ORIGINAL ARTICLE

A multicentric study on accurate grading of prostate cancer with systematic and MRI/US fusion targeted biopsies: comparison with final histopathology after radical prostatectomy

R. Diamand[1] · M. Oderda[3] · W. Al Hajj Obeid[1] · S. Albisinni[2] · R. Van Velthoven[1] · G. Fasolis[3] · G. Simone[4] · M. Ferriero[4] · J-B. Roche[5] · T. Piechaud[5] · A. Pastore[6] · A. Carbone[6] · G. Fiard[7] · J-L. Descotes[7] · G. Marra[8] · P. Gontero[8] · E. Altobelli[9] · R. Papalia[9] · P. Kumar[10] · D. Eldred-Evans[11] · A. Giacobbe[12] · G. Muto[12] · V. Lacetera[13] · V. Beatrici[13] · T. Roumeguere[2] · A. Peltier[1]

Abstract

Objective To evaluate the accuracy in histologic grading of MRI/US image fusion biopsy by comparing histopathology between systematic biopsies (SB), targeted biopsies (TB) and the combination of both (SB + TB) with the final histopathologic outcomes of radical prostatectomy specimens.

Materials and methods Retrospective, multicentric study of 443 patients who underwent SB and TB using MRI/US fusion technique (Urostation® and Trinity®) prior to radical prostatectomy between 2010 and 2017. Cochran's Q test and McNemar test were conducted as a post hoc test. Uni-multivariable analyses were performed on several clinic-pathological variables to analyze factors predicting histopathological concordance for targeted biopsies.

Results Concordance in ISUP (International Society of Urological Pathology) grade between SB, TB and SB + TB with final histopathology was 49.4%, 51.2%, and 63.2% for overall prostate cancer and 41.2%, 48.3%, and 56.7% for significant prostate cancer (ISUP grade ≥ 2), respectively. Significant difference in terms of concordance, downgrading and upgrading was found between SB and TB (ISUP grade ≥ 2 only), SB and SB + TB, TB and SB + TB (overall ISUP grade and ISUP grade ≥ 2) ($p < 0.001$). Total number of cores and previous biopsies were significant independent predictive factors for concordance with TB technique.

Conclusion In this retrospective study, combination of SB and TB significantly increased concordance with final histopathology despite a limited additional number of cores needed.

Keywords Targeted · Biopsy · MRI/US fusion · Prostate cancer · Concordance

Introduction

Prostate cancer (PCa) is the most common non-cutaneous malignancy in men and is a major health concern in developed countries. Traditionally, clinical diagnosis is made by digital rectal examination (DRE) in association with serum PSA level and confirmation by 10–12-core systematic biopsies [1]. However, this blind diagnostic method leads on one hand to a risk of under-detection of potentially significant index lesions, on the other hand, systematic biopsies may lead to detection of clinically indolent, low-risk PCa, with a consequent risk of overtreatment [2].

Undeniably, it is known that Gleason score (GS) remains one of the most important prognostic factors and an essential component for determining the best choice of treatment. However, several large studies have shown a limited correlation between systematic biopsies and final histopathologic outcomes, reaching values of 50%, with disease upgrading and downgrading in more than 30% and 20% of cases, respectively [3, 4]. This upgrading can in fact lead to inappropriate or under-treatment in a subgroup of patients [5].

Multiparametric magnetic resonance imaging (mp-MRI) has been studied as a new tool for early detection of prostate cancer before performing initial biopsies and recent studies confirm its high sensitivity especially for clinically significant cancer [6–9]. Suspicious foci can be targeted during biopsy and several modalities have been developed for clinical practice, including MRI/ultrasound (MRI/US) image fusion and cognitive techniques [10]. Few prospective studies comparing image fusion and cognitive techniques have not clearly shown a significant difference in terms of cancer detection and grade concordance with final specimen [11–13]. However, it appears that MRI/US image fusion biopsy shows better reproducibility with a fairly rapid learning curve and can be used to improve accuracy for focal treatments and/or radiotherapy [14–16]. Although randomized studies have shown contradictory results in identifying significant difference in terms of cancer detection between targeted and systematic biopsies, it appears that targeted biopsies would improve the accuracy of biopsy [17–20]. Indeed, it seems that they improve histopathological concordance with the final prostatectomy specimen [21–24].

The aim of this multicentric study was to evaluate the accuracy in histologic grading of MRI/US image fusion biopsy by comparing histopathology between systematic biopsies (SB), targeted biopsies (TB) and the combination of both (SB + TB) with the final histopathologic outcomes of radical prostatectomy.

