Re-biopsy of the Prostate Using a Stereotactic Transperineal Technique

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Purpose: In this study we investigated the detection rate and morbidity of stereotactic transperineal prostate re-biopsy with 3-dimensional mapping for diagnosis of nonpalpable isoechoic occult prostate malignancy.

Materials and Methods: A total of 180 consecutive patients with continued increasing total prostate specific antigen and at least 1 prior benign transrectal prostate biopsy underwent stereotactic transperineal prostate biopsy at a single outpatient institution between April 2004 and March 2006. Similar to a prostate brachytherapy procedure, patients were placed in the dorsal lithotomy position. With the patient under general anesthesia, and using transrectal ultrasound, a perineal brachytherapy template and stabilizing device, the prostate was positioned on the implant grid. It was equally divided into 8 sections (octants) according to x and y coordinates on the mid gland axial image. The midplanes of axial and sagittal prostate gland images for each patient determined the x, y and z coordinates that would occupy each octant. Tissue cores were initially obtained from the apical octants, followed by identical x and y coordinates of the basilar octants. Specimens from each specific octant were placed in 1 of 8 specimen jars and pathological review was reported accordingly.

Results: Stereotactic transperineal prostate biopsy yielded positive biopsies identifying adenocarcinoma in 68 of 180 (38%) patients. Acute urinary retention developed in 18 of 180 (10%) patients requiring an indwelling urinary catheter upon discharge home. In all patients estimated blood loss was less than 5 cc and median pain score was 1 of 10.

Conclusions: Stereotactic transperineal prostate biopsy is extremely well tolerated and useful for diagnosis of nonpalpable isoechoic occult prostate malignancy. Additionally, stereotactic transperineal prostate biopsy provides comprehensive tissue sampling with accurate 3-dimensional mapping of malignancy in this select group of patients.

Key Words: biopsy, prostatic neoplasms, prostate-specific antigen

Few glands in the human body have been subjected to more variations of biopsy techniques than the prostate. The diagnosis of prostate cancer has evolved from patients presenting predominantly with locally advanced and/or metastatic disease to present day asymptomatic, nonpalpable, isoechoic, PSA detected occult prostate malignancy.

Numerous studies have demonstrated superiority of transrectal ultrasound guided transrectal prostate biopsy vs digitally directed prostate biopsy.[1] In 1989 Hodge et al recommended a systematic sextant biopsy technique. This approach was more likely to detect cancer than was targeted biopsy of either palpable disease or echogenically abnormal areas on ultrasound.[2] The PSA era was about to begin and it was embraced with a fury of effort to further understand this concept of occult malignancy.

Occasionally, a patient will continue to have negative biopsies while other indicators remain to strongly suggest that indeed a malignancy may exist. Such a scenario presents a true diagnostic dilemma for the physician, in addition to significant anxiety for the patient.[3] This study investigates the detection rate and morbidity of TRUS template guided STPB with 3-dimensional mapping of malignancy.

MATERIALS AND METHODS

180 consecutive patients underwent STPB at a single outpatient institution between April 2004 and March 2006 (table 1). The criteria to perform STPB were continued increasing total PSA along with at least 1 prior benign TRPB. Similar to a prostate brachytherapy procedure using general anesthesia using a laryngeal mask airway, patients were placed in dorsal lithotomy position. The prostate was positioned on the implant grid using TRUS B&K Medical Falcon stepper stabilizer device and perineal brachytherapy template.

It was equally divided into 8 sections (octants) according to x and y coordinates on the mid gland axial image. The midplanes of axial and sagittal prostate gland images for each patient determined the x, y and z coordinates that would occupy each octant. Octants were assigned accordingly as I—right anterior base, II—left anterior base, III—right posterior base, IV—left posterior base, V—right anterior apex, VI—left anterior apex, VII—right posterior apex and VIII—left posterior apex (fig. 1). Comprehensive tissue cores using the MaxCore™ disposable biopsy instrument

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Nothing to disclose.
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TABLE 1. *Patient characteristics*

