Oncology

How Many Cores Should be Obtained During Saturation Biopsy in the Era of Multiparametric Magnetic Resonance? Experience in 875 Patients Submitted to Repeat Prostate Biopsy

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OBJECTIVE To evaluate the number of needle cores combined with multiparametric magnetic resonance imaging (mpMRI) findings needed to diagnose all clinically significant cases of prostate cancer (csPCa) in men subject to transperineal saturation biopsy (SPBx; 30 cores).

METHODS From January 2016 to June 2019, 875 men (median age 63 years) underwent repeat SPBx (median 30 cores) for the suspicion of cancer. All of the patients underwent for the first time 3.0 Tesla pelvic mpMRI before SPBx, and the lesions with Prostate Imaging-Reporting and Data System category ≥3 underwent additional transperineal-targeted fusion prostate biopsies (TPBx).

RESULTS StageT1c PCa was found in 306/875 (34.5%), and 222/306 (72.5%) of them were classified as csPCa. SPBx missed 2/222 (1%) csPCa with International Society of Urologic Pathology Grade Group (GG) 3. TBPx missed 33/222 (14.9%) csPCa (21 vs 12 cases were GG1 vs GG3). The initial 20 needle SPBx cores obtained from the peripheric (16 cores) and anterior gland (4 cores) diagnosed all of the 222 (100%) csPCa only missing 84/129 (65.1%) indolent PCa thus presenting diagnostic accuracy, sensitivity, and specificity equal to 83.1%, 100%, and 65.1%, respectively.

CONCLUSION In men subject to mpMRI and/or TPBx, a maximum of 20 systematic transperineal needle cores detected all cases of csPCa and minimized the diagnosis of indolent cancers. UROLOGY 00: 1–5, 2019. © 2019 Elsevier Inc.

Prostate cancer (PCa) is the most frequent tumor diagnosed in older/elderly men with more than 1.3 million prostate biopsies per year performed in the United States,[1] but the main goal at present is to reduce the number of unnecessary biopsies and diagnose only clinically significant PCa (csPCa).[2] In this respect, multiparametric magnetic resonance imaging (mpMRI) combined with transrectal ultrasound (TRUS) fusion-targeted biopsies have improved the accuracy of standard biopsy schemes; the estimated detection rate for csPCa of suspicious mpMRI lesions performing targeted transperineal biopsy ranges from 65.3% to 83.8% of the cases.[3,4] Nevertheless, mpMRI has demonstrated a false negative rate of 15% to 20% in detection of low volume csPCa.[5] In addition, mpMRI/TRUS fusion biopsy platforms[6] have shown different diagnostic accuracy in diagnosing PCa; therefore, at present, a systematic prostate biopsy (at least 10-12 cores) should be combined with mpMRI/TRUS fusion biopsy.[7,8] Finally, the number of cores that should be obtained during systematic prostate biopsy in the presence of negative mpMRI and/or added to targeted fusion biopsy to diagnose csPCa has not been established.

In this report, the number of needle cores combined with mpMRI findings needed to diagnose all the csPCa in men who underwent transperineal saturation biopsy (SPBx) was prospectively evaluated.

MATERIALS AND METHODS

From January 2016 to June 2019, 875 men (median age: 63 years; range: 47-78 years) with negative digital rectal examination and previous negative (absence of cancer) extended biopsy underwent repeat transperineal SPBx for the suspicion of cancer

Conflict of Interest: *The authors declare no conflict of interest exists in regard to this study. The authors contributed equally to this article.*

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Submitted: October 22, 2019, accepted (with revisions): November 13, 2019