Materials and methods

We performed a retrospective multicentric study with a European database (Belgium, Italy, France and UK) on patients who underwent MRI/US image fusion biopsy with Koelis® device (Koelis®, La Tronche, France) between 2010 and 2017. A total of 2115 cases were found, of which 443 underwent radical prostatectomy in the same institution in which biopsies were performed, with complete data available.

Clinical and pathologic data was retrospectively gathered. Mp-MRI was performed prior to biopsy when a prostate cancer was suspected by an elevated PSA and/or a positive DRE although it is not currently recommended by EAU guidelines in biopsy-naïve patients [1]. The mp-MRI protocol was dependent on the institution and followed the European Society of Urogenital Radiology (ESUR) guidelines with at least T2-weighted (T2W), diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) sequences. Suspicious lesions were defined by a Prostate Imaging Reporting and Data System score (PI-RADS version 1 was used for 110 patients until 2015 which were converted to the PI-RADS version 2 after retrospective

analysis of the images, and version 2 thereafter for 333 patients) and then were delineated by the radiologist using the Koelis® software.

Urostation® (93%) and Trinity® (7%) devices (Koelis®, La Tronche, France) were used to create highly detailed 3D maps of the prostate combining elastic MRI/US fusion, 3D ultrasound and Organ-Based Tracking® technology. Biopsies were performed exclusively transrectally by experienced urologists (> 100 biopsies performed) who knew the MRI results before the procedure. All the patients gave informed consent and biopsies were performed according to EAU guidelines; quinolones were used before biopsies and enema was performed according to the operator's choice [1]. They underwent systematic biopsies (SB) (median 12 cores) and then targeted biopsies (TB) (median 3 cores), depending on the prostate anatomy and size of suspicious lesions. Systematic biopsies were performed using an extended pattern 12-core biopsy. No matter the location or the size of the target area, systematic biopsies were always carried out in the same, standardized manner. Biopsies of hypoechoic area were left to the discretion of operators as well as the transitional zone.

Each prostate biopsy was individualized, labeled and embedded in paraffin. For each case, biopsy and prostatectomy specimens were evaluated by the same uropathologist in each institution. For the needle biopsy and prostatectomy specimens, the overall grade was assigned based on the part with the highest Gleason score which is usually associated with the grade of the dominant nodule in concordance with the recommendations of the International Society of Urological Pathology (ISUP) [25]. Gleason scores were reported as five groups (ISUP grades 1–5) as recommended in recent ISUP guidelines. Significant prostate cancer was defined by an ISUP grade equal or superior to 2.

Indication for radical prostatectomy was taken in line with the EAU guidelines [1]. All RPs were performed with pure laparoscopic or robot-assisted laparoscopic approach by experienced urologists, according to the institutional policy.

Cochran's Q test was used to test for the difference in concordance with final histopathology between systematic (SB), targeted (TB) and combined biopsies (SB + TB). McNemar test was conducted as a post hoc test. Univariable and multivariable logistic regressions were performed to analyze factors predicting histopathological concordance for targeted biopsies. Variables tested included: PSA (categoric < 10 vs. 10–20 vs. > 20), prostate volume (categoric < 30 vs. 30–60 vs. > 60), previous biopsy (categoric), number of targets (continuous), PI-RADS score (categoric 3 vs. 4 vs. 5), diameter of target (continuous), and number of cores per target (continuous). We assumed a significance level of 0.05. Statistical analysis was performed using SPSS version 25 (IBM Corp®, New York, USA).

Results

Patient characteristics are shown in Table 1. In total, 126 cases (28.4%) had positive digital rectal examination and 45% of the patients were biopsy naïve. The median prostate volume was 45.5 cc (IQR 25). Mp-MRI identified a single index lesion with a PI-RADS score of 3, 4 and 5 in 17.6%, 45.6% and 30.9% of the patients, respectively. Of note, there was insufficient data regarding the PI-RADS score for 25 patients (5.6%) because of incomplete protocols at the time of the PI-RADS version 1. The median number of cores taken per lesion was 3 (IQR 2) for targeted biopsy and 12 (IQR 3) for systematic biopsies.

