# Functional and oncological outcomes of salvage external beam radiotherapy following robot-assisted radical prostatectomy in a Canadian cohort

*Khaled Ajib, MD[1,2]; Marc Zanaty, MD[1,2]; Mansour Alnazari, MD[1,2]; Emad Rajih, MD[1,2]; Pierre-Alain Hueber, MD[1]; Mila Mansour, MD[1]; Roger Valdivieso, MD[1]; Cristina Negrean, MD[1]; Pierre I. Karakiewicz, MD[1]; Daniel Taussky, MD[3,4]; Guila Delouya, MD[3,4]; Assaad El-Hakim, MD[1,2]; Kevin C. Zorn, MD[1]*

[1]Section of Urology, Department of Surgery, Centre Hospitalier de l'Université de Montréal; [2]Division of Robotic Urology, Department of Surgery, Hôpital du Sacré Cœur de Montréal; [3]Department of Radiation Oncology, Centre Hospitalier de l'Université de Montréal, Hôpital Notre-Dame; [4]CRCHUM-Centre Hospitalier de Recherche du Centre Hospitalier de l'Université de Montréal; Montreal, QC, Canada

Cite as: *Can Urol Assoc J* 2018;12(2)45-9. http://dx.doi.org/10.5489/cuaj.4641

Published online December 1, 2017

See related commentary on page 50

## Abstract

**Introduction**: We sought to determine the impact of salvage radiotherapy (SRT) on oncological and functional outcomes of patients with prostate cancer after biochemical recurrence (BCR) following robot-assisted radical prostatectomy (RARP).

**Methods**: Data of 70 patients with prostate cancer treated with SRT after developing BCR were retrospectively analyzed from a prospectively collected RARP database of 740 men. Oncological (prostate-specific antigen [PSA]) and functional (pads/day, International Prostate Symptom Score [IPSS], and Sexual Health Inventory for Men [SHIM]) outcomes were reported at six, 12, and 24 months after RT and adjusted for pre-SRT status.

**Results**: Men who underwent SRT had a mean age, PSA, and time from radical prostatectomy (RP) to RT of 61.8 years (60.1–63.6), 0.5 ng/ml (0.2–0.8), and 458 days (307–747), respectively. Freedom from biochemical failure (FFBF) post-SRT, defined as a PSA nadir <0.2 ng/mL, was observed in 89%, 93%, and 81%, at six, 12, and 24 months, respectively. Undetectable PSA was observed in 14%, 35%, and 40% at the same time points, respectively. There was no significant difference in urinary continence post-SRT (p=0.56). Rate of strict continence (0 pads/day) was 71% at 24 months compared to 78% pre-SRT. Mean IPSS at six, 12, and 24 months was 3.4, 3.6, and 3.6, respectively compared to pre-RT score of 3.3 (p=0.61). The mean SHIM score pre-SRT was comparable at all time points following treatment (p=0.86).

**Conclusions:** In this unique Canadian experience, it appears that early SRT is highly effective for the treatment of BCR following RARP with little impact on urinary continence and potency outcomes.

## Introduction

Prostate cancer is considered to be the most common cancer in men. There are an estimated 151 360 new cases each year.[1] Robot-assisted radical prostatectomy (RARP) has been adapted increasingly in Canada. In the U.S., nearly 80% of all prostatectomies are performed with this technique.[1]

Post-prostatectomy radiotherapy (RT) is commonly used to maximize oncological outcomes in patients. Adjuvant radiotherapy (ART) is used with certain pathological features, including the pathological stage and margin status. In the absence of ART, the five-year risk of biochemical recurrence (BCR) is 50–75% in high-risk patients;[2] however, salvage radiotherapy (SRT) is used in cases with elevated prostate-specific antigen (PSA) postoperatively or BCR. The European guidelines state that early SRT provides a possibility of cure for patients with an increasing or persistent PSA after radical prostatectomy (RP). Roughly, 60% of patients who are treated before the PSA level rises to >0.5 ng/mL will achieve an undetectable PSA level. Therefore, patients will have an 80% chance of being progression-free five years later.[3] Stish et al states that the outcomes of SRT are positively affected when initiated at lower PSA levels.[4]

It is well-established that radiotherapy has an impact on the prognostic and functional status of the patient. One study demonstrated that the delayed administration of RT has a positive effect on erectile dysfunction and urinary continence post-RP.[5]

The aim of this study is to question and determine the real impact of early SRT on the patients' oncological outcome in relation to their PSA levels. Moreover, it will discuss the effect of early SRT on the functional status of the patients.

