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## Radiotherapy after Radical Prostatectomy: Effect of Timing of Post-Prostatectomy Radiation on Functional Outcomes

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## Abstract

**Introduction and Objective**—The timing of radiotherapy after prostatectomy is controversial, and its effect on sexual, urinary, and bowel function is unknown. This study seeks to compare patient-reported functional outcomes after radical prostatectomy (RP) and post-prostatectomy radiation as well as elucidate the timing of radiation to allow optimal recovery of function.

**Methods**—The Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study is a prospective, population-based, observational study of men with localized prostate cancer. Patient-reported sexual, urinary, and bowel functional outcomes were measured using the 26-item Expanded Prostate Index Composite (EPIC-26) at baseline and at 6, 12, 36, and 60 months after enrollment. Functional outcomes were compared among men undergoing RP alone, post-RP adjuvant radiation (RP+aRT), and post-RP salvage radiation (RP+sRT) using multivariable models controlling for baseline clinical, demographic, and functional characteristics.

**Results**—Among 1482 CEASAR participants initially treated with RP for clinically localized prostate cancer, 11.5% ( $N=170$ ) received adjuvant (aRT,  $N=57$ ) or salvage (sRT,  $N=113$ ) radiation.

Men who received post-RP radiotherapy (RT) had worse scores in all domains [sexual function ( $-9.0$ , 95% CI [ $-14.5$ ,  $-3.6$ ],  $p<0.001$ ), incontinence ( $-8.8$ , [ $-14.0$ ,  $-3.6$ ],  $p<0.001$ ), irritative voiding ( $-5.9$ , [ $-9.0$ ,  $-2.8$ ],  $p<0.001$ ), bowel irritative ( $-3.5$ , [ $-5.8$ ,  $-1.2$ ],  $p=0.002$ ), and hormonal function ( $-4.5$ , [ $-7.2$ ,  $-1.7$ ],  $p=0.001$ )] compared to RP alone at 5 years of follow up.

Compared to men treated with RP alone in an adjusted linear model, sRT was associated with significantly worse scores in all functional domains. aRT was associated with significantly worse incontinence, urinary irritation, and hormonal function domain scores compared to RP alone at 5 years of follow up.

On multivariable modeling, RT administered approximately 24 months after RP was associated with the smallest decline in sexual domain score, with an adjusted mean decrease of 8.85 points (95% CI [ $-19.8$ ,  $2.1$ ]) from post-RP, pre-RT baseline.

**Conclusions**—In men with localized prostate cancer, post-RP RT was associated with significantly worse sexual, urinary, and bowel function domain scores at 5 years compared to RP alone. Radiation delayed for approximately 24 months after RP may be optimal for preserving erectile function compared to radiation administered closer to the time of RP.

## Keywords

Prostate cancer; Outcomes; Prostatectomy; Radiation; Erectile function

## 1. Introduction

Radical prostatectomy (RP) is the most commonly utilized treatment option for men with intermediate- or high-risk clinically localized prostate cancer<sup>1,2</sup>. Despite refinements in preoperative risk stratification, patient selection, and surgical technique, approximately 25% to 41% of men will develop local recurrence with prostate-specific antigen (PSA) elevation in the absence of radiographic distant disease within 10 years after surgery<sup>3-6</sup> prompting evaluation for salvage therapy. Additionally, four randomized trials have demonstrated reduction in the risk of biochemical recurrence (BCR), local recurrence, and clinical

progression of cancer with adjuvant radiotherapy in men with adverse features at prostatectomy such as positive margins, seminal vesical invasion, and/or extraprostatic extension<sup>7–10</sup>. Despite broad recommendations for consideration of adjuvant radiotherapy in these men in both the AUA and EUA guidelines, adjuvant therapy is utilized in only 6–51% of men and is declining over time<sup>11,12</sup>.

Variations in adjuvant (aRT, administered within one year of RP) and salvage radiotherapy (sRT, administered greater than one year after RP) patterns worldwide for localized prostate cancer managed with initial RP stem from multiple factors. Studies in aRT versus early sRT differ regarding freedom from BCR, freedom from androgen deprivation therapy (ADT), and freedom from distant metastases but are largely concordant in demonstrating no change in overall survival (OS)<sup>13–16</sup>. As a result, patients and providers may delay post-RP radiation due to uncertainty regarding the survival benefit and concern about the adverse functional effects of post-RP radiation.