(increasing or persistently elevated prostate-specific antigen [PSA] values). After institutional review board and ethical committee approval were granted, informed consents were obtained from all participants included in the study. Ten days before SPBx, all patients underwent for the first time pelvic mpMRI in conjunction with SPBx (median of 30 cores; range: 28-34 cores) performed transperineally using a GE Logiq P6 ecograph (General Electric; Milwaukee, WI) and supplied with a biplanar transrectal probe (5-7.5 MHz) using a tru-cut 18 gauge needle (Bard; Covington, GA). Patients were sedated and received antibiotic prophylaxis (intravenous administration of 2 g of cefazolin before prostate biopsy). All mpMRI examinations were performed using a 3.0 Tesla scanner, (ACHIEVA 3T; Philips Healthcare Best, the Netherlands) equipped with surface 16-channel phased-array coil placed around the pelvic area with the patient in the supine position. Multi-planar turbo spin-echo T2-weighted, axial diffusion weighted imaging (high b-value—2000 s/mm^2), and axial dynamic contrast enhanced MRI were performed for each patient. The mpMRI procedure was well-tolerated and successfully performed in all cases (men with claustrophobia, cardiac pacemakers, and hip replacements were not included in the study). The mpMRI lesions characterized by Prostate Imaging Reporting and Data System (PI-RADS) version 2[12] scores ≥3 were considered suspicious for cancer.[3] Two radiologists blinded to preimaging clinical parameters evaluated the mpMRI data separately and independently; moreover, 1 urologist with more than 25 years of experience performed the biopsy procedure. The data were collected following the Screening Tool to Alert to Right Treatment criteria.[9] In the presence of mpMRI lesions suggestive of cancer (490/875 equal to 56% of the cases), a fusion-targeted biopsy (4 cores) was added to SPBx using a transperineal fusion guided-biopsy device (Hitachi 70 Arietta ecograph, Chiba, Japan).[10] The Hitachi Arietta 70 platform allowed processing of a software-based rigid registration of pelvic mpMRI and TRUS (biplanar probe, respectively) with the use of a fusion device; moreover, an electromagnetic tracking system showed needle localization.

The diagnostic accuracy of mpMRI and TPBx for the diagnosis of csPCa (Gleason score ≥6 and/or greatest percentage of cancer >50% and/or more than 2 positive cores) has previously been evaluated[2] and compared with SPBx results. In addition, the minimum number of needle cores during SPBx combined with mpMRI findings to diagnose all the csPCa was recorded. The SPBx protocol included at least 12 cores in the peripheric zone of each lobe (apex, med, and base), beginning parasagittally and extending to reach the outer edges of the gland (lateral margins) and 4 cores in the anterior zone were obtained. Each needle core was progressively numbered to indicate the prostatic zone.[11,12] The Clavien-Dindo grading system for the classification of biopsy complications was used.[13] For statistical analysis, the Student's t-test was used, and a P value <.05 was considered statistically significant.

RESULTS

In 306/875 (34.5%) patients, stage T1c PCa was diagnosed, and 222/306 (72.5%) of them were classified as csPCa (Table 1). In detail, 117/222 (79.8%) and 45/222 (20.2%) csPCa were located in the peripheric and anterior zones of the gland, respectively. The median total PSA was 9.8 ng/ml (range: 4.2-51 ng/ml); moreover, the prostate volume, PSA density, the quantitative histology, and the PI-RADS scores are listed in Table 2. None of the patients had significant complications (only Clavien-Dindo grade I) resulting from the prostate biopsy, requiring hospital admission. The Gleason score and International Society of Urologic Pathology Grade Groups (GG)[14] were directly correlated with the PI-RADS scores and the number of positive needle cores (P < .001; Table 2); moreover, the number of positive cores was higher in small prostate tumors with higher PSA density values (Table 2). The detection rate for overall cancers vs csPCa using SPBx vs TPBx is listed in Table 3. In detail, SPBx missed 2/54 (3.7%) csPCa GG3, and TBPx missed 21/45 (46.7%) vs 12/54 (22.2%) of csPCa GG1 vs GG3; on the contrary, SPBx and TPBx diagnosed equally all csPCa GG2 (Table 1).

