la Taille et al.[29]	52	68.0 (45.0–70.0)	27.7 (6.0–69.0) mo	51.0 (3.0 yr)
Liauw et al.[30]	51	65.7 (61.2–72.3)	3.8 yr	56.0 (3.0 yr) 16.0 (5.0 yr)
Symon et al.[31]	50	66.6	39.6 mo	54.0 (3.0 yr)
Leventis et al.[32]	49	66.0 (60.0–75.5)	29.0 mo	24.0 (5.0 yr)
Morris et al.[33]	48	(60.0–64.0)	32.0 mo	47.0 (3.0 yr)
Kundel et al.[34]	48	66.6	34.3 mo	67.0
Crane et al.[35]	41	60.0 (58.0–66.0)	55.0 (36.0–96.0) mo	20.0

PSA = prostate-specific antigen; PSADT = prostate-specific antigen doubling time.
*The summary is limited to case series with 40 or more patients.
†Unless otherwise indicated.
‡149 patients received photon irradiation and 21 patients received a combination of photon and neutron irradiation.
§Prognostic groups were analyzed separately.
¶Group A, persistently detectable serum PSA level.
**Group B, delayed rise of serum PSA level.
††Group C, local recurrence.

increase the likelihood of urinary incontinence.[13–15,26,39] There is little data available on the effect of radiotherapy in this setting on the long-term risk of impotence.

Radiation treatment planning issues

One key area central to the issue of postoperative (adjuvant or salvage) radiotherapy following radical prostatectomy is proper target volume delineation, that is, the area at risk of harbouring gross or microscopic residual disease. There is considerable variability in the area that received treatment in the published series and there is little agreement in the literature regarding the appropriate definition of the target area.

The recent use of endorectal magnetic resonance imaging (MRI) in defining patterns of local relapse following radical prostatectomy may help to guide radiation oncologists in delineating the appropriate target area.[40,41] Sella and colleagues[40] analyzed the distribution of clinically documented local recurrence in 41 patients with biochemical recurrence after surgery using endorectal MRI. The majority of recurrences were retrovesical (40%), perianastomotic (29%) or within retained seminal vesicles (22%). A small number of recurrences occurred at the anterior or lateral surgical margins (9%). In contrast, Miralbell and colleagues[40] observed that most progressive or residual disease in the primary tumour bed was located in the inferior and posterior region of the vesicourethral anastomosis.

