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Reduced Core Targeted (RCT) biopsy: Combining multiparametric magnetic resonance imaging - transrectal ultrasound fusion targeted biopsy with laterally-directed sextant biopsies – An alternative template for prostate fusion biopsy

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ABSTRACT

Purpose: To introduce and assess the efficacy of a Reduced Core Targeted (RCT) biopsy template (image-targeted + laterally directed *sextant* biopsy) to detect clinically-significant cancer in patients with elevated PSA and a previous negative biopsy or on active surveillance. The performance and added value of either targeted alone vs random sextant vs combined biopsy template was appraised.

Methods: Data from 113 patients with a suspicious lesion on mpMRI and previous history of extended 10–12 core standard biopsy who subsequently had a RCT-biopsy were analyzed. These patients had at least one prior negative standard 10–12 core biopsy (n = 70) or were on active surveillance (n = 43). At least two samples were taken from each mpMRI lesion as a targeted biopsy together with the classic laterally-directed sextant biopsy.

Results: In patients having previous negative biopsy (n = 70), the RCT biopsy detected any cancer versus clinically-significant cancer in 62.9% versus 32.9%, respectively. Targeted biopsy diagnosed more clinically-significant cancers than sextant biopsy (31.4% versus 25.7%, $p < 0.01$). In this cohort, the use of targeted fusion biopsy upgraded the biopsy grade group (GrGp) in 15 (21.4%) patients compared to sextant biopsy. In patients on active surveillance, the RCT biopsy identified any cancer versus clinically-significant cancer for detection rates of 74.4% versus 39.5%, respectively. Fusion targeted biopsy diagnosed more clinically-significant cancers than sextant biopsy did (37.2% versus 18.6%, $p = 0.002$). The use of targeted biopsy upgraded the biopsy GrGp in 12 (27.9%) patients.

Conclusion: As a preliminary study, among men with MRI suspicious lesions and previous negative prostate biopsy or those under active surveillance, an image-targeted plus sextant biopsy platform can be associated with increased efficiency of detecting clinically-significant prostate cancer with fewer random cores. Future large series are needed to validate the clinical implication of this reduced core template in comparison with targeted fusion biopsy plus standard 12-core schema.

1. Introduction

The transrectal ultrasound (TRUS) - guided extended 12-core biopsy is the current standard of care biopsy platform to obtain histologic tissue to enable the diagnosis of prostate cancer (PCa) in men with an elevated prostate-specific antigen (PSA) level and/or abnormal digital rectal exam [1]. The overall cancer detection rate utilizing this modality based on the level of PSA and PSA density is between 35.1%–64.5% [1–3]. In the era of risk stratified PCa management, the detection of “clinically-significant” PCa is essential in that it may benefit men with reasonable life expectancy to subsequently seek curative therapy. On the other hand, patients with low risk PCa can be monitored to avoid the potential complications of overtreatment [4,5]. When cancer is detected by the standard extended 10–12 core biopsy, it

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has been shown that the correct risk attribution is not higher than 50% and this may not increase by repeating the standard biopsy [6–8]. Therefore, accurate risk attribution is always a challenge in the setting of rising PSA with initial negative prostate biopsy as well as in patients under active surveillance seeking to reassess if their disease still medically qualifies for observation.

In recent years, the introduction of multiparametric magnetic resonance imaging (mpMRI) and adoption of prostate imaging reporting and data system (PI-RADS™) version-2 have revolutionized the image identification and characterization of clinically significant PCa foci. The ability to visualize lesions comprising clinically significant (i.e. prostate grade group (GrGp) ≥2) PCa foci coupled to the high negative predictive value of mpMRI are major advancements over the conventional biopsy technique since it can change the management plan of patients that have undergone previous biopsy [9,10]. When mpMRI images are co-registered with real-time TRUS (i.e. mpMRI/TRUS fusion), the suspicious lesion can be purposefully targeted. As expected, mpMRI/TRUS fusion targeted biopsy can be associated with the detection of more (as high as 67%) GrGp ≥ 2 cancers while missing up to one-third of low risk lesions [11,12]. Despite this intuitive approach for the detection of clinically significant lesions, the current practice of image-guided biopsy includes a concurrent standard extended 10–12 core biopsy in addition to several mpMRI/TRUS fusion biopsies from mpMRI-suspicious lesions [10–12]. Obviously, these several additional core biopsies can increase the morbidity of the procedure especially in patients who are experiencing repeat biopsy session(s) [13].

