HSOA Archives of Urology

Research Article

Do Biopsies of the Transition Zone Impact Prostate Cancer Treatment Planning?

Gregory S Merrick[1,2*], Seraj Singh[1], Robert Galbreath[1,3], Whitney Scholl[4], BrianKurko[1], Ryan Fiano[1], and Edward Adamovich[4]

[1]Schiffler Cancer Center, Urologic Research Institute, USA

[2]Department of Urology, Wheeling Hospital, USA

[3]Ohio University Eastern, USA

[4]Department of Pathology, Wheeling Hospital, USA

Abstract

Objectives: To determine whether Transition Zone (TZ) biopsies as part of a Transperineal Template guided Mapping Biopsy (TTMB) impacted Gleason score upgrading and prostate cancer treatment decisions when compared to a standard Trans Rectal Ultrasound (TRUS) guided biopsy.

Methods: One thousand two hundred and thirty consecutive patients underwent TTMB for an elevated PSA. The position of each biopsy core was recorded in three dimensions. For every patient, the location of each positive biopsy core, the number of positive cores, the Gleason score, the percent involvement of each core and the status of perineural invasion was documented. Multiple parameters were evaluated to determine predictors of TZ upgrading when compared to standard TRUS biopsy.

Results: The mean patient age was 65.3 years with a median pre-biopsy PSA of 7.5ng/mL.The mean volumetric prostate volume was 56.2cm 3 with an ellipsoid transition zone volume of 27.0cm 3. Seven hundred and fifty-nine patient (61.7%) were diagnosed with prostate cancer and 358 patients (47.2%) had involvement of the TZ. Forty patients (5.4%) had TZ cancer only. Compared to a standard 12 core TRUS biopsy, TZ biopsy upgraded Gleason score in 13.2% of patients.

Conclusion: 47.2% of patients had TZ involvement with 5.4% having prostate cancer isolated to the TZ. TZ biopsies resulted in Gleason score upgrading in 13.2% of patients with resultant possible implications concerning treatment approaches to include eligibility for focal therapies and active surveillance.

Keywords: Prostate cancer; Transition zone biopsy; Transition zone cancer; Transperineal template guided mapping biopsy

***Corresponding author:** Gregory S Merrick, Schiffler Cancer Center, Wheeling Hospital, 1 Medical Park, Wheeling, WV 26003, USA, Tel: +1 3042433490; Fax: +1 3042435047; E-mail: gmerrick@urologicresearchinstitute.org

Citation: Merrick GS, Singh S, Galbreath R, Scholl W, Kurko B, et al. (2020) Do Biopsies of the Transition Zone Impact Prostate Cancer Treatment Planning? Arch Urol 3: 012.

Received: November 09, 2020; **Accepted:** December 10, 2020; **Published:** December 17, 2020

Introduction

Contemporary prostate biopsy series have demonstrated the prevalence of dominate anterior-based malignant lesions including those of the transition zone (TZ) [1-4]. Prostate cancer involves the TZ in up to 60% of cases [5]. TZ cancers are difficult to detect by Digital Rectal Examination (DRE) and often poorly visualized on imaging studies [6]. Overall, Transrectal ultrasound guided needle biopsies directed at the transition zone increase the detection of prostate cancer by only 1.5 - 13% [7]. In addition, the reliability of TZ detected Trans rectal ultrasound guided needle biopsies has been called into question [6]. Hearer and colleagues reported that 40% of patients with Transrectal biopsy diagnosed TZ cancers did not have TZ cancer at the time of radical prostatectomy (RP) [6]. Individual variability in peripheral zone tissue volume, the presence and extent of benign prostatic hyperplasia (BPH) and relative resistance of the TZ to needle penetration may affect the ability to accurately sample the TZ [6].

The diagnosis of anterior prostate cancer malignancies is often difficult due to the posterior approach of Trans Rectal Ultrasound (TRUS) guided needle biopsies. Transperineal Template-guided Mapping Biopsy (TTMB) techniques have emerged to address the potential shortcoming of TRUS biopsies [8-10]. Advantages of Transperineal biopsy techniques include the ability to systematically map the gland and provide more accurate information regarding prostate cancer grade, volume, and spatial distribution of cancer decreases the infectious morbidity of TRUS biopsy. TTMB has been demonstrated to accurately identify high-grade cancers when compared to whole-mount Radical Prostatectomy (RP) pathology [11]. The majority of clinically significant prostate cancers missed at TRUS biopsy are located in the anterior prostate with Gleason score upgrading in approximately 39% of patients [12,8].

