Original Article



Magnetic resonance imaging targeted biopsy in biopsy-naïve patients and the risk of overtreatment: a grading issue

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Objective

To evaluate the impact of applying the 2014 and 2019 International Society of Urological Pathology (ISUP) recommendations on grade group distribution and concordance with radical prostatectomy (RP).

Materials and Methods

Overall, 655 biopsy-naïve patients diagnosed by magnetic resonance imaging (MRI) targeted and systematic biopsies for Prostate Imaging Reporting and Data System score \geq 3 lesions were identified from a prospectively maintained database from 2016 and 2022. Clinically significant prostate cancer was detected in 249 patients, of whom 69 underwent RP. Wilcoxon signed rank and McNemar's tests were used to compare the ISUP grade group distribution and concordance with RP after applying the 2014 (i.e., highest grade) and 2019 (i.e., global grade) ISUP recommendations, respectively.

Results

Compared to the 2014 ISUP recommendations, the 2019 ISUP recommendations were associated with a significant decrease in ISUP Grade Group 4 (range of difference from -13% to -5%) and an increase in ISUP Grade Group 2 (range of difference from +6% to +11%) in MRI targeted biopsy only, MRI targeted with perilesional biopsies, and MRI targeted with systematic biopsies (all P < 0.01). In patients who underwent RP, a significant decrease in downgrading was observed with all biopsy strategies (range of difference from -19% to -12%; $P \le 0.008$), along with an increase in concordance with RP specimen (range of difference from +12% to +13%; $P \le 0.02$). The use of the 2019 ISUP recommendation was associated with RP specimen a lower treatment burden.

Conclusions

The use of the 2019 ISUP recommendations mitigates the grade migration induced by MRI targeted biopsy and improves the concordance with the final RP specimen.

Keywords

grade migration, overtreatment, MRI, prostate cancer, biopsy

Introduction

Gleason score remains the most important prognostic factor in prostate cancer (PCa) and forms the basis for treatment decisions [1,2]. The Gleason grading system has significantly evolved from its original description to a five-grade-group system after successive consensus meetings conducted by the International Society of Urological Pathology (ISUP) in 2005, 2014 and 2019 [3]. The use of multiparametric MRI and MRI targeted biopsy in biopsy-naïve patients is associated with improved detection of clinically significant PCa (csPCa) [4–7]. However, the clinical implications of this newly unmasked PCa are a matter of growing debate in the urological community given the massive impact of biopsy grading on risk stratification and patient management [8–11]. Indeed, it is questionable whether this increase in the detection of csPCa is the result of higher-grade disease otherwise missed by systematic biopsies or the selective representation of a high-grade area within an overall less aggressive pathology. On this basis, Vicker et al. [8] argued that the broad use of MRI potentially induces grade migration and overtreatment.

By focusing on a suspicious MRI lesion, a larger number of positive biopsy cores is more likely to be obtained. This not only results in higher Gleason pattern yields but would most likely lead to greater grade heterogeneity within biopsy samples. While most urologists prefer to rely on the worst grade (i.e., the highest grade group) for treatment decisions, as mentioned in the 2014 ISUP recommendations, the ISUP Consensus Conference in 2019 suggested providing a global grade group for each suspicious MRI lesion, taking into account perilesional biopsies [12,13]. However, data to evaluate the clinical impact of such a grading modification are not yet available.

In the present study, we aimed to evaluate the distribution of grade groups in patients diagnosed by MRI targeted and systematic biopsies by applying the 2014 and 2019 ISUP recommendations. We then evaluated the ISUP grade group concordance between biopsy and radical prostatectomy (RP) specimens.

Patients and Methods

Population

The study was performed according to the Declaration of Helsinki after obtaining institutional review board approval (Jules Bordet Institute Central Ethics Committee, CE3477). For a detailed account of the study protocol, please refer to the supplementary material section of this publication. Data from 1313 successive patients who underwent MRI targeted and systematic biopsies at Jules Bordet Institute between June 2016 and December 2022 were retrospectively identified from a prospectively maintained database Appendix A. Only MRI targeted biopsy-naïve patients with positive MRI, defined by a Prostate Imaging Reporting and Data System (PI-RADS) score ≥ 3 lesion, were included (n = 890). Among these, we excluded patients with fewer than two MRI targeted biopsy cores (n = 79) and fewer than six systematic biopsy cores (n = 156). Patients with ISUP Grade Group 1 disease were subsequently excluded (n = 406) given that these patients would have no change regardless of the ISUP recommendations applied. This resulted in a cohort of 249 patients eligible for final analysis (Fig. S1). The indication for surgical intervention was left to the discretion of the treating physician after exploring all treatment options. All surgeries were performed by fully trained urologists (n = 69).