The initial 20 needle cores of SPBx performed in the peripheric (16 cores: 3 cores of the apex, 3 Med, and 2 base for each lobe) and anterior gland (4 cores) were diagnosed all

Table 1. Number of positive needle cores in 306 patients with prostate cancer (PCa) submitted to transperineal saturation biopsy (SPBx) combined with transperineal targeted fusion biopsy (TPBx)

Number of Positive Needle Cores Overall PCa 306 Patients (pts)	csPCa 222 (pts) (75.5%)	SPBx 1 Core	SPBx 2 Cores	SPBx 3 Cores	SPBx 4 Cores	SPBx >4 Cores	Positive TPBx 1-4 Cores	Negative TPBx 0 Cores
GS* 3 + 3 GG1** 129 PCa	45 (pts) (34.9%)	51	33	15	3	27	24 (pts) (53.3%)	21 (pts)
GS* 3 + 4 GG2** 99 PCa	99 (pts) (100%)	3	15	18	6	57	99 (pts) (100%)	0 (pts)
GS* 4 + 3 GG3** 54 PCa	54 (pts) (100%)	3	3	0	3	45	42 (pts) (77.8%)	12 (pts) (22.2%)
GS* 4 + 4 GG4** 6 PCa	6 (pts) (100%)	0	0	0	0	6	6 (pts) (100%)	0 (pts)
GS* 4 + 5 GG5** 18 PCa	18 (pts) (100%)	0	0	0	0	18	18 (pts) (100%)	0 (pts)

* Gleason score (GS).
** International Society of Urological Pathology (ISUP) grading group (GG); csPCa: clinically significant prostate cancer; pts: patients.

Table 2. Clinical parameters, quantitative biopsy histology, and Prostate Imaging Reporting and Data System (PI-RADS) category in the 222 men with csPCa

Quantitative Histology Gleason Score (ISUP Grade Group-GG)	PI-RADS 3 (112 pts)	PI-RADS 4 (93 pts)	PI-RADS 5 (17 pts)
3 + 3 (GG1)	42	3	-
3 + 4 (GG2)	45	54	-
4 + 3 (GG3)	25	29	-
4 + 4 (GG4)	-	4	2
4 + 5 (GG5)	-	3	15
	Median number of positive cores (range)		
3 + 3 (GG1)	5.2 (1-12)	5.0 (4-7)	-
3 + 4 (GG2)	6.3 (1-17)	6.5 (4-9)	-
4 + 3 (GG3)	7.0 (1-20)	7.5 (5-15)	-
4 + 4 (GG4)	-	8.0 (7-19)	12 (10-16)
4 + 5 (GG5)	-	12.0 (10-18)	15 (12-21)
Median Greatest Percentage of Cancer (range)	50% (30%-70%)	60% (40%-100%)	80% (50%-100%)
Median prostate volume (g)	52	42	40
Median prostate-specific antigen (PSA) density	0.19	0.21	0.24

pts, patients; SPBx, saturation prostate biopsy; TPBx: targeted fusion biopsy.

Table 3. Detection rate for clinically significant prostate cancer (csPCa) related to the number of needle cores during transperineal saturation biopsy

Number of needle cores	csPCa (222 cases)	16 Cores 12* + 4**	17 Cores 13* + 4**	18 Cores 14* + 4**	19 Cores 15* + 4**	20 Cores 16* + 4**
TPBx	189 (84.1%)	189 (84.1%)	189 (84.1%)	189 (84.1%)	189 (84.1%)	189 (84.1%)
SPBx	220 (96.6%)	208 (93.7%)	210 (95.5%)	215 (96.8%)	216 (97.3%)	220 (99%)
SPBx + TPBx	222 (30 cores) (100%)	208 (93.7%)	212 (95.5%)	215 (96.8%)	216 (97.3%)	222 (100%)

SPBx, saturation prostate biopsy; TPBx, targeted fusion biopsy.
* Peripheric needle cores.
** Anterior needle cores.