	Age	PSA (ng/ml)	Prostate Vol (cm^3)	No. Prior TRPB Sets	No. Tissue Cores Obtained on Prior TRPB Sets
Mean	63.1	9.3	46.5	1.8	13.6
Median	62.7	8.1	42.9	2	12
Range (min–max)	44.5–81.6	0.8–40.1	12.9–123.0	1–6	5–22
Interquartile range	11.2	6.0	25.3	1	4

were obtained initially from the apical octants using 5 mm spacing on the template grid followed by identical x and y coordinates of the basilar octants. The larger the gland volume the more specimens were obtained. Prostates 30 cm^3 or less in which the anterior apical specimen adequately sampled the tissue, did not require a basilar specimen of the identical x and y coordinates. Thus, these specimens were assigned to the respective apical octant. Each specific octant was sampled as described. Upon retrieval specimens were deposited on telfa and placed in the respective octant's formalin filled specimen jar. Pathological review was reported accordingly.

Using the National Cancer Institute's pain intensity scale, patients verbally reported the level of pain they experienced during 3 periods of recovery room, discharge and at time of postoperative phone call, which occurs the next working day following implant. On the 0 to 10 numeric pain intensity scale, 0 represents no pain and 10 is equivalent to the worst possible pain. Each patient's pain rating, location of pain and any action taken to alleviate pain was documented by a registered nurse. All statistical tests were calculated using SPSS® 12.0 software. Statistical significance was established with $p < 0.05$.

RESULTS

We were able to differentiate the precise location of malignant vs benign regions of the prostate gland. In all patients estimated blood loss was less than 5 cc and pain was reported to be minimal. Mean pain ratings for the recovery room, time of discharge and at time of postoperative telephone call were 1.00 ± 1.76, 0.59 ± 1.09 and 0.46 ± 1.02, respectively. Perineal discomfort followed by urethral burning were the first and second most commonly reported sites of pain in all 3 study areas. Of 180 patients acute urinary retention developed in 18 (10%) requiring an indwelling Foley catheter upon discharge. STPB identified adenocarcinoma in 68 of 180 (38%) patients (table 2). Interestingly, findings included that the number of biopsy cores per patient approximated the prostate gland volume in cubic cm (fig. 2).

Of the malignant cores 69% were Gleason score 6 with 31% Gleason score 7 or higher (fig. 3). Of the positive cores 77% contained 50% or less carcinomatous involvement (fig. 4). Of these patients 24% exhibited only 1 malignant octant, while 35% had 4 or more octants involved (fig. 5). Of the 68 patients with positive biopsy, 42 (62%) had a prostate volume less than or equal to the cohort median prostate volume of 42.9 cm^3, while 26 (38%) patients had a prostate volume greater than 42.9 cm^3.

Of the 180 patients in the study group 19 (11%) were diagnosed with high grade PIN on initial negative TRUS biopsy, 33 (18%) had prostatitis and 6 (3%) patients were found to have PIN and prostatitis. Of these patients 11 of 19 (58%), 7 of 33 (21%) and 3 of 6 (50%), respectively, were found to have adenocarcinoma after STPB. Using cross-tabs a diagnosis of PIN and/or prostatitis on prior TRPB was a significant predictor of diagnosis of adenocarcinoma upon STPB ($p = 0.023$). Furthermore, among the variables age, total PSA, prostate volume, previous number of biopsy sets and number of cores sampled, multivariate analysis determined that only total PSA ($p = 0.003$) and prostate volume ($p = 0.043$) were significant predictors of detecting adenocarcinoma (table 3).

More specimens were obtained from the apical half than the basilar half and this was attributed to smaller glands in which the apical specimen sufficiently sampled the anterior curvature of the gland. Pathology was also reviewed individually as a component of the anterior/posterior and/or apical/basilar halves in addition to quadrants of the prostate gland (fig. 6). Independent samples t tests determined that there were no significant differences in the number of cores obtained or the number of malignant cores in each of the octants, quadrants (anterior base, posterior base, anterior apex, posterior apex) and halves (base, apex, anterior. posterior). All p values were greater than 0.05, indicating that the prostate was indeed sampled systematically. No one octant, quadrant or half of the gland was sampled significantly more than the other.