Histopathological concordance with final specimen is shown in Table 2 and Fig. 1a (overall ISUP grade), b

Table 1 Patient characteristics of 443 patients

Age, median (IQR), years	65 (8)
PSA, median (IQR), ng/mL	7.1 (5)
Rectal examination, n (%)	
Positive	126 (28.4)
Negative	271 (61.1)
Unknown	46 (10.4)
Prostate volume, median (IQR), mL	45.5 (25)
Previous biopsy, n (%)	
Yes	161 (36.3)
No	200 (45.1)
Unknown	82 (18.5)
Koelis® device, n (%)	
Urostation®	412 (93)
Trinity®	31 (7)
Number of target lesions per prostate, n (%)	
1	329 (74.3)
2	95 (21.4)
3	17 (3.8)
4	1 (0.2)
Unknown	1 (0.2)
PI-RADS score, n (%)	
2	1 (0.2)
3	78 (17.6)
4	202 (45.6)
5	137 (30.9)
Unknown	25 (5.6)
Diameter target lesion, median (IQR), mm	11 (8)
Number of cores per target, median (IQR), n	3 (2)
Number of cores, median (IQR), n	
Target biopsy	4 (3)
Systematic biopsy	12 (3)
Total	15 (2)

IQR interquartile range

Table 2 Histopathologic results

ISUP grade (target biopsy only), n (%)	
Negative	101 (22.8)
1	108 (24.4)
2	109 (24.6)
3	60 (13.5)
4	50 (11.3)
5	15 (3.4)
ISUP grade (systematic biopsy only)	
Negative	108 (24.4)
1	137 (30.9)
2	102 (23)
3	52 (11.7)
4	31 (7)
5	13 (2.9)
ISUP grade (target and systematic biopsy)	
Negative	26 (5.9)
1	141 (31.8)
2	134 (30.2)
3	61 (13.8)
4	65 (14.7)
5	16 (3.6)
ISUP grade (prostatectomy)	
1	118 (26.6)
2	161 (36.3)
3	101 (22.8)
4	41 (9.2)
5	22 (5)
TNM	
2a	34 (7.7)
2b	22 (5)
2c	249 (56.2)
3a	95 (21.4)
3b	36 (8.1)
4	2 (0.4)
Unknown	5 (1.1)
N+	30 (6.8)

(ISUP grade ≥ 2). Cochran's Q test was performed to test the difference between the three groups: systematic biopsy only (SB group), targeted biopsy only (TB group) and the association of both techniques (SB + TB group). The test was positive in all the categories whether the analysis was for the downgrading ($p < 0.001$), upgrading ($p < 0.001$) or concordance ($p < 0.001$) and it can be concluded that the proportions in at least two of the groups were significantly different from each other. McNemar test was then performed to compare each set of groups head to head. Table 3 illustrates concordance in ISUP grade across biopsy techniques and radical prostatectomy specimen. For overall ISUP grade, a significant difference was found between SB group and