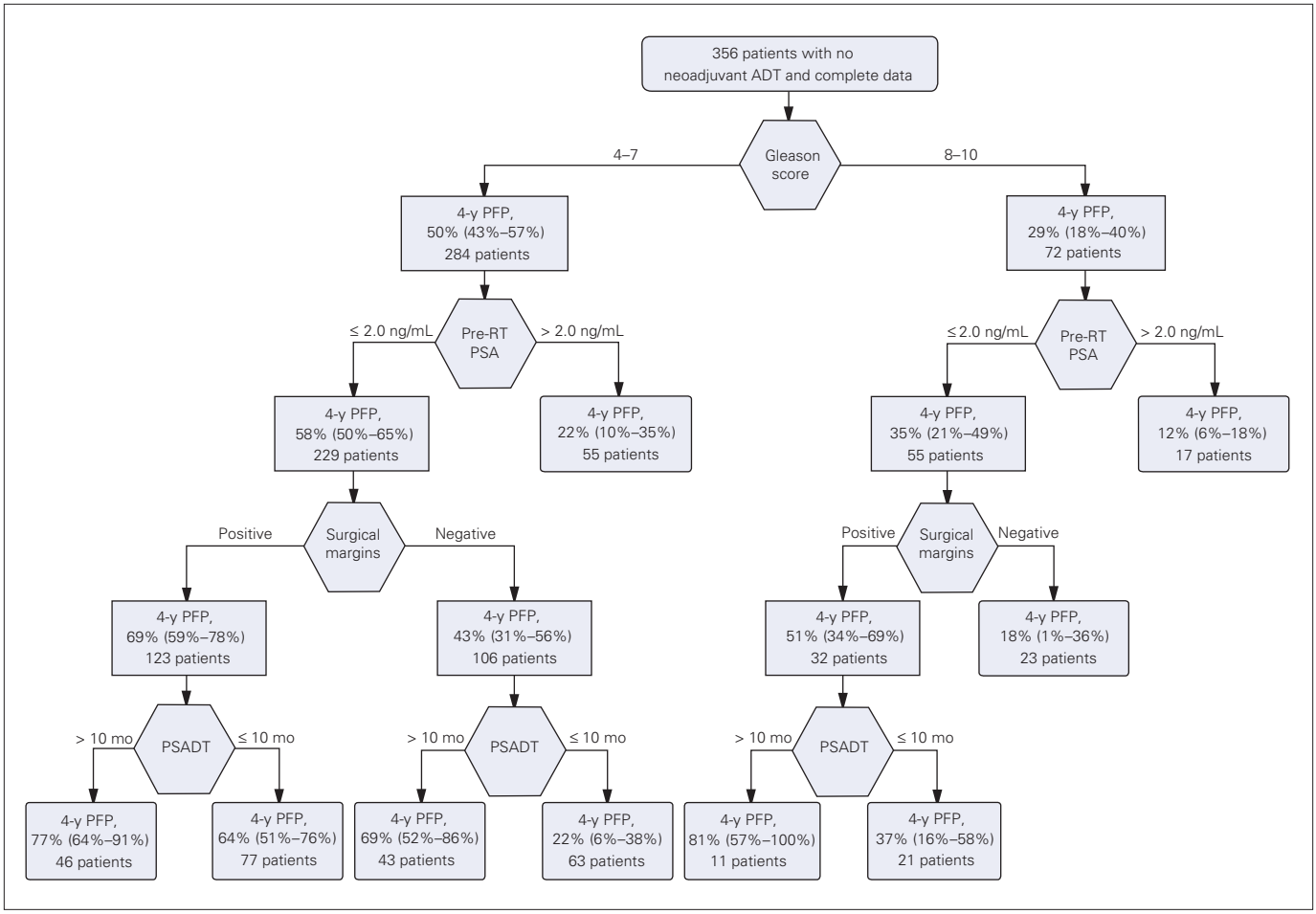

Fig 1. Four-year actuarial progression-free probability (PFP) after salvage radiotherapy. ADT = androgen deprivation therapy; PSA = prostate-specific antigen; PSADT = prostate-specific antigen doubling time; RT = radiotherapy. Adapted with permission from Stephenson AJ, Shariat SF, Zelefsky MJ, et al. (*JAMA* 2004;291:1325-1332).[36] (Note: the conversion factor between ng/mL and µg/L is 1.0.)

A study outlining the boundaries of the surgical bed after radical prostatectomy considered at risk of microscopic tumour cell contamination developed at Princess Margaret Hospital was presented at the conference.[42] It was agreed that further study was needed before this issue could be resolved.

