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FULL PAPER

In-bore MRI-guided biopsy: can it optimize the need for periodic biopsies in prostate cancer patients undergoing active surveillance? A pilot test-retest reliability study

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Objective: To evaluate the test-retest reliability of repeated in-bore MRI-guided prostate biopsy (MRGB).

Methods: 19 lesions in 7 patients who had consecutive MRGBs were retrospectively analysed. Five patients had 2 consecutive MRGBs and two patients had 3 consecutive MRGBs. Both multiparametric MRI and MRGBs were performed using a 3T MRI scanner. Pathology results were categorized into benign, suspicious and malignant. Consistency between first and subsequent biopsy results were analysed as well as the negative predictive value (NPV) for prostate cancer.

Results: 15 lesions (~79%) had matching second biopsy and 4 (21%) had non-matching second biopsy. Lesions with both Prostate Imaging – Reporting and Data System (PIRADS) categories 1 and 4 were all benign and had matching pathology results. Lesions with

non-matching results had PIRADS categories 2, 3 and 5. NPV for prostate cancer in first biopsy was 87.5%. Overall agreement was 78.9% and overall disagreement was 21.1%. $\kappa = 0.55$ denoting moderate agreement ($p = 0.002$). 10/19 lesions had a third biopsy session. 9/10 (90%) had matching pathology results across the three biopsy sessions and all matching lesions were benign.

Conclusion: In-bore MRI-guided prostate biopsy may have a better reliability for repeat biopsies compared to TRUS biopsy. Final conclusion awaits a prospective analysis on a larger cohort of patients.

Advances in knowledge: This pilot study showed that repeated prostate in-bore MRI-guided prostate biopsy may have better reliability compared to TRUS biopsy with a suggested high NPV.

INTRODUCTION

Active surveillance is a viable management option for many patients with low-risk prostate cancer. Generally, protocols rely on repeated transrectal ultrasound-guided biopsies (TRUS-Bx) to detect missed clinically significant cancer and identify biological tumour progression.¹ The concept of repeated biopsies is based on the considerable risk of underestimation of tumour grade and the possible false negative results associated with TRUS-Bx.^{2,3}

Obtaining consistent results from repeated biopsy sessions is an essential feature for a successful sampling tool. Adopting a reliable and reproducible sampling test can help optimize the current paradigm of periodic biopsies for prostate cancer patients undergoing active surveillance, leading to a decrease in the number of biopsied cores, possible elimination of annual/frequent biopsies altogether and potentially help provide a better insight into the notion of true tumour progression.

TRUS-Bxs are inherently imprecise.⁴ They show a wide variation in both Gleason scores (GS) and tumour volumes^{4,5} with an overall mild to moderate agreement across repeated sessions.⁶ Therefore, there has been no consensus regarding the recommended frequency of TRUS-Bx in the setting of active surveillance. For instance, current protocols range from recommending an annual biopsy after diagnosis,^{7,8} to a more conservative approach where biopsies are repeated every 2–3 years.^{9,10}

The use of MRI/Ultrasound fusion biopsy represents a step toward ensuring more reliable biopsy results; however, it may suffer from inaccurate sampling due to issues related to tissue deformability, varied fusion algorithms with required manual adjustments and hence user dependence, as well as lack of true real-time monitoring of target selection that eventually leads to misregistration of targets. Discrepancies in pathology results were observed when targeting the same lesions during repeated biopsy sessions utilizing the MRI/Ultrasound fusion technology missing 39% of previously detected targets in first biopsy in one study.¹¹

Direct in-bore MRI-guided biopsy (MRGB) may conceivably be suitable for active surveillance due to adequate visualization of prostate lesions, thereby facilitating precise real-time targeting. The precision of MRGB has been proven at both experimental and clinical settings^{12,13} with superior cancer detection rates (37–59%) compared to traditional TRUS-Bx (27–40%), more accurate Gleason grading (88%) and less complication rates.^{2,14–19} However, no data are, to our knowledge, available on the reproducibility of in-bore transrectal MRI-guided biopsy when targeting the same suspicious foci during repeated biopsy sessions.

The aim of this pilot study is to evaluate the test-retest reliability of repeated in-bore MRI-guided prostate biopsies in the setting of repeated targeting of individual lesions.

