Journal of Cellular Biochemistry, Supplement 16H:74-77 (1992)

Prostate Cancer Tumor Location as Predicted by Digital Rectal Examination Transferred to Ultrasound and Ultrasound-Guided Prostate Needle Biopsy

Michael K. Brawer, M.D.*, Nelson R. Ploch, M.D., and Steven A. Bigler, M.D.

Departments of Urology and Pathology, Seattle Veterans Administration Medical Center and University of Washington, Seattle, Washington 98108

Abstract The advent of transrectal ultrasound (TRUS) and the Biopty instrument (Bard Urologic) has revolutionized prostate biopsy (PNB). Theoretically the systematic multiple biopsy approach offers the advantage of less sampling error with respect to presence of carcinoma, grade of carcinoma and sites of tumor within the gland. These parameters may be important in selecting the therapeutic approach and, if radical prostatectomy is contemplated, in modifying the operation as indicated based on tumor location.

In the present investigation, we received specimens obtained from 100 men with clinically localized prostatic carcinoma who had previously undergone ultrasound-guided systematic random biopsy (TRUSPNB) along with TRUS and digital rectal exam (DRE). Among the 372 sectors with carcinoma identified in the 100 radical prostatectomy specimens, significant underrepresentation by TRUSPNB was noted (39% false negative). When an abnormality on either DRE, TRUS or TRUSPNB was observed, the sensitivity was 65%. The specificity was 89% when all three tests were abnormal. It would appear that preoperative assessment of tumor location is inadequate with the current modalities available. There may, however, be subsets of patients which would benefit by tumor location utilizing DRE, TRUS and TRUSPNB.

Key words: DRE, prostate cancer location, random biopsy, TRUS

Adenocarcinoma of the prostate represents the number one malignancy in men and the second most common cause of cancer deaths in the United States [1]. Extirpative surgery remains the best method of providing cure from this common malignancy. Advances in the surgical procedure have resulted in decreasing morbidity. An understanding of the sites of egress of carcinoma from the prostate, as well as the relationship of the neurovascular bundles, has allowed more successful removal of tumors as well as maintenance of potency in a significant number of men [2–6].

Accurate identification of the site(s) of the tumor within the prostate would allow better preoperative prognostication and, potentially, tailoring of therapy based on tumor extent and location. Specifically, if the clinician knows the tumor location in a patient electing radical prostatectomy, decisions concerning the apical dissection as well as preservation of one or both of the neurovascular bundles may be more rationally made. For patients electing brachy therapy, knowledge of tumor extent and location may allow more accurate dosimetry. Finally, if expectant therapy is planned, knowledge of the extent of tumor may provide more accurate prognosis. In the present investigation we compared digital rectal examination (DRE), transrectal ultrasound (TRUS), and six ultrasound-guided systematic random biopsies (TRUSPNB) with tumors located following radical prostatectomy in a series of patients with clinically localized prostate carcinoma.

• Recipient of a career development award from the American Cancer Society

Supported in part by a merit review grant from the Veterans Affairs Administration

MATERIALS AND METHODS

Patients undergoing radical retropubic prostatectomy with clinically localized adenocarcinoma of the prostate at the University of Washington or the Seattle Veterans Affairs Medical Center were entered into the protocol. Prior to the surgery, the patients underwent DRE, TRUS, and TRUSPNB by a urologist.

The results of DRE were carefully recorded on a schematic which divided the prostate into six sectors (*i.e.*, right—base, mid-gland and apex; left—base, mid-gland and apex). Abnormalities including asymmetry, induration or frank nodules were recorded within each sector and graded as 0, normal; 1, asymmetry; 2, induration; 3, palpable abnormality, strongly suspicious of malignancy.

TRUS was performed in the lateral, decubitus position after the patient received a Fleet's enema, 80 mg of gentamycin (im), and 500 mg of ciprofloxacin (po). Scanning was performed with the Bruel Kjaer 1846 scanner with a 7.5 MHz probe as previously described [7]. Imaging was performed in the axial and sagittal planes. The prostate was divided into six sectors as described above, and the presence of hypoechoic areas within any of these sectors was recorded. Hypoechoic peripheral zone lesions were the only sonographic abnormalities examined.

Following completion of imaging, TRUSPNB was performed as previously described [8]. If a hypoechoic area within any of the six sectors was identified, it was biopsied utilizing the Bard biopty instrument (Covington, GA) and an 18G needle. If no hypoechoic regions were recognized, random sector biopsies were performed.

All biopsies were submitted separately for histologic examination. Radical retropubic prostatectomy was performed in the standard fashion; however, nerve sparing operation was carried out only on the contralateral side to carcinoma identified upon biopsy.

The surgical specimen was heavily inked and fixed in 10% formalin for 24 hours. The specimen was sectioned at 5 mm intervals in the plane perpendicular to the rectal surface. Five-μm histologic sections stained with hematoxylin and eosin were examined. The margins were carefully scrutinized and the carcinoma was staged as follows: OC, organ-confined; C_1, capsular penetration without perforation; C_2, complete capsular perforation (*i.e.*, cancer cells stained with ink); C_3, seminal vesicle extension; and D_1, pelvic lymph node metastasis. Presence of one or more carcinomas within any of the six sectors described above was recorded, as well as large cancers which extended to more than one sector.

