Original Article

DOI: 10.4274/uob.galenos.2021.2021.2.4

Bull Urooncol 2022;21(2):35-39

Is Cognitive MR Fusion Biopsy Superior to Standard TRUS Guided Prostate Biopsy? Our Clinical Experience

Bahadır Şahin, Doğancan Dörücü, İlker Tinay, Deniz Filinte, Haydar Kamil Çam

Marmara University Faculty of Medicine, Department of Urology, İstanbul, Turkey

Abstract

Objective: To share our clinical experience with cognitive prostate biopsy and compare results of cognitive biopsies with standard biopsies.

Materials and Methods: The data of patients for whom prostate biopsy was performed at Marmara University Faculty of Medicine, Department of Urology in 2020 were retrospectively reviewed. All biopsies, including repeat biopsies are included in the study. Basic clinical characteristics and pathological outcomes were compared between the groups. Clinically significant prostate cancer (PCa) was defined as gleason grade group 2 or more in biopsy pathology.

Results: The mean age of all patients included in the study was 64.9±8.16 years. Median prostate specific antigen (PSA) level was 7.7 (5.0-12.8) ng/dL. There were no statistically significant differences between the two groups with respect to patient age, total and free PSA values, digital rectal examination and radiologic prostate volume. Biopsy pathologies were also similar between the groups. Our data demonstrated that patients with advanced age and higher levels of total PSA value were more likely to have clinically significant PCa. The positive predictive value of digital rectal exam (DRE) was 43.5% for clinically significant cancers and 59.0% for all PCa, which was higher than Prostate Imaging-Reporting and Data System 4 and 5 lesions.

Conclusion: Clinical experience could be the main determining factor in cognitive fusion biopsy results. Our results show that cognitive biopsy is not superior than standard systematic biopsy. So taking standard biopsy core should not be neglected, especially in inexperienced clinics. Our results also support the fact that DRE is still one of the most cost-effective diagnostic tools for clinically significant PCa.

Keywords: Prostate cancer, prostate biopsy, multiparametric prostate MRI, PI-RADS, fusion biopsy, cognitive biopsy

Introduction

Diagnosing clinically significant prostate cancer (PCa) without overdiagnosis is one of the main goals in the diagnostic process PCa. Multiparametric prostate magnetic resonance imaging (mpMRI) has been a promising modality for this purpose (1,2). It is now regarded as one of the first line imaging modalities before prostate biopsy in the European Association of Urology guidelines with a strong recommendation (3). Studies demonstrated that mpMRI with the help of Prostate Imaging-Reporting and Data System (PI-RADS) (v2.1) could improve clinically significant PCa diagnosis rates as well as reduce unnecessary biopsies (4,5). This technological advancements made targeted biopsies a possibility in the diagnosis of PCa diagnosis instead of standard transrectal ultrasound (TRUS) guided biopsies. Targeted prostate biopsy along with standard biopsy is a strong recommendation in The European Association of Urology guidelines for PI-RADS ≥3 lesions in the biopsy naïve patient group (3).

Although targeted biopsies are recommended, there are some technical and economic factors limit their routine use. The need of special instruments and software for fusion biopsies comes with a significant economic burden to the health-care and insurance systems. Although there are some studies demonstrating fusion biopsy as a cost-effective modality for the diagnosis of PCa, economic factors still limit the use of software-enhanced fusion biopsies (6).

Cognitive prostate biopsy, which is defined as taking extra biopsy cores during classical TRUS guided biopsy from the localization of the observed lesions in mpMRI, is an alternative to fusion biopsy. Since cognitive biopsy does not require any additional instruments, it could easily be performed in daily clinical practice. In this study, we shared our clinical experience on cognitive prostate biopsy and compare the results of cognitive biopsies with those of standard biopsies.

Materials and Methods

The data of patients for whom prostate biopsy was performed at Marmara University Faculty of Medicine, Department of Urology in 2020 were reviewed retrospectively. Cognitive biopsies which

Cite this article as: Şahin B, Dörücü D, Tinay İ, Filinte D, Çam HK. Is Cognitive MR Fusion Biopsy Superior to Standard TRUS Guided Prostate Biopsy? Our Clinical Experience. Bull Urooncol 2022;21(2):35-39