MRI and Biopsy Technique

All men underwent MRI of the prostate within the 6-month period before the biopsy session. The MRI studies were performed using a 1.5-T or 3-T scanner with or without an

All suspicious lesions on MRI defined as PI-RADS \geq 3 lesions were subject to biopsy. After contouring of the index lesion, MRI targeted biopsies combined with systematic biopsies of the prostate were performed in the same session transrectally. Of note, systematic biopsies were taken beyond the suspicious MRI lesions and included the perilesional area (Fig. 1). Biopsies were carried out by one of two expert urologists using real-time TRUS guidance via the KOELIS Trinity[®] (KOELIS[®], La Tronche, France) software platform.

Pathology Reporting

A dedicated genitourinary pathologist analysed both individual biopsy and whole-mount prostatectomy specimens using the 2014 ISUP recommendations. Each biopsy core was submitted in an individual container for pathological analysis. The Gleason score for each core was the sum of the most prevalent pattern graded as primary and any amount of a worst pattern graded as secondary, before being converted to ISUP grade group. Although patients with a final ISUP Grade Group 1 were not included in the analysis, the presence of ISUP Grade Group 1 within a heterogeneous biopsy session was indeed considered for the calculation of the final ISUP





grade group. Patients with only ISUP Grade Group 1 in all biopsy cores were excluded. In RP specimens, a minor pattern constituting <5% was mentioned as a tertiary pattern but was not considered for the present study.

Applying the 2014 ISUP recommendations, the biopsy core with the highest ISUP grade group was considered the final (i.e., patient-level) ISUP grade group given. Applying the 2019 ISUP recommendations, a global ISUP grade group was assigned for the MRI targeted biopsy with or without perilesional biopsy cores. Perilesional biopsies were defined as systematic biopsy cores that were retrieved within 10 mm of the periphery of the suspicious MRI lesion [15]. Systematic biopsies that harboured a more aggressive pathology than the global score given to the MRI targeted and perilesional biopsy cores were considered for the final ISUP grade group assignment. Indeed, such distant positive cores were hypothesized to arise from secondary foci and were excluded from the global score. All biopsies were reviewed by a genitourinary pathologist fellow to provide the global ISUP grade group for MRI targeted and perilesional biopsies per the 2019 ISUP recommendations.

Variables and Outcomes

Patient characteristics were obtained for age, PSA, tumour clinical stage on DRE, and PSA density. Radiological characteristics included the PI-RADS score on MRI, the maximum diameter of the index suspicious MRI lesion, and the number of suspicious MRI lesions. Pathology characteristics included ISUP grade group obtained by applying the 2014 and 2019 ISUP recommendations and using three different biopsy strategies (MRI targeted biopsy only; MRI targeted with perilesional biopsies; MRI targeted with systematic biopsies).

The primary outcome of the study was the ISUP grade group distribution when applying the 2014 and 2019 ISUP recommendations. Secondary outcomes were ISUP grade group concordance with RP specimens and impact on biopsy strategy.

Statistical Analysis

Descriptive statistics were presented using frequency for categorical variables and median with interquartile range (IQR) for continuous variables. For the primary outcome, the distribution of ISUP grade groups according to the 2014 and 2019 ISUP recommendations using one of the three biopsy strategies was compared using Wilcoxon signed rank test. For the secondary outcomes, the ISUP grade group accuracy (i.e., downgrading, concordance and upgrading rates) compared with final specimens according to the 2014 and 2019 ISUP recommendations for each biopsy strategy was compared using McNemar's test. We used the adjusted Wald interval to calculate confidence intervals. For the investigation of the relationship between PSA density and upgrading of ISUP grade group at final pathology with respect to the global grade group of each biopsy technique, Spearman's rank correlation coefficient was employed. Regarding the impact on treatment strategy, an MRI targeted and systematic biopsy strategy was used as recommended by current international guidelines. We used externally validated risk prediction models that included MRI-related parameters [16,17]. The statistical analysis was performed using STATA 14.1 (StataCorp, College Station, TX, USA).