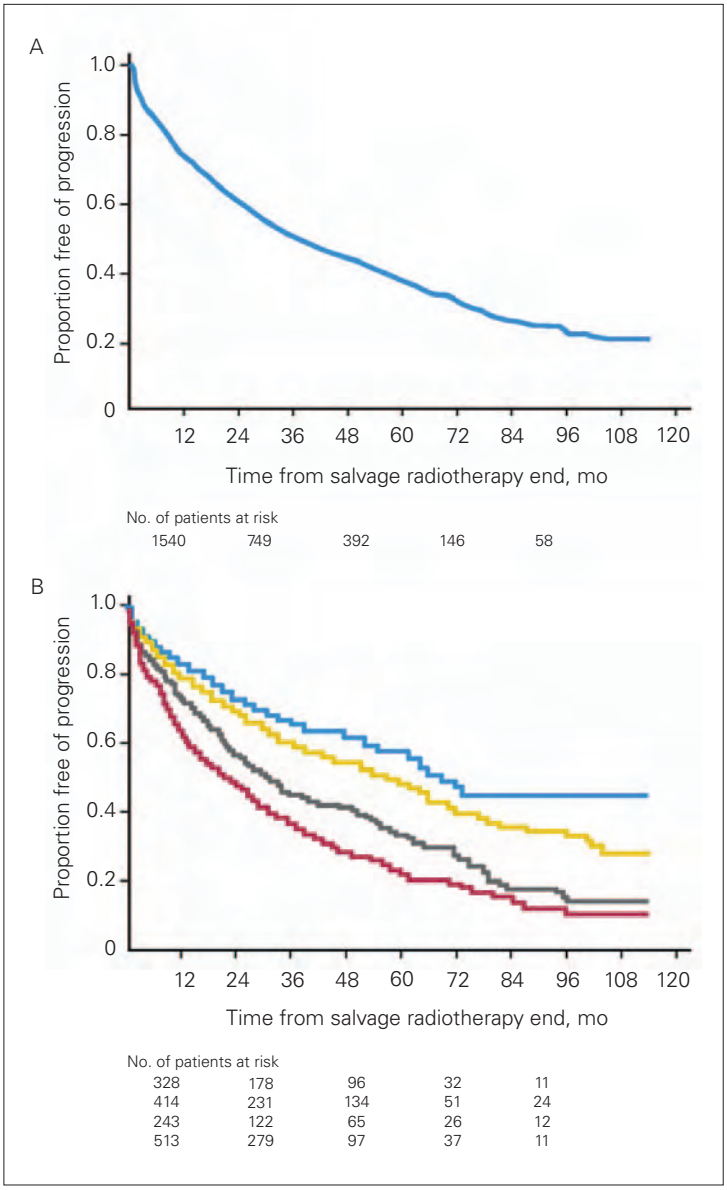

Fig 2. **(A)** Kaplan–Meier estimate of the overall progression-free probability after salvage radiotherapy. **(B)** Progression-free probability after salvage radiotherapy stratified by preradiotherapy prostate-specific antigen level ≤ 0.50 µg/L (blue), 0.51–1.00 µg/L (yellow), 1.01–1.50 µg/L (grey) and > 1.50 µg/L (red). Adapted with permission from Stephenson AJ, Scardino PT, Kattan MW, et al. (*J Clin Oncol* 2007;25:2035-41).[37]

Clinical trials

Completed (but results pending), ongoing and planned clinical trials that will help address the many unresolved issues were presented and discussed. The role of hormonal therapy with salvage radiotherapy was studied in a large, intergroup phase III trial conducted by the Radiation Therapy Oncology Group (study RTOG 9601). Eligible patients included those who underwent a radical prostatectomy (either retropubic or perineal) and pelvic lymphadenectomy (either open or laparoscopic) for carcinoma of the prostate, pathological stage T3N0 or pT2N0 with positive inked resection margin. At entry, the serum PSA level must have been between 0.2 µg/L and 4.0 µg/L. More than 1200 patients were randomly assigned to radiotherapy with or without bicalutamide given at a dose of 150 mg daily starting at the initiation of radiotherapy and continued for 2 years. This study closed to accrual in 2003 and results should be available within the next 2 years. There was considerable support at the meeting for the upcoming Medical Research Council/National Cancer Institute of Canada Clinical Trials Group Radiotherapy and Androgen Deprivation in Combination after Local Surgery (RADICALS) trial (study NCIC-CTG PR.13) (Fig. 3). The protocol has 2 separate randomizations with most post–radical prostatectomy patients potentially eligible at some point in their clinical course. This study will help to elucidate 2 important areas of uncertainty for post–radical prostatectomy patients:[1] the need for and timing of postoperative radiotherapy, that is, immediate (adjuvant) versus salvage (deferred or early salvage);[3] the use and duration of hormone therapy with postoperative radiotherapy, that is, none versus short-term (6 mo) versus long-term (24 mo). The trial will open in Canada in 2008.

Summary

Radical prostatectomy is a well-established curative treatment modality for localized prostate cancer, but a significant number of patients will develop biochemical failure and require secondary treatment. Salvage radiotherapy following radical prostatectomy for a persistently detectable serum PSA level or a rising serum PSA level out

of the undetectable range can provide long-term disease control and is a potentially curative treatment in patients with truly localized disease. Prognostic factors, for example, serum PSA level, serum PSA level doubling time, time to failure, margin positivity, seminal vesicle invasion and Gleason score, are potential predictors for ultimate disease control. The most consistent predictor of disease control is the serum PSA level before salvage radiotherapy. A key point from recent studies is that durable responses can be achieved, even in subsets of patients with high-risk disease (those with a Gleason score of 8–10, a rapid serum PSA level doubling time or seminal vesicle involvement), when salvage radiotherapy is administered early in the course of disease recurrence. The benefit seen in some high-risk patients suggests that salvage radiotherapy may prevent metastatic disease progression and emphasizes the need for early referral. In addition to the potential for long-term disease control, the potential benefit of salvage radiotherapy in delaying the initiation of androgen deprivation should be considered. Toxicity from radiotherapy remains modest, but may also be improved with more conformal therapy. Better delineation of the postoperative target area for radiotherapy will likely improve its effectiveness and allow for the possibility of reducing toxicity and possibly increasing the radiotherapy dose to the target area. The role of hormonal therapy as an adjunct to radiotherapy is not well established at the present time. Ongoing accrual to clinical trials is essential.

