Central European Journal of Urology

ORIGINAL PAPER

UROLOGICAL ONCOLOGY

The influence of the operator's experience on the outcomes of fusion prostate biopsy

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Citation: Rempega G, Rajwa P, Ryszawy J, et al. The influence of the operator's experience on the outcomes of fusion prostate biopsy. Cent European J Urol. 2023; 76: 287-292.

Article history
Submitted: June 12, 2023
Accepted: Sept. 16, 2023
Published online: Sept. 22, 2023

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Introduction Magnetic resonance imgaing (MRI) targeted biopsy is the gold standard for prostate cancer (PCa) diagnosis. In this study, we examined the association between the operator's experience and the improvement in the precision of the MRI prostate biopsy procedure and the detection of PCa.

Material and methods We included consecutive patients who underwent prostate fusion biopsy. Data on biopsy duration, prostate-specific antigen (PSA) value, lesion size, number of samples taken, number of cores involved, and International Society of Urological Pathology (ISUP) grade were subjected to statistical analysis, with the study group divided into three consecutive time periods (tertiles).

Results There were statistically significant differences in biopsy duration between tertiles ($p < 0.001$). The greatest difference in the involved/taken cores ratio occurred between the first and third tertile ($p = 0.002$). The difference between the first and second tertile was insignificant ($p = 0.4$), while the difference between the second and third tertile was statistically significant ($p = 0.004$). The differences between tertiles in Prostate Imaging and Reporting Data System v2.1 were also significant ($p = 0.003$). The PSA value ($p = 0.036$) was statistically significant, unlike prostate volume ($p = 0.16$), digital rectal examination (DRE) ($p = 0.7$), and ISUP grade ($p = 0.7$). There was no statistical difference between tested tertiles in the number of detected PCa ISUP ≥2 ($Z = 0.191$; $p = 0.8$).

Conclusions The abilities and precision of the operator increase with the increase in the number of procedures performed. The biopsy duration is shortened, and the detection of PCa during the procedure seems to improve with the operator's experience.

Key Words: biopsy ‹› prostate cancer ‹› image-guided biopsy

INTRODUCTION

Diagnostics of prostate cancer (PCa) focuses on performing imaging tests, such as multiparametric magnetic resonance imaging (mpMRI). These tests are necessary for risk stratification and tumor location visualization to perform a targeted biopsy. Standardization of the prostate mpMRI images is obtained by using Prostate Imaging and Reporting and Data System v2. (PI-RADS v2.) which enables the assessment of the cancer risk. [1, 2, 3].

Fusion biopsy is the guidelines' recommended standard for PCa diagnosis [4]. It is characterized by greater sensitivity and specificity compared

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to systematic biopsy. It allows for the precise collection of the incised tissue due to simultaneous mpMRI and ultrasound imaging [5, 6, 7]. Fusion biopsy facilitates the histological assessment of the tumour tissue (based on the Gleason score), which enables further prognosis and response to treatment [5, 8, 9, 10].

The amount of experience needed to precisely perform a fusion biopsy procedure is determined by the learning curve. There are numerous publications analyzing changes in biopsy duration and clinically significant prostate cancer detection in given time intervals, both for transrectal and transperineal biopsies. Most of them indicate a relatively short learning curve for transperineal fusion biopsy in particular with regard to the duration of the procedure [11, 12, 13].

This study aimed to assess the relationship between the increasing experience of the operator and the improvement in the precision of the MRI prostate biopsy procedure and the detection of PCa. Changes in number of PCa diagnosed, percentage of positive target biopsy results, taken cores, cancer involved cores, involved/taken cores ratio and biopsy duration were also analyzed. In addition, differences in prostate-specific antigen (PSA), digital rectal examination (DRE), lesion size, ISUP grade, Gleason group (GG), and PI-RADS v2 values between individual tertiles were analyzed to assess their possible impact on the obtained results.

MATERIAL AND METHODS

Study design

This single-centre prospective study included male patients with suspected prostate cancer who underwent prostate fusion biopsy. Biopsy procedures were performed over three years from December 2018 to December 2021 by one urologist during a residency course, studying in one research center, without experience in the field of MRI-guided prostate biopsy. Before collecting cores, 11 ml of 2% lidocaine gel was administered to the rectum. Then, 5 ml of 1% lidocaine was injected around the periprostatic nerve bundle. Transrectal biopsy was performed using ultrasound BK Medical Flex Focus 400 - BioJet System (DK Technologies) and the Pro-Mag Ultra biopsy gun with an AIOU 14G 250 mm needle. During the procedure, a minimum of 2–4 samples were collected from the suspicious region, and then systematically 8–12 samples were collected from the right and left lobes of the prostate. The number of collected samples was variable depending on patients' clinical characteristics and operator preferences.

The mpMRI examinations performed in many laboratories were used for the analysis. The result of the imaging examination was evaluated by one radiologist with many years of work experience.

Histopathological examination was performed by one experienced pathologist. The evaluation was based on the Gleason score. Histopathological Gleason score 6 (3+3) was defined as clinically insignificant cancer.

During the study, the number of targeted biopsies increased from <4 to ≥4 due to scientific reports which proved