Fig. 1 Histopathological concordance with final specimen, **a** overall ISUP grade, **b** ISUP ≥ 2 and **c** ISUP ≥ 2 (biopsy-naïve patients)
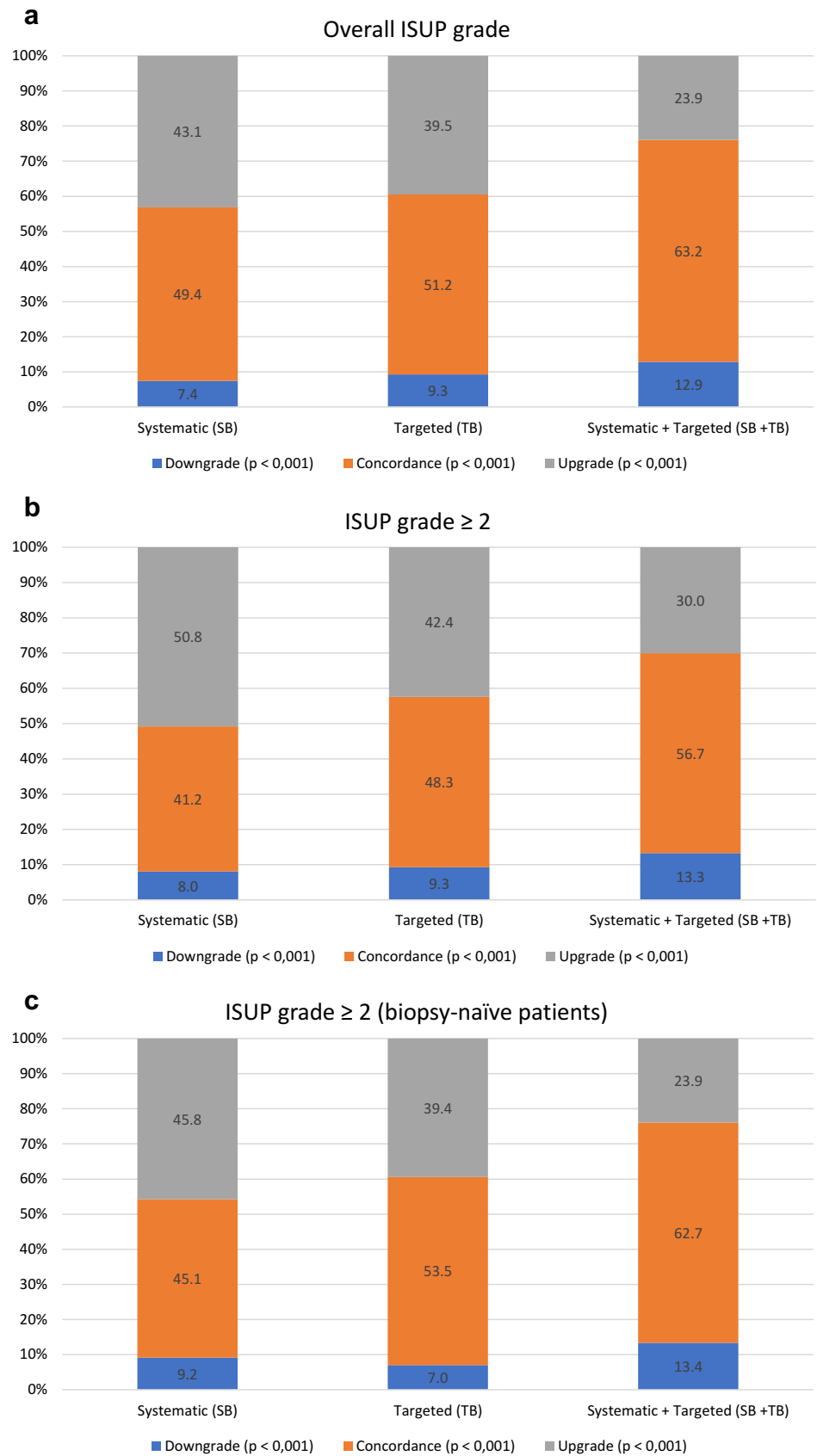

a

Overall ISUP grade

	Systematic (SB)	Targeted (TB)	Systematic + Targeted (SB +TB)
Upgrade	43.1	39.5	23.9
Concordance	49.4	51.2	63.2
Downgrade	7.4	9.3	12.9

■ Downgrade (p < 0,001) ■ Concordance (p < 0,001) ■ Upgrade (p < 0,001)

b

ISUP grade ≥ 2

	Systematic (SB)	Targeted (TB)	Systematic + Targeted (SB +TB)
Upgrade	50.8	42.4	30.0
Concordance	41.2	48.3	56.7
Downgrade	8.0	9.3	13.3

■ Downgrade (p < 0,001) ■ Concordance (p < 0,001) ■ Upgrade (p < 0,001)

c

ISUP grade ≥ 2 (biopsy-naïve patients)

	Systematic (SB)	Targeted (TB)	Systematic + Targeted (SB +TB)
Upgrade	45.8	39.4	23.9
Concordance	45.1	53.5	62.7
Downgrade	9.2	7.0	13.4

■ Downgrade (p < 0,001) ■ Concordance (p < 0,001) ■ Upgrade (p < 0,001)

Table 3 Histopathology concordance between biopsy (systematic + targeted) and final specimen

ISUP grade at biopsy	ISUP grade at prostatectomy						Concordance (%)
	Grade I	Grade II	Grade III	Grade IV	Grade V	Total	
0	9	10	6	1		26	
Grade I	97	32	9	3		141	68.8
Grade II	11	100	18	4	1	134	74.6
Grade III		10	43	5	3	61	70.5
Grade IV	1	9	23	27	5	65	41.5
Grade V			2	1	13	16	81.2
Total	118	161	101	41	22	443	

SB + TB group for downgrading, upgrading and concordance ($p < 0.001$). Same results were found between TB group and SB + TB group ($p < 0.001$). However, there was an absence of significant difference between SB group and TB group (upgrading $p = 0.2$, downgrading $p = 0.2$, concordance $p = 0.6$). For ISUP grade ≥ 2, a significant difference was found between SB group and SB + TB group for upgrading, downgrading and concordance ($p < 0.001$), between TB group and SB + TB group (upgrading $p < 0.001$, downgrading $p < 0.001$, concordance $p = 0.001$), and between SB group and TB group (upgrading $p < 0.001$, concordance $p = 0.001$) except for downgrading ($p = 0.2$).