Address for Correspondence: Bahadır Şahin, Marmara University Faculty of Medicine, Department of Urology, İstanbul, Turkey
Phone: +90 216 657 06 06 **E-mail:** drbahadirsahin@gmail.com **ORCID-ID:** orcid.org/0000-0002-4874-4178
Received: 19.02.2021 **Accepted:** 11.08.2021

were performed in 63 patients were included as the study group and the most recent consecutive standard biopsies matching the number of cognitive ones were included as the control group. Patients with missing critical data (total PSA, pathology result etc.) were excluded from the study. All biopsies, including repeat biopsies are included. At least 12 cores were taken in each biopsy and in some patients core numbers are adjusted based on the clinical characteristics of the patient. Preoperatively, all patients were informed about the procedure and gave informed consent. Given the retrospective case control nature of this study ethics board approval was not applicable. In standard prostate biopsy, cores were obtained under periprostatic block (10 mL of 1% lidocaine) from the peripheral zone of the prostate at the apex, mid, gland and base (7). For cognitive biopsies, standard TRUS biopsy with at least 12 cores was performed. According to the mpMRI, extra cores were obtained. Core numbers of targeted biopsies are decided per patient, based on factors like lesion size and lesion PI-RADS score. The final patient cohort consisted of 125 patients (59 cognitive vs. 66 standard biopsies). Basic clinical characteristics and pathological outcomes were compared between the groups. Clinically significant PCa was defined as gleason grade group 2 or more in biopsy pathology.

Statistical Analysis

Statistical analyses were performed in the python programming language with the help of pandas, numpy and scipy libraries (8,9,10). JupyterLab was used as the coding interface (11). The scaler variables were investigated using visual (Histograms, QQ Plots) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk, D'Agostino's K^2 tests) to determine whether they are normally distributed. Independent samples t-test was used for the comparison of two groups if the variable is normally distributed in each group, otherwise Mann-Whitney U test was used. Categorical variables were compared with the chi-square test if the assumptions of the test were met. When the assumptions of the chi-square do not hold, for two groups Fisher Exact test and for more than two groups likelihood ratio was used to compare categorical variables. Numbers are given as the mean and standard deviation for normally distributed variables and median and interquartile range for non-normally distributed variables. For categorical variables, case number and pe percent were given for each category. For all statistical analyses p values less than 0.05 were statistically significant.

Results

The mean age of all patients included in the study was 64.9±8.16 years. Median PSA level was 7.7 (5.0-12.8) ng/dL. There were no statistically significant differences between the two groups with respect to patient age, total and free PSA values, digital rectal examination and radiologic prostate volume (Table 1). Since it must take more cores from the lesions total core count was higher in the cognitive biopsy group, as expected.

Biopsy pathologies were also similar between the groups. The median-targeted core number was 3 (2-3) cores per lesion. In the cognitive biopsy group, there were 18 (30.5%) patients whose targeted biopsy specimens were diagnosis with adenocarcinoma. This ratio was lower than the general cancer diagnosis ratio of the cognitive biopsy group (40.7%). There was only one (1.7%) patient who was diagnosed with gleason grade group 1 PCa with targeted biopsy while his all-standard biopsy cores resulted benign. Whereas 6 (10.2%) patients had tumor-positive cores in classical biopsy although their targeted biopsy cores were benign and 2 (3.3%) of these patients had clinically significant PCa.

Our data demonstrated that patients with advanced age and higher levels of total PSA value were more likely to have clinically significant PCa. Also, 58.7% of patients with International Society of Urological Pathology (ISUP) grade 2 or more cancer had positive signs on the digital rectal examination (DRE) (Table 2). Positive predictive value (PPV) of DRE was 43.5% for clinically significant cancers and 59.0% for all PCa. DRE had a higher PPV than PI-RADS 4 or 5 lesions for both clinically significant and all PCa groups. (PPV for PI-RADS 4-5 lesions: 31.6% and 50.0%, respectively)

Discussion

The diagnosis of clinically significant PCa without over diagnosing and overeating patients has been the focus of many studies recently. With the technological advancements, mpMRI has been highlighted as the technique of choice for discriminating clinically significant PCa (12). PI-RADS has high PPV for clinically significant PCa (13). Recently the PROstate MRI Imaging Study (PROMIS) trial demonstrated that using mpMRI in the first line evaluation of patients could decrease unnecessary biopsies up to 27% and could reduce the diagnosis of clinically insignificant PCa by 5% (5). The negative predictive value (NPV) of mpMRI was 89% in the PROMIS trial. In our study, NPV of PI-RADS 4 and 5 lesions combined was 69.4% that was lower than that of the PROMIS trial. This difference could be explained by factors like regional variability of PCa and the effect of the experience of both radiologists and urologists on the diagnostic value of mpMRI, as some previous studies demonstrated (14).

