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Topography of Prostate Cancer Recurrence After Radiation Therapy: A Detailed Mapping Study of Salvage Radical Prostatectomy Specimens

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Abstract

In men who do not respond to initial radiation therapy, accurate knowledge of the site of cancer recurrence or persistence is necessary to understand treatment failure. We evaluated the pathologic characteristics of recurrent/persistent prostate cancer with tumor maps from the whole-mount slides of salvage radical prostatectomies performed between 2000 and 2014. Of 216 consecutive patients, detailed tumor maps were available for 77. Sixty-nine patients (90%) were found to have tumor in the apex, of which 46% occurred in the most apical 3 mm. Fifty-three patients (69%) had tumors at a distance of ≤5 mm from the urethra. Five patients had tumor directly involving the

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urethra, all of whom had urethral invasion at the apex. Seminal vesicle involvement was seen in 32 patients (42%), two of whom had tumor only in the seminal vesicles. Sixty-two patients (81%) had tumors in the distal apex, periurethral area, or seminal vesicles, that is, areas that are not routinely biopsied. Targeting these areas could improve the accuracy of biopsy when cancer recurrence is suspected.

Patient summary—When recurrence is suspected, clinicians should include biopsy of the distal apex, areas surrounding the urethra, and seminal vesicles. This information will help tailor successful salvage treatments.

Keywords

Prostatic neoplasms; Recurrence; Salvage therapy

A major challenge for nonextirpative therapies is ensuring the complete and successful delivery of treatment to affected areas in close proximity to the urethra, rhabdosphincter, neurovascular bundles, and anterior rectal wall. Approximately one-third of men treated with radiation therapy (RT) for clinically localized prostate cancer will experience treatment failure [1,2], and salvage radical prostatectomy (SRP) has been shown to provide the best long-term cure [3]. Analysis of pathologic recurrence patterns in prostate cancer can help identify factors associated with primary treatment failure and may also be important for evaluating options for salvage therapy. In the present study, we reviewed detailed tumor maps from patients who underwent SRP and assessed the patterns of tumor recurrence after RT.

After receiving approval from the Institutional Review Board, we identified 216 consecutive patients who underwent SRP after RT for prostate cancer at our institution between 2000 and 2014. We evaluated clinical and pathologic characteristics of the 77 patients with tumor maps. Detailed methods are reported in the Supplementary material.

We found significant differences between the two patient groups (tumor map vs no tumor map) only in age at SRP; patients with tumor maps were slightly older (66 vs 65 yr old; $p = 0.046$; Supplementary Table 1). Clinical and pathologic characteristics of patients with tumor maps are shown in Tables 1 and 2. Tumors involved the apex, midgland, and base of the prostate in 69 (90%; 95% confidence interval [CI] 81%, 95%), 73 (95%; 95% CI 87%, 99%), and 44 (57%; 95% CI 45%, 68%) patients, respectively. Among patients with tumors involving the apex, 46% (95% CI 34%, 59%) had tumors in the most apical 3 mm. Forty-seven patients (61%; 95% CI 49%, 72%) had a single-cancer focus. Two patients (2.6%; 95% CI 0.3%, 9.1%) had tumor only in the seminal vesicles. Periurethral tumors were found in 53 patients (69%; 95% CI 57%, 79%). Among these patients, the location of the minimum distance between the tumor and the urethra was the apex in 28 patients (53%; 95% CI 39%, 67%) and midgland in 23 (43%; 95% CI 30%, 58%). Five patients had tumors directly involving the urethra, all of whom had urethral invasion at the apex. Forty-five patients (58%; 95% CI 47%, 70%) had extraprostatic extension (EPE); of them, 39 (87%; 95% CI 73%, 95%) had EPE at the posterior prostate, 35 (78%; 95% CI 63%, 89%) at the base, and 34 (76%; 95% CI 60%, 87%) at the posterior base. Among the 32 patients (42%; 95% CI 30%, 53%) with seminal vesicle involvement (SVI), two had tumors only in the

seminal vesicles. Among the 77 patients with tumor maps, 81% (95% CI 70%, 89%) had a tumor in the distal apex, periurethral area, or seminal vesicles. None of these sites are routinely biopsied.