In an effort to optimize the mpMRI/TRUS fusion biopsy, several investigators evaluated the performance of targeted "only" biopsy to detect clinically significant PCa. For example, Siddiqui et al. showed that the overall cancer detection rate of targeted only biopsy can be the same as standard TRUS biopsy but with significantly fewer cores (5.7 versus 12 cores: i.e. double the detection efficiency). Furthermore, targeted biopsy detected 30% more clinically significant cancers than standard biopsy did [11]. Similarly, Sonn et al. showed the superior efficacy of targeted biopsy compared to repeated conventional 12-core biopsy in patients with previous negative biopsies (diagnostic rate: 37%; almost 2/3 of them were GrGp ≥ 2) [12]. Recently, in a multicenter randomized trial comparing the diagnostic yield of MRI-targeted only versus standard TRUS-guided biopsy, more (+12%) clinically significant cancer versus less (-13%) low grade cancer was detected with MRI guided biopsy. The authors cited that by omitting standard biopsy sampling from MRI-targeted biopsy, up to 10% of clinically significant cancers might have been missed [13].

In response to the need to further optimize the mpMRI/TRUS fusion biopsy [14] while keeping the overall number of cores low (biopsy efficiency) we aim to evaluate the efficacy of mpMRI fusion targeted plus a random *sextant* biopsy template (i.e. Reduced Core Targeted (RCT) biopsy template) to detect clinically significant cancer in patients with a previous negative biopsy or on active surveillance. We specifically focused on how this biopsy approach can potentially *change* the management plan of these patients. To our knowledge, this is the first report of fusion image-targeted in combination with a random sextant biopsy schema to detect clinically significant PCa.

2. Patients and methods

2.1. Patient selection

Our institutional review board approved this Health Insurance Portability and Accountability Act-compliant retrospective study and granted a waiver of informed consent. Between January 2014 and March 2017, data from 113 consecutive patients with previous history of extended 10–12 core conventional biopsy who subsequently had a mpMRI/TRUS fusion targeted plus random sextant biopsies (RCT-biopsy) were analyzed. The inclusion criteria were patients who underwent 3 T mpMRI with an endorectal coil including high-resolution multiplanar T2 weighted (T2W) images, Diffusion-weighted imaging (DWI), and Dynamic Contrast Enhanced (DCE)-MRI. These patients either had a prior negative standard 10–12 core biopsy and had a rising PSA (n = 70) or had been diagnosed with clinically insignificant prostate cancer and were on an active surveillance protocol (n = 43). All patients in the cancer-naïve group had documented persistent elevated PSA after their standard biopsies but were excluded if they had received any treatment for prostate cancer in the interval between the initial standard and fusion biopsies in the AS group. Patients in either group were excluded if they had an incomplete mpMRI or had a contraindication to mpMRI. All men evaluated had at least one suspicious lesion on their mpMRI.

2.2. Imaging

2.2.1. Multiparametric MRI technique

MRI was performed using a single-channel endorectal coil (eCoil, Medrad, Indianola, PA) as well as multichannel surface coils on 3-T MRI scanners (Skyra, Siemens Healthcare, Erlangen, Germany). Imaging sequences included thin-section (3-mm section thickness) fast spin-echo T2-weighted images in the coronal, axial, and sagittal planes. DW images were obtained using multiple b values (b = 50 and 800 s/mm^2 with matched 3 mm slice thickness to T2W images in the axial plane, matrix size of 80 × 128, and field of view of 150 mm), and calculation of apparent diffusion coefficient (ADC) maps as well as high b value imaging (b = 1400s/mm^2) was also performed. DCE-MRI sequences were obtained after administration of a weight-based dose of extracellular MRI contrast agent (gadobenate dimeglumine, Multihance, Bracco Diagnostics, Princeton, NJ) with 4- to 5-second temporal resolution for 5–6 min.

2.2.2. Reading protocol

All mpMRIs were interpreted as per our standard clinical protocol by one of seven board-certified, fellowship trained abdominal radiologists with post-fellowship experience of at least five years. PI-RADS v2 scoring was utilized for all identified lesions. Lesion and gland segmentation were performed on third party software linked to our biopsy hardware (DynaCAD, Invivo Corp., Milwaukee, WI). All lesion and gland segmentation were checked prior to MR-TRUS fusion biopsy by a single board-certified radiologist with completed fellowship training in abdominopelvic imaging, special interest and expertise in prostate imaging, and over 7 years of experience reading prostate mpMRI (RG). This was done to optimize performance and consistency of mpMRI-TRUS fusion. Clinical interpretations of these cases were maintained throughout this process with no additions or deletions to the clinically marked lesions to maintain integrity of the quality improvement aspect of the project and to mimic real-life clinical practice.