Despite current prospective investigations into the timing of post-RP radiation with regard to BCR, cancer-specific survival, and OS, there remains a paucity of prospective data on the functional outcomes of men undergoing post-RP radiation and the association between the timing of radiation with functional outcomes. Anecdotally, urologists often counsel patients that longer duration between prostatectomy and radiation improves the chance of recovery of continence and erectile function. However, data to support this are scarce. This study aims to examine the effect of post-RP radiation on patient-reported functional outcomes as well as the timing of aRT or sRT to allow optimal recovery of continence, sexual function, and bowel function after radical prostatectomy using data from the prospective, population-based Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) cohort.

## 2. Methods

### 2.1 Study Population

The Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study is a prospective, population-based observational cohort designed to measure the effectiveness and harms of contemporary management strategies for men diagnosed with localized prostate cancer (NCT0136286). Patients were accrued from five Surveillance Epidemiology, and End Results (SEER) registry catchment areas (Louisiana, New Jersey, Utah, Atlanta, and Los Angeles) augmented with a sample of men enrolled in Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE)<sup>17</sup>. The CEASAR methodology has previously been described.<sup>18</sup> Briefly, a total of 3,709 participants were enrolled in CEASAR between 2011 and 2012 and completed at least one follow up survey, of which, 3,277 men met inclusion criteria: age  $\geq$  80 years old, clinical stage cT1 or cT2 disease, prostate-specific antigen (PSA)  $<$ 50 ng/dl, English- or Spanish-speaking, able to give consent, and enrolled within 6 months after pathologically diagnosed localized adenocarcinoma of the prostate.

Among 3,277 eligible men, 1,482 who underwent RP as initial treatment were analyzed. Men excluded from this study were those who had missing treatment dates, reported both RP and RT on the same date, or underwent ablation before RP or between RP and RT (Supplemental Figure 1). aRT was defined as radiotherapy administered within one year

after RP regardless of pathologic risk factors or intent of treatment, and sRT was defined as radiotherapy administered greater than one year after RP regardless of known recurrence or progression of disease.

The coordinating site at Vanderbilt, SEER sites, and CaPSURE each obtained approval from the corresponding local Institutional Review Board.

## 2.2 Survey instruments and medical chart abstraction<sup>19</sup>

Surveys were completed at baseline (time of study enrollment within 6 months of diagnosis) and at 6, 12, 36, and 60 months after enrollment. The validated 26-item Expanded Prostate Index Composite (EPIC-26) was used to evaluate patient-reported disease-specific function with summary scores calculated for urinary irritative, urinary incontinence, bowel, sexual, and hormonal domains ranging from 0 to 100, with higher scores representing better function. Surveys captured patient-reported race, age, income, education, marital status, and insurance. Validated instruments assessing general health and function, emotional health, cancer-related anxiety, and illness management style were previously described<sup>18</sup>. Total Illness Burden Index for Prostate Cancer (TIBICAP) measured comorbidity, with higher scores corresponding to greater severity<sup>20</sup>. Tumor characteristics, treatment, and treatment dates were obtained from medical charts by participating registries one year after enrollment. For patients without available chart information, treatment was determined from self-reported surveys and data from cancer registries.

## 2.3 Statistical Analysis

Patients' demographic and baseline characteristics were summarized by treatment groups (RP-alone versus RP+aRT or RP+sRT). Differences among groups were compared with the Kruskal-Wallis or Wilcoxon rank-sum test for continuous variables and the Pearson  $\chi^2$  test for categorical variables.

The primary outcomes measured at baseline and each follow-up included the five EPIC-26 domain scores: sexual function, urinary incontinence, urinary irritative, bowel irritative, and hormonal function. Among the men who underwent RP and any type of radiation, we defined the secondary outcomes as the changes in the five domain scores from the post-RP-baseline to the last follow-up.

In the primary analyses, we first evaluated the overall effects of RT on outcomes by comparing patients who underwent RP-only with those who underwent any radiation following RP. The effect of timing of radiation was investigated by comparing men who underwent RP+aRT or RP+sRT separately. Linear regression models were used, and mean differences in domain scores among groups was reported along with 95% confidence intervals (95% CIs). Models adjusted for age (continuous), race (white, nonwhite), TIBICAP comorbidity score ( $\leq 4$ ,  $>5$ ), D'Amico risk (low, intermediate, high), bilateral nerve-sparing prostatectomy technique (yes, no), use of ADT (yes, no), margin status (positive, negative), and corresponding baseline domain scores (continuous). Restricted cubic splines terms were included for age to allow for flexible association with the outcomes. To account for potential correlations among multiple records collected from the same individual at different follow-ups, robust covariance matrix estimates by the Huber-White method was used<sup>21,22</sup>.