In our current analysis, the majority of recurrent tumors after RT were solitary (61%), and located within 5 mm of the urethra (69%), at the apex (90%), or at the midgland (95%). Our findings are consistent with two previous studies of prostate cancer recurrence after RT, which evaluated 46 and 50 SRP tumor maps, respectively [4,5]. Both studies reported that recurrent tumors tend to be solitary (72% and 66%) and located near the urethra (67% and 74%) and apex (93% and 72%). Our data also showed that, approximately half of the patients had tumors at the apex and the tumor occurred in the most apical 3 mm. Furthermore, despite almost the same number of patients with the minimum distance between the periurethral tumor and the urethra occurring at the apex and midgland, direct urethral invasion occurred much more frequently at the apex. The apex was at increased risk for direct urethral invasion. We believe that biopsy of the very distal apex and periurethral area is necessary for successful salvage treatment when recurrence is suspected.

Our results disclosed some remarkable findings regarding EPE and SVI. Among our cohort, in three-quarters of the patients with EPE, involvement occurred at the posterior base of the prostate. In contrast, Ohori et al [6] previously reported that, among men undergoing primary radical prostatectomy, EPE occurred in the posterior base, posterior midgland, posterior apex, and anterior in 35%, 44%, 21%, and 13% of their patients, respectively. In the present study, base tumor was found in only 44 patients (57%), but in 34 of them (76%) EPE occurred at the posterior base. When recurrent tumor is detected at the base on biopsy, physicians should be aware of the high rate of EPE occurrence at the posterior base. Regarding SVI, more than one-third of patients presented with SVI in our cohort. Only 10 patients underwent seminal vesicle biopsy, four were positive for disease, and the remaining six were negative, coinciding with the results from their SRP, including two with tumor occurring only in the seminal vesicles. Therefore, when recurrence is suspected, biopsy of seminal vesicles is warranted to assess the need for treatment of the seminal vesicles in the salvage setting.

In the present study, we could not assess the tumor maps of all our patients. When we compared the characteristics of patients with and without tumor maps to evaluate possible selection bias, we found a significant difference in age at SRP ($p = 0.046$). However, because we did not find a significant difference in other characteristics, particularly prostate-specific antigen and Gleason score, we do not believe that this finding affected our results. This paper describes the largest series of patients with SRP tumor maps thus far reported in the literature.

The majority of patients had recurrent tumors in the distal apex, periurethral area, and seminal vesicles, areas that are not routinely biopsied. When recurrence is suspected, biopsy of these areas is warranted for successful salvage treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Vora SA, Wong WW, Schild SE, et al. Outcome and toxicity for patients treated with intensity modulated radiation therapy for localized prostate cancer. J Urol. 2013; 190:521–6. [PubMed: 23415964]
2. Zelefsky MJ, Kuban DA, Levy LB, et al. Multi-institutional analysis of long-term outcome for stages T1-T2 prostate cancer treated with permanent seed implantation. Int J Radiat Oncol Biol Phys. 2007; 67:327–33. [PubMed: 17084558]
3. Chade DC, Eastham J, Graefen M, et al. Cancer control and functional outcomes of salvage radical prostatectomy for radiation-recurrent prostate cancer: a systematic review of the literature. Eur Urol. 2012; 61:961–71. [PubMed: 22280856]
4. Huang WC, Kuroiwa K, Serio AM, et al. The anatomical and pathological characteristics of irradiated prostate cancers may influence the oncological efficacy of salvage ablative therapies. J Urol. 2007; 177:1324–9. [PubMed: 17382724]
5. Leibovici D, Chiong E, Pisters LL, et al. Pathological characteristics of prostate cancer recurrence after radiation therapy: implications for focal salvage therapy. J Urol. 2012; 188:98–102. [PubMed: 22578724]
6. Ohori M, Scardino PT, Lapin SL, Seale-Hawkins C, Link J, Wheeler TM. The mechanisms and prognostic significance of seminal vesicle involvement by prostate cancer. Am J Surg Pathol. 1993; 17:1252–61. [PubMed: 8238732]