2.3. Biopsy protocol

As mentioned above, following a standard mpMRI read at our institution, men electing fusion biopsy had their mpMRIs segmented and lesion target(s) assigned by one experienced prostate MRI radiologist (RG). Patients were scheduled for mpMRI/TRUS fusion biopsy at another separate session. Briefly, for RCT- biopsy the target lesions on a T2-weighted sequence were co-registered with real-time TRUS images as per the standard protocol of our MR-TRUS fusion system (UroNav, Invivo Corp., Milwaukee, WI). At least two samples were taken from each lesion guided by an end-fire TRUS probe. Following completion of the image-guided biopsy phase, classic laterally-directed sextant biopsies were taken randomly from the prostate base, mid- and apical aspects of the right and left lobes in the peripheral zone (Fig. 1).

2.4. Data analysis

All sextant and targeted fusion biopsy results were collected and

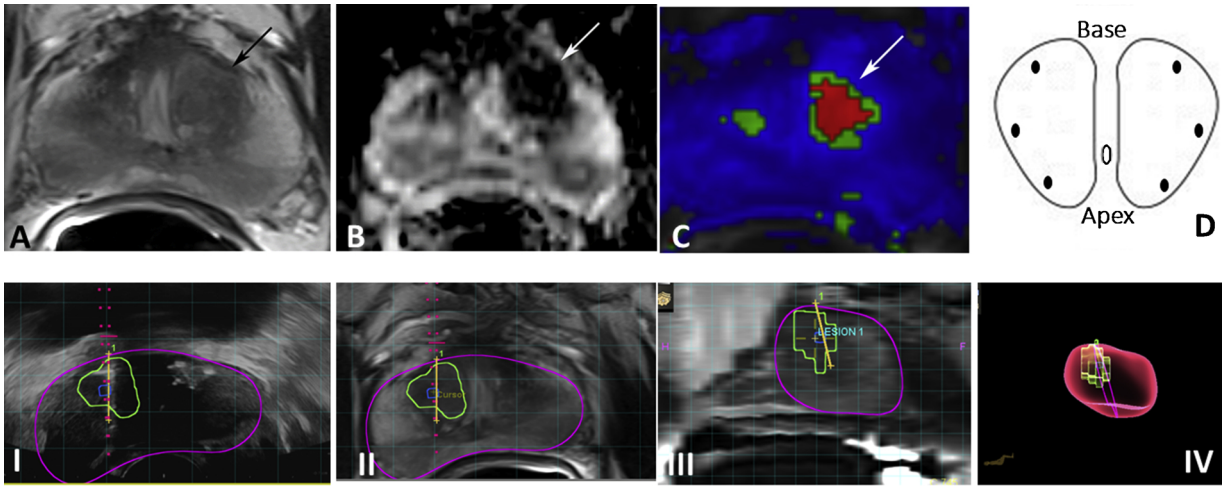

Fig. 1. A 57-year-old man with serum PSA of 7.6 ng/mL, PSA density of 0.19 ng/mL^2 and TRUS-guided biopsy demonstrating Gleason 3 + 3 = 6 prostate cancer involving the left base and left mid gland. He was referred for mpMRI with endorectal coil to ensure appropriate AS candidacy and to assess for any higher grade disease.

Upper panel: (A) Axial T2-weighted (T2W) image reveals ill-defined decreased T2 signal at the level of the left anterior transition zone of the mid-gland (arrow). **(B)** Diffusion-weighted imaging (DWI) and axial apparent diffusion coefficient (ADC) mapdemonstrate markedly restricted diffusion in this region (arrow). **(C)** Colored perfusion map created using post-processing software from dynamic contrast-enhanced (DCE) - MRI acquisition demonstrates suspicious perfusion kinetics for prostate cancer (arrow), corresponding to the findings seen on T2W and DWI. Lesion was scored PI-RADS 4 and patient elected RCT biopsy (mpMRI/TRUS fusion plus laterally directed sextant biopsy - schematic shown in **(D)**) revealing Gleason 3 + 5 = 8 prostate cancer (60% pattern 3, 35% pattern 4 and 5% pattern 5, GrGp 4) involving 30 mm of aggregate length and 70% of biopsy tissue. **Lower panel:** Screen capture from mpMRI/TRUS fusion biopsy of the lesion in the left anterior transition zone showing the needle within the lesion (outlined in green) with the center of the lesion denoted by the small blue circle on both the real-time TRUS image (I) and fused mpMRI image (II). Also, included are sagittal reformatted images from mpMRI (III) and three dimensional model of the prostate and the lesion with the biopsy cores within the lesion (IV). Based on the biopsy results and mpMRI findings, patient was deemed a poor AS candidate and elected radical prostatectomy revealing Gleason 4 + 3 = 7 (GrGp 3) prostate cancer (45% pattern 3, 50% pattern 4 and 5% pattern 5).