Results

Patient Characteristics

Descriptive characteristics of the patients are shown in Table 1. Patients had a median (IQR) age of 70 (64–75) years and a median (IQR) pre-biopsy PSA value of 9 (6.3– 14) ng/mL. The median (IQR) prostate volume on MRI was 41 (32–60) cc with a median (IQR) PSA density of 0.22 (0.14–0.38) ng/mL/cc. Most of the patients had one MRI lesion (174/249, 70%). A median (IQR) of 4 (3–4) MRI targeted biopsy cores per lesion were taken with a median (IQR) of 3 (2–4) positive cores. A median (IQR) of 8 (7–9) systematic biopsy cores were taken with a median (IQR) of 2 (1–4) positive cores.

Table 1 Characteristics of the 249 patients included in the final analysis.

Characteristic	Total (<i>N</i> = 249)
Age, median (IQR) years	70 (64–75)
PSA, median (IQR) ng/mL	9 (6.3–14)
Tumour clinical stage, <i>n</i> (%)	
TI	158 (63)
T2	91 (37)
Prostate volume on MRI, median (IQR) cm ³	41 (32–60)
PSA density, median (IQR) ng/mL/cc	0.22 (0.14–0.38)
PI-RADS score, n (%)	
3	5 (2)
4	117 (47)
5	127 (51)
Maximum diameter of index lesion, median	15 (11–20)
(IQR) mm	
Number of MRI suspicious lesion, n (%)	
1	174 (70)
2	67 (27)
2	7 (2.8)
Number of MRI targeted biopsy cores, median (IQR)	4 (3–4)
Number of positive cores on MRI targeted biopsy, median (IQR)	3 (2–4)
Number of systematic biopsy cores, median (IQR)	8 (7–9)
Number of positive cores on systematic biopsy, median (IQR)	2 (1–4)

IQR, interquartile range; MRI, multiparametric MRI; PI-RADS, Prostate Imaging Reporting and Data System. International Society of Urological Pathology Grade Group Distribution

The comparison of the ISUP grade group distribution according to the 2014 and 2019 ISUP recommendations is shown in Table 2, Fig. 2 and Figs S2 and S3. Applying the 2019 ISUP recommendations, a significant decrease in ISUP Grade Group 4 (difference from -13% to -5%) and an increase in ISUP Grade Group 2 (difference from 6% to 11%) were observed for MRI targeted biopsy only, MRI targeted with perilesional biopsies, and MRI targeted with systematic biopsies (all $P \le 0.01$).

Concordance with Final Specimens

For the 69 patients who underwent RP, a significant decrease in downgrading (difference from -19% to -12%; $P \le 0.008$) and an increase in concordance (difference from 12% to 13%; $P \le 0.02$) were observed for all three biopsy strategies (Fig. 3, Table 3 and Table S1).

No strong correlation was demonstrated between PSA density and upgrading at final pathology across the three biopsy techniques with Spearman's correlation coefficient for MRI targeted biopsy only, MRI targeted with perilesional biopsies

 Table 2
 International Society of Urological Pathology grade group distribution according to (a) MRI targeted biopsy only, (b) MRI targeted including perilesional biopsies and (c) MRI targeted and systematic biopsies.

	ISUP Grade Group	2014 recommendations	2019 recommendations	Difference (CI) 2019–2014	P value
(a) MRI-targeted biopsy	2 3 4 5	100 (40) 55 (22) 59 (24) 14 (6)	115 (46) 55 (22) 46 (18) 12 (5)	0.06 (0.02, 0.1) - -0.05 (-0.09, -0.01) -0.008 (-0.02, 0.007)	0.003
(b) MRI-targeted and perilesional biopsies	2 3 4 5	104 (42) 57 (23) 63 (25) 13 (5)	144 (51) 57 (23) 43 (17) 11 (4)	0.09 (0.04, 0.14) - -0.08 (-0.13, -0.03) -0.008 (-0.02, 0.007)	<0.001
(c) MRI-targeted and systematic biopsies	2 3 4 5	110 (44) 56 (23) 68 (27) 15 (6)	138 (55) 63 (25) 36 (15) 12 (5)	0.11 (0.06, 0.16) 0.03 (-0.05, 0.1) -0.13 (-0.19, -0.07) -0.01 (-0.03, 0.006)	<0.001

Fig. 2 Sankey diagram illustrating the International Society of Urological Pathology (ISUP) grade group (GG) distribution between 2014 (left column) and 2019 (right column) ISUP recommendations when considering MRI targeted and perilesional biopsies.