A post hoc subgroup analysis including only biopsy-naïve patients with ISUP grade ≥ 2 at radical prostatectomy showed similar results with a significant difference between SB group and SB + TB group (upgrading $p < 0.001$,

downgrading $p = 0.03$, concordance $p < 0.001$), between TB group and SB + TB group (upgrading $p < 0.001$, downgrading $p = 0.004$, concordance $p = 0.02$) but there was no significant difference between SB group and TB group (upgrading $p = 0.3$, downgrading $p = 0.5$, concordance $p = 0.1$) (Fig. 1c).

In univariable logistic analysis, previous biopsy [OR = 0.6, 95% CI (0.4–0.9), $p = 0.04$] was associated to a significant reduction in concordance and number of cores taken [OR = 1.2, 95% CI (1.1–1.3), $p = 0.004$] was significant predictive factors for concordance (Table 4). Multivariable analysis revealed that these same factors were independently associated with histopathological concordance [previous biopsy OR = 0.6, 95% CI (0.4–0.9), $p = 0.01$; number of cores taken OR = 1.2, 95% CI (1.1–1.3), $p = 0.004$].

Of note, 26 patients (5.9%) had negative prostate biopsies with previous positive biopsies. In this subset, patients were

Table 4 Logistic regression for targeted biopsy concordance

Variable	Univariable[a]			Multivariable[a]		
	OR	95% CI	p	OR	95% CI	p
PSA, ng/mL						
<10	1					
10–20	1.1	(0.7–1.7)	0.7			
>20	1.4	(0.6–3.3)	0.5			
Prostate volume, mL						
<30	1					
30–60	0.6	(0.3–1.1)	0.08			
>60	0.8	(0.4–1.5)	0.5			
Previous biopsy	0.6	(0.4–0.9)	0.04	0.6	(0.4–0.9)	0.01
Number of target	1.1	(0.8–1.5)	0.7			
PI-RADS score						
≤3	1					
4	0.9	(0.6–1.5)	0.8			
5	1.1	(0.7–1.9)	0.6			
Diameter, mm						
<10	1					
10–20	0.8	(0.5–1.4)	0.5			
>30	0.6	(0.3–1.4)	0.3			
Number of cores per target	1.2	(1.1–1.3)	0.004	1.2	(1.1–1.3)	0.004

[a]Variables with $p < 0.05$ in the univariable analysis were included in the multivariable analysis

under active surveillance but chose to carry out a surgical intervention after discussion with their surgeon. Final histopathology at radical prostatectomy was 9 ISUP grade 1, 10 ISUP grade 2, 6 ISUP grade 3 and 1 ISUP grade 4. The final TNM stage was 9 T2a, 16 T2c and 1 T3b. In total, nine patients (2%) with grade I (acute urinary retention) and nine patients (2%) with grade II (severe hematuria and prostatitis) complications according to the Clavien–Dindo classification were reported.

Discussion

The last decade has witnessed a revolution in PCa diagnosis, with the introduction of mp-MRI and the inverse stage migration allowing for a better identification of aggressive cancers requiring radical therapy and indolent cancers as potential candidates for active surveillance [6, 26]. The ultimate goal should be to decrease the risk of overtreating young adults and undertreating the older generation [27]. The purpose of mp-MRI is to help the urologist to better characterize suspicious lesions, to be able to delineate potentially clinically significant PCa which can be biopsied later despite having a challenging location such as the apex and the anterior zone of the prostate and eventually reducing the number of useless biopsies for indolent cancer [6, 7]. This technology is even more important because targeted biopsies may be helpful in causing a breakthrough in focal tumor treatment without the need of radical therapy in the absence of definitive histopathology.

Our study found no significant difference in terms of concordance between systematic and targeted biopsies for all the cancers but a better accuracy for targeted biopsy when significant cancers were taken into account. This finding suggests that the use of targeted biopsies alone can detect as accurately as systematic biopsies prostate cancer and support the conclusion of several studies using different platforms of MRI/US fusion (Artemis®, BioJet®, Urostation®) [21–24]. If we only take into account studies using Koelis® device, Baco found a concordance for targeted biopsy of 70%, an upgrading of 14% and downgrading of 16% in a retrospective analysis of 135 patients [21]. Lanz found similar results with a concordance for targeted biopsy of 67%, an upgrading of 29% and a downgrading of 4% with a retrospective analysis of 125 patients [24]. Of note, these studies evaluated the accuracy of targeted biopsy without a direct comparison with systematic biopsy or the association of both. It is, therefore, reasonable to raise the question of the usefulness of systematic biopsies. Of note, our study revealed that significant prostate cancers were found in cases of negative targeted biopsies with 38 ISUP grade I (8.6%) and 63 ISUP grade $\geq$ 2 [14.2%: 40 ISUP grade II (9%), 17 ISUP grade III (3.8%), 5 ISUP