The diagnostic value of mpMRI is supported with level 1 evidence and clearly recommended in most guidelines. With the advancement in mpMRI techniques and concatenation of mpMRI images with biopsy procedures made targeted biopsies are a possibility for the prostate. Although some reports on these fusion biopsy procedures combined with standard biopsy demonstrated a possible advantage of these techniques in PCa diagnosis, the need of special enhancements and equipment limit the widespread use of software-enhanced fusion biopsies (15,16). The question of whether or not it is possible to achieve the favorable results with cognitive biopsies without any special instrumentation in biopsy has also been studied by some studies.

Results on the effectiveness of cognitive prostate biopsies are conflicting. Although some studies suggested a clear benefit of cognitive biopsies over routine biopsies in the diagnosis of clinically important PCa, there are also some reports with no clear benefit shown of cognitive biopsy. A recent study showed that cognitive prostate biopsy could increase cancer detection rates in patients with previous cancer negative biopsies (17). Another study with 510 patients showed that no clinically significant difference on biopsy outcomes between cognitive and fusion biopsies whereas both these techniques

were superior than standard biopsy (18). In a meta-analysis conducted by Schoots et al. (19), although cognitive fusion biopsies did not have a statistically significant advantage over standard biopsies, their success rate on the diagnosis of all and significant PCa was comparable with software enhanced fusion biopsies. Furthermore a prospective designed study showed that although pre-biopsy mpMRI increased diagnostic accuracy of prostate biopsy, no difference had been detected between cognitive and software enhanced biopsies (20). Wysock et al. (21) demonstrated that although software enhanced fusion biopsies were more informative histologically than visual targeting there were statistically significant difference in cancer detection rates.

Table 1. General characteristics of patients in two groups

		Standard Bx (n=66) (3rd comment of reviewer 2)	Cognitive Bx (n=59) (3rd comment of reviewer 2)	p-value
Patient age	**Median (IQR)**	64.0 (60.0-70.0)	64.0 (59.0-71.0)	0.538[1]
Total PSA value	**Median (IQR)**	8.72 (4.74-17.98)	7.14 (5.66-11.44)	0.423[1]
Free PSA value	**Median (IQR)**	1.46 (1.02-3.63)	1.36 (1.03-1.98)	0.299[1]
Radiologic prostate diameter	**Median (IQR)**	70.0 (48.25-97.5)	58.5 (41.5-83.0)	0.098[1]
t-PSA/f-PSA ratio	**Median (IQR)**	4.34 (3.85-5.79)	4.8 (3.99-7.41)	0.306[1]
Digital rectal examination n (%)	**Normal**	43 (65.15)	43 (72.88)	0.352[2]
	Abnormal	23 (34.85)	16 (27.12)	
Biopsy pathology n (%)	**Benign**	36 (54.55)	35 (59.32)	0.590[2]
	Malign	30 (45.45)	24 (40.68)	
ISUP grades n (%)	**1**	12 (41.38)	12 (50.0)	0.874[2]
	2	8 (27.59)	4 (16.67)	
	3	2 (6.9)	2 (8.33)	
	4	2 (6.9)	1 (4.17)	
	5	5 (17.24)	5 (20.83)	
Clinically significant cancer n (%)	**No**	49 (74.24)	47 (79.66)	0.474[2]
	Yes	17 (25.76)	12 (20.34)	
Post-op complication n (%)	**0**	59 (89.39)	56 (94.92)	0.332[2]
	1	7 (10.61)	3 (5.08)	

[1]Mann-Whitney U, [2]Chi-square, Bx: Biopsy, IQR: Interquartile range, t-PSA: Total PSA, f-PSA: Free PSA, ISUP: International society of urological pathology, PSA: Prostate specific antigen

Table 2. Comparison of patients who were diagnosed as clinically significant PCa and not