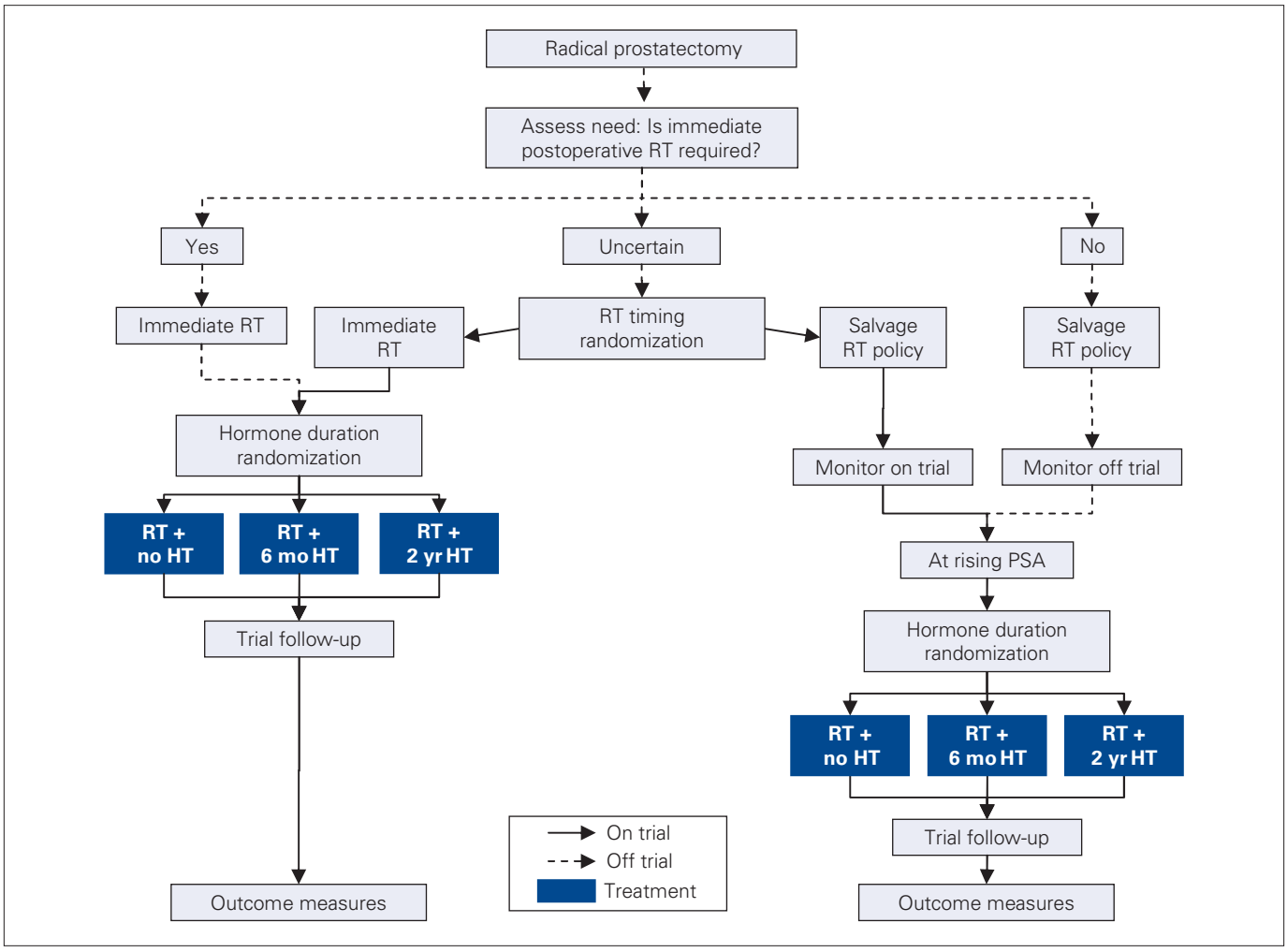

Fig 3. Schema of the NCIC-CTG PR.13 randomized trial. HT = hormone therapy; PSA = prostate-specific antigen; RT = radiotherapy.