For the secondary analysis, with the goal of identifying the optimal timing for post-RP radiation for functional recovery, we used linear regressions to model the association between time from RP to post-RP radiation (RP-RT-interval) and changes in domain scores from the post-RP, pre-RT baseline to last follow-up. Restricted cubic splines for RP-RT-interval were included in these models. The time from radiation to last follow-up and covariates included in the primary analysis were included in this model. Mean changes in domain scores were estimated as a function of RP-RT-interval.

Results were interpreted in light of both statistical and clinical significance according to previously published minimally clinically important differences (MCIDs: 4–6 points for bowel and hormonal, 5–7 for urinary irritation, 6–9 for urinary incontinence, and 10–12 points for sexual function domains)<sup>28</sup>. Statistical significance was considered for all two-sided p-values  $\leq 5\%$ . All analyses were conducted using R software version 3.5<sup>23</sup>.

### 3. Results

There were 1,482 men in the CEASAR cohort with clinically localized prostate cancer who underwent initial treatment with RP. Of those, 170 men (11%) underwent post-RP RT within 5 years, including 57 men (34%) who received aRT and 113 men (66%) who received sRT. The median time from RP to aRT was 7.3 months, and median time from RP to sRT was 28.5 months. Age at prostate cancer diagnosis, race, education, marital status, comorbidities, clinical tumor stage, and pre-prostatectomy baseline EPIC-26 domain scores were similar among treatment groups (Table 1). There were expected statistically significant differences in the RP-alone versus RP+aRT versus RP+sRT groups with regard to PSA at diagnosis, Gleason score, D'Amico risk, clinical and pathologic stages, margin status, and exposure to ADT as these covariates are related to the indications for subsequent radiation exposure after RP.

Unadjusted comparisons between RP-alone, RP+aRT, and RP+sRT demonstrated that each group had distinct functional recovery trajectories following RP, depending on whether and when they received radiation (Figure 1). For example, men who underwent aRT had lower hormonal domain scores in the first two years after RP compared to men who underwent RP-alone or RP+sRT (Figure 1E).

#### 3.1 Comparison between RP alone and any additional RT

Compared to men who underwent RP alone, men who received post-RP RT had worse scores in all domains regardless of the timing of receiving RT [sexual function (–9.0 point difference in EPIC-26 score, 95% CI [–14.5, –3.6],  $p<0.001$ ), incontinence (–8.8, [–14.0, –3.6],  $p<0.001$ ), irritative voiding (–5.9, [–9.0, –2.8],  $p<0.001$ ), bowel irritative (–3.5, [–5.8, –1.2],  $p=0.002$ ), and hormonal function (–4.5, [–7.2, –1.7],  $p=0.001$ )] at 5 years of follow up (Supplemental Table 1 and Supplemental Figure 2).

#### 3.2 Comparisons between RP alone, aRT, and sRT

When taking the timing of RT into consideration, RP+aRT was associated with significant decrements in incontinence (–11.9, [–20.7, –3.1],  $p=0.008$ ), urinary irritation (–5.9, [–11.2, –0.6],  $p=0.030$ ), and hormonal function (–7.3, [–13.6, –1.0],  $p=0.023$ ) at five years of

follow up versus RP alone. RP+sRT was also associated with a significant decline in sexual function ( $-11.1$ ,  $[-17.0, -5.3]$ ,  $p<0.001$ ), incontinence ( $-7.6$ ,  $[-13.6, -1.6]$ ,  $p=0.014$ ), urinary irritative ( $-6.1$ ,  $[-9.7, -2.4]$ ,  $p=0.001$ ), bowel irritative ( $-4.5$ ,  $[-7.4, -1.7]$ ,  $p=0.002$ ), and hormonal function ( $-3.3$ ,  $[-6.0, -0.6]$ ,  $p=0.017$ ) domain scores versus RP alone at 5 years of follow up (Table 2). Irritative voiding and hormonal function scores were affected by aRT in the first year after RP; however, no statistically significant differences were found between RP+aRT and RP+sRT with regard to any functional domain scores beyond 1 year.

### 3.3 Multivariable modeling of change from baseline domain score over time from RP

We modeled the change in domain score from post-RP, pre-RT baseline to the longest follow-up outcome in order to identify the optimal timing for post-RP radiation for functional recovery (Figure 2). The smallest decline in sexual function score occurred when RT was administered approximately 24 months after RP (mean 8.9 point decline on EPIC-26 sexual domain,  $p=0.016$ ). RT administered before 19 months or after 29 months from RP was associated with a mean decline of at least 10 points, which meets the threshold for MCID. These models did not identify optimal timing of radiation to preserve urinary incontinence, urinary irritative, bowel, or hormonal function.