Although the presence of TZ malignancies are common, malignancies exclusively restricted to the TZ are noted in only 2-5% of cases [3,13]. In this study, we evaluate whether biopsy of the TZ provides information regarding Gleason score upgrading which may influence prostate cancer treatment decisions.

Materials and Methods

From January 2005 - June 2012, 1,230 consecutive patients underwent TTMB for an elevated PSA or following a negative TRUS biopsy for a persistently elevated PSA and/or the presence of Atypical Small Acinar Proliferation (ASAP) or High-Grade Prostatic Intraepithelial Neoplasia (HGPIN). TTMB was performed via an anatomic technique with sampling of 24 regional biopsy regions performed by a single operative (GSM) [8,9].

Two days prior to TTMB, tamulosin (0.8mg) was initiated and continued for two weeks. TTMB was performed in the operating room in the dorsal lithotomy position under general anesthesia. All patients received perioperative antibiotics. The prostate gland was scanned from the proximal seminal vesicles/base of the prostate gland to the apex using the 5.0-7.5MHz transducer. A volumetric ultra-sonographic evaluation was obtained to determine prostate size. In addition, the prostate gland and TZ volumes were estimated as an ellipsoid with the formula: length x width x height x $\pi/6$. Transperineal biopsies were obtained through template apertures corresponding to the 24 regional biopsy locations [8,9]. For each of the 24 regions, as many as 4 biopsy cores were taken depending on prostate size. Eighteen gauge, 25cm long Max-Core biopsy needles (C.R. Bard Inc., Covington, GA, USA) were used. For each biopsy core, the template coordinate and the offset from the base were recorded. Biopsies were taken to sample the entire gland including the TZ (sites 7, 8, 17, 18), the posterior (sites 3, 4, 12, 13, 21, 22), posterior lateral (sites 2, 5, 11, 14, 20, 23), anterior lateral (sites 1, 6, 9, 10, 15, 16) and anterior apex (sites 19, 24). All pathologic assessment was performed by a pathologist with significant expertise in prostate pathology (EA).

For each patient, the location of each positive biopsy core, the number of positive cores, the percentage involvement of each core and the presence/absence of perineural invasion was recorded. Evaluated predictors for TZ Gleason score upgrading included age, PSA, body mass index (BMI), number of TRUS biopsies and cores, prostate volume, transition zone volume, PSA density (PSAD=PSA/prostate volume), transition zone PSA density (TZPSAD=PSA/TZ volume), Transition Zone Index (TZI=transition zone volume/prostate volume), total number of TTMB cores, hypertension and TURP.

Independent sample t-tests, one-way analysis of variance and 2-sided Pearson chi-square tests were applied to the clinical and biopsy parameters to determine the significance of any differences between the groups. Predictors for positive diagnosis of prostate cancer were determined by binary logistic regression, as were predictors of Gleason score upgrading by TZ biopsy alone. For all test, a p value $\leq$ 0.05 was considered statistically significant. Statistical analysis was performed using STATA (version 15.0, STATA Corporation, LP and College station, TX).

Results

Table 1 summarizes the clinical parameters of the 1,230 consecutive patients undergoing TTMB. The mean and median age of the entire cohort was 65.3 and 66.0 years, respectively. Seven hundred and fifty-nine patients (61.7%) were diagnosed with prostate cancer. Patients with prostate cancer were statistically older (66.1 vs. 64.0 years, p<0.001), underwent fewer prior TRUS biopsies and a lesser number of TRUS biopsy cores (p<0.001) and were less likely to present with diabetes mellitus (p=0.012). No statistical differences in pre-biopsy PSA, BMI or prior tobacco usage were noted.