## Methods

### Patient characteristics

After institutional review board approval, a prospectively collected database of patients who underwent RARP for localized prostate cancer at our institution, which included 740 men between 2006 and 2014, was retrospectively reviewed. All men had RARP using our standardized surgical approach.[6]

### Salvage radiation therapy

Among these, 70 node-negative patients underwent standardized SRT at one of two academic centres performed by dedicated uro-radiation oncologists. The patients undertook 33 sessions of radiotherapy (66 Gy) with an intensity of 2 Gy per day. Patients were followed up for a period of two years. Patients with ART or usage of any hormonal therapy were not included for the analysis. Our study retrospectively analyzes data from these patients.

### Definitions and statistical analysis

The oncological outcome was related to the PSA level, which was measured pre- and post-RT. Biochemical failure after SRT was defined as serum PSA rising above the post-treatment nadir to a level of 0.2 ng/mL or more with a confirmatory value.

With no international consensus for the definition of post-prostatectomy incontinence,[7] in our study, continence was clinically assessed using the number of pads used per day. Patients who use no pads or one security pad (PRN) were considered continent; however, patients using one or more pads were considered incontinent. With respect to the lower urinary tract symptoms, the validated International Prostate Symptom Score (IPSS) score was used, including the quality of life (QOL) score. Moreover, both the validated erection hardness score (EHS) and the Sexual Health Inventory for Men (SHIM) scores were used to evaluate potency.[8] Outcomes were reported at six, 12, and 24 months after SRT. Additionally, adjustment of these values was done and compared with pre-RT status. Categories were compared using Chi-square test and Fisher exact test for categorical variables. A p value <0.05 was considered clinically significant.

## Results

This study included 70 patients who had undergone RARP and SRT. Table 1 demonstrates the baseline characteristics of the men participating in our study. Patients are categorized according to pre-RT PSA value (< or ≥0.2 ng /ml). The mean age, PSA value prior to SRT, and time from RP to RT were 61 years, 0.50 ng/mL (confidence interval [CI] 0.21–0.79), and 458 days (CI 307–747), respectively. Nerve-sparing techniques were bilateral, unilateral, and non-nerve-sparing in 48.57%, 15.71%, and 35.71%, respectively. The average PSA doubling time among our population was 15.97 months (CI 11.97–19.97). Mean post-surgical Cancer of the Prostate Risk Assessment (CAPRA-S) score in the cohort was 4.14 (CI 2.18–6.11), with a range from 1–8 (Mode: 4). Before initiation of SRT, 62.9% of men had a PSA ≥0.2 ng/ml. Pathological features of all 70 are summarized in Table 1. The majority of men had pathological Gleason score of 7 (3+4) (38.57%). Forty-seven (67.14%) of the patients had positive surgical margins, the majority of which had a pathological stage of T3 (74%). SRT was initiated at a PSA <0.2 ng/ml in 44.68% of the men with positive surgical margins; 16% of the patients had documented seminal vesicle invasion.

Patients were followed up for a period of 24 months. After 24 months, 42 of 52 (80.77 %) patients had a PSA <0.2 ng/ml; 21 of these 42 men (50%) had an undetectable PSA of 0 ng/ml at 24 months. Forty-one percent of the patients with extracapsular extension had a PSA <0.2 ng/ml before RT. This value increased up to 80% 24 months post-RT. With respect to surgical margins, the percentage of patients with positive surgical margins with a PSA value <0.2 ng/ml was 44% and 81% pre- and post-RT, respectively (p =0.80).

The Kaplan-Meier curve for both populations is shown in Fig. 1. The first curve (smooth line) is for the population with a pre-RT PSA of <0.2 ng/ml that included 26 patients. Three out of 26 men had a PSA >0.2 ng/ml two years after SRT. To add, 27% of the patients who started RT at a PSA <0.2 ng/ml had an undetectable PSA two years later. The 44 patients with a pre-RT PSA ≥0.2 ng/ml are demonstrated in the second curve (jagged line).