## 4. Discussion

In this study, both adjuvant and salvage radiation were associated with worse EPIC-26 incontinence, urinary irritative, and hormonal function; with sRT also affecting sexual function and bowel irritative domain scores compared to RP alone at 5 years of follow up. Furthermore, an interval of approximately 24 months between RP and RT was associated with the least pronounced decline in sexual function associated with post-RP radiation when compared to RT administration at other time points.

This prospective analysis is consistent with reports of lower long-term continence rates in men who undergo radiation at any time point after prostatectomy in retrospective analyses<sup>24–28</sup>. However, retrospective data assessing the impact of post-RP RT on sexual function are more varied. Zaffuto *et al* observed a significantly decreased 3-year erectile function recovery rate of 11.6% after aRT versus 29.0% after sRT compared to 35.0% after RP suggesting that time from surgery to radiation administration does play a role in recovery<sup>25</sup>. Adam *et al* also demonstrated that post-RP radiotherapy was associated with an 18% lower potency rate compared to RP alone, with aRT significantly lowering potency compared to sRT (37% vs 45%)<sup>26</sup>. This is in contrast to studies by Hegarty *et al* and Showalter *et al* that showed no difference in rates of erectile dysfunction after RP versus post-RP radiotherapy with subgroup analysis demonstrating no increased rate of erectile dysfunction between aRT and sRT<sup>27,28</sup>. Differences between our findings and those studies may reflect the fact that we were able to adjust for baseline function and disease severity, which substantially influence outcomes<sup>29</sup>.

While the EPIC-26 domain scores employed in our study are increasingly being utilized for patient-reported functional outcomes among prostate cancer survivors, consideration should be given to the clinical implication of these findings. The 10–12 point minimally-important

difference (MID) previously established by Skolarus *et al*<sup>31</sup> for erectile function is observed when RT is administered before 19.0 months and after 29.0 months after RP.

Time from radical prostatectomy to radiation was associated with a significant change in sexual domain score from baseline with the least decline in erectile function achieved at approximately 24 months. This suggests that an approximately two-year recovery period after surgery may be optimal for erectile function preservation, and, therefore, sRT would be preferred if there is no compromise in oncologic control. Whereas older studies have demonstrated differences in progression free survival between aRT and sRT, interim analysis of the ongoing RADICALS- RT trial did not show a benefit for aRT versus early sRT with regard to biochemical progression free survival<sup>30</sup>. Patient-reported urinary incontinence for the aRT group was worse at one year, but other functional measures of the RADICALS-RT trial have not yet been reported. Taken together with the current study, this suggests that men considering selective sRT may preserve function compared to aRT without compromising oncologic outcomes. Final results of RADICALS- RT and the ongoing RAVES and GETUG-17 trials comparing aRT and sRT will help to better understand the impact of delayed radiotherapy on survival outcomes.

There are several limitations of this study, including confounding to indication inherent to this type of nonrandomized study which may limit outcome comparisons between RP, aRT, and sRT groups in the CEASAR cohort. Nevertheless, we controlled for prostate cancer risk group, Gleason score, PSA at diagnosis, pathologic stage, margin status, and ADT exposure, which are related to the indications for subsequent radiation exposure. The knowledge of additional radiation treatment could influence patient assessment and reporting of symptoms, and utilization of interventions for symptomatic management of erectile dysfunction and bladder symptoms in the time period after prostate cancer treatment were not reported. Given the relatively small sample size of 170 men undergoing post-RP radiotherapy in our study, negative results for the other domains may be a reflection of being underpowered to discern statistical significance.

These findings help describe the potential harms of post-prostatectomy radiation on sexual, urinary, and bowel function, and the differential outcomes based on the timing of radiation. This information may assist physicians in counseling men with localized prostate cancer with high risk features, PSA persistence, or biochemical recurrence after RP, particularly when used in conjunction with emerging data on comparative oncologic effectiveness of aRT and sRT. Balancing the effect of the timing of radiation on both the optimization of functional outcomes and maintenance of disease-specific and OS will be of critical value to prostate cancer survivors participating in shared decision making regarding future treatments.