Table 2 summarizes the TTMB parameters of patients with and without prostate cancer. Patients with prostate cancer presented with statistically smaller glands (51.4cm^3 vs 77.9cm^3, p<0.001), fewer TTMB cores were obtained (55.6 vs 57.2, p=0.019), had a smaller transition zone volume (20.1cm^3 vs 38.2cm^3, p<0.001), a higher PSAD (0.195 vs 0.122, p<0.001) a higher TZPSAD (0.597 vs 0.271, p<0.001) and a smaller transition zone index (0.398 vs 0.507, p<0.001). Of the 759 patients with prostate cancer, 454 (58.8%) presented with clinically significant prostate cancer table 3. The mean and median number of positive prostate cancer cores were 9.1 and 7.0, respectively with 86 patients (11.3%) having more than 20 positive cores. 358 patients (47.2%) had involvement of the transition zone with 40 patients (5.4%) having TZ involvement only. One hundred patients (13.2%) had Gleason score upgrading based on the TZ pathology when compared to a standard 12 core TRUS biopsy (sites 3, 4, 5, 6, 11, 12, 13, 14, 20, 21, 22, 23). Of those TZ upgraded patients, 50 (6.6%) were diagnosed with Gleason 3+4, 28 (3.7%) with Gleason 4+3, 15 (2.0%) with Gleason score 8 and 7 (0.9%) with Gleason score 9-10. In multivariate analysis table 4, predictors of TZ upgrading were limited to the number of prior TRUS biopsy sessions.

Discussion

Anterior prostate cancers (TZ and anterior apex) are often poorly visualized on imaging studies [6]. In our current study, 47.2% of all cancers involved the TZ but only 40 patients (5.4%) had cancers exclusively confined to the TZ. Consequently, 94.6% of all prostate cancers would have been diagnosed without a TZ biopsy.

	Negative Biopsy (n = 471)			Positive Biopsy (n = 759)				All patients (n = 1230)		
Continuous variables	**Mean**	**(±SD)**	**Median**	**Mean**	**(±SD)**	**Median**	**p**	**Mean**	**(±SD)**	**Median**
Age	64	-7.1	64	66.1	-8	66	**<0.001**	65.3	-7.7	66
Pre-Biopsy PSA	7.4	-4.2	6.3	7.6	-7.8	6	0.617	7.5	-6.6	6.1
BMI	28.7	-4.9	28	29.1	-5.1	28.4	0.131	29	-5.1	28.3
No. of TRUS Biopsies	1.6	-1.2	1	1.1	-1	1	**<0.001**	1.3	-1.1	1
No. of TRUS Biopsy Cores	17.6	-10.3	12	14.9	-7.8	12	**<0.001**	16	-9	12
Categorical Variables	**Count**	**(%)**		**Count**	**(%)**	**P**		**Count**	**(%)**	
Pre-biopsy TURP/TUIP: Yes	7	-1.5		19	-2.5	0.228		26	-2.1	
No	464	-98.5		740	-97.5			1204	-97.9	
Tobacco: Never	323	-49.3		334	-44	0.192		566	-46	
Former	185	-39.3		325	-42.8			510	-41.5	
Current	54	-11.5		100	-13.2			154	-12.5	
Hypertension: No	224	-47.6		329	-43.4	0.149		553	-45	
Yes	247	-52.4		430	-56.6			677	-55	
Diabetes: No	411	-87.3		625	-82.4	**0.012**		1036	-84.2	
Yes	60	-12.7		134	-17.6			194	-15.8	

Table 1: Clinical Parameters of the study population.

	Negative Biopsy			Positive Biopsy				All patients		
Continuous variables	**Mean**	**(±SD)**	**Median**	**Mean**	**(±SD)**	**Median**	**p**	**Mean**	**(±SD)**	**Median**
Number of TTMB Cores	57.2	-14.9	61	55.6	-9	57	**0.019**	56.2	-11.7	59
Prostate Volume: Volumetric	77.9	-44	67.3	51.4	-24.5	45.5	**<0.001**	61.6	-35.7	53.2
Ellipsoid	69.2	-38.5	60.7	45.6	-22.7	39.6	**<0.001**	54.6	-31.9	47.3
TZ Volume (Ellipsoid)	38.2	-28.2	30.1	20.1	-16.6	15	**<0.001**	27	-23.5	19.6
Prebiopsy PSA	7.4	-4.2	6.3	7.6	-7.8	6	0.617	7.5	-6.6	6.1
PSAD	0.122	-0.07	0.105	0.195	-0.211	0.146	**<0.001**	0.167	-0.157	0.131
TZ PSAD	0.271	-0.215	0.22	0.597	-0.82	0.406	**<0.001**	0.019	-0.676	0.301
TZ index	0.507	-0.127	0.516	0.398	-0.127	0.372	**<0.001**	0.44	-0.167	0.422

Table 2: Clinical Parameters of the study population.