METHODS AND MATERIALS

Study population and design

After approval of the institutional review board and obtaining written informed consents, we searched our 244-patient MRGB database between 2013 and 2017 to retrospectively identify patients who had repeated transrectal MRGBs with the same lesion being biopsied in successive biopsy episodes. Our search resulted in 7 patients having 19 repeatedly targeted lesions. Those patients were typically referred for MRGB either with elevated prostate-specific antigen (PSA) for primary biopsy, seeking focal therapy or for negative initial TRUS-Bx with persistently elevated PSAs and heightened clinical suspicion for prostate cancer. A repeat MRGB was performed due to rising PSA after the initial negative MRGB, mismatching PSA/clinical suspicion with a low-risk cancer diagnosed on initial MRGB or as a part of active surveillance plan where MR guidance was elected in order to target the same lesions in the previous biopsy. Patient's clinical data, radiology and pathology reports were obtained from electronic medical records. Analysis was performed on a per lesion basis.

Lesion selection and analysis

As a part of the routine clinical care, each lesion was assigned a constant number by the reporting radiologist that is maintained through biopsy procedures, pathological analyses and reports as well as through subsequent repeated diagnostic scans and biopsy episodes allowing accurate tracking and re-biopsy of those lesions. We selected lesions that were repeatedly biopsied in various biopsy sessions. The largest lesion diameter was measured and recorded. For the study purposes, pathology results were classified as benign (including inflammatory lesions), suspicious [high grade prostatic intra-epithelial neoplasia (HGPIN)] or malignant [low-risk: GS ≤ 6 "Grade Group 1 (GG 1)", intermediate-risk: GS 7 "GG 2 and 3", or high-risk: GS ≥ 8 "GG 4 and 5"]. Lesions were considered matching when the initial and repeat biopsies were concordant regarding (i) presence of cancer; (ii) location; and (iii) Gleason score. Discrepancies in any of these three parameters disqualified the lesions as matching ones. PIRADS v2 score was assigned to each lesion in retrospect by the consensus of two radiologists blinded to the pathology results.

Multiparametric MRI protocol & interpretation

Multiparametric MRI (mpMRI) scans were performed on separate sessions prior to MRGBs. A 3T MRI scanner (Magnetom Trio, Siemens, Germany) was used with 32-channel surface pelvic coil to obtain the following sequences: Axial high-resolution T_2 imaging of the pelvis using a sampling perfection with application optimized contrasts using different flip angle evolution (SPACE) sequence with 1 mm contiguous slices and no fat suppression [repetition time (TR)/echo time (TE)/number of signal averages(NSA)/flip angle(FA) = 1200/120/2/95°]; Pre and post contrast three-dimensional volumetric interpolated breath-hold sequence (VIBE) with fat saturation with slice thickness of 3.0 mm, scan time of 14 s and a 256 × 256 resolution matrix (TR/TE/NSA/FA = 3.54/1.27/1/10°); A turbo spin echo T_2 weighted imaging sequence in three planes with slice thickness of 3 mm (TR/TE/NSA/FA = 3000/101/4/150°) and 320 × 256 resolution matrix; Dynamic contrast-enhanced sequences were performed with slice thickness of 3.0 mm following i.v. administration of 20 ml of Multihance (Gadobenate dimeglumine, Bracco) contrast delivered at a rate of 3 ml second⁻¹ (TR/TE/NSA/FA = 3.66/1.23/4/10°) with acquisition time of 2:55 min; Diffusion-weighted imaging (DWI) sequences were performed with slice thickness of 3 mm (TR/TE/NSA/Field of view = 6000/89/7/300, b -values = 0, 1000, 1500 and 2000 s mm⁻²). Image interpretation and perfusion analysis post-processing were performed on a satellite workstation using the Dynacad® software (Invivo corp., Gainesville, FL, USA). Images were interpreted by an experienced radiologist (SN, 19 years of experience).