DISCUSSION

Few would disagree that TRUS and systematic sextant biopsy have had a pivotal role in the early detection of prostate cancer. Published data have clearly demonstrated a higher yield of malignant biopsies when a more comprehensive approach obtaining more specimens is used.[4] Further investigation promoted the concept of laterally directed biopsies

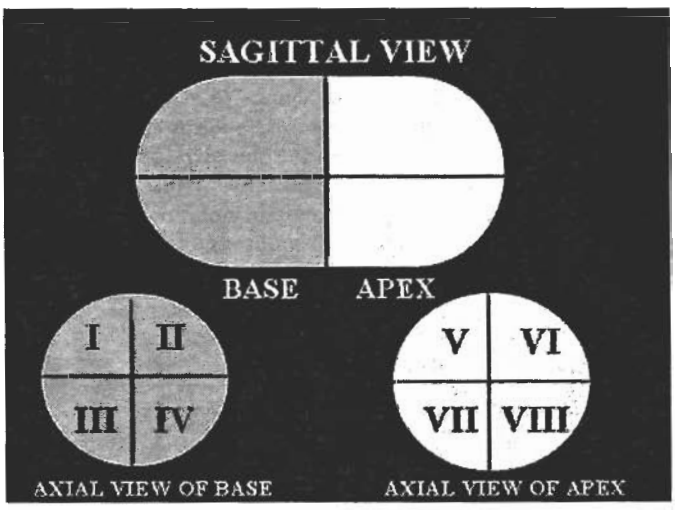

FIG. 1. Prostate octant schematics

TABLE 2. *Biopsy results*

	No. Tissue Cores Obtained on STPB	No. Malignant Tissue Cores in 68 Pts With Pos STPB	Highest % Involvement of Malignant Tissue Cores	Procedure Mins	Recovery Mins
Mean	41.3	3.9	30.8	28.7	84.4
Median	41	3	20	28	80
Range (min–max)	13–117	1–17	1–95	9–57	50–185
Interquartile range	18	3	44.5	15	22.8

of the peripheral zone of the prostate, which has been referred to as the extended systematic sextant technique. Extensive data strongly support this modification of the standard sextant technique.[5] It has been shown to increase the diagnostic yield of malignancy an additional 35%.[6] Despite these advances to detect isoechoic, nonpalpable occult malignancy, a subset of patients remains in which total PSA continues to increase despite having had prior negative TRUS TRPB.

New data began to emerge regarding extensive saturation TRPB of the prostate (table 4).[7–10] Stewart et al evaluated ultrasound guided transrectal extensive saturation biopsy of the prostate in 224 patients in whom previous negative sextant TRPB had been performed in the office.[10] Carcinoma was identified in 77 of 224 (34%) patients. The overall complication rate was 12% with 27 of 224 experiencing an adverse event. Hematuria requiring an overnight hospitalization occurred in 12 of 224 patients (5%). Of 224 patients urinary retention developed in 10 (4.5%). In another study Pushkar et al reported transrectal saturation biopsy complications in 612 patients, which included hematuria in 220 (35.9%), hematospermia in 166 (27.1%), pain in the perineum and rectum in 189 (30.9%), acute prostatitis in 21 (3.4%), acute orchiepididymitis in 7 (1.1%), acute urinary retention in 9 (1.5%), long-term rectal hemorrhage in 13 (2.1%) and loss of consciousness during the biopsy in 7 (1.1%).[11]