Tables 2 and 3 assess the urinary and sexual functional outcome, respectively, of men undertaking radiotherapy. Table 2 demonstrates that 78.5% (55) of men were continent at the time of RT. Throughout the followup of these 55 men, continence was maintained in 37 men, with a followup to 24 months. Only five of these 55 patients started to use one pad 24 months after RT. With respect to possible detrusor impact of SRT, the IPSS was also studied. The mean value was 3.6 after RT compared to 3.38 before (all p values NS). Table 2 also demonstrates that there is no significant relationship between RT and the quality of life of the patients (p=0.98).

The relation between SRT and erection is reported in Table 3. Analysis demonstrates that there appears to be no significant relation between SRT and EHS (p=0.98). Among the 25 men who had an EHS ≥3 (potent) pre-RT, 21 remained in the study beyond 12 months, 19 of which continued to report an EHS ≥3. At 24 months, the 16 patients (originally 25 pre-RT) who remained in the study had an EHS ≥3.

The overall mean SHIM score of the men was 8.82 before RT compared to 8.18 24 months after RT (p=0.66). Two years after initiation of radiotherapy, 86% of men had a

**Table 1. Baseline characteristics of the 70 patients**

| | Overall (n=70) | PSA <0.2 at SRT (n=26) | PSA ≥0.2 at SRT (n=44) | p |
|---|---|---|---|---|
| Age (years) | 61.86 (60.15–63.57) | 61.58 (58.99–64.16) | 62.02 (59.69–64.35) | 0.43 |
| BMI (kg/m$^2$) | 27.84 (26.74–28.94) | 27.60 (25.33–29.86) | 27.99 (26.81–29.18) | 0.28 |
| CAPRA-S score | 4.14 (2.18–6.11) | 4.04 (3.25–4.83) | 4.20 (3.73–4.68) | 0.61 |
| PSADT (months) | 15.97 (11.97–19.97) | 22.16 (13.16–31.16) | 12.31 (8.89–15.72) | 0.09 |
| Pre-RARP PSA (ng/dl) | 8.53 (7.36–9.71) | 8.01 (5.99–10.01) | 8.84 (7.35–10.33) | 0.02 |
| Pre-RT PSA (ng/ml) | 0.50 (0.21–0.79) | 0.14 (0.13–0.16) | 0.75 (0.29–1.22) | 0.01 |
| Mean time between RARP and RT (days) | 458 (307–747) | 518 (402–635) | 398 (277–519) | 0.28 |
| Surgical pathology details<br>pT – stage (%) | | | | |
| pT2 | 26 (37.14) | 11 | 15 | 0.49 |
| pT3a | 32 (45.71) | 12 | 20 | 0.16 |
| pT3b | 12 (15.71) | 3 | 9 | 0.13 |
| Pathological Gleason score (%) | | | | |
| 6 | 4 (5.71) | 1 | 3 | 0.27 |
| 7 (3+4) | 27 (38.57) | 10 | 17 | 0.18 |
| 7 (4+3) | 17 (24.29) | 8 | 9 | 0.81 |
| 8–10 | 22 (31.43) | 7 | 15 | 0.09 |
| Positive surgical margins (%) | | | | |
| Overall | 47 (67.14) | 21 | 26 | |
| pT2 | 15 | 8 | 7 | 0.98 |
| pT3 | 32 | 10 | 22 | 0.82 |
| Nerve-sparing (NS) technique (%) | | | | |
| Bilateral NS | 34 (48.57) | 13 | 21 | 0.62 |
| Unilateral NS | 11 (15.71) | 2 | 9 | 0.43 |
| Non-NS | 25 (35.71) | 11 | 14 | 0.67 |

BMI: body mass index; CAPRA-S: Cancer of the Prostate Risk Assessment score; PSA: prostate-specific antigen; PSADT: PSA doubling time; RARP: robot-assisted radical prostatectomy; RT: radiotherapy.

SHIM score less than 21 compared to 82 % before RT (Table 3). When subanalysis of the pre-SRT men with EHS ≥3 was conducted, the mean SHIM for these 25 men was 18.32, 15.8, 16.62, and 16.76 at pre-SRT, six months, 12 months, and 24 months, respectively (p =0.6).