Continuous Variable	**Mean**	**(±SD)**	**Median**
# TTMB Cores	55.6	-9	50
# Positive Cancer Cores	9.1	-8.3	7
Percent Positive Biopsies	17.1	-16	12.2
Categorical Variables	**Count**	**(%)**	
Gleason Score: 6	305	-40.2	
7 (3+4)	209	-27.5	
7 (4+3)	109	-14.4	
8	72	-9.5	
9 - 10	64	-8.4	
Positive Cores: 1	96	-12.7	
2-3	153	-20.2	
4-12	310	-40.8	
13-20	114	-15	
> 20	86	-11.3	

Table 3: Characteristics of prostate cancer patients.

	Univariate		Multivariate	
Continuous variable	**p**	**OR**	**p**	**OR**
Age at biopsy	**0.004**	**0.967**	0.066	
PSA prior to biopsy	0.382			
BMI	0.205			
Number of TRUS biopsies	**0.001**	**1.379**	**0.003**	**1.569**
Number of TRUS biopsy cores	**0.026**	**1.013**	0.811	
Prostate volume (ellipsoid)	**<0.001**	**0.971**	0.142	
TZ volume (ellipsoid)	**<0.001**	**0.959**	0.897	
PSAD	0.334			
TZPSAD	0.194			
TZ index	**<0.001**	**0.0316**	0.54	
Total number of TTMB cores	0.692			
Categorical variables				
Hypertension	0.146			
TURP/TUIP	0.754			
Diabetes	0.287			

Table 4: Predicting TZ upgrading (logistic regression).

However, TZ biopsies did potentially influence treatment decisions in 13.2% of patients by upgrading Gleason scores compared to a standard 12-core TRUS biopsy. Of those 13.2%, 6.6% of patients had Gleason score 4+3 histology or higher. In addition, the fact that approximately half of all prostate cancers involved the TZ has implications regarding patient eligibility for focal therapies and potentially active surveillance.

TTMB techniques may be more effective in obtaining biopsies of the TZ due to the ability to easily access the anterior gland [2,8,9]. TRUS biopsy techniques may be hampered by the fact that TZ tissue can be relatively resistant to needle penetration [6]. McNeal and Noldus observed that TZ needle biopsies selectively sampled tissue between BPH nodules and spared hyperplastic nodules [14]. They postulated this phenomenon was secondary to the mobility of hyperplastic nodules and extended this argument to include TZ-localized prostate cancer nodules. In contrast, TTMB is less likely to be influenced by such because of the use of a fixed template with Transperineal needle stabilization of the prostate gland prior to biopsy and visualization of the biopsy needles in the transverse and sagittal planes [2,8,9].

Strengths of our study include its prospective nature. All patients underwent the same intensive TTMB procedure by one investigator. Weaknesses of our study include the necessity for general anesthesia and operating room time which have limited wide spread adoption of TTMB. In the future, refinements in MRI and/or genomic testing will play greater roles in determining patient selection for prostate biopsy to include TZ biopsy.

Conclusion

47.2% of patients had TZ involvement with 5.4% having prostate cancer isolated to the TZ. TZ biopsies resulted in Gleason score upgrading in 13.2% of patients with resultant possible implications concerning treatment approaches to include eligibility for focal therapies and active surveillance.

References

1. Bratt O, Holmberg E, Andren O, Stefan C, Linda D, et al. (2019) The value of extensive transrectal repeat biopsy with anterior sampling in men on active surveillance for low-risk prostate cancer: A comparison from the randomized study of active monitoring in Sweden (SAMS). Eur Urol 76: 461-466.

2. Merrick GS, Delatore A, Butler WM, Bennett A, Fiano R, et al. (2017) Transperineal Template-guided Mapping Biopsy Identifies Pathologic Differences Between Very-Low-risk and Low-risk Prostate Cancer: Implications for Active Surveillance. Am J Clin Oncol 40: 53-59.

3. Patel V, Merrick GS, Allen ZA, Andreini H, Taubenslag W, et al. (2011) The incidence of transition zone prostate cancer diagnosed by transperineal template-guided mapping biopsy: Implications for treatment planning. Urol 77: 1148-1154.

4. Queiroz M, Falsarella P, Valle L, Mariotti GC, Lemos GC, et al. (2020) Is a sampling transition zone important to increase the detection of prostate cancer in systematic prostate biopsies. Acta Radiologica 2: 1-2

5. Davis JW, Kim J, Ward JF, Wang X, Nakanishi H, et al. (2009) Radical prostatectomy findings in patients predicted to have low volume/low-grade prostate cancer diagnosed by extended-core biopsies: an analysis of volume and zonal distribution of timor foci. Brr J Urol 105: 1386-1391.