MRI Targeted and Perilesional Biopsies

ISUP 2014 vs ISUP 2019



Fig. 3 International Society of Urological Pathology (ISUP) grade group accuracy after whole-mount radical prostatectomy between 2014 and 2019 ISUP recommendations according to (A) MRI targeted biopsy only, (B) MRI targeted including perilesional biopsies, and (C) MRI targeted and systematic biopsies.



Table 3 International Society of Urological Pathology grade group accuracy after whole-mount radical prostatectomy according to (a) MRI targeted biopsy only, (b) MRI targeted including perilesional biopsies and (c) MRI targeted and systematic biopsies.

	2014 recommendations	2019 recommendations	Difference (CI) 2019–2014	P value 2014 vs 2019
(a) targeted biopsy				
Upgrading	9 (13)	9 (13)	-	-
Concordance	45 (65)	53 (77)	0.12 (0.02, 0.21)	0.008
Downgrading	15 (22)	7 (10)	-0.12 (-0.21, -0.02)	0.008
(b) MRI targeted and perile	sional biopsies			
Upgrading	8 (12)	9 (13)	0.01 (-0.02, 0.05)	1
Concordance	44 (64)	53 (77)	0.13 (0.02, 0.24)	0.01
Downgrading	17 (25)	7 (10)	-0.14 (-0.25, 0.04)	0.002
(c) MRI targeted and system	natic biopsies			
Upgrading	7 (10)	10 (14)	0.04 (-0.02, 0.1)	0.2
Concordance	43 (62)	53 (77)	0.13 (0.009, 0.28)	0.02
Downgrading	19 (28)	6 (8.7)	-0.19 (-0.3, -0.07)	<0.001

MRI, multiparametric MRI.

and MRI targeted with systematic biopsies being 0.07, 0.15 and 0.17, respectively. This correlation showed no statistically significant difference.

Impact on Treatment Strategy

The proportion of candidates for active surveillance according to European Association of Urology (EAU) criteria [18] (i.e., ISUP Grade Group 2 with <10% of pattern 4, PSA < 10 ng/ mL, \leq cT2a, low biopsy extent) increased from 8% (20/249) to 12% (30/249) (P < 0.001) when 2014 and 2019 ISUP recommendations were applied.

Considering the impact on radiation therapy and the need for short- or long-term androgen deprivation therapy, the proportion of high-risk patients according to the EAU risk groups [18] decreased from 40% (99/249) to 30% (74/249; P < 0.001) when 2019 ISUP recommendations were applied. Concerning brachytherapy, the proportion of patients that fulfilled the criteria for low-dose-rate treatment only (i.e., National Comprehensive Cancer Network favourable intermediate-risk disease: one intermediate-risk factor, ISUP Grade Group 2, <50% biopsy cores positive) increased from 27% (66/249) to 29% (72/249) (P < 0.001) when 2019 ISUP recommendations were applied.

The need for extended pelvic lymph node dissection decreased from 63% (135/249) to 54% (157/249; P < 0.001) using the Briganti 2019 nomogram [17], with a 7% cut-off when the updated recommendations were applied. No significant difference was found when the risk of extracapsular extension was evaluated using the Soeterik nomogram [16] with a 20% cut-off (94% vs 95%; P > 0.05).

Discussion

The present study provides valuable insights into the impact of assigning a global grade group on the distribution of ISUP grade groups and the concordance rate with RP specimens. The results demonstrate that applying the 2019 ISUP recommendations reduces the rate of high-grade PCa compared to the 2014 recommendations. Moreover, it can reduce the rate of downgrading at final pathology by up to 19%, while maintaining a higher concordance. This aims to better account for the tumour heterogeneity observed in MRI targeted biopsy cores and improve the accuracy of biopsy grading. To our knowledge, this is the first study to compare the 2014 ISUP with the 2019 ISUP recommendations concerning MRI targeted biopsy grading.