grade IV (1.1%) and 1 ISUP grade V (0.2%)], a result which appears validated by other studies confirming that targeted biopsies alone might miss 3.8–17% of the significant prostate cancer [28]. Furthermore, around 10% of the tumors were undetected by MRI and in few cases, the delineated target volume does not always reflect the real tumor volume with a 16% over estimation and a 32% underestimation according to Cornud [7, 8, 29]. However, Baco showed a 100% match in terms of localization of targeted biopsies for the index lesion and an overall 95% precision rate with a 5% error margin attributable to missing the tumor on MRI using Koelis® system [21]. Therefore, taking into account systematic biopsies allows adjusting for the lack of precision in tumor volume on MRI and, to a lesser extent, to improve the performance of targeted biopsies. In fact, combining both techniques (systematic and targeted) achieves a 63.2% in concordance with final histopathology, an upgrade of 23.9% and a downgrade of 12.9%. This same trend is seen whenever we take into account the subcategory of significant cancers (ISUP grade $\geq$ 2) with a significant difference in comparison with the two biopsy techniques separately. This proposal goes in the opposite direction of the conclusion of the PRECISION trial that supports the fact of doing only targeted biopsy [20]. However, the primary outcome of this study was the detection of men with clinically significant cancer and not the histopathologic concordance. Of note, 30 patients underwent radical prostatectomy with sufficient data and percentages of concordance, upgrading and downgrading were similar between targeted biopsy group and systematic biopsy group. To our point of view, the association of both techniques remains the standard for PCa detection and our results reinforce these recommendations [1].

The study included patients over a 7-year period and different versions of the fusion system were used (Urostation® and Trinity® in 93% and 7% of cases, respectively). However, it is known that MRI/US fusion targeted biopsies are associated with a short learning curve [14] and all operators had a vast experience with both targeted and systematic biopsies. Moreover, the histopathologic concordance between targeted biopsies and final specimen for the first 100 cases (2010–2014) and last 100 cases (2016–2017) was 57% and 59%, respectively.

Although recommendations have been proposed at the International Society of Urological Pathology (ISUP) consensus meeting in 2005 and 2014, discordance among pathologists remains in assigning Gleason score and ISUP grades [25]. In the case of multiple cores having different Gleason grades, some pathologists choose to give an overall Gleason score rather than the highest Gleason score. In general, the pathologist should report the grades of core separately and in our study, we used the highest

Gleason score (biopsy and final specimen) to calculate the histopathologic concordance. Nonetheless, as the same pathologist performed the analysis for the biopsy and the final prostatectomy specimen, this discordance is limited.

The number of cores taken during targeted biopsy was an independent predictive factor for concordance with final histopathology and it is currently recognized that two cores per lesion are generally sufficient while the median number was 3 per lesion in our study. Number of cores depends on lesion sizes and appreciation of the operator and it is important to note that multiple studies confirmed the absence of correlation between the number of cores taken and the potential risk of infection or bleeding [30]. Given our results, we advise urologists should not hesitate to perform additional biopsies to maximize the accuracy of diagnosis.

Although this is to our knowledge the largest study comparing histopathology between biopsy and final specimens, we acknowledge its limitations. This is a retrospective study with heterogeneity in the data collection and looks at a population who underwent radical prostatectomy with a significant disease. Mp-MRI and biopsies were performed by a large number of specialists with a variability of experience and habits in different centers without a central pathologic revision. Urologists were also not blinded to MRI results so there could be an influence on how systematic biopsies were performed. However, the same pathologist for each center evaluated the biopsies and the correlated prostatectomy specimen, thus such bias is reduced.

Conclusions

In this retrospective study, MRI/US image fusion and systematic biopsies were found to be complementary, significantly increasing concordance with final histopathology and causing a significant decrease in disease upgrading. Combining these two techniques may aid in tailoring the adequate treatment for each patient. Prospective studies are awaited to validate our findings.