MRI-guided biopsy

All biopsy procedures were performed under conscious sedation on the same 3T MRI unit used for the diagnostic mpMRI. Patients were placed in the prone position. The rectal needle sleeve of the Dyna-TRIM® (Invivo corp, Gainesville, FL) system, which serves as a needle holder and a fiducial marker, was inserted following lubrication with lidocaine gel and then pre-procedure scans were performed using turbo spin echo axial and sagittal T_2 weighted images (TR/TE/NSA/FA = 6,883/96/1/150°) as well

Table 1. Patients' characteristics

	Prostate volume (ml)	PSA			Number of targeted lesions in each session	Previous TRUS-Bx
		First session (ng ml ⁻¹)	Second session (ng ml ⁻¹)	Third session (ng ml ⁻¹)		
Patient 1	47	3.6	4.38	N/A	1	Yes, GS = 3 + 3 = 6 "GG 1"
Patient 2	51	6.76	6.9	N/A	3	No
Patient 3	104	5.9	5.2	N/A	4	Yes, HGPIN
Patient 4	47	3.9	4.6	Not available	2	Yes, GS = 3 + 3 = 6 "GG 1"
Patient 5	105	12	14	17.7	7	Yes, benign
Patient 6	30	4	6.3	N/A	1	No
Patient 7	22.7	7.5	9.7	N/A	1	Yes, GS = 3 + 3 = 6 "GG 1"

HGPIN, High grade prostatic intra-epithelial neoplasia; GG, Grade group; GS, Gleason score; N/A, not applicable; PSA, Prostate-specific antigen; TRUS-Bx, Transrectal ultrasound-guided biopsy.

as DWI (b -values = 0, 1000, 1500 and 2000) with same imaging parameters, as above. Images were then transferred to a satellite station with the DynaCAD® software (Invivo corp, Gainesville, FL), to identify the transrectal fiducial line, the target lesions and to calculate the trajectory angles in three planes. Targets were correlated with the previous mpMRI diagnostic scan and further localized with T_2 weighted imaging and DWI on the updated pre-procedure MRI scan. All lesions were biopsied regardless of level of suspicion. All biopsy procedures were performed by an experienced interventional radiologist (SN, 19 years of experience) who interpreted the diagnostic scans.

Subsequently, an 18-gauge MR compatible core biopsy needle was introduced into the target lesions. A median of 3 cores (range 2–4 cores) were obtained from each lesion. Samples were labelled with reference to lesion number mentioned in the mpMRI report and submitted for histopathological assessment. Histopathology reports were issued referring to lesions' location and number as depicted on MRI report. Pathology slides were read by pathologists at our institution as part of routine clinical care.

Statistical analysis

Categorical variables were interpreted as frequencies and percentages. Quantitative variables were summarised as median and range. Statistical significance was defined as p value < 0.05 tested by Fisher's exact test for categorical variables and Mann-Whitney U test for non-parametric quantitative variables. The negative predictive values (NPV) (including the non-malignant lesions) of first biopsy for prostate cancer was calculated (in reference to the second biopsy session).

Consistency between first and second biopsy session results was assessed by Kappa statistics. Kappa statistics is used to measure agreement as corrected for chance.²⁰ It is interpreted as 0.01–0.20 Slight agreement, 0.21–0.40 Fair agreement, 0.41–0.60 Moderate

agreement, 0.61–0.80 Substantial agreement and 0.81–0.99 Almost perfect agreement.²¹ Overall agreement and positive and negative agreement were calculated.²² Data were analysed by SPSS (v. 23, IBM) for Microsoft Windows.

RESULTS

Patients' characteristics

Seven patients were included in this pilot study (Table 1). Median age was 62 years (range 49–67). Median prostate gland volume was 47 ml (range 22.7–105). Median PSA at first session was 5.9 ng ml⁻¹ (range 3.6–12). Median PSA at second session was 6.3 ng ml⁻¹ (range 4.38–14). Five of the seven patients had TRUS-Bx prior to the initial MRGBs. Three patients had clinically insignificant cancer (3 + 3 = 6) diagnosed by TRUS-Bx before the first MRGB session. The median interval between mpMRI and MRGB was 2 months (range 1–5). Five patients had two consecutive MRGBs and two patients had three consecutive MRGB sessions. The intervals between the initial and second biopsy sessions ranged between 6 and 21 months. The intervals between second and third biopsy sessions ranged between 6 and 11 months.

Lesion characteristics

Lesions biopsied in two sessions

A total of 19 lesions were assessed in this study. As illustrated in Table 2, 15 lesions (~79%) had matching second biopsy and 4 (21%) had non-matching second biopsy. Regarding lesion locations, most matching lesions were in the central gland (11/15, 73.3%) while most non-matching lesions were at the peripheral zone (3/4, 75%) (p value = 0.1). For gland level, most matching lesions were at mid gland levels (10/15, 66.6%) while most non-matching lesions were evenly distributed between apex and mid gland levels (p value = 0.49). Pathology results of matching lesions are illustrated in Table 3.