## 5. Conclusions

In men with localized prostate cancer, post-prostatectomy radiation was associated with worse erectile function, incontinence, urinary irritative, bowel function, and hormonal function domain scores at 5 years compared to RP alone. RT delayed for approximately 24 months after RP was associated with a smaller decline in sexual function than radiation



administered closer to the time of RP, suggesting that an approximately two-year recovery period after surgery may be optimal for erectile function preservation if there is no compromise in oncologic control.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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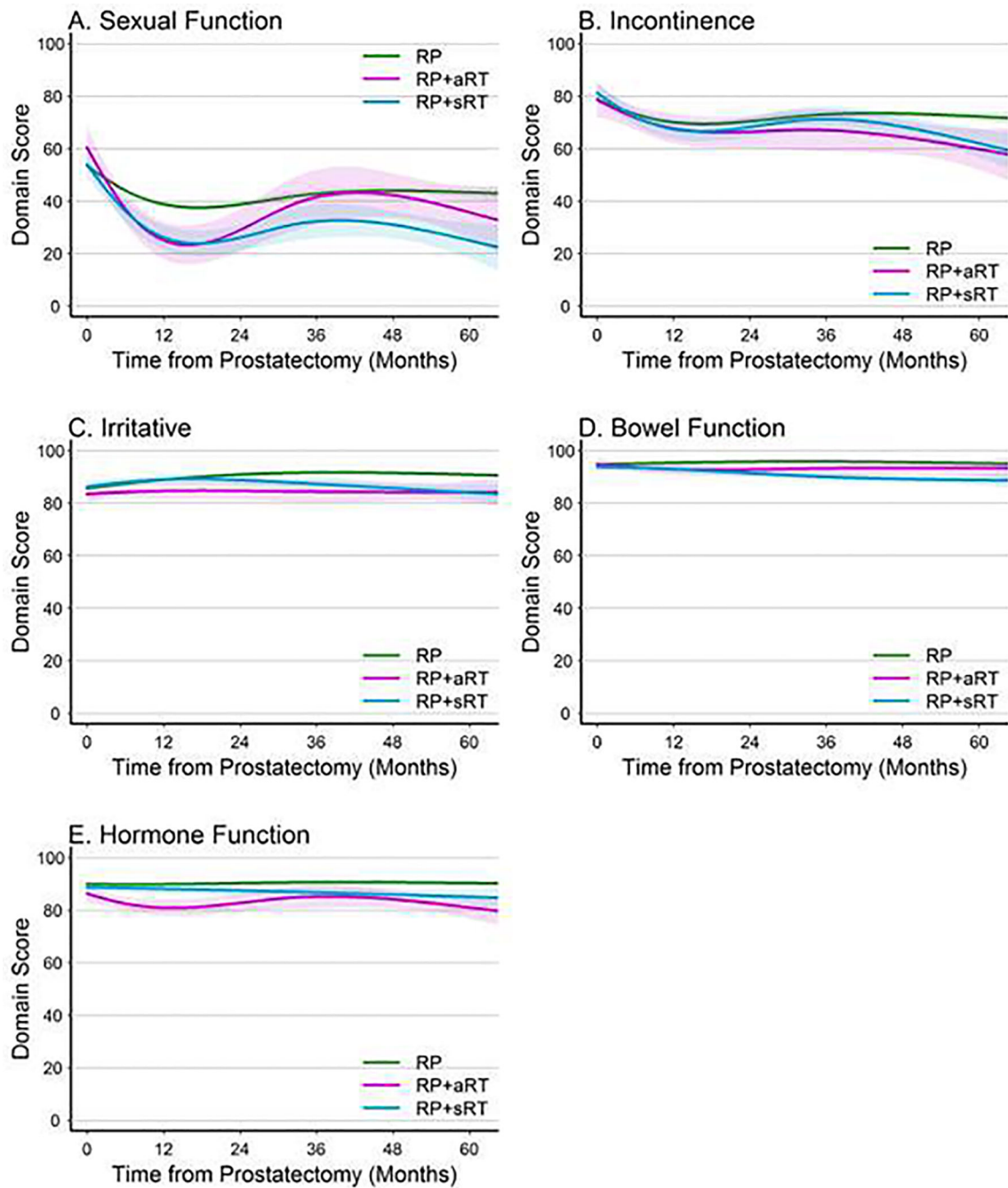
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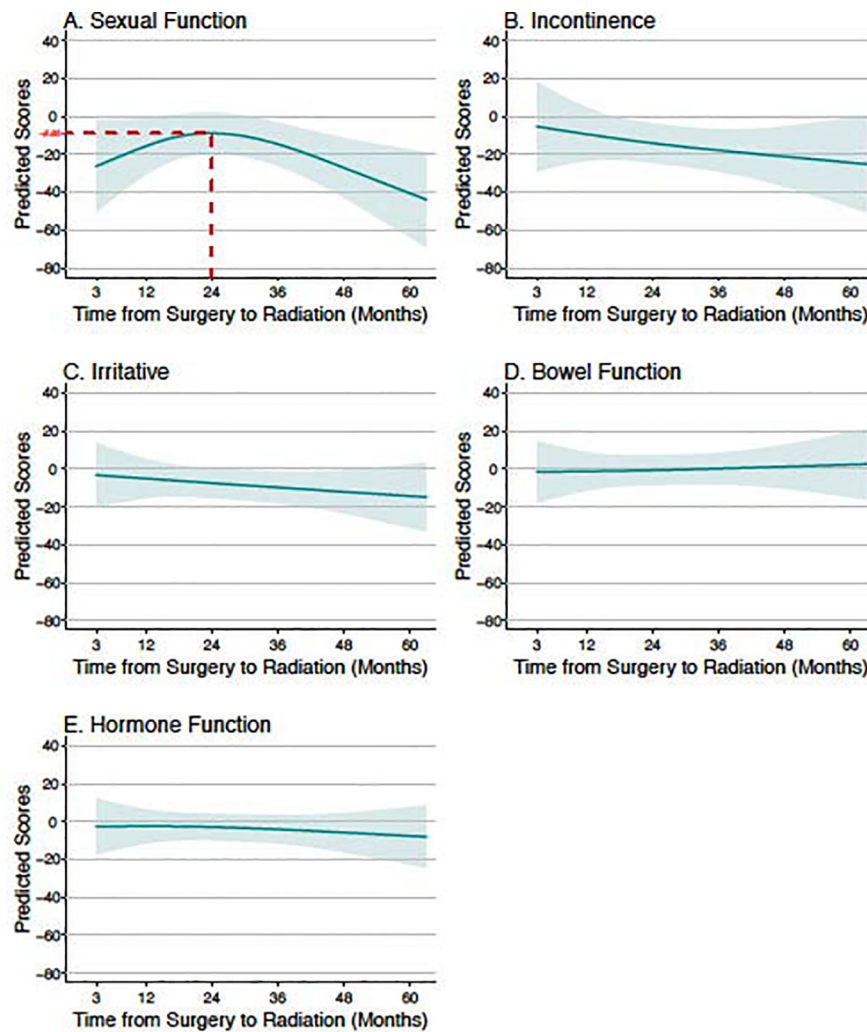
### Highlights