		Clinically significant PCa		
		No	**Yes**	**p-value**
Patient age	**Median (IQR)**	63.0 (58.0-68.0)	72.0 (65.0-75.0)	**<0.001[1]**
Total PSA value	**Median (IQR)**	6.72 (4.76-11.39)	12.71 (9.26-33.24)	**<0.001[1]**
Free PSA value	**Median (IQR)**	1.41 (1.02-2.56)	1.54 (1.04-4.84)	0.553[1]
Radiologic prostate diameter	**Median (IQR)**	68.0 (49.0-94.0)	50.0 (37.0-59.5)	0.018[1]
t-PSA/f-PSA ratio	**Median (IQR)**	4.39 (3.75-5.9)	7.65 (4.23-9.01)	0.051[1]
Lesion diameter (mm)	**Median (IQR)**	10.0 (8.0-15.0)	14.0 (8.0-18.0)	0.269[1]
PI-RADS category n (%)	**≤3**	34 (56.67)	2 (14.29)	0.004[2]
	>3	26 (43.33)	12 (85.71)	
Digital rectal examination n (%)	**Benign**	74 (77.08)	12 (41.38)	**<0.001[2]**
	Malign	22 (22.92)	17 (58.62)	
Biopsy type n (%)	**Standard**	49 (51.04)	17 (58.62)	0.474[2]
	Cognitive	47 (48.96)	12 (41.38)	

[1]Mann-Whitney U, [2]Chi-square, PCa: Prostate Ca, IQR: Interquartile range, t-PSA: Total PSA, f-PSA: Free PSA, PI-RADS: Prostate Imaging-reporting and data system, PSA: Prostate specific antigen

On contrary to these results Yamada et al. (22) showed that software enhanced fusion biopsies can yield higher cancer detection rates compared to cognitive biopsies. Aslan et al. (23) showed that combined mpMRI targeted and systematic biopsy is superior to detect high-grade disease, than either systematic or MPMR-targeted biopsy alone. A recent prospective trial showed that the cancer detection rate by cognitive biopsy alone was lower than the standard biopsy combined with cognitive biopsy (24). Our results did not show the net benefit of cognitive biopsy. In our study, targeted biopsy was detected cancer in only one patient, whose standard biopsy was benign, and this patient had a gleason grade group 1 tumor. No patient was diagnosed with clinically significant PCa only with targeted biopsy in our study; on the other hand, two patients were diagnosed significant PCa with standard biopsy while targeted biopsy cores of these patients were benign.

Although technological advancements have revolutionized the diagnostic process of PCa recently, the importance of DRE has not change. Abnormal DRE is associated with an increased rate of higher ISUP grade PCa (25,26). Gosselaar et al. (25) showed that an abnormal DRE along with elevated PSA value has a PPV of 48.6% for the diagnosis of PCa. Our results were also quite close to these findings. We found that the PPV of DRE 43.5% for clinically significant cancers and 59.0% for all PCa.

Study Limitations

Our study does not without its limitations. As stated before, it is known that operator experience could affect the success rate of cognitive biopsies. Since our clinic is an education clinic, it was impossible to maintain the same standard for the operator experience for all biopsies. Biopsies were not taken by the same physician. This was also the case for standard biopsies, so we believe this factor could have a minimal effect on our results. Also, mpMRI was not performed in every patient who underwent standard biopsy procedure and this was a limiting factor in our study to make comments on the success rate of mpMRI. Furthermore, interobserver variability of mpMRI could affect our results since this study was conducted as a retrospective series, it was impossible to ensure that all mpMRI was evaluated by the same radiologist.

Conclusion

Our study shows that although cognitive biopsy seems as a tempting alternative because no additional funds, education or tools needed to perform it, the net benefit of this procedure is still debatable. Clinical experience could be the main determining factor of cognitive fusion biopsy results and taking a standard biopsy core should not be neglected, especially in inexperienced clinics. Our results also support the fact that DRE is still one of the most cost-effective diagnostic tools for clinically significant PCa.

Acknowledgements

Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as authors.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Ethics

Ethics Committee Approval: Given the retrospective case control nature of this study ethics board approval was not applicable.

Informed Consent: All patients were informed about the procedure and gave informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.Ş., H.K.Ç., Design: B.Ş., H.K.Ç., Supervision: İ.T., H.K.Ç., Data Collection or Processing: B.Ş., D.D., İ.T., D.F., Statical Analysis: B.Ş., Literature Review: B.Ş., D.D., Writing: B.Ş., D.D.