Table 2. Characteristics of lesions biopsied in two consequent sessions

		Matching (N = 15)		Non-Matching (N = 4)		p value
		N	%	N	%	
Lesion location	Peripheral	4	57.1	3	42.9	0.11
	Central	11	91.7	1	8.3	
	Apex	3	60	2	40	0.71
	Mid	10	83.3	2	16.7	
	Base	2	100	0	0	
PIRADS v2	1	2	100	0	0	0.5
	2	1	33.3	2	66.7	
	3	6	85.7	1	14.3	
	4	5	100	0	0	
	5	1	50	1	50	
Lesion size	≤10 mm	3	60	2	40	0.27
	>10 mm	12	85.7	2	14.3	
		Median	Range	Median	Range	
Interval between biopsies (in months)		11	6–20	12	NA	0.02 ^a

^aStatistically significant.

Most of the lesions in the matching group were larger than 10 mm (11/15, 73.3%), while lesions in the non-matching group were evenly distributed in both size categories with no statistically significant difference between both groups (p value = 0.27).

There was no statistically significant difference between matching and non-matching lesions in terms of PIRADS scores. Lesions with both PIRADS categories 1 and 4 were all benign and had matching pathology results. Four of the five lesions with PIRADS 4 scores were in the central gland and the fifth was in the peripheral zone. Lesions with non-matching results had PIRADS categories 2, 3 and 5, as illustrated in Figure 1. PIRADS scores were the same across repeated diagnostic scans.

The median interval duration for re-biopsy was 11 months (range 6–20 months) for matching lesions and 12 months for non-matching lesions (p value = 0.02). NPV for prostate cancer in first biopsy was 87.5%. All non-matching lesions characteristics are illustrated in Table 4.

Table 3. Pathology results for matching lesions

Pathology	N	%
Benign	12	80
Suspicious		
Malignant		
Low-risk (GS 3 + 3 = 6) "GG 1"	1	6.7
Intermediate-risk (GS 3 + 4 = 7) "GG 2"	1	6.7
Suspicious	1	6.7

GS, Gleason score; GG, Grade group.

Lesions biopsied in three sessions

10 out of the 19 lesions had a third biopsy session. 9/10 (90%) had matching pathology results across the three biopsy sessions and 1/10 (10%) was not matching in the third time. All matching lesions were benign. The non-matching lesion characteristics are illustrated in Table 4.

Test-retest reliability

Overall agreement was 78.9% and overall disagreement was 21.1%. Positive agreement between first and second biopsy sessions was 50% and negative agreement was 86.7%. Kappa statistics was used to assess agreement between first and second MRGBs as corrected for chance, $\kappa = 0.55$ denoting moderate agreement beyond chance (p value = 0.002).

DISCUSSION

Patients with low-risk prostate cancer have increasingly been placed on active surveillance programs in the recent years with

Figure 1. Comparison between pathology results on repeated biopsy sessions per each PIRADS category.

Table 4. Lesions with non-matching pathology results on repeat MRGBs

	Size in (mm)	Interval between biopsies (months)	PIRADS	Lesion location	First biopsy	Second biopsy	Third biopsy	Previous TRUS-Bx (before first MRGB)
Lesion A	12	20	3	Peripheral-Apex	Benign	Malignant (GS = 3 + 3 "GG 1"); 1/3 cores; cancer core %=10	N/A	Positive (3 + 3 = 6 "GG 1") 30%
Lesion B	5	12	2	Peripheral-Apex	Suspicious (HGPIIN)	Benign	N/A	Negative
Lesion C	8	12	2	Peripheral-Mid gland level	Malignant (GS = 3 + 3 "GG 1"); 1 of 4 cores; cancer core %=5	Malignant (GS = 4 + 3 "GG 3"); 1/3 cores; cancer core %=15	N/A	Negative
Lesion D	16	First-Second = 11 Second-Third = 17	1	Peripheral- Mid gland level	Benign	Benign	Suspicious (HGPIIN)	Not done
Lesion E	19	21	5	Central-Mid gland level	Benign	Malignant (GS = 3 + 3 = 6 "GG 1"); 3/3 cores; cancer core %=60, 60, 40	N/A	Not done