In their paper, Vickers et al. [8] implied that the broad application of MRI and MRI targeted biopsies in biopsy-naïve men potentiates the risk of overtreatment in patients diagnosed with PCa. Risk stratification systems in PCa need to be reconsidered as staging is being disrupted with the widespread reliance on MRI instead of DRE. The present study demonstrated that the risk of grade migration induced by MRI targeted biopsy could be mitigated using novel ISUP recommendations [19,20]. The 2019 ISUP recommendations on grading heterogeneous PCa as a global grade group for each MRI index lesion comes in the context of recalibrating risk stratification systems to prevent the risk of overtreatment as illustrated in the present study.

Although the decrease in ISUP Grade Group 4 was statistically significant in our study, its clinical significance is yet to be demonstrated. Previous studies have compared the prognostic value of the global and highest grade group assignments on systematic biopsy [21–25]. Berney et al. [24] showed that relying on the global or highest grade group has similar predictive value for PCa death in conservatively treated patients. A similar prognostic value for the two grading approaches in terms of biochemical recurrence-free survival after hormone therapy was also demonstrated [25]. In fact, Verhoef et al. [26] have proven that, in patients with an overall ISUP Grade Group 2 and a highest ISUP Grade Group >2 within the cores, biochemical recurrence-free survival after RP or radiotherapy was not statistically different from that in patients with an overall ISUP Grade Group 2 without a higher grade. This needs to be further demonstrated by future studies evaluating the prognostic value of assigning a global grade group on MRI targeted biopsies. However, the decrease in high-grade PCa would result in a considerable change in management. This implies a decreased treatment burden, especially concerning the indication for extended pelvic lymph node dissection if decisions are based on multivariable prediction models. It would also impact the duration of androgen deprivation therapy in case of treatment by radiotherapy.

Arias-Stella et al. sought to assess whether an overall Gleason score for systematic biopsy would more accurately predict the RP findings. Their results demonstrated a higher rate of upgrading while having a higher rate of correlation with the final grade. An overall Gleason score was less likely to be downgraded and more likely to be upgraded than a highest Gleason score while maintaining a better correlation overall [27]. These latter findings are consistent with our results that showed a decrease of up to 19% in the rate of downgrading and an increase of up to 13% in the rate of concordance using the 2019 ISUP recommendations. The nonsignificant difference in upgrading observed in the present study is probably due to the exclusion of patients with ISUP Grade Group 1 lesions on biopsy. When compared to RP findings, we previously proved that the biopsy method that yielded the lowest upgrading rates (24% for ISUP grade group) and the highest concordance rates (60% for ISUP grade group) was the combination of MRI targeted and systematic biopsies [28]. While the former relied on the 2014 ISUP recommendations for biopsy reporting, our study demonstrates an even higher rate of concordance, reaching 77% when an overall grade group was assigned, with a 13% statistically significant increase in concordance. A similar rate of concordance was achieved using only MRI targeted biopsy with or without perilesional biopsy, and the role of systematic biopsy is unclear. It is worth noting that, even though the increase in concordance was statistically significant, its clinical significance remains debatable. The clinical significance of these findings lies in the decrease in downgrading observed in the study population with the use of the 2019 ISUP recommendations.

Although the present study highlights the outcomes of assigning a global grade group to biopsy samples, some limitations need to be considered. We acknowledge the single-centre, retrospective nature of the analysis, which confers a potential selection bias. Limitations of this study also include the presence of non-index lesions that might alter ISUP grade group distribution and concordance rate. It is worth noting that not all patients included had a positive perilesional or a positive systematic biopsy. Hence the overall grade group represents mostly that of MRI targeted biopsies. In addition, the use of RP specimens has an inherent population bias toward patients who do not have low-volume, low-grade disease. Similarly, patients who have very highstage disease also do not tend to undergo RP. Moreover, the study was conducted in a single institution with dedicated physicians for each step of the procedure, which may limit the generalizability of the findings. There is still uncertainty concerning the assignment of the final ISUP grade group when systematic biopsy cores beyond the perilesional area are involved by the highest grade. Although this concerns a minority of the patients (4.4%, 11/249 in the present study), this unresolved issue needs to be addressed. Additionally, the

study did not evaluate the impact of assigning a global grade group on patient outcomes, such as biochemical recurrence or overall survival. Further studies with larger sample sizes and long-term follow-up are needed to confirm the impact of assigning global grade group on patient outcomes.