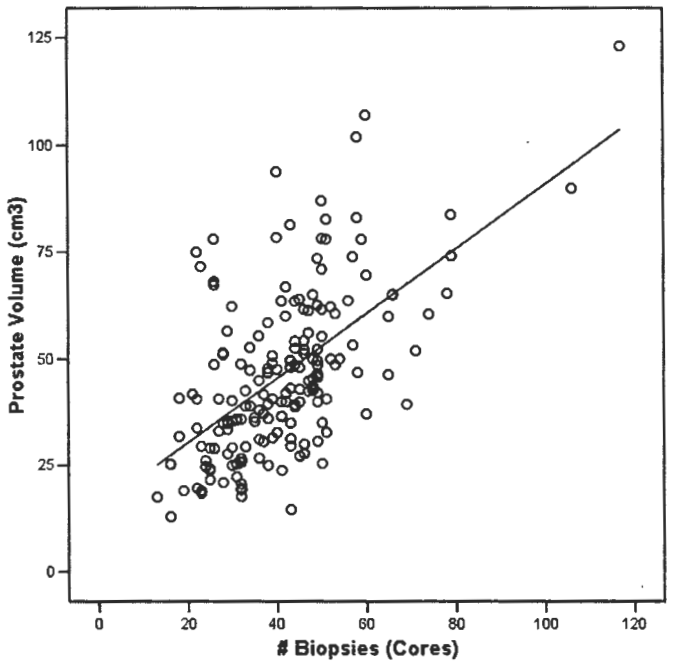

FIG. 2. Biopsy cores vs prostate volume

In addition to complications, there is no doubt that TRPB may also include a significant risk of discomfort. In fact De Sio et al reported on a study in which 19% of patients refused to undergo additional TRPB without analgesia.[12] In another study 22% of 89 patients who had systematic sextant core biopsies experienced significant pain.[12] It should be noted that much of the literature regarding TRPB and pain consists of patient groups that had 6 or fewer cores taken. Today most clinicians perform extended systemic biopsies with up to 12 cores. Thus, the potential for patient discomfort may even be greater. However, in an effort to improve patient tolerance, periprostatic nerve block has been shown to significantly decrease the amount of discomfort men experience undergoing TRPB.[12]

For patients undergoing re-biopsy, percent positivity using the transperineal approach ranged from 37% to 43%, possibly suggesting a higher detection rate with transperineal saturation biopsy than that of transrectal saturation biopsy.[13–19] It does not appear that the higher detection rate is necessarily due to increased number of biopsies taken since, except the present study, the median number of cores using transperineal saturation biopsy was less than transrectal saturation biopsy.

There are numerous technical advantages to a transperineal approach compared to a transrectal approach. Rectal wall penetration by the biopsy needle is avoided and may translate into a lower risk of infection. Using sagittal imaging the anterior apical biopsy specimen can be obtained with excellent visualization. Finally, the use of a perineal template provides valuable information regarding localization of biopsy cores.

Literature from Europe, Asia and to a lesser extent, the United States, suggests that transperineal biopsy using ultrasound guidance is not only superior to transrectal biopsy, but may be preferred for select patients.[20] Igel et al reported on 88 men with prior negative TRPB with persistent PSA increase and concluded that the only significant independent variable predictive of a positive biopsy was prostate

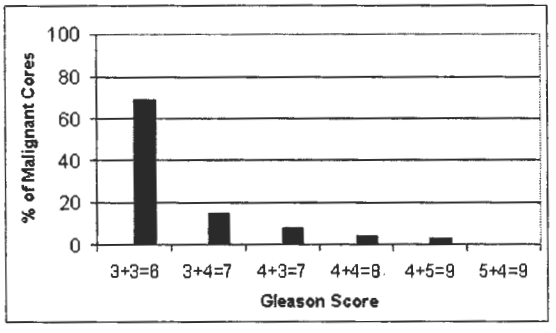

FIG. 3. Gleason scores of malignant cores

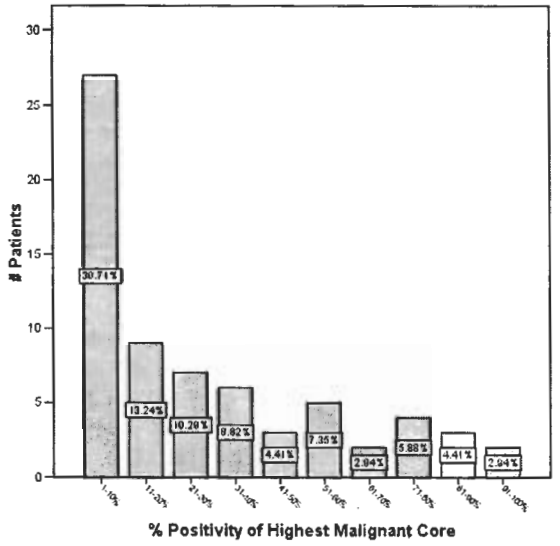

FIG. 4. Percent positivity of malignant cores

volume.[16] Mean volume in the positive and negative biopsy groups was 48 and 73 gm, respectively ($p < 0.001$). Furuno et al were the first to report that carcinoma was more prevalent in the anterior half of the prostate in patients with prior negative TRPB.[15] Additionally, they reported that patients who had never previously undergone biopsy had an equal distribution of malignancy anteriorly and posteriorly ($p < 0.001$).