- Adjuvant and salvage radiation affect outcomes after prostate cancer surgery
- Radiation after prostatectomy worsens erectile function, incontinence, and voiding
- Radiotherapy given two years after prostatectomy best preserves erectile function
- Salvage radiation preferred for sexual function preservation if oncologically sound



**Figure 1.**

Unadjusted trajectory plot of EPIC-26 scores for a) sexual function, b) incontinence, c) urinary irritative, d) bowel function, e) hormonal function domains for men undergoing RP, RP+aRT, and RP+sRT over time from RP. (Median time from RP to aRT 7.3 months; median time from RP to sRT 28.5 months).



**Figure 2.** Predicted changes in EPIC-26 domain scores from post-RP, pre-RT baselines to the longest follow up outcome [for a) sexual function, b) incontinence, c) urinary irritative, d) bowel function, e) hormonal function] as functions of time interval from RP to administration of post-RP radiation. (Red dotted line denotes smallest decrease {mean  $-8.85$  points, 95% CI  $[-19.8, 2.1]$ } in sexual function domain score was achieved when the post-RP radiation was administered approximately 24 months after RP.)

**Table 1.**

## Demographics and Baseline Characteristics

	RP only (n = 1312)	RP + aRT (n = 57)	RP + sRT (n = 113)	p-value
Median age at diagnosis (IQR), years	62 (57, 66)	62 (56, 65)	63 (58, 66)	0.23 <sup>1</sup>
Race, N(%)				0.35 <sup>3</sup>
White	996 (77)	37 (65)	84 (75)	
Black	152 (12)	12 (21)	11 (10)	
Hispanic	98 (8)	5 (9)	10 (9)	
Asian	38 (3)	1 (2)	5 (4)	
Other	17 (1)	2 (4)	2 (2)	
Education, N(%)				0.14
Less than high school	91 (7)	7 (13)	12 (11)	
High school graduate	257 (21)	9 (16)	15 (14)	
Some college	276 (22)	13 (24)	21 (19)	
College graduate	310 (25)	10 (18)	24 (22)	
Graduate/professional school	297 (24)	16 (29)	37 (34)	
Marital Status, N(%)				0.49 <sup>3</sup>
Not married	198 (16)	10 (18)	22 (20)	
Married	1031 (84)	45 (82)	86 (80)	
Comorbidity Score, N(%)				0.44 <sup>3</sup>
0–2	422 (34)	19 (35)	29 (27)	
3–4	530 (43)	21 (38)	55 (50)	
>5	286 (23)	15 (27)	25 (23)	
PSA at diagnosis, median (IQR), ng/mL	5 (4, 7)	7 (5, 12)	6 (4, 8)	<0.001 <sup>1</sup>
Biopsy Gleason score, N(%)				<0.001 <sup>3</sup>
6 or less	718 (55)	13 (23)	23 (20)	
3 + 4	380 (29)	13 (23)	43 (38)	
4 + 3	127 (10)	9 (16)	20 (18)	
8, 9, 10	82 (6)	22 (39)	27 (24)	
D'Amico prostate cancer risk, N(%)				<0.001 <sup>3</sup>
Low	628 (48)	8 (14)	17 (15)	
Intermediate	518 (40)	22 (39)	59 (52)	
High	163 (12)	27 (47)	37 (33)	
Clinical stage, N(%)				0.013 <sup>3</sup>
cT1	1007 (77)	42 (74)	73 (65)	
cT2	303 (23)	15 (26)	40 (35)	
Pathologic pT stage, N(%)				<0.001 <sup>3</sup>