Table 1
Baseline characteristics of men having mpMRI/TRUS fusion biopsy plus random sextant [RCT] biopsy.

	Men with previous negative standard biopsy (n = 70)	Men under active surveillance (n = 43)	P value
Age (Mean SD) [Years]	65.4 (6.2)	67.8 (7.2)	P = 0.03
Median PSA (IQR) [ng/mL]	9.9 (6.6)	6.1 (4.1)	P = 0.04
Median prostate volume (IQR) [cc]	40.4 (27.2)	39.8 (26.3)	P = 0.08
Median PSA density (IQR) [ng/mL/cc]	0.26 (0.19)	0.2 (0.17)	P = 0.01
Number biopsy cores before fusion biopsy Median (IQR) [Range]	12 (12) [6–45]	12 (12) [6–74]	P = 0.03
Number suspicious lesions on mpMRI[a] Median (IQR) [Range]	1 (1) [1–3]	1 (1) [1–3]	–
Lesion volume [cc] Median (IQR)	0.9 (1.3)	0.94 (1.4)	P = 0.42
Number targeted biopsy cores Median (IQR) [Range]	2 (2) [2–6]	2 (2) [2–6]	–
Total biopsy cores Median (IQR) [Range]	8 (8) [8–12]	8 (8) [8–12]	–

TRUS: Transrectal ultrasound, PSA: Prostate-specific antigen, mpMRI: multiparametric magnetic resonance imaging.
[a] All are PI-RADS 4 or 5 lesions.

scored based on the five-tiered prostate cancer grade grouping system [15]. Specimens with GrGp ≥ 2 were considered clinically significant PCa and the highest GrGp on targeted or random biopsy was recorded and analyzed. The main objective of this study was to assess the performance of RCT-biopsy as a potentially "optimized" biopsy scheme (Fusion image-targeted + random sextant biopsy) to detect clinically significant disease and to evaluate how the results from this biopsy platform can potentially *change* the management of patients with either a previous negative biopsy or those on active surveillance. The management protocol was defined based on the first line of treatment as proposed for the ideal patient in each risk group by the National Comprehensive Cancer Network (NCCN) Guidelines® [https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf]. This simply includes observation/ active surveillance for benign/ low risk disease (GrGp1), respectively, and encouragement of active treatment/ intervention for GrGp ≥ 2 if clinically appropriate.

Patient demographics such as age, PSA level, prostate volume, PSA density and image characteristics were also recorded but management planning was solely based on the biopsy results in order to specifically assess the role of this biopsy protocol on management planning. Univariate comparisons were performed using parametric (student's *t*-test) and non-parametric (Wilcoxon's rank sum) testing for continuous variables and Fisher's exact or chi squared tests for categorical variables, as appropriate. Results for continuous variables are reported as median with interquartile ranges (IQR) unless otherwise specified. All tests were two-tailed and p values < 0.05 were considered statistically significant. All analyses were performed using the R v3.3.1 software (the R Foundation for Statistical Computing, Vienna, Austria) with 'Hmisc' and 'gmodels' libraries.

3. Results

During the study period, 113 patients with a previous history of at least one extended 10–12-core standard biopsy underwent mpMRI/TRUS fusion plus sextant biopsy and their data were categorized into two distinct cohorts (Table 1). Patients with previous negative 10–12-core standard biopsy (n = 70) had higher median pre-biopsy PSA level (9.9 ng/mL versus 6.1 ng/mL, P = 0.04), similar prostate volume and

higher median PSA density (0.26 versus 0.2 ng/mL^2, P = 0.01) compared to those on active surveillance. Both groups had similar patterns with regards to the number and volume of suspicious lesion (s) on mpMRI and the total biopsy cores taken during the mpMRI/TRUS fusion plus sextant biopsy (Table 1). All regions of interest on mpMRI in both groups were PI-RADS 4 or 5 lesions.