Recommendations

- **All patients (including those with Gleason scores of 8–10 and other high-risk features) should be referred to a radiation oncologist for consideration of treatment as soon as possible after biochemical failure is recognized, certainly before the serum PSA level reaches 0.5 µg/L.**
- **Patients with persistently elevated serum PSA levels after surgery should also be referred to a radiation oncologist for consideration of treatment.**
- **Ongoing research is necessary to fully define the appropriate treatment volume, radiotherapy dose and treatment technique.**
- **The potential benefit of adjunctive hormonal therapy is not established and awaits the results of clinical trials.**
- **GUROC recognizes the need for ongoing clinical trials in this area and supports accrual to the NCIC-CTG PR.13 study.**

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References

1. Grossfeld GD, Stier DM, Flanders SC, et al. Use of second treatment following definitive local therapy for prostate cancer: data from the caPSURE database. *J Urol* 1998;160:1398-404.
2. Pickles T, Morgan S, Morton G, et al. Adjuvant radiotherapy following radical prostatectomy: Genito-Urinary Radiation Oncologists of Canada Consensus Statement. *CUAJ* 2008;2:95-9.
3. Moul JW. Prostate specific antigen only progression of prostate cancer. *J Urol* 2000; 163:1632-42.
4. Pound CR, Partin AW, Epstein JI, et al. Prostate-specific antigen after anatomic radical retropubic prostatectomy. Patterns of recurrence and cancer control. *Urol Clin North Am* 1997;24:395-406.
5. Han M, Partin AW, Zahurak M, et al. Biochemical (prostate specific antigen) recurrence probability following radical prostatectomy for clinically localized prostate cancer. *J Urol* 2003;169:517-23.
6. Ravery V. The significance of recurrent PSA after radical prostatectomy: benign versus malignant sources. *Semin Urol Oncol* 1999;17:127-9.
7. Ornstein DK, Colberg J, Virgo KS, et al. Evaluation and management of men whose radical prostatectomies failed: results of an international survey. *Urology* 1998;52:1047-54.
8. Duchesne GM, Millar, JL, Moraga V, et al. What to do for prostate cancer patients with a rising PSA? A survey of Australian practice. *Int J Radiat Oncol Biol Phys* 2003; 55:986-91.
9. Morris SL, Parker C, Huddart R, et al. Current opinion on adjuvant and salvage treatment after radical prostatectomy. *Clin Oncol (R Coll Radiol)* 2004;16:277-82.
10. Buskirk SJ, Pisansky TM, Schild SE, et al. Salvage radiotherapy for isolated prostate specific antigen increase after radical prostatectomy: evaluation of prognostic factors and creation of a prognostic scoring system. *J Urol* 2006;176:985-90.
11. Pazona JF, Han M, Hawkins SA, et al. Salvage radiation therapy for prostate specific antigen progression following radical prostatectomy: 10-year outcome estimates. *J Urol* 2005;174:1282-6.
12. Ward JF, Zincke H, Bergstralh EJ, et al. The impact of surgical approach (nerve bundle preservation versus wide local excixion) on surgical margins and biochemical recurrence following radical prostatectomy. *J Urol* 2004;172:1328-32.
13. Maier J, Forman J, Tekyi-Mensah S, et al. Salvage radiation for a rising PSA following radical prostatectomy. *Urol Oncol* 2004;22:50-6.
14. Pisansky TM, Kozelsky TF, Myers RP, et al. Radiotherapy for isolated serum prostate specific antigen elevation after prostatectomy for prostate cancer. *J Urol* 2000;163: 845-50.
15. Katz MS, Zalefsky MJ, Ennapadam S, et al. Predictors of biochemical outcome with salvage conformal radiotherapy after radical prostatectomy for prostate cancer. *J Clin Oncol* 2003;21:483-9.
16. Brooks JP, Albert PS, Wilder RB, et al. Long-term salvage radiotherapy outcome after radical prostatectomy and relapse predictors. [discussion 2208]. *J Urol* 2005;174: 2204-8.
17. MacDonald OK, Schild SE, Vora SA, et al. Radiotherapy for men with isolated increase in serum prostate specific antigen after radical prostatectomy. *J Urol* 2003;170:1833-7.
18. Choo R, Morton G, Danjoux C, et al. Limited efficacy of salvage radiotherapy for rising PSA or clinically isolated local recurrence after radical prostatectomy. *Int J Radiat Oncol Biol Phys* 2002;53:269-76.
19. Anscher MS, Clough R, Dodge R. Radiotherapy for a rising prostate-specific antigen after radical prostatectomy: the first 10 years. *Int J Radiat Oncol Biol Phys* 2000;48:369-75.
20. Cadeddu JA, Parting AW, Deweese TL, et al. Long-term results of radiation therapy for prostate cancer recurrence following radical prostatectomy. [discussion 177-8]. *J Urol* 1998;159:173-7.
21. Garg MK, Tekyi-Mensah S, Bolton S, et al. Impact of postprostatectomy prostate-specific antigen nadir on outcomes following salvage radiotherapy. *Urology* 1998;51: 998-1002.
22. Song DY, Thompson TL, Ramakrishnan V, et al. Salvage radiotherapy for rising or persistent PSA after radical prostatectomy. *Urology* 2002;60:281-7.
23. Nudell DM, Grossfeld GD, Weinberg VK, et al. Radiotherapy after radical prostatectomy: treatment outcomes and failure patterns. *Urology* 1999;54:1049-57.
24. Peyromaure M, Allouch M, Eschwege F, et al. Salvage radiotherapy for biochemical recurrence after radical prostatectomy: a study of 62 patients. Urology 2003;62:503-7.
25. Do T, Parker RG, Do C, et al. Salvage radiotherapy for biochemical and clinical failures following radical prostatectomy. *Cancer J Sci Am* 1998;4:324-30.
26. Catton C, Gospodarowicz, Warde P, et al. Adjuvant and salvage radiation therapy after radical prostatectomy for adenocarcinoma of the prostate. *Radiother Oncol* 2001;59: 51-60.
27. Chawla AK, Thakral HK, Zeitman AL, et al. Salvage radiotherapy after radical prostatectomy for prostate adenocarcinoma: analysis of efficacy and prognostic factors. *Urology* 2002;59:726-31.
28. Vanuytsel L, Janssensa G, Van Poppelb H, et al. Radiotherapy for PSA recurrence after radical prostatectomy. *Eur Urol* 2001;39:425-9.
29. de la Taille A, Flam TA, Thiounn N, et al. Predictive factors of radiation therapy for patients with prostate specific antigen recurrence after radical prostatectomy. *BJU Int* 2002;90:887-92.
30. Liauw SL, Webster WS, Pistenmaa DA, et al. Salvage radiotherapy for biochemical failure of radical prostatectomy: a single-institution experience. *Urology* 2003;61:1204-10.
31. Symon Z, Kundel Y, Sadetzki S, et al. Radiation rescue for biochemical failure after surgery for prostate cancer: predictive parameters and an assessment of contemporary predictive models. *Am J Clin Oncol* 2006;29:446-50.
32. Leventis AK, Shariat SF, Kattan MW, et al. Prediction of response to salvage radia-