	RP only (n = 1312)	RP + aRT (n = 57)	RP + sRT (n = 113)	p-value
pT0	1 (0)	0 (0)	0 (0)	
pT2 (NOS)	44 (4)	2 (4)	2 (2)	
pT2a	125 (12)	3 (6)	5 (5)	
pT2b	24 (2)	0 (0)	0 (0)	
pT2c	736 (70)	16 (31)	46 (48)	
pT3 (NOS)	5 (0)	2 (4)	2 (2)	
pT3a	96 (9)	15 (29)	30 (31)	
pT3b	18 (2)	13 (25)	11 (11)	
pT4	1 (0)	0 (0)	0 (0)	
Margin status, <i>N</i> (%)				<0.001 <sup>3</sup>
Negative	865 (8%)	19 (40)	62 (65)	
Positive	212 (20)	29 (60)	33 (35)	
Any hormone therapy, <i>N</i> (%)				<0.001 <sup>3</sup>
Yes	83 (6)	28 (49)	39 (35)	
No	1229 (94)	29 (51)	74 (65)	
Nerve-sparing surgery, <i>N</i> (%)				<0.001 <sup>3</sup>
Nerve-sparing	759 (82)	25 (61)	53 (68)	
Non-nerve-sparing or unilateral nerve-sparing	165 (18)	16 (39)	25 (32)	
Time from radiation to final survey, median (IQR), months		51 (41, 55)	25 (11, 39)	<0.001 <sup>2</sup>
Time from surgery to radiation, median (IQR), months		7 (5, 9)	29 (20, 40)	<0.001 <sup>2</sup>
Pre-RP baseline EPIC-26 score (IQR)				
Sexual function	80 (40, 95)	69 (48, 99)	75 (44, 90)	0.84
Urinary incontinence	100 (79, 100)	100 (73, 100)	100 (79, 100)	0.85 <sup>I</sup>
Urinary irritative	88 (75, 100)	88 (69, 100)	88 (75, 100)	0.97 <sup>I</sup>
Bowel function	100 (96, 100)	100 (96, 100)	100 (92, 100)	0.78 <sup>I</sup>
Hormonal	95 (85, 100)	90 (80, 100)	95 (81, 100)	0.16 <sup>I</sup>
Baseline EPIC-26 score between RP and RT (IQR)				
Sexual function	80 (40, 95)	43 (5, 65)	22 (0, 50)	<0.001 <sup>I</sup>
Urinary incontinence	100 (79, 100)	76 (51, 100)	76 (54, 98)	<0.001 <sup>I</sup>
Urinary irritative	88 (75, 100)	88 (80, 100)	94 (81, 100)	0.003 <sup>I</sup>
Bowel function	100 (96, 100)	100 (100, 100)	100 (92, 100)	0.053 <sup>I</sup>
Hormonal	95 (85, 100)	90 (80, 100)	90 (80, 100)	0.007 <sup>I</sup>

Tests used:

<sup>I</sup>Kruskal-Wallis test

<sup>2</sup>Wilcoxon test



<sup>3</sup>Pearson test

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**Table 2.**

Unadjusted and adjusted linear regression model comparing sexual function, incontinence, urinary irritative, bowel irritative, and hormonal function EPIC-26 domain scores over time for RP-alone versus RP+aRT versus RP+sRT.