## Discussion

RARP has gained rapid adoption in the U.S. and globally since its description in early 2002. Over the past decade, RARP has been demonstrated as a safe procedure with acceptable oncological and functional outcomes, and with the benefit of shorter hospital stay, convalescence, and blood loss as the forefront of reduced morbidity.[9]

The current guidelines define BCR as a rising PSA after surgery with two documented consecutive rises over the value of 0.2 ng/ml.[10] RT represents a curative therapeutic option that can be offered to men with postoperative detectable PSA.[11] The purpose behind the modality of SRT is to reduce the PSA values and to maintain PSA recurrence-free status.[12] The three-year BCR rate after RARP and SRT was 36% comparable to the rates post-open or laparoscopic prostatectomies.[13]

Kwon et al indicated that there are significant outcomes for patients who receive SRT for BCR after primary RP. They highlight the significance of certain predictors that might lead to a favourable outcome. Some of the recognized predictors of success were: low pre-RT PSA values, longer PSA doubling time before SRT, concomitant androgen-deprivation therapy administration, and positive surgical margins.[14]

The early administration of salvage RT to patients with BCR after RP has a good long-term outcome.[15] A pooled analysis has showed that the five-year BCR-free survival in patients receiv-

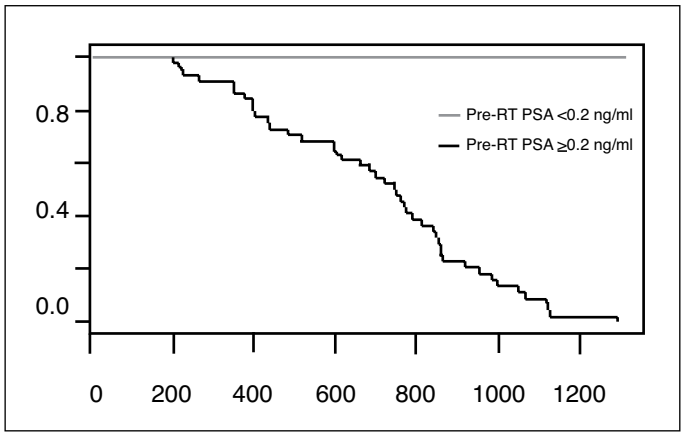


***Fig. 1.*** Kaplan-Meier curve for patients with a pre-radiotherapy (RT) prostate-specific antigen (PSA) of <0.2 ng/ml and ≥0.2 ng/ml.

**Table 2. Functional urinary outcome (continence rate [p= 0.56], IPSS, QOL)**

| Time (months) | Continent: 0 pads or 1 security pad, n (%) | Incontinent: ≥1 pad, n (%) | Total number of patients |
|---|---|---|---|
| Pre-RT | 55 (78.57) | 15 (21.43) | 70 |
| 6 | 54 (81.82) | 12 (18.18) | 66 |
| 12 | 46 (75.41) | 15 (24.59) | 61 |
| 24 | 37 (71.15) | 15 (28.85) | 52 |
| | **IPSS** | **CI** | **p** |
| Pre-RT | 3.39 | (2.79–3.97) | |
| 6 | 3.44 | (2.67–4.21) | 0.9121 |
| 12 | 3.62 | (2.72–4.51) | 0.6666 |
| 24 | 3.66 | (2.75–4.57) | 0.6123 |
| | **QOL score** | **CI** | **p** |
| Pre-RT | 1.62 | (1.05–2.19) | |
| 6 | 1.70 | (1.22–2.18) | 0.8214 |
| 12 | 1.61 | (0.97–2.25) | 0.9846 |
| 24 | 1.61 | (0.86–2.36) | 0.9859 |

CI: confidence interval; IPSS: International Prostate Symptom Score; QOL: quality of life; RT: radiotherapy.

ing early salvage RT was 71%.[14] Gandaglia et al described certain clinical features that may benefit from early SRT. They talked about patients with Gleason score ≥8, pT3b/4, and lymph node invasion.[16] On the other hand, another study that included 2460 patients with a median followup of five years stated that early SRT at low PSA levels after RP has a better outcome in patients. They reported improvement in freedom from biochemical failure and distant metastasis rates.[17]