6. Haarer CF, Anuradha G, Tickoo SK, Scardino PT, Eastham JA, et al. (2009) Prostatic transition zone directed needle biopsies uncommonly sample clinically relevant transition zone tumors. J Urol 182: 1337-1341.

7. Ishizuka O, Mumura Y, Oguchi T, Kawakami M, Nishizawa O, et al. (2005) Importance of transition zone biopsies in patients with gray-zone PSA levels undergoing the ultrasound guided systematic ten-biopsy regimen for the first time. Urol Int 74: 23-26.

8. Taira AV, Merrick GS, Galbreath RW, Andreini H, Taubenslag W, et al. (2010) Performance of transperineal template-guided mapping biopsy in detecting prostate cancer in the initial and repeat biopsy setting. Prostate Cancer PD 13: 71-77.

9. Bittner N, Merrick GS, Butler WM, Bennett A, Galbreath RW, et al. (2013) Incidence and pathologic features of prostate cancer detected on transperineal template guided mapping biopsy after negative transrectal ultrasound guided biopsy. J of Urol 109: 509-514.

10. Merrick GS, Rohmann G, Galbreath R, Scholl W, Fiano R, et al. (2020) Impact of age on prostate cancer progression and quality of life in active surveillance patients. BJUI Compass 2: 1-6.

11. Tosoian JJ, Trock BJ, Landis P, Feng Z, Epstein JI, et al. (2011) Active surveillance program for prostate cancer: An update of the Johns Hopkins experience. J Clin Oncol 29: 2185-2190

12. Crawford ED, Rove KO, Barqawi AB, Maroni PD, Werahera PN, et al. (2013) Clinical-pathologic correlation between transperineal mapping biopsies of the prostate and three-dimensional reconstruction of prostatectomy specimens. Prostate 73: 778-787.

13. McNeal JE, Redwine EA, Freiha FS, Stamey TA, et al. (1988) Zonal distribution of prostatic adenocarcinoma. Correlation with histologic pattern and direction of spread. Am J Surg Pathol 12: 897- 906.

14. McNeal J, Noldus J (1996) Limitatoins of transition zone needle biopsy findings in the prediction of transition zone cancer and tissue composition of benighn nodular hyperplasia. Urol 48: 721-756.

Advances In Industrial Biotechnology | ISSN: 2639-5665

Advances In Microbiology Research | ISSN: 2689-694X

Archives Of Surgery And Surgical Education | ISSN: 2689-3126

Archives Of Urology

Archives Of Zoological Studies | ISSN: 2640-7779

Current Trends Medical And Biological Engineering

International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X

Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276

Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292

Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370

Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594

Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X

Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562

Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608

Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879

Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397

Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751

Journal Of Aquaculture & Fisheries | ISSN: 2576-5523

Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780

Journal Of Biotech Research & Biochemistry

Journal Of Brain & Neuroscience Research

Journal Of Cancer Biology & Treatment | ISSN: 2470-7546

Journal Of Cardiology Study & Research | ISSN: 2640-768X

Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943

Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771

Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844

Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801

Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978

Journal Of Cytology & Tissue Biology | ISSN: 2378-9107

Journal Of Dairy Research & Technology | ISSN: 2688-9315

Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783

Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X

Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798

Journal Of Environmental Science Current Research | ISSN: 2643-5020

Journal Of Food Science & Nutrition | ISSN: 2470-1076

Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X

Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566

Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485

Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662

Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999

Journal Of Hospice & Palliative Medical Care

Journal Of Human Endocrinology | ISSN: 2572-9640

Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654

Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493

Journal Of Light & Laser Current Trends

Journal Of Medicine Study & Research | ISSN: 2639-5657

Journal Of Modern Chemical Sciences

Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044

Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X

Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313

Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400

Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419

Journal Of Obesity & Weight Loss | ISSN: 2473-7372

Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887

Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052

Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X

Journal Of Pathology Clinical & Medical Research

Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649

Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670

Journal Of Plant Science Current Research | ISSN: 2639-3743

Journal Of Practical & Professional Nursing | ISSN: 2639-5681

Journal Of Protein Research & Bioinformatics

Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150

Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177

Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574

Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060

Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284

Journal Of Toxicology Current Research | ISSN: 2639-3735

Journal Of Translational Science And Research

Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193

Journal Of Virology & Antivirals

Sports Medicine And Injury Care Journal | ISSN: 2689-8829

Trends In Anatomy & Physiology | ISSN: 2640-7752