222 (100%) csPCa, including the 21 cases of GG1 cancer with quantitative histology suggestive for csPCa (Table 1). In addition, a number of needle cores equal to 20 missed 84/129 cases (65.1%) of indolent PCa (GG1) and thus presented diagnostic accuracies, sensitivities, and specificities in diagnosing csPCa equal to 83.1%, 100% and 65.1%, respectively.

COMMENT

Although mpMRI is strongly recommended in patients recommended for prostate biopsy[15,16] or enrolled in active surveillance protocols,[9,17] at present, systematic prostate biopsies should be always combined with mpMRI/TRUS fusion biopsy due to the false negative rate[4,5,18] of mpMRI (csPCa with low volume and Gleason score $\geq$ 7).[3,19,20] On the other hand, mpMRI improves the cost-effectiveness of prostate biopsy; in fact, mpMRI constitutes a significant saving of healthcare resources by reducing the risk of overdiagnosis and the number of unnecessary procedures.[21] Complications from prostate biopsy are also expensive, and methods to reduce their incidence may be cost-effective. The risk of sepsis with the related costs (such as hospitalization, antibiotic therapy) in men subject to transrectal biopsy is between 2% and 5%.[22] In addition, overall healthcare spending for prostate biopsies should include the cost of the follow-ups for clinically indolent PCa (active surveillance) and the related overtreatment of definitive therapy (erectile dysfunction and urinary incontinence).[23] In this scenario, the number of required cores that should be obtained during systematic prostate biopsy has not been established in the presence of negative mpMRI and/or added to targeted-fusion biopsy used to diagnose all the csPCa. In fact, in the era before mpMRI, SPBx was recommended as a way to increase the diagnosis of PCa with a detection rate for cancer between 22.9% and 40%[11] and a high percentage of indolent PCa[24]; nevertheless, transperineal SPBx, is presently suggested in men enrolled in clinical trials for focal therapy[25] and/or in men included in AS protocols.[8]

In our series, SPBx diagnosed 306 PCa, and only 222 (72.5%) of them were classified as csPCa; conversely, TPBx missed 33/222 (14.9%) csPCa characterized by 21/45 (46.7%) vs 12/54 (22.2%) International Society of Urologic Pathology GG1 vs GG3. The initial 20 needle cores of SPBx plus TPBx obtained from the peripheric (16 cores) and anterior gland (four cores) diagnosed all 222 cases (100%) of csPCa missing 84/129 (65.1%) indolent PCa. These data could be useful for reducing the complication rate (such as acute urinary retention) following a high number of needle cores during transperineal SPBx.[26,27] These data are also useful for planning of prostate biopsy under local anesthesia in an office setting[28]

thus reducing the cost of the procedure (hospitalization, sedation, surgery room) and the risk of overdiagnosis. Finally, the feasibility of an office biopsy procedure could propagate the transperineal approach in clinical practice in order reset the risk of sepsis and improve the detection rate for csPCa located in anterior zone.[29,30]

Regarding our results, some considerations should be made. First, the results were evaluated on biopsy specimens and not on the entire prostate gland or from a template mapping biopsy. Second, the use of an in-bore mpMRI-targeted biopsy, probably, would have probably improved the diagnosis of csPCa. Third, our data refer only to men who underwent repeat prostate biopsies. Fourth, the detection rate for csPCa of the peripheric cores (12 vs 16) significantly correlated with the prostate weight and PSA density values; in contrast, the 4 needle cores of the anterior zone demonstrated that all cases were csPCa irrespective of prostate volume. Fifth, the patient population was mainly derived from men with persistently elevated PSA values after previously negative systematic prostate biopsies; therefore, the results might not be transferable to a screening population. Finally, our results might change if the definition of csPCa had included only PCa with Gleason score ≥7 (GG2 or more).[22]

CONCLUSION

In men subject to mpMRI and/or TPBx, a maximum of 20 systematic transperineal needle cores detected all of the cases of csPCa thus minimizing the diagnosis of indolent cancers.

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