GG, Gleason group; GS, Gleason score; HGPIIN, High grade prostatic intra-epithelial neoplasia; MRGB, In-bore MRI-guided biopsy; N/A, not applicable; TRUS-Bx, Transrectal ultrasound-guided biopsy.

the goal of avoiding treatment-related morbidity while identifying those whose cancers are likely to progress and offering them proper management in a timely manner. The tools for active surveillance include serum PSA monitoring, digital rectal examinations and periodic TRUS-Bx. There has been, however, no validated strategy regarding the ideal testing frequency during active surveillance nor has been one regarding the test results that should trigger the initiation of active therapy.

TRUS-Bxs are central to the practice of active surveillance. In most practices, a repeat TRUS-Bx is obtained after 1 year of initial biopsy, and then repeated periodically at various intervals that vary with the practice pattern and with the level of concern for possible disease progression. In many instances, patients may receive up to an annual TRUS-Bx during this process. The need for repeat TRUS-Bx is justified by their inherent low cancer detection rates^{2,14} along with the mild to moderate agreement reported between repeated episodes of 12-core systematic TRUS-Bx.⁶

In our pilot study, there was a high overall (78.9%), and negative (86.7%) agreements with moderate positive (50%) agreement between the first and second biopsy sessions and all lesions that had a third biopsy showed absence of cancer in all the biopsy sessions. The test-retest reliability was found to be $\kappa = 0.55$ denoting moderate agreement as corrected for chance. The reliability of MRI targeted biopsy has been previously studied by Sonn et al using MRI/Ultrasound fusion biopsy with electronic tracking.¹¹ They showed that MRI/Ultrasound fusion biopsy detected 61% of cancers in the second biopsy session for lesions with corresponding MRI targets. MRGBs have shown a more favourable agreement between the first and second biopsy results in our pilot study. Our investigation does, however, include benign and suspicious targets in addition to the malignant lesions and is limited by the small sample size.

Four lesions in this study (lesions A, B, D and E, Table 4) demonstrated mismatching pathology results between the consecutive MRGB episodes. The pathology results from lesions A and E were benign on the first MRGB attempt but revealed low-risk prostate cancer (GS 3 + 3 = 6 "GG 1") on the second MRGB episode. Of note, lesion A was positive for cancer (GS 3 + 3 = 6 "GG 1") on an earlier TRUS-Bx prior to the first MRGB, confirming a false negative first MRGB. Lesion B showed suspicious pathological results (HGPIIN) on the first MRGB but only benign samples were retrieved on the repeat biopsy. Lesion D showed benign results in the first and second biopsy sessions and changed into HGPIIN in the third biopsy session. False negative MRI Targeted biopsy after positive TRUS-Bx was studied by Cash et al.²³ They suggested that a false negative MRI targeted biopsy could be due to prostate movement or deformation with probe placement, patient movement, incorrect image registration, sampling error, discrepancy between imaged lesion size and true size (MRI underestimates the lesion size) or due to an error in lesion diagnosis as potential cancer on mpMRI. As their study was carried out on MRI/Ultrasound fusion biopsies, we believe that some of their conclusions can be applied to MRGB. The rectal piece placement causes movement of the prostate and

Figure 2. Both images (a, b) were obtained for the same patient while targeting two different targets at the same level. The needle sleeve indents the prostate gland leading to change in gland contour and gland displacement which may potentially lead to incorrect needle placement. Fast confirmatory scans are necessary to confirm needle placement.

can cause gland deformation with tissue compression compromising both the T_2 weighted imaging and DWI scans used for biopsy planning (Figure 2). To minimize this effect, we believe it is important to acquire a fast confirmatory scan to document the biopsy needle location relative to the target while attempting each lesion for biopsy.

Sampling errors during in-bore MRI-guided biopsy could also be due to needle placement errors. This issue was tested on phantoms at both 3T and 1.5T systems with errors of needle placement reported between 2.5 and 3 mm^{12,13} and in clinical settings for in-bore template biopsy with needle placement errors reported at 5.4 mm.¹² We therefore obtain 2–4 cores at 1–2 mm intervals from each lesion to ensure proper sampling of the targeted abnormalities. Smaller lesions (<1 cm) may conceivably be more subject to sampling errors than larger ones; however, this assumption requires validation with a larger data set and cannot be made based on the results from this pilot study.

