



Original contribution

Does the distance between tumor and margin in radical prostatectomy specimens correlate with prognosis: relation to tumor location

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Summary The posterior half of the prostate has a smooth well-defined edge unlike anteriorly. Often, tumor extends close to the posterior margin, where it is controversial whether pathologists should measure the distance between the tumor and the margin. There are no published data regarding the significance of a close margin factoring in the anatomical location within the radical prostatectomy (RP). We identified 158 RPs with 39 anterior-predominant carcinomas and 119 cases with posterior-predominant cancer. Distances between the tumor and inked margin were measured with an ocular micrometer. Eighty-seven cases had no progression with a minimum 6-year follow-up (median, 8; range, 6-9). Eighteen cases had progression with a median time to progression of 2 years with all men progressing within 6 years after RP. There was no statistically significant difference in the risk of progression relative to distance of tumor to the posterior margin ($P = .09$). The mean distance of tumor to the anterior margin for the cases that progressed was 0.6 mm (median, 0.5 mm; range, 0.05-1.18) compared to 1.9 mm (median, 1.1; range, 0.02-4) for the cases that did not progress ($P = .02$). Of 7 cases with anterior-predominant tumors that progressed, 5 had tumor located less than 1 mm from the anterior margin. In conclusion, if cancer is present less than 1 mm from the anterior margin, there is an increased tendency to recur, and this finding should be included in pathology reports. However, close margins posteriorly are not clinically significant and should not be reported.

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1. Introduction

The prostate is a pyramidal fibromuscular gland lying in the deep lesser pelvis and surrounded by vulnerable structures. Radical prostatectomy (RP) can achieve only 1 to 2 mm margins around the prostate due to these anatomical restrictions [1]. The anterior part of the prostate is relatively deficient in

glandular tissue and is largely composed of fibromuscular tissue. The posterior surface of the prostate has a well-defined edge consisting of condensed smooth muscle [2]. Posteriorly, it is easier for the urologist to discern where the edge of the prostate is located. Anteriorly, the boundaries of the prostate are more ill defined where the anterior fibromuscular stroma is indistinguishable and continuous with extraprostatic smooth muscle [3]. Hence, RP specimens have a well-rounded smooth posterior surface and irregular anterior surface. There have been several studies with conflicting results analyzing whether there is any prognostic significance to the distance between prostatic carcinoma and margins of

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resection [4–9]. The current study is the first to assess whether there is any prognostic significance to the anatomical location of the closest margin.

2. Materials and methods

We identified 1564 cases of RP cases from 2005 to 2012 with Gleason score 6 or with a minor (<5%) higher grade component based on the modified Gleason grading system [10]. Sequential cases were analyzed, which had tumor located only in the posterior half or anterior half of the prostate and had a minimum 6-year follow-up in cases without progression. We identified 39 cases with carcinoma located predominantly in the anterior half, and 119 cases with carcinoma located predominantly in the posterior half of the prostate. Minor (<5%) pattern 4 was present in 6 cases, and minor pattern 5 was present in 1 case.

Patients did not receive adjuvant therapy until progression. Prostate-specific antigen (PSA) was checked yearly, and *progression* was defined as a postoperative serum PSA level of greater than or equal to 0.2 ng/mL, local progression, or distant metastases. All the prostatectomy specimens were grossed following the protocol given at an International Society for Urological Pathology (ISUP) consensus [11]. The prostates were weighed and fixed in formalin for 18 to 24 hours before grossing. The outer surface of the prostate was inked. Margins from the base/bladder neck/proximal end of the prostate were taken as a thin shave (en face) section. The distal 1 cm of the apex was removed, and the apical margins were processed as perpendicular margins parallel to the urethra. Sections of the base of the seminal vesicle where it joined the prostate were submitted. The remaining prostate was serially sectioned at 3-mm intervals and totally submitted in routine cassettes; each slice was sectioned into half or quarter to fit into standard cassettes. All of the cases were graded using the modified Gleason score [10]. The distance between the cancer and the closest inked resection margin was measured using a micrometer with an objective 10x.

To test the statistical significance of distance relative to progression, a *t* test for quality of means was performed. Cox regression analysis was performed to evaluate the significance of the distance to margin relative to progression using an actuarial analysis. Statistics were performed using STATA (College Station, TX). The work has been carried out in accordance with the code Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, and the privacy rights of the subjects were adhered to.

3. Results

Of the 158 RPs that satisfied the study criteria, 39 cases had anterior-predominant carcinoma, and 119 cases were located predominantly posteriorly. Of 124 cases without progression,

Table 1 Anterior-predominant prostatic cancer cases

Progression status	Percentage of cases with distance to margin < 1 mm	Mean distance between cancer and margin in mm (95% confidence interval)
Progressed	71%	0.6 (0.1-1.1)
Not progressed	13%	1.9 (1.3-2.5)

there was a minimum follow-up of 6 years (median, 8 years; range, 6-9 years).

Of 39 cases with anterior-predominant tumor, 7 cases progressed (Table 1). The mean distance of tumor to the anterior margin for cases with progression was 0.6 mm (median, 0.5 mm; range, 0.05-1.5) compared to 1.9 mm (median, 1.1; range, 0.02-5) for cases without progression ($P = .02$). Of cases with progression, 5 (71%) of 7 had tumor less than 1 mm from the margin, compared to 13 (40%) of 32 of cases without progression. Of the 7 cases with progression, 1 had a minor (<5%) pattern 5 in the anterior-predominant cancer. A minor (<5%) component of pattern 4 was seen in 7 cases with no progression. Extraprostatic extension was present in 6 cases, of which 1 progressed. Of 18 (5/18) (27.7%) cases with less than 1 mm distance from the anterior margin, 5 progressed. In contrast, only 2 (9.5%) of 21 cases with greater than or equal to 1 mm distance from the anterior margin progressed.

Twenty-seven cases with predominant posterior tumor progressed (Table 2). The mean distance of tumor to the posterior margin for cases with progression was 1.1 mm (median, 0.74 mm; range, 0.03-6 mm) compared to 0.7 mm (median, 0.36 mm; range, 0.02-8 mm) for cases without progression. Eight of the cases with progression had a minor component of pattern 4. Twenty-one cases with a minor pattern 4 component and 1 case with less than 5% pattern 5 did not progress. Of 99 cases with less than 1 mm distance from the posterior margin, 18 (18%) progressed. Of 20 with greater than or equal to 1 mm distance from the posterior margin, 9 (45%) progressed. Of cases with progression, 67% had tumor less than 1 mm from the margin, compared to 88% of cases without progression. There was no statistically significant difference in the risk of progression based on the proximity of tumor to the posterior margin ($P = .09$) (Fig. 1).

4. Discussion

A positive surgical margin is defined as the presence of tumor cells at the inked cut surface of the RP specimen [12,13].

Table 2 Posterior-predominant prostatic cancer cases

Progression status	Mean distance between cancer and margin in mm (95% confidence interval)
Progressed	1.1 (0.6-1.7)
Not progressed	0.7 (0.4-0.9)

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