In conclusion, the broad application of MRI targeted biopsies comes with a risk of grade migration. The 2019 ISUP recommendations were made in the context of consolidating our knowledge of PCa pathology rather than mitigating this effect. Implementing the 2019 ISUP recommendations and assigning a global grade to MRI targeted biopsies can result in a grading shift and enhances the accuracy of PCa grading, thereby potentially reducing unnecessary treatment which would imply shorter-duration androgen deprivation therapy, decreased extended pelvic lymph node dissection, and more recruitment to active surveillance.

Disclosure of Interests

The authors have no conflicts of interest to disclose.

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Appendix A

Biopsy Protocol

Approved by the Jules Bordet Institute Central Ethics Committee (CE3477).

Magnetic Resonance Imaging

Multiparametric MRI is performed within 6 months before biopsy and reported according to European Society of Urogenital Radiology guidelines using PI-RADS v2.1 score.

Fig. A1 Automatic tridimensional prostate map generated by the Trinity system (KOELIS®, La Tronche, France) after biopsy.

Rapport d'intervention Cartographie 3D de la prostate: Biopsie

INFORMATIONS CLINIQUES

Patient :		Examen :	
Nom	DE PRAET	Date d'examen	05/09/2823
Prénom	1.1.00	Clinicien référent	ROUM
Deuxième prénom		Clinicien opérateur	SKI .
Date de naissance	83/12/1958		
Age	63		
Patient ID	14.28 PVB		
Sexe	Mesculin		

COMMENTAIRES



В



Passers ID 11408/08

Fig. A2 Illustration of the biopsy report automatically generated by the Trinity system (KOELIS®, La Tronche, France).



Scan quality is defined as a Prostate Imaging Quality (PI-QUAL) score \geq 3. Suspicious lesion is reported on a dedicated prostate diagram.

The MRI contouring is performed using dedicated software (MrDraw[®], KOELIS, La Tronche, France) by two dedicated radiologists and sent to the local Picture Archiving and Communication System (PACS).

Biopsy Procedure

Prostate biopsies are performed by two dedicated urologists in the outpatient department via the transrectal route using software-assisted registration with elastic fusion of MRI and tridimensional ultrasound images (Trinity[®], KOELIS).

Anticoagulant and antiplatelet treatments were to be suspended 2–10 days before biopsy. A fleet enema is given 2 h before biopsy. Targeted antibiotics are given for 3 days.

Patient is placed in a left lithotomy position.

A total of 3–5 biopsy cores per target are taken, with a minimum of 1 biopsy core in the centre of the target and 1 biopsy core in the lateral part of the target. A total of 8–12 systematic biopsy cores (including perilesional biopsies that are taken in the area 10 mm around the index MRI lesion) are then performed outside the MRI targeted lesions.

Biopsy cores are potted separately before being sent to the Pathology Department for analysis.

At the end of the procedure, an automatic biopsy report is generated by the biopsy system and sent to the local PACS (Figs A1, A2).

Pathologist Analysis

The pathology report is generated using the 2019 ISUP guidelines and each biopsy core is analysed separately. A global ISUP grade group is assigned for each MRI targeted lesion as recommended. csPCa is defined as a ISUP Grade Group ≥ 2 (Gleason score ≥ 7 [3 + 4]).

Pathological results are then included in the biopsy report.

Data are then entered into the database including all the parameters detailed above.

Patients are enrolled in the database at the time of their initial PCa diagnosis.

Clinical and pathological data are collected at various time points during the patient's journey, including at diagnosis, during treatment, and at follow-up visits.

Data entry is performed by trained research personnel, who enter information into a secure electronic database in real time.

Data analysis: Data from the prospectively maintained database can be analysed using statistical methods to investigate multiple correlations.

This allows for robust data collection and analysis, minimizing the risk of selection bias and providing highquality information to support research objectives.

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Abbreviations: csPCa, clinically significant prostate cancer; EAU, European Association of Urology; ISUP, International Society of Urological Pathology; PCa, prostate cancer; RP, radical prostatectomy.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1. Flow diagram of study design and participants.

Fig. S2. Sankey diagram illustrating the ISUP grade group distribution between 2014 (left column) and 2019 (right column) ISUP recommendations when considering MRI targeted biopsies only.

Fig. S3. Sankey diagram illustrating the ISUP grade group distribution between 2014 (left column) and 2019 (right column) ISUP recommendations when considering MRI targeted and systematic biopsies.

Table S1. Cross tabulation of ISUP grade group concordance with whole mount radical prostatectomy according to biopsy strategy.