In our study, RT was initiated at an average PSA level of 0.5 ng/ml (CI 0.2–0.79). The figures have shown that the PSA value is <0.2 ng/ml in 93% of the patients 12 months after RT (p<0.001). This value reaches 81% after 24 months, knowing that the total number of patients at the end of the study is 52 due to loss of followup. Such values prove the oncological success of early SRT, which is defined as a PSA nadir of <0.2 ng/ml. In cases of pT3, capsule rupture, or seminal vesicle invasion with a PSA <0.1 ng/ml post-RP, the European guidelines offer two options. Those options are initiation of ART after urinary function recovery, or monitoring the patient and offering SRT before the PSA exceeds 0.5 ng/ml.[3] In our study, the percentage of patients with a PSA <0.2 ng/ml 24 months after RT is 80%, 81%, and 55% for patients with extracapsular extension, positive surgical margins, and seminal vesicle invasion, respectively compared to 41%, 45%, and 36% pre-RT.

There is also better cancer control with administration of SRT at the first sign of PSA rise.[18] Moreover, such method of treatment improves the long-term outcome on patients with prostate cancer.[19] In the era of ultrasensitive PSA detection, our data suggests that early administration of SRT can lead to a better oncological outcome (Fig. 1). The long-term effect was not discussed in our study because the median followup was 24 months. Further studies are needed to determine the optimal cutoff of PSA at which salvage RT should be given to patients with BCR.

Moreover, the dosage of RT has always been a controversial topic. It differs among patients undergoing primary RT, ART, or SRT. With respect to our study, the dosage was 66 Gy for all 70 patients. Most studies considering early SRT have used, on average, a dosage of 66.2 Gy.[20] Current guidelines report that the minimum dosage that should be used in SRT is 64 Gy.[21] In contrast, trials evaluating ART use dosages between 60 and 64 Gy.[22] In patients who undergo primary RT, a minimum dose of >74 Gy is recommended for RT + HT. The European guidelines recommend a total dose of 76–78 Gy in intermediate- and high-risk patients.[3]

Some of the patients will experience urinary incontinence with or without impotency after RP. In the era of RARP, the weighted mean potency rate and the mean rate of urinary continence (no pad) at 24 months were 64.9% and 91.4%, respectively.[9] In spite of the above-mentioned data, the possibility of post-treatment deterioration should be addressed to the patients before initiation of RT. One of the important points highlighted in our study is that the functional outcome of the patients is not significantly affected with early SRT. This study has revealed that RT doesn't aggravate lower urinary tract symptoms. Strict continence, defined as the usage of 0 pads, was seen in 71% of the patients after SRT vs. 78% before SRT. Hegarty et al report there is no significant relationship between early RT and higher rates of gastrointestinal, geni-

**Table 3. Functional sexual outcome (EHS [p= 0.982], SHIM score)**

| Time (months) | EHS ≤2, n (%) | EHS >2, n (%) | Total number of patients | | | |
|---|---|---|---|---|---|---|
| Pre-RT | 45 (64.29) | 25 (35.71) | 70 | | | |
| 6 | 41 (65.08) | 22 (34.92) | 63 | | | |
| 12 | 36 (63.07) | 22 (37.93) | 58 | | | |
| 24 | 31 (64.58) | 17 (35.42) | 48 | | | |
| **Time (months)** | **SHIM score <21, n (%)** | **SHIM score ≥21, n (%)** | **Total number of patients** | **Mean** | **Mean CI** | **p** |
| Pre-RT | 58 (82.86) | 12 (17.14) | 70 | 8.823 | (6.89–10.76) | |
| 6 | 57 (81.43) | 13 (18.57) | 70 | 11.07 | (9.25–12.89) | 0.09335 |
| 12 | 51 (86.44) | 8 (13.56) | 59 | 8.32 | (6.22–10.42) | 0.7247 |
| 24 | 43 (86) | 7 (14) | 50 | 8.18 | (5.88–10.48) | 0.6669 |

CI: confidence interval; EHS: erection hardness score; SHIM: Sexual Health Inventory for Men; RT: radiotherapy.