3.1. Patients with previous negative standard biopsy (n = 70)

A total of 37 of 70 (52.8%) cancer-naïve patients had two, 10 of 70 (14.3%) had three biopsy sessions and 23 of 70 (32.9%) had one biopsy before mpMRI/TRUS fusion plus sextant biopsy. Combined mpMRI/TRUS fusion plus sextant biopsy findings of any cancer versus clinically significant cancer detection rates were 62.9% versus 32.9%. The overall cancer detection rate with targeted biopsy was 54.3% versus 48.6% with random sextant biopsy within the same session ($p < 0.01$). Targeted biopsy diagnosed 5.7% more clinically significant cancers than sextant biopsy (31.4% versus 25.7%, $p < 0.01$). Compared to the sextant biopsy, the addition of targeted biopsy upgraded the highest GrGp category on pathologic analysis in 15 of 70 (21.4%) patients and it would have been associated with a potential change in management of 5 of 70 (7.1%) patients from conservative to active treatment. Adding sextant biopsy to targeted biopsy alone lead to upgrading in the GrGp category group in 8 of 70 (11.4%) patients, including five patients from benign pathology to GrGp 1, however this combination would have changed the management plan in only one case (1.4%). The number needed to biopsy with sextant biopsy in addition to targeted biopsy to diagnose one additional GrGp ≥ 2 disease was 71.5 (Table 2).

3.2. Patients in the active surveillance protocol (n = 43)

All patients on active surveillance were monitored due to GrGp1 PCa. A total of 16 of 43 (37.2%) patients had two, 8 of 43 (18.6%) had three and the 19 of 43 (44.2%) had one biopsy session before mpMRI-TRUS fusion biopsy. Combined mpMRI/TRUS fusion plus sextant biopsy findings of any cancer versus clinically significant cancer detection rates were 74.4% versus 39.5%, respectively. The overall cancer detection rate with targeted biopsy alone was 65.1% versus 58.1% with sextant biopsy alone (p = 0.02). Targeted biopsy diagnosed 18.6% more clinically significant cancers than sextant biopsy did (37.2% versus 18.6%, p = 0.002). The addition of targeted biopsy to the random biopsy template upgrades the GrGp in 12 of 43 (27.9%) patients and would have been associated with a potential change in management of 9 of 43 (20.9%) patients from conservative to active treatment. Adding sextant biopsy to targeted biopsy alone leads to upgrading of the diagnosis in 6 of 43 (13.9%) patients (Five patients had benign pathology in their targeted biopsy but GrGp 1 in their sextant), however this combination would change the management plan of only one case (2.3%). The number needed to biopsy with sextant biopsy in addition to targeted biopsy to diagnose one additional GrGp ≥ 2 disease was 43.5 (Table 3). Fig. 1 demonstrates the value of the RCT- biopsy template for reclassification of patients on active surveillance.

In both cohorts, median PSA density was significantly higher in men with versus without any cancer on combined biopsy, with clinically significant versus low risk disease on combined biopsy, and in men upgraded to any or GrGp ≥ 2 cancer by the addition of targeted biopsy to random biopsy (all $P < 0.005$) (Figs. 2 and 3).

Table 2
mpMRI/TRUS fusion biopsy compared to random sextant biopsy outcome for cohort of 70 men with previous negative biopsy. Light brown cells indicate patients in whom targeted biopsy upgraded the prostate grade group (GrGp) in relation to sextant biopsy. In eight patients, random sextant biopsy upgraded the prostate cancer grade group in relation to targeted biopsy (red cells), with one upgraded from benign to clinically significant disease. (For interpretation of the references to colour in this table legend, the reader is referred to the web version of this article.)

	Random sextant biopsy results						
Targeted biopsy results	Benign	GrGp1	GrGp2	GrGp3	GrGp4	GrGp5	Total
Benign	26	5	0	0	0	1	32
GrGp1	9	7	0	0	0	0	16
GrGp2	0	3	5	1	0	0	9
GrGp3	1	0	3	1	2	0	7
GrGp4	0	1	0	0	0	1	2
GrGp5	0	0	0	1	2	1	4
Total	36	16	8	3	4	3	70

mpMRI: multiparametric magnetic resonance imaging; GrGp: Prostate cancer grade group.