Lesion C was positive for malignancy on both MRGB episodes, but re-biopsy resulted in GS upgrading from $3 + 3 = 6$ “GG 1” to $4 + 3 = 7$ “GG 3” (Figure 3). Upgrading could be due to sampling error during the first MRGB, interobserver error by pathologists, or possibly true tumour progression. Upgrading on repeat biopsy was reported by different investigators evaluating TRUS-Bx.^{4,24,25} They attributed the upgrading to under-sampling associated with

Figure 3. Axial T_2 weighted imaging-TSE images (a, b) illustrating needle placement (arrow) in a target in a 67-year-old patient with persistently elevated PSA and a prior negative TRUS-Bx. Initial MRGB revealed a GS $3 + 3 = 6$ lesion (lesion C) in peripheral zone at 7 o'clock (a). A repeat biopsy of the same lesion (b) after 12 months showed disease upgrade to GS $4 + 3 = 7$.

uncertainty of targeting rather than to true tumour progression. Despite these few sampling errors associated with repeat MRGB, accurate grading of prostate cancer with MRGB was reported by Hambrock et al.²⁶ They studied the performance of 3T DWI targeted MRGB in comparison to radical prostatectomy and demonstrated high accuracy in tumour grading (88%) compared to TRUS-Bx (55%). This could support an argument that the upgrading of lesion C in our series upon re-biopsy was related to possible true tumour progression rather than sampling error, a finding that may raise interest in the use of MRGB in studying whether grade progression in prostate cancer over time is a true phenomenon.

We retrospectively categorized lesions using the new PIRADS score v. 2. Lesions with PIRADS Categories 1 and 4 were benign in both initial and repeated biopsies except for lesion D that showed HGPIN on the third biopsy. Non-matching lesions had PIRADS score 3 (lesion A) and 2 (lesion B and C) and 5 (lesion E). 4/5 of the PIRADS Category 4 lesions were in the central gland. In their evaluation of the PIRADS v.2 using whole mount pathology as reference standard, Vargas et al²⁷ had a low cancer detection rate of PIRADS Category 4 in the transitional zone (about 20%); their results in addition to our small sample size may explain the herein reported findings.

Most benign lesions in our series had matching pathology results on re-biopsy with NPV of first biopsy 87.5% for cancers as compared to the second biopsy session. Even when a subset of this sample was re-biopsied for the third time, 9/10 confirmed benignity and 1/10 showed HGPIN with no frank malignancy detected. These results corroborate the findings of the recently published PROMIS study showing that multiparametric MRI has a higher NPV compared to TRUS-Bx (89 vs 74%, p value < 0.0001).²⁸ Results are also in-line with the findings of Hoeks et al²⁹ who showed that the NPV of a cancer-negative MRGB for risk re-stratification at repeated examinations was 79%.

Our study has some limitations; the retrospective nature of the study does not allow for proper control of confounders and is subject for poor representation. As different pathologists interpret the results, Interobserver variability can also be a source of bias. Although the primary goal of the study is to insure reproducibility of pathological results across repeated biopsy sessions, the relative high prevalence of benign findings in repeated biopsies may still be due to potential mistargeting, correlation with whole mount pathology results may still be required. Another limitation is the small sample size that affects generalization of findings, although findings were statistically significant. Despite the small sample size, this patient population has not been addressed before in the in-bore biopsy literature and number of patients having repeated in-bore biopsy is currently very limited in the clinical practice. As we used many categories for comparison between pathology results, this lowered the Kappa value beyond the high overall agreement. Despite these limitations, the findings of this pilot study may contribute to formulating paradigms for less invasive active surveillance programs and warrant further investigation in a prospective study design performed on a larger cohort of subjects.

CONCLUSION

This pilot study indicates that in-bore MRI-guided biopsy may have a better reliability for repeat biopsies compared to TRUS-Bx. A reliable demonstration of consistent biopsy results may obviate or at least reduce the need for the current paradigm of obtaining periodic prostate biopsies in patients undergoing active surveillance. This test–retest reliability may also help provide a better insight into the notion of GS upgrades and whether true tumour

progression occurs or that upgrades are always related to missed cancers on TRUS-Bx. The conclusion awaits a prospective analysis on a larger cohort of patients.

FUNDING

The study has been approved by the Institutional Review Board (IRB).

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