References

1. Bratan F, Niaf E, Melodelima C, et al. Influence of imaging and histological factors on prostate cancer detection and localisation on multiparametric MRI: a prospective study. Eur Radiol 2013;23:2019-2029.
2. Le JD, Tan N, Shkolyar E, et al. Multifocality and prostate cancer detection by multiparametric magnetic resonance imaging: correlation with whole-mount histopathology. Eur Urol 2015;67:569-576.
3. Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 2021;79:243-262.
4. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS prostate imaging–reporting and data system: 2015, version 2. Eur Urol 2016;69:16-40.
5. Ahmed HU, Bosaily AE-S, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017;389:815-822.
6. Cerantola Y, Dragomir A, Tanguay S, et al. Cost-effectiveness of multiparametric magnetic resonance imaging and targeted biopsy in diagnosing prostate cancer. Urol Oncol 2016;34:119.e1-9.
7. Haffner J, Lemaitre L, Puech P, et al. Role of magnetic resonance imaging before initial biopsy: comparison of magnetic resonance imaging-targeted and systematic biopsy for significant prostate cancer detection. BJU Int 2011;108:E171-178.
8. Reback J, McKinney W, Den Van Bossche J, et al. pandas-dev/pandas: Pandas 1.0. 3. Zenodo. 2020.
9. McKinney W, editor. Data structures for statistical computing in python. Proceedings of the 9th Python in Science Conference; 2010: Austin, TX.
10. Virtanen P, Gommers R, Oliphant TE, et al. SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methos. 2020;17:261-272.
11. Kluyver T, Ragan-Kelley B, Pérez F, et al. Jupyter Notebooks-a publishing format for reproducible computational workflows. 2016;87-90.
12. Fütterer JJ, Briganti A, De Visschere P, et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. Eur Urol 2015;68:1045-1053.
13. Vargas HA, Hötker AM, Goldman DA, et al. Updated prostate imaging reporting and data system (PIRADS v2) recommendations for the detection of clinically significant prostate cancer using

multiparametric MRI: critical evaluation using whole-mount pathology as standard of reference. Eur Radiol 2016;26:1606-1612.

14. Marra G, Ploussard G, Futterer J, et al. Controversies in MR targeted biopsy: alone or combined, cognitive versus software-based fusion, transrectal versus transperineal approach? World J Urol 2019;37:277-287.
15. van der Leest M, Cornel E, Israël B, et al. Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study. Eur Urol 2019;75:570-578.
16. Rouvière O, Puech P, Renard-Penna R, et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. Lancet Oncol 2019;20:100-109.
17. Kuliš T, Zekulić T, Alduk AM, et al. Targeted prostate biopsy using a cognitive fusion of multiparametric magnetic resonance imaging and transrectal ultrasound in patients with previously negative systematic biopsies and non-suspicious digital rectal exam. Croat Med J 2020;61:49-54.
18. Monda SM, Vetter JM, Andriole GL, et al. Cognitive Versus Software Fusion for MRI-targeted Biopsy: Experience Before and After Implementation of Fusion. Urology 2018;119:115-120.
19. Schoots IG, Roobol MJ, Nieboer D, et al. Magnetic resonance imaging–targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol 2015;68:438-450.
20. Puech P, Rouvière O, Renard-Penna R, et al. Prostate cancer diagnosis: multiparametric MR-targeted biopsy with cognitive and transrectal US–MR fusion guidance versus systematic biopsy—prospective multicenter study. Radiology 2013;268:461-469.
21. Wysock JS, Rosenkrantz AB, Huang WC, et al. 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 2014;66:343-351.
22. Yamada Y, Shiraishi T, Ueno A, et al. Magnetic resonance imaging-guided targeted prostate biopsy: Comparison between computer-software-based fusion versus cognitive fusion technique in biopsy-naïve patients. Int J Urol 2020;27:67-71.
23. Aslan G, Çelik S, Sözen S, et al. Comparison of TRUS and combined MRI-targeted plus systematic prostate biopsy for the concordance between biopsy and radical prostatectomy pathology. Int J Clin Pract 2020;75:e13797.
24. Elkhoury FF, Felker ER, Kwan L, et al. Comparison of Targeted vs Systematic Prostate Biopsy in Men Who Are Biopsy Naive: The Prospective Assessment of Image Registration in the Diagnosis of Prostate Cancer (PAIREDCAP) Study. JAMA Surg 2019;154:811-818.
25. Gosselaar C, Roobol MJ, Roemeling S, Schröder FH. The role of the digital rectal examination in subsequent screening visits in the European randomized study of screening for prostate cancer (ERSPC), Rotterdam. Eur Urol 2008;54:581-588.
26. Okotie OT, Roehl KA, Han M, et al. Characteristics of prostate cancer detected by digital rectal examination only. Urology 2007;70:1117-1120.