Table 1

Clinical characteristics of 77 patients with tumor maps

Type of primary therapy	
EBRT	48 (62%)
Brachytherapy	22 (29%)
EBRT and brachytherapy	7 (9.1%)
Type of surgery	
Open	68 (88%)
Laparoscopic	7 (9.1%)
Robotic	2 (2.6%)
ADT	26 (34%)
Diagnostic clinical classification	
T1c	33 (43%)
T2	30 (39%)
T3	6 (7.8%)
Unknown	8 (10%)
Pre-SRP clinical classification	
T1c	23 (30%)
T2	45 (58%)
T3	8 (10%)
Unknown	1 (1.3%)

EBRT = external beam radiation therapy; ADT = androgen deprivation therapy; SRP = salvage radical prostatectomy.

All values are frequency (proportion).

Table 2

Pathologic characteristics in 77 patients with tumor maps

Tumor location	
Apex	69 (90%)
Most apical 3 mm of the apex	32 (42%)
Midgland	73 (95%)
Base	44 (57%)
Only in SV	2 (2.6%)
No tumor	1 (1.3%)
Dominant tumor origin zone	
Peripheral zone	70 (91%)
Transition zone	3 (3.9%)
SV	2 (2.6%)
No tumor	1 (1.3%)
Unknown	1 (1.3%)
Number of cancer foci	1 (1, 2)
Number of patients with single-cancer foci	47 (61%)
Tumor volume (cm^3)	1.4 (0.5, 3.5)
Number of patients with periurethral tumor	53 (69%)
Location of minimum distance between periurethral tumor and urethra ($N = 53$)	
Apex	28 (53%)
Apex and midgland	1 (1.9%)
Midgland	23 (43%)
Base	1 (1.9%)
Laterality	
Unilateral	21 (27%)
Bilateral	53 (69%)
Only in SV	2 (2.6%)
No tumor	1 (1.3%)
Pathologic classification	
T0	1 (1.3%)
T2	29 (38%)
T3	41 (53%)
T4	6 (7.8%)
EPE	45 (58%)
EPE location (apex vs midgland vs base; $N = 45$)	
Apex	1 (2.2%)
Midgland	4 (8.9%)
Base	16 (36%)
Apex and midgland	2 (4.4%)
Midgland and base	14 (31%)
Apex and midgland and base	5 (11%)

SV	3 (6.7%)
EPE location (anterior vs posterior; *N* = 45)	
Anterior	3 (6.7%)
Posterior	35 (78%)
Anterior and posterior	4 (8.9%)
SV	3 (6.7%)
SVI	32 (42%)
LNI	22 (29%)
PSM	15 (19%)
Type of surgery	
Open (*N* = 68)	11 (73%)
Laparoscopic (*N* = 7)	2 (13%)
Robotic (*N* = 2)	2 (13%)
Type of primary therapy	
EBRT (*N* = 48)	8 (53%)
Location of PSM	
Apex	5 (63%)
Midgland	1 (13%)
Base	2 (25%)
SV	0 (0%)
Brachytherapy (*N* = 22)	5 (33%)
Location of PSM	
Apex	1 (20%)
Midgland	0 (0%)
Base	2 (40%)
SV	1 (20%)
Unknown	1 (20%)
EBRT and brachytherapy (*N* = 7)	2 (13%)
Location of PSM	
Apex	0 (0%)
Midgland	0 (0%)
Base	1 (50%)
SV	1 (50%)

EBRT = external beam radiation therapy; SV = seminal vesicle; EPE = extraprostatic extension; SVI = seminal vesicle involvement; LNI = lymph node involvement; PSM = positive surgical margin.

All values are median (interquartile range) or frequency (proportion).