Table 3
mpMRI/ultrasound fusion biopsy compared to random sextant biopsy outcome for the cohort of 43 men with low risk prostate cancer under active surveillance. Light brown cells indicate patients in whom targeted fusion biopsy upgraded the grade group in relation to sextant biopsy. In six patients, random sextant biopsy upgraded the grade group in relation to targeted fusion biopsy (red cells); only one was upgraded from low risk to clinically significant disease. (For interpretation of the references to colour in this table legend, the reader is referred to the web version of this article.)

	Random sextant biopsy results						
Targeted biopsy results	Benign	GrGp1	GrGp2	GrGp3	GrGp4	GrGp5	Total
Benign	10	5	0	0	0	0	15
GrGp1	3	8	0	1	0	0	12
GrGp2	3	3	6	0	0	0	12
GrGp3	1	1	0	0	0	0	2
GrGp4	1	0	0	0	1	0	2
GrGp5	0	0	0	0	0	0	0
Total	18	17	6	1	1	0	43

mpMRI: multiparametric magnetic resonance imaging; GrGp: Prostate cancer grade group.

4. Discussion

In the era of risk stratified diagnosis and management of prostate cancer, several modalities have been proposed to increase the detection rate of clinically significant (i.e. GrGp ≥ 2) prostate cancer on standard TRUS-guided biopsy that simultaneously minimize morbidity. In addition to the use of several biomarkers such as free-PSA, Prostate Cancer Antigen-3, the Prostate Health Index, 4 K Score, and exosomes, increasing the number of biopsy sessions and/or cores have been examined [16,17]. In men with initial negative conventional biopsy, increasing the number of biopsy sessions is associated with a lower rate of cancer detection (18% to 7% on second through fifth biopsy sessions) [16]. Furthermore, while classic sextant biopsy may miss up to 20% of prostate cancer cases [17], increasing the number of cores may not always improve the rate of clinically significant cancer detected or add more prognostic information [18]. In recent years, largely due to a higher efficacy of mpMRI/TRUS fusion-guided biopsy to detect overall and clinically significant cancers (37–67%) [11,12,19], its application has been recommended for the diagnosis of prostate cancer in patients with negative biopsy or monitoring those under active surveillance [5,20,21]. This new application of fusion biopsy has been associated with a simultaneous extended 12-core biopsy, maintaining the standard of care, to avoid inadvertent cancer under-detection. Therefore, with

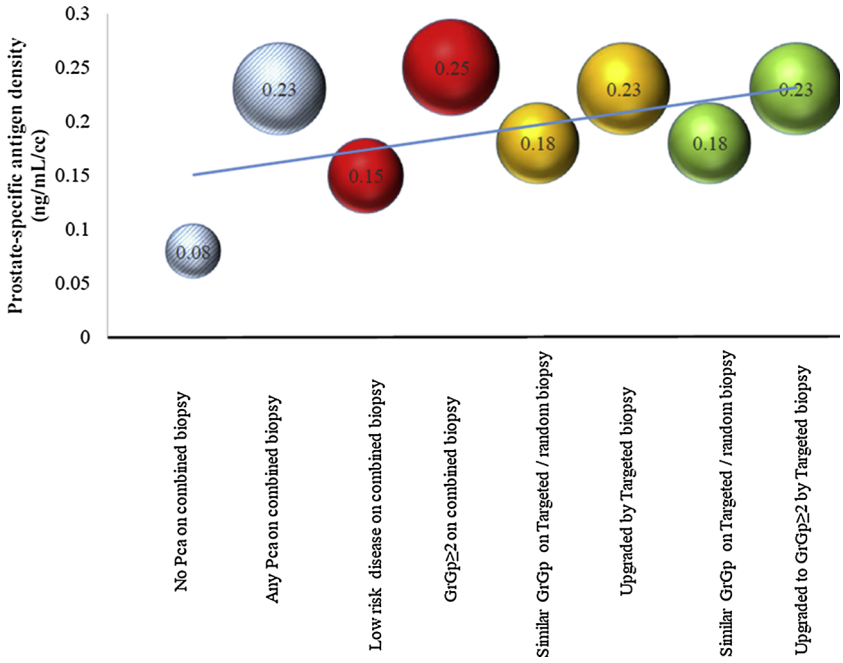

Fig. 2. Median PSAD values in different subgroups of men with previous negative biopsy who underwent RCT biopsy.
PCa: Prostate cancer, GrGp: Prostate cancer Grade Group.

standard mpMRI/TRUS fusion biopsy, patients are receiving *more* biopsy cores, rather than fewer, as should occur when making improvements to technology. At the same time, the majority of publications in the literature do not support the ability to obviate a randomly sampled biopsy altogether to rely solely on image-guided cores only at this time.