tourinary, or sexual events.[23] With respect to the IPSS score, the mean value after 24 months post-SRT was 3.6 compared to 3.3 pre-SRT. This endorses the idea that early SRT doesn't affect the patients' QOL using the IPSS score as part of the evaluation criteria. Another study manifested that the IPSS and QOL had returned to baseline 12 months after SRT.[24]

With respect to the sexual health, our study has shown that the average SHIM score was 8 24 months post-SRT compared to 8.8 pre-SRT. It was stated that preoperative erectile function has an impact on recovery after RT regardless of the timing and dosage.[5] Fourteen percent had a SHIM score greater than 21 post-RT compared to 17 % pre-RT. In our study, we considered a subcategory of men with an EHS ≥3 pre-RT because the average SHIM score pre-RT was low (8.83). Out of the 25 patients who had an EHS of 3 or 4 before RT, 16 patients were followed up for two years. Their EHS after two years was 3 or 4. The average SHIM score for this same subcategory was 18.32 pre-RT compared to 16.76 24 months post-RT. Our figures eliminate the misconception that SRT causes sexual health deterioration.

Despite all this, our study has certain limitations. The number of patients undergoing SRT post-RARP in the study was around 70. This number will surely increase in the coming years because of the growing number of patients undergoing RARP. The data was collected in a retrospective manner, so some of the confounders cannot be controlled. Long-term effect (>5 years) was not assessed in this article, but will be addressed in future articles. Despite these limitations, we believe our results indicate that SRT post-RARP is a safe procedure with valuable oncological outcomes for patients.

## Conclusion

SRT is an effective treatment for patients who experience BCR following RARP. It was shown that it improves the prognosis of the patients. This study has revealed that early SRT has a very little midterm impact on urinary continence and potency. To note, further studies will be needed to evaluate the long-term side effects of this treatment modality.

**Competing interests:** Dr. Taussky has received grants/honoraria from Bayer and Sanofi. Dr. Zorn has been a consultant for Boston Scientific. The remaining authors report no competing personal or financial interests.

This paper has been peer-reviewed.