Compliance with ethical standards

References

1. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M et al (2017) EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 71(4):618–629

2. Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P et al (2016) 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 375(15):1415–1424. https://doi.org/10.1056/NEJMoa1606220

3. Cohen MS, Hanley RS, Kurteva T, Ruthazer R, Silverman ML, Sorcini A et al (2008) Comparing the Gleason prostate biopsy and Gleason prostatectomy grading system: the Lahey Clinic Medical Center experience and an international meta-analysis. Eur Urol 54(2):371–381

4. King CR, Long JP (2000) Prostate biopsy grading errors: a sampling problem? Int J Cancer 90(6):326–330

5. Gordetsky J, Epstein J (2016) Grading of prostatic adenocarcinoma: Current state and prognostic implications. Diagn Pathol 11:25

6. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK et al (2017) Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 389(10071):815–822

7. Tan N, Margolis DJ, Lu DY, King KG, Huang J, Reiter RE et al (2015) Characteristics of detected and missed prostate cancer foci on 3-T multiparametric MRI using an endorectal coil correlated with whole-mount thin-section histopathology. Am J Roentgenol 205(1):W87–W92

8. Russo F, Regge D, Armando E, Giannini V, Vignati A, Mazzetti S et al (2016) Detection of prostate cancer index lesions with multiparametric magnetic resonance imaging (mp-MRI) using whole-mount histological sections as the reference standard. BJU Int 118(1):84–94

9. Peltier A, Aoun F, Lemort M, Kwizera F, Paesmans M, Van Velthoven R (2015) MRI-targeted biopsies versus systematic transrectal ultrasound guided biopsies for the diagnosis of localized prostate cancer in biopsy naïve men. Biomed Res Int 2015:571708. https://doi.org/10.1155/2015/571708

10. Wegelin O, van Melick HHE, Hooft L, Bosch JLHR, Reitsma HB, Barentsz JO et al (2017) Comparing three different techniques for magnetic resonance imaging-targeted prostate biopsies: a systematic review of in-bore versus magnetic resonance imaging-transrectal ultrasound fusion versus cognitive registration is there a preferred technique? Eur Urol 71:517–531

11. Lee DJ, Recabal P, Sjoberg DD, Thong A, Lee JK, Eastham JA et al (2016) Comparative effectiveness of targeted prostate biopsy using magnetic resonance imaging ultrasound fusion software and visual targeting: a prospective study. J Urol 196(3):697–702

12. Valerio M, McCartan N, Freeman A, Punwani S, Emberton M, Ahmed HU (2015) Visually directed vs. software-based targeted biopsy compared to transperineal template mapping biopsy in the detection of clinically significant prostate cancer. Urol Oncol Semin Orig Investig 33(10):424.e9–424.e12

13. Wysock JS, Rosenkrantz AB, Huang WC, Stifelman MD, Lepor H, Deng FM et al (2014) A prospective, blinded comparison of magnetic resonance (MR) imaging-ultrasound fusion and visual estimation in the performance of MR-targeted prostate biopsy: the profus trial. Eur Urol 66(2):343–351

14. Lista G, Lughezzani G, Lazzeri M, Bini V, Hurle R, Buffi N et al (2017) Absence of learning curve impact may let MRI-TRUS fusion guided biopsy up for early diagnosis of prostate cancer. Eur Urol Suppl 16:p1086–p1087

15. Cool DW, Zhang X, Romagnoli C, Izawa JI, Romano WM, Fenster A (2015) Evaluation of MRI-TRUS fusion versus cognitive registration accuracy for MRI-targeted, TRUS-guided prostate biopsy. Am J Roentgenol 204:83–91

16. Kwak JT, Hong CW, Pinto PA, Williams M, Xu S, Kruecker J et al. (2015) Is visual registration equivalent to semiautomated registration in prostate biopsy? Biomed Res Int 2015:394742. https://doi.org/10.1155/2015/394742

17. Baco E, Rud E, Eri LM, Moen G, Vlatkovic L, Svindland A et al (2016) A randomized controlled trial to assess and compare the outcomes of two-core prostate biopsy guided by fused magnetic resonance and transrectal ultrasound images and traditional 12-core systematic biopsy. Eur Urol 69(1):149–156

18. Tonttila PP, Lantto J, Pääkkö E, Piippo U, Kauppila S, Lammentausta E et al (2016) Prebiopsy multiparametric magnetic resonance imaging for prostate cancer diagnosis in biopsy-naive men with suspected prostate cancer based on elevated prostate-specific antigen values: results from a randomized prospective blinded controlled trial. Eur Urol 69(3):419–425

19. Porpiglia F, Manfredi M, Mele F, Cossu M, Bollito E, Veltri A et al (2017) Diagnostic pathway with multiparametric magnetic resonance imaging versus standard pathway: results from a randomized prospective study in biopsy-naïve patients with suspected prostate cancer. Eur Urol 72(2):282–288

20. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH et al (2018) MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med. https://doi.org/10.1056/NEJMoa1801993

21. Baco E, Ukimura O, Rud E, Vlatkovic L, Svindland A, Aron M et al (2015) Magnetic resonance imaging-transectal ultrasound image-fusion biopsies accurately characterize the index tumor: correlation with step-sectioned radical prostatectomy specimens in 135 patients. Eur Urol 67(4):787–794

22. Borkowetz A, Platzek I, Toma M, Renner T, Herout R, Baunacke M et al (2016) Direct comparison of multiparametric magnetic resonance imaging (MRI) results with final histopathology in patients with proven prostate cancer in MRI/ultrasonography-fusion biopsy. BJU Int 118(2):213–220

23. Porpiglia F, De Luca S, Passera R, Manfredi M, Mele F, Bollito E et al (2016) Multiparametric-magnetic resonance/ultrasound fusion targeted prostate biopsy improves agreement between biopsy and radical prostatectomy Gleason score. Anticancer Res 36(9):4833–4840

24. Lanz C, Cornud F, Beuvon F, Lefèvre A, Legmann P, Zerbib M et al (2016) Gleason score determination with transrectal ultrasound-magnetic resonance imaging fusion guided prostate biopsies—are we gaining in accuracy? J Urol 195(1):88–93

25. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA (2016) The 2014 international society of urological pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma definition of grading patterns and proposal for a new grading system. Am J Surg Pathol 40(2):244–252

26. Albisinni S, Joniau S, Quackels T, De Coster G, Dekuyper P, Van Cleynenbreugel B et al (2017) Current trends in patient enrollment for robotic-assisted laparoscopic prostatectomy in Belgium. Cancer 123(21):4139–4146

27. Lunardi P, Ploussard G, Grosclaude P, Roumiguié M, Soulié M, Beauval JB et al (2017) Current impact of age and comorbidity assessment on prostate cancer treatment choice and over/under-treatment risk. World J Urol 35(4):587–593

28. Radtke JP, Teber D, Hohenfellner M, Hadaschik BA (2015) The current and future role of magnetic resonance imaging in prostate cancer detection and management. Transl Androl Urol 4(3):326–341

29. Cornud F, Khoury G, Bouazza N, Beuvon F, Peyromaure M, Flam T et al (2014) Tumor target volume for focal therapy of prostate cancer—does multiparametric magnetic resonance imaging allow for a reliable estimation? J Urol 191(5):1272–1279

30. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, Nam R et al (2013) Systematic review of complications of prostate biopsy. Eur Urol 64:876–892

Affiliations

R. Diamand[1] · M. Oderda[3] · W. Al Hajj Obeid[1] · S. Albisinni[2] · R. Van Velthoven[1] · G. Fasolis[3] · G. Simone[4] · M. Ferriero[4] · J-B. Roche[5] · T. Piechaud[5] · A. Pastore[6] · A. Carbone[6] · G. Fiard[7] · J-L. Descotes[7] · G. Marra[8] · P. Gontero[8] · E. Altobelli[9] · R. Papalia[9] · P. Kumar[10] · D. Eldred-Evans[11] · A. Giacobbe[12] · G. Muto[12] · V. Lacetera[13] · V. Beatrici[13] · T. Roumeguere[2] · A. Peltier[1]

1   Department of Urology, Jules Bordet Institute, Université Libre de Bruxelles, Boulevard de Waterloo 121, 1000 Brussels, Belgium

2   Department of Urology, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

3   Department of Urology, San Lazzaro Hospital, Alba, Italy

4   Department of Urology, Regina Elena National Cancer Institute, Rome, Italy

5   Department of Urology, Saint Augustin Clinic, Bordeaux, France

6   Department of Medico-Surgical Sciences and Biotechnologies, Urology Unit, Sapienza University of Rome, Latina, Italy

7   Department of Urology, Grenoble University Hospital, Grenoble, France

8   Department of Surgical Sciences, Urology Unit, University of Turin, Turin, Italy

9   Department of Urology, Campus Bio-medico University, Rome, Italy

10 Department of Urology, Royal Marsden Hospital, London, UK

11 Department of Urology, Charing Cross Hospital, London, UK

12 Department of Urology, Humanitas Gradenigo Hospital, Turin, Italy

13 Department of Urology, Azienda Ospedaliera Ospedali Riuniti Marche Nord Hospital, Pesaro Fano, Italy