In the present study, we coupled the strength of the image-guided targeted biopsy to the random sampling nature of sextant biopsy. We conceptualized that the high performance of targeted biopsy can potentially cover the missed cancer detection rate of sextant biopsy, a technique that relies on a minimum number of randomly-sampled cores, resulting in an efficient biopsy template with optimum biopsy cores [17]. Therefore, we proposed and examined a new mpMRI/TRUS fusion biopsy schema consisting of two biopsy cores per mpMRI-identified lesion plus laterally-directed random sextant biopsies (i.e. RCT-biopsy). Depending on the number of regions of interests on the mpMRI, the total number of cores in the present study ranged between 8 (i.e. for 1 mpMRI-detected lesion) to 12 cores (i.e. two cores for each of 3 suspicious mpMRI-detected lesions + sextant biopsies). We believe that this strategy can potentially reduce the morbidity of the biopsy procedure especially in men undergoing repeat biopsy. We show that in patients with a previous negative biopsy, the overall and clinically significant prostate cancer detection rates were 62.9% and 32.9%, respectively, using a RCT- biopsy schema (median cores = 8). These

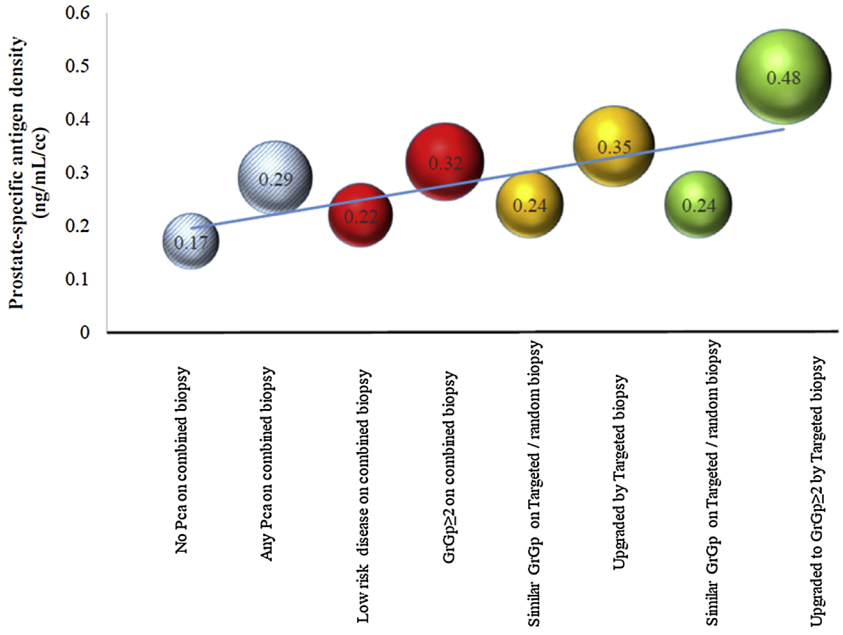

Fig. 3. Median PSAD values in different subgroups of men under active surveillance who underwent RCT biopsy.
PCa: Prostate cancer, GrGp: Prostate cancer Grade Group.

detection rates are consistent with previous reports when a combined targeted and a *12*-core biopsy template is used [11,12,19,22]. Interestingly, we show that when image-guided fusion biopsy is added to the sextant biopsy, the biopsy result is upgraded to clinically significant disease in about one in five patients with a tendency toward detection of GrGp ≥ 2 lesions (Δ +5.7%) and potential change in management (7.1%) with targeted biopsy. Conversely, the addition of a sextant biopsy diagnosed 8.5% more PCa but only 1.4% additional clinically significant cancers. A systematic review of standard mpMRI/TRUS fusion biopsy outcomes showed that the targeted versus standard extended biopsies detect 5–16% versus 2.1% additional clinically significant cancers, respectively [8]. The authors recommended that the standard biopsy should not be omitted from the protocol. Nonetheless, in the present report, we showed that decreasing the number of random biopsy cores to 6 may not negatively influence the outcome.