Time from Prostatectomy (Months)	Unadjusted*				Adjusted <sup>†</sup>								
	N	RP (n=1265)	RP + aRT (n=57)	RP + sRT (n=112)	RP vs RP + aRT			RP vs RP + sRT			RP + aRT vs RP + sRT		
					B	95% CI	P-value	B	95% CI	P-value	B	95% CI	P-value
Sexual Function													
12	1315	33 (10, 65)	15 (0, 58)	17 (5, 43)	-3.5	[-10.9, 3.9]	0.356	-4.5	[-10.2, 1.2]	0.121	-1	[-9.5, 7.5]	0.817
36	1202	38 (12, 73)	24 (0, 70)	27 (0, 49)	-2.2	[-12.5, 8.2]	0.68	-5.1	[-10.4, 0.2]	0.057	-2.9	[-13.9, 8.0]	0.598
60	1100	39 (10, 75)	20 (0, 75)	12 (0, 49)	-4.2	[-14.4, 6.0]	0.417	-11.1	[-17.0, -5.3]	<b>&lt;0.001</b>	-6.9	[-18.0, 4.1]	0.219
Incontinence													
12	1289	75 (52, 100)	79 (46, 100)	73 (52, 100)	1.4	[-6.2, 9.1]	0.714	-0.7	[-6.3, 4.8]	0.796	-2.2	[-11.1, 6.7]	0.635
36	1208	79 (54, 100)	71 (46, 88)	76 (58, 98)	-7	[-16.6, 2.5]	0.149	-1	[-6.5, 4.5]	0.724	6	[-4.5, 16.6]	0.259
60	1106	75 (58, 100)	66 (38, 86)	67 (46, 85)	-11.9	[-20.7, -3.1]	<b>0.008</b>	-7.6	[-13.6, -1.6]	<b>0.014</b>	4.3	[-5.9, 14.5]	0.407
Irritative													
12	1312	94 (88, 100)	88 (77, 94)	94 (88, 100)	-5.1	[-8.7, -1.6]	<b>0.005</b>	-0.3	[-2.5, 1.8]	0.759	4.8	[0.9, 8.7]	<b>0.015</b>
36	1208	94 (88, 100)	88 (75, 100)	94 (81, 100)	-5.7	[-10.9, -0.4]	<b>0.035</b>	-3	[-6.2, 0.2]	0.07	2.7	[-3.3, 8.6]	0.38
60	1102	94 (88, 100)	88 (75, 100)	88 (75, 100)	-5.9	[-11.2, -0.6]	<b>0.03</b>	-6.1	[-9.7, -2.4]	<b>0.001</b>	-0.2	[-6.4, 6.0]	0.947
Bowel Irritative													
12	1328	100 (96, 100)	96 (88, 100)	100 (92, 100)	-3	[-5.4, -0.5]	<b>0.016</b>	-1.3	[-3.8, 1.2]	0.306	1.6	[-1.6, 4.9]	0.323
36	1224	100 (96, 100)	100 (92, 100)	100 (83, 100)	-1.3	[-4.3, 1.6]	0.382	-4.6	[-8.1, -1.2]	<b>0.008</b>	-3.3	[-7.8, 1.1]	0.144
60	1117	100 (96, 100)	100 (88, 100)	96 (83, 100)	-1.1	[-4.1, 1.8]	0.46	-4.5	[-7.4, -1.7]	<b>0.002</b>	-3.4	[-7.4, 0.5]	0.088

Time from Prostatectomy (Months)	Unadjusted*				Adjusted <sup>†</sup>									
	N	RP (n=1265)	RP + aRT (n=57)	RP + sRT (n=112)	RP vs RP + aRT			RP vs RP + sRT			RP + aRT vs RP + sRT			
					$\beta$	95% CI	P- value	$\beta$	95% CI	P- value	$\beta$	95% CI	P- value	
Hormonal function														
12	1314	95 (85, 100)	90 (66, 99)	90 (80, 100)	-7.2	[-12.1, -2.2]	<b>0.005</b>	-0.4	[-3.0, 2.1]	0.747	6.7	[1.3, 12.1]	<b>0.014</b>	
36	1209	95 (85, 100)	95 (75, 100)	92 (79, 100)	-2.8	[-8.1, 2.6]	0.312	-2	[-5.0, 1.1]	0.208	0.8	[-5.3, 6.9]	0.796	
60	1108	95 (85, 100)	90 (70, 100)	90 (75, 100)	-7.3	[-13.6, -1.0]	<b>0.023</b>	-3.3	[-6.0, -0.6]	<b>0.017</b>	4	[-2.8, 10.8]	0.247	

\* Omitted 48 patients who had surgery after one year.

<sup>†</sup> Covariates included age, race, TIBICAP, D'Amico risk, use of ADT, bilateral nerve-sparing technique, time from RT administration to final survey completion, and corresponding baseline domain scores.