RESULTS

Analysis of 100 radical prostatectomy specimens identified 372 sectors with carcinoma (Table I). Of these, 226 were identified by systematic random biopsy, a 39% incidence of false negatives (Table I). As expected there was a higher incidence of carcinoma in the mid-gland sectors.

Table II lists the sensitivity, specificity, and positive and negative predictive values for DRE, TRUS, and TRUSPNB alone and in combination, as confirmed by radical prostatectomy. As

Table I. Carcinomas in Sectors

Sector	TRUSPNB	Prostatectomy	% False (–)
Right Base	36	46	22
Right Mid	31	79	61
Right Apex	32	51	37
Left Base	40	54	26
Left Mid	47	85	45
Left Apex	40	57	30
Total	226	372	39

Table II. Test Performance Characteristics (by Patient)

Test	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
DRE	44	71	69	47
TRUS	53	57	59	51
TRUSPNB	53	77	80	49
DRE & TRUS	35	74	67	45
DRE & TRUSPNB	36	88	84	45
TRUS & TRUSPNB	40	87	87	46
DRE & TRUS & TRUSPNB	30	89	82	45
DRE or TRUS	61	51	60	56
DRE or TRUSPNB	58	65	71	53
TRUS or TRUSPNB	61	56	60	57
DRE or TRUS or TRUSPNB	65	54	60	59

expected, the highest sensitivity was obtained when an abnormality on one of a combination of DRE, TRUS or TRUSPNB was present (65%). However, the overall sensitivity was disappointingly low. Specificity was greatest when all three tests were abnormal (89%). When at least two of the tests were combined, specificity was quite reasonable and probably at a clinically significant level.

The positive predictive values varied from a low of 59% for TRUS to a high of 87% for TRUS and TRUSPNB. The negative predictive values ranged from a low of 45% (for DRE & TRUS; or DRE & TRUSPNB; or DRE, TRUS & TRUSPNB) to a high of 59% when any of the three tests were abnormal.

While the performance characteristics depicted in Table II were disappointing, TRUSPNB was reasonably accurate in predicting the site of positive margin (C_2). Failure to detect more than two sectors with positive margins by TRUSPNB occurred in only five of 40 men (12.5%) with stage C_2 carcinoma (Table III).

Table III. Sectors With Positive Margins (C_2)

False Negative Sectors	No. Patients (%)
0	17(43)
1	18(45)
2	3(8)
3	1(3)
4	1(3)
5	0
6	0
Total:	40

DISCUSSION

One of the great problems in the area of prostatic carcinoma today is our relative inability to accurately stage the neoplasm. Advances in imaging had previously been inadequate to accurately localize carcinoma preoperatively. The advent of transrectal ultrasound revolutionized our biopsy approach; however, its utility in staging remains controversial. Utilizing ultrasound to guide biopsies has been well established as the optimum technique. The ability to selectively sample isolated sectors of the prostate leads to the possibility that improvement in

mapping location of carcinoma may be realized.

The data presented herein demonstrate that all three diagnostic tests—DRE, TRUS and TRUSPNB—are inadequate in assessing tumor locations preoperatively. While the specificity is reasonable, particularly if the tests are used in combination, the relative lack of sensitivity would seem to preclude the use of this approach to significantly modify therapeutic approaches. Other investigations may, however, identify a subset of patients in which these techniques may provide useful information and improve therapy for this neoplasm.

REFERENCES

1. Silverberg E, Boring CC, Squires TS: Cancer statistics, 1990. CA: Cancer J Clin 40:9–26, 1990.
2. Eggleston JC, Walsh PC: Radical prostatectomy with preservation of sexual function: Pathologic findings in the first 100 cases. J Urol 134:1146–1148, 1985.
3. Catalona WJ, Bigg SW: Nerve-sparing radical prostatectomy: Evaluation of results after 250 patients. J Urol 143:538–544, 1990.
4. Walsh PC, Lepor H, Eggleston JC: Radical prostatectomy with preservation of sexual function: Anatomical and pathological considerations. Prostate 4:473–485, 1983.
5. Stamey TA, McNeal JE, Freiha FS, Redwine E: Morphometric and clinical studies on 68 consecutive radical prostatectomies. J Urol 139:1235–1241, 1988.
6. Villers A, McNeal JE, Redwine EA, Freiha FS, Stamey TA: The role of perineural space invasion in the local spread of prostatic adenocarcinoma. J Urol 142:763–768, 1989.
7. Takayama TK, Brawer MK: Prostate ultrasonography in normal and benign conditions. World J Urol, 1991 (in press).
8. Brawer MK, Chetner MP, Beatie J, Buchner DM, Vessella RL, Lange PH: Screening for prostatic carcinoma with prostate specific antigen. J Urol 147:841–845, 1992.