The value of PSA density for improving the predictive accuracy of PI-RADS™ as well as the detection rate of high-grade cancer using targeted biopsy has been shown [23,24]. A similar pattern was observed in our RCT- biopsy template. The PSA density was significantly higher in those having GrGp ≥ 2 cancers. Similarly, the PSA density was significantly higher in men whose biopsy results were upgraded in general or upgraded to a GrGp ≥ 2 by targeted biopsy (Fig. 2).

The use of mpMRI and mpMRI/TRUS fusion biopsy for tracking a cancer lesion over time, targeting new suspicious lesions and whole gland mapping for systematic biopsy is emerging in active surveillance programs. Recently, Elkhoury et al. reviewed the role of targeted prostate biopsy for enrolling patients into or monitoring them during active surveillance protocols. Using MRI to monitor and target biopsies of suspicious lesions, the rate of upgrading from GrGp 1 to GrGp ≥ 2 in these patients varied between 10–42% [25]. In another systematic review on the role of mpMRI in active surveillance, Schoots et al. concluded that the addition of MRI can be associated with detection of 33–50% clinically significant cancers and a reclassification rate of 33% during follow up [26]. In the present study, we evaluated the performance of the RCT-biopsy template in low risk patients (GrGp 1) with known region(s) of interest. Almost 40% of patients with clinically significant disease were detected with the RCT-biopsy approach. As expected, targeted biopsies favored the detection of GrGp ≥ 2 cancers (Δ +18.6%) and were associated with a potential reclassification rate of approximately 21%. Therefore, reducing the number of random cores in the setting of active surveillance can be comparable with previous reports using a standard fusion biopsy protocol [25,26]. The PSA density was significantly higher in patients reclassified to clinically significant disease using the RCT-biopsy template (Fig. 3). This finding is also consistent with previous reports evaluating the performance of mpMRI/TRUS fusion with a standard 12-core schema in the setting of active surveillance [27]. We believe that increasing the biopsy efficiency is an important and emerging viewpoint. In recent years, newer technologies such as MRI- guided in-bore biopsy have been presented based on this concept. A recent systematic review of pure targeted in-bore MRI-guided biopsy in men with previous negative biopsy or on AS showed an overall versus csPCa detection rate of 23–74% versus 26–94% (median 63%) with this technology [28].

To our knowledge, this is the first report showing the feasibility of reducing the overall number of biopsy cores during mpMRI/TRUS fusion procedures in patients having a prior history of extended core biopsy. As a preliminary study, when assessed with the series of standard mpMRI/TRUS fusion with a 12-core random biopsy template we demonstrate the performance of a "*Reduced- Core-Targeted*" fusion/random biopsy paradigm was comparable. Approximately 10–15% of clinically significant cancer foci may be missed on mpMRI [29]. Until such time that random biopsies are deemed no longer necessary, utilizing a sextant biopsy template retains some of the benefits of sampling while minimizing the impact of additional needle passes that may not be necessary.

A number of potential limitations of this study deserve mention. The reproducibility of the proposed fusion/sextant template should be further assessed in a large sample size and in a biopsy-naïve screening population. Ideally, the radical prostatectomy specimen should be utilized as the gold standard to assess performance. However, radical prostatectomy can also bias the cohort towards higher grade disease so we feel that our results are still valuable in those patients who have a combination of low and high risk disease. Moreover, we carefully selected active surveillance patients with MRI-positive lesions in this cohort. A positive mpMRI is significantly associated with upgrading (to GrGp ≥ 2) in men reclassified to radical prostatectomy from active surveillance (43% versus 27%) [26]. Currently, surveillance of MRI-negative individuals with imaging only is not yet considered a standard of care [28], therefore we focused on MRI-positive men but this needs to be verified in large series. Previous studies have shown that if a "lesion-only" aimed biopsy was applied, the overall pathology costs could have been reduced by 80% [22]. Therefore, comparative studies are warranted to analyze how reduction of biopsy cores can mitigate the morbidity, psychologic burden and costs associated with mpMRI/TRUS fusion biopsy.

5. Conclusion

As a preliminary study, among men with MRI-suspicious lesions and previous negative prostate biopsy or those under active surveillance, a fusion image-targeted plus sextant biopsy platform can be associated with increased efficiency of detecting clinically significant prostate cancer with fewer cores. Future Comparative studies seems advisable to validate the clinical implication of this reduced core template in comparison with targeted fusion biopsy plus standard 12-core schema.

Conflict of interest

Dr. Gupta has a consultant agreement with Invivo Corporation.

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