Kawakami et al analyzed location of malignancy as a function of T stage with specimens obtained by transperineal prostate biopsy.[17] The cancer detection rate for T2 lesions was positive most frequently in the posterior peripheral zone while patients with T1c disease were most often positive in the anterior peripheral zone. Emilliozzi et al evaluated the number of cores obtained with transperineal technique to identify if there is a minimum number of samples that should be obtained.[13] In their prospective randomized study, it was shown that 12-core transperineal biopsy was superior to 6-core biopsy, regarding diagnostic yield of malignancy (49% vs 30%, respectively ($p = 0.016$)). Additionally, Ficarra et al evaluated optimal core sampling as a function of prostate volume. In prostates larger than 50 cc, even a 14-core scheme may have been inadequate with a diagnostic yield of only 24.2%, whereas the 14-core scheme in patients with less than 30 cc volume, the diagnostic yield was 43.8%.[14] In the present study as prostate volume increased, so did the number of biopsy cores obtained. This was a necessary result of an effort to provide comprehensive sampling.

TABLE 3. *Detection rate variables*

	No./Total No. (%) Detected of Pts With Pos Biopsy	p Value
Age:		0.120
50 or Younger	3/68 (4.4)	
51–60	20/68 (29.4)	
41–60	36/68 (52.9)	
Older than 60	9/68 (13.2)	
PSA (ng/ml):		0.003
0–10	40/68 (58.8)	
10–20	23/68 (33.8)	
Greater than 20	5/68 (7.4)	
Prostate vol (cm^3):		0.043
Less than 20	4/68 (5.9)	
20–40	32/68 (47.1)	
40–60	20/68 (29.4)	
Greater than 60	12/68 (17.6)	
Previous No. biopsy sets:		0.052
1	38/68 (55.9)	
2	25/68 (36.8)	
3	2/68 (2.9)	
4 or Greater	3/68 (4.4)	
No. cores sampled:		0.571
Less than 20	4/68 (5.9)	
20–40	37/68 (54.4)	
41–60	23/68 (33.8)	
Greater than 60	4/68 (5.9)	

Today transperineal prostate brachytherapy has earned acceptance as a viable treatment option for early stage prostate cancer. It is not surprising that clinicians have taken advantage of this technology to perform biopsy of the prostate gland. There has been much speculation as to how previously undetected malignancies have become so apparent using a transperineal approach. We believe that the transperineal template approach incorporates more objective comprehensive tissue sampling using needle guidance based on x, y and z coordinates compared to the conventional transrectal biopsy, which relies more heavily on skill of the practitioner for needle localization and subsequent tissue sampling, which is more subjective.

From a technical perspective we experienced the octant concept to be practical and reproducible regardless of prostate size. Our support staff quickly adapted to the octant concept as it pertained to specimen handling, labeling and interpretation of pathology reports. We were surprised to