tion therapy in patients with prostate cancer recurrence after radical prostatectomy. *J Clin Oncol* 2001;19:1030-9.
33. Morris MM, Dallow KC, Zeitman AL, et al. Adjuvant and salvage irradiation following radical prostatectomy for prostate cancer. *Int J Radiat Oncol Biol Phys* 1997;38:731-6.
34. Kundel Y, Pfeffer R, Lauffer M, et al. Salvage prostatic fossa radiation therapy for biochemical failure after radical prostatectomy: the Sheba experience. *Isr Med Assoc J* 2004;6:329-31.
35. Crane CH, Rich TA, Read PW, et al. Preirradiation PSA predicts biochemical disease-free survival in patients treated with postprostatectomy external beam irradiation. *Int J Radiat Oncol Biol Phys* 1997;39:681-6.
36. Stephenson AJ, Shariat SF, Zelefsky MJ, et al. Salvage radiotherapy for recurrent prostate cancer after radical prostatectomy. *JAMA* 2004;291:1325-32.
37. 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.
38. Freedland SJ, Humphreys EB, Mangold LA, et al. Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. *JAMA* 2005; 294:433-9.
39. Parker C, Warde P, Catton C. Salvage radiotherapy for PSA failure after radical prostatectomy. *Radiother Oncol* 2001;61:107-16.
40. Miralbell R, Vees H, Lozano J, et al. Endorectal MRI assessment of local relapse after surgery for prostate cancer: a model to define treatment field guidelines for adjuvant radiotherapy in patients at high risk for local failure. *Int J Radiat Oncol Biol Phys* 2007; 67:356-61.
41. Sella T, Schwartz LH, Swindle PW, et al. Suspected local recurrence after radical prostatectomy: endorectal coil MR imaging. *Radiology* 2004;231:379-85.
42. Wiltshire KL, Brock KK, Haider MA, et al. Anatomic boundaries of the clinical target volume (prostate bed) after radical prostatectomy. *Int J Radiat Oncol Biol Phys* 2007; 69:1090-9.

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