## References

1. Patel VR, Sivaraman A. Current status of robot-assisted radical prostatectomy: Progress is inevitable. *Oncology* 2012;26:616-9.
2. Abugharib A, Jackson WC, Tumati V, et al. Very early salvage radiotherapy improves distant metastasis-free survival. *J Urol* 2017;197:662-8. https://doi.org/10.1016/j.juro.2016.08.106
3. Habchi H, Mottet N. Management of prostate cancer: EAU guidelines on screening, diagnosis, and local primary treatment. *Management of Prostate Cancer* 2017;399-411. https://doi.org/10.1007/978-3-319-42769-0_26
4. Stish B, Pisansky T, Harmsen W, et al. Early salvage radiation therapy is associated with improved metastasis-free, prostate cancer-specific, and overall survival in men with detectable PSA following radical prostatectomy. *Int J Rad Oncol Biol Physics* 2016;96:E237. https://doi.org/10.1016/j.ijrobp.2016.06.1218
5. Zaffuto E, Gandaglia G, Fossati N, et al. Early postoperative radiotherapy is associated with worse functional outcomes in patients with prostate cancer. *J Urol* 2017;197:669-75. https://doi.org/10.1016/j.juro.2016.09.079
6. Valdivieso RF, Hueber P, Zorn K. Robot assisted radical prostatectomy: How I do it. Part II: Surgical technique. *Can J Urol* 2013:20:7073-8.
7. Ficarra V, Sooriakumaran P, Novara G, et al. Systematic review of methods for reporting combined outcomes after radical prostatectomy and proposal of a novel system: The survival, continence, and potency (SCP) classification. *Eur Urol* 2012;61:541-8. https://doi.org/10.1016/j.eururo.2011.11.042
8. Matsuda Y, Hisasue S, Kumamoto Y, et al. Correlation between erection hardness score and nocturnal penile tumescence measurement. *J Sex Med* 2014;11:2272-6. https://doi.org/10.1111/jsm.12617
9. Zorn KC, Tholomier C, Bienz M, et al. Oncological and functional outcomes of 722 robot-assisted radical prostatectomy (RARP) cases: The largest Canadian 5-year experience. *Can Urol Assoc J* 2014;8:195-201. https://doi.org/10.5489/cuaj.2016
10. Su MZ, Kneebone AB, Woo HH. Adjuvant versus salvage radiotherapy following radical prostatectomy: Do the AUA/ASTRO guidelines have all the answers? *Exp Rev Anticancer Ther* 2014;14:1265-70. https://doi.org/10.1586/14737140.2014.972381
11. Herrera FG, Berthold DR. Radiation therapy after radical prostatectomy: Implications for clinicians. *Front Oncol* 2016 9;6:117. https://doi.org/10.3389/fonc.2016.00117
12. Mizowaki T, Aoki M, Nakamura K, et al. Current status and outcomes of patients developing PSA recurrence after prostatectomy who were treated with salvage radiotherapy: A JROSG surveillance study. *J Rad Res* 2015;56:750-6. https://doi.org/10.1093/jrr/rrv027
13. Van der Poel H, Tillier C, de Blok W, et al. Salvage radiotherapy after robot-assisted laparoscopic radical prostatectomy. *Urology* 2013;82:834-9. https://doi.org/10.1016/j.urology.2013.04.057
14. Kwon O, Kim KB, Lee YI, et al. Salvage radiotherapy after radical prostatectomy: Prediction of biochemical outcomes. *Plos One* 2014;9:e103574. https://doi.org/10.1371/journal.pone.0103574
15. Pfister D, Bolla M, Briganti A, et al. Early salvage radiotherapy following radical prostatectomy. *Euro Urol* 2014;65:1034-43. https://doi.org/10.1016/j.eururo.2013.08.013
16. Gandaglia G, Karakiewicz PI, Briganti A, et al. Early radiotherapy after radical prostatectomy improves cancer-specific survival only in patients with highly aggressive prostate cancer: Validation of recently released criteria. *Int J Urol* 2014;22:89-95. https://doi.org/10.1111/iju.12605
17. Tendulkar R, Agrawal S, Efstathiou J, et al. Contemporary update of a multi-institutional predictive nomogram for salvage radiation therapy after prostatectomy. *Int J Rad Oncol Biol Physics* 2015;93:S131. https://doi.org/10.1016/j.ijrobp.2015.07.313
18. Fossati N, Karnes RJ, Cozzarini C, et al. Assessing the optimal timing for early salvage radiation therapy in patients with prostate-specific antigen rise after radical prostatectomy. *Eur Urol* 2016;69:728-33. https://doi.org/10.1016/j.eururo.2015.10.009
19. Gandaglia G, Cozzarini C, Mottrie A, et al. The role of radiotherapy after radical prostatectomy in patients with prostate cancer. *Curr Oncol Rep* 2015;17:53. https://doi.org/10.1007/s11912-015-0478-5
20. Briganti A, Wiegel T, Joniau S, et al. Early salvage radiation therapy does not compromise cancer control in patients with pT3N0 prostate cancer after radical prostatectomy: Results of a match-controlled multi-institutional analysis. *Eur Urol* 2012;62:472-87. https://doi.org/10.1016/j.eururo.2012.04.056
21. Valicenti RK, Thompson I, Albertsen P, et al. Adjuvant and salvage radiation therapy after prostatectomy: American Society for Radiation Oncology/American Urological Association guidelines. *Int J Rad Oncol Biol Physics* 2013;86:822-8. https://doi.org/10.1016/j.ijrobp.2013.05.029
22. Thompson IM, Tangen CM, Paradelo J, et al. Adjuvant radiotherapy for pathologically advanced prostate cancer. *JAMA* 2006;296:2329-35. https://doi.org/10.1001/jama.296.19.2329
23. Hegarty SE, Hyslop T, Dicker AP, et al. Radiation therapy after radical prostatectomy for prostate cancer: Evaluation of complications and influence of radiation timing on outcomes in a large, population-based cohort. *Plos One* 2015;10:e0118430 https://doi.org/10.1371/journal.pone.0118430
24. Miyake M, Tanaka N, Asakawa I, et al. Changes in lower urinary tract symptoms and quality of life after salvage radiotherapy for biochemical recurrence of prostate cancer. *Radiother Oncol* 2015;115:321-6. https://doi.org/10.1016/j.radonc.2015.04.026

**Correspondence:** Dr. Khaled Ajib, Section of Urology, Department of Surgery, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; khaled.ajib@gmail.com