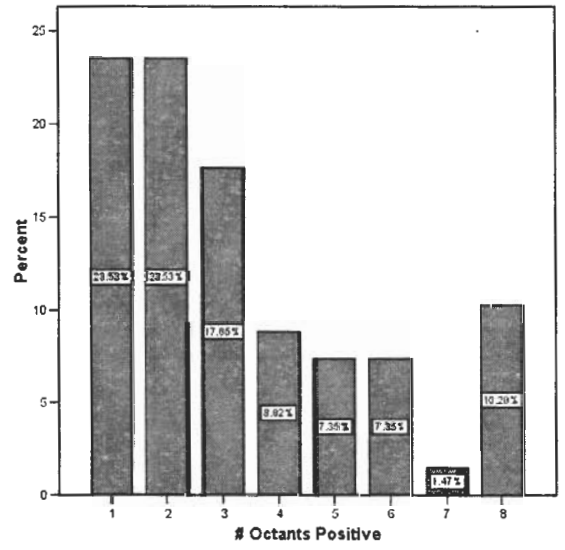

FIG. 5. Octants involved with positive cores

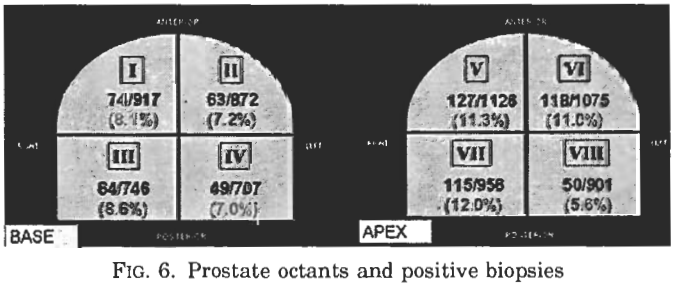

FIG. 6. Prostate octants and positive biopsies

TABLE 4. *Review of referenced literature*

References	No. Pts	No. Previous Biopsy (range)	Median No. Cores (range)	% Positivity	% Urinary Retention
		Transrectal			
Patel et al[7]	100	1.65	24	25	Not available
Pryor and Schellhammer[8]	35	2 or More	20	20	Not available
Fleshner and Klotz[9]	37	3 or Greater (3–6)	32–38	13.50	Discharged with catheter
Stewart et al[10]	224	1.8 (1–7)	23 (14–45)	34	12
		Transperineal freehand (without prior biopsy)			
Ficarra et al[14]	480	0	14	35.2	0.6
Kawakami et al[17]	289	0	14	36	Not available
Emiliozzi et al[13]	214	0	6–12	38–51	0
Kojima et al[18]	679	0	6–12	18–24	Not available
		Transperineal template guided (with prior biopsy)			
Current Study	180	1–6	41	38	10
Pinkstaff et al[19]	210	1 (81% had 2 or more)	21.2 (12–41)	37	11
Furuno et al[15]	113	86 Pts had 0, 27 with 1 or more	18.4	43	Not available
Igel et al[16]	88	2	15.4	43	2

find that no one octant was statistically more likely to contain malignancy than any other octant. This is in contrast to a similar group of patients who had prior negative TRPB. As previously cited, Furuno et al did in fact report a statistically significant difference with anterior biopsies more likely to be positive.[15]

In the analysis of the 68 patients found to have malignancy, treatment decisions were prostate brachytherapy in 37 of 68 (54%), radical prostatectomy in 11 of 68 (16%), cryotherapy in 2 of 68 (3%), IMRT in 2 of 68 (3%) and undecided in 16 of 68 (24%). In the patients undergoing radical prostatectomy, whole mount specimen pathology was reviewed and retrospectively correlated to the location of malignancy identified on STPB. In all 11 patients adenocarcinoma was located in the identical octant that was defined at the time of STPB.

CONCLUSIONS

During the last 2 decades there has been a dramatic improvement regarding the ability to diagnose early stage prostate cancer. Despite the enhanced diagnostic yield of obtaining additional lateral cores from the peripheral zone, occasional patients continue to have increasing total PSA associated with benign pathology. Transrectal saturation biopsies have increased the yield of malignant diagnosis, however, accuracy of carcinomatous location and patient discomfort remain an issue.

Our experience using STPB has been informative and rewarding. It has proven value to establish the presence not only of occult carcinomas, but also to define its localization within the prostate. Using a concept of geographic octants, we were able to identify malignant biopsy cores and assign them to 1 or more of 8 octants within the prostate gland. STPB is well tolerated, practical and effective for the diagnosis of malignancy.

In the future STPB will have a significant role in the diagnosis of prostate cancer. It may also definitively eliminate carcinoma from the differential diagnosis of patients with an increased PSA. Because of the comprehensive nature of this procedure, a benign outcome will be welcomed as it may relieve much anxiety for the patient and physician. As a result the clinician will be less inclined to continue repeating TRPB. Finally, if patients are aware of this technique as an option they too will be unlikely to prefer repeated TRUS TRPB as an alternative.

Abbreviations and Acronyms

PIN = high grade prostatic intraepithelial neoplasia
PSA = prostate specific antigen
STPB = stereotactic transperineal prostate biopsy
TRPB = transrectal prostate biopsy
TRUS = transrectal ultrasound

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EDITORIAL COMMENT

The authors have provided a well written analysis of a biopsy method that 5 years ago was viewed as sui generis, but has now achieved widespread use for specific clinical situations (reference 16 in article). Its role in identifying clinically significant prostate carcinoma will continue to be defined. This method may give rise to discussion or exploration of the controversial arena of targeted therapy for prostatic carcinoma because the location of the positive biopsies closely mirrors cancer found in the radical prostatectomy specimen.

As this biopsy method has evolved in our practice, we have noted patient observation and complaint regarding the relative billing for the procedure. The pathologist often charges per biopsy analysis and has an exponentially higher fee than the umbrella reimbursement the urologist receives for his/her labor and time, whether completing 6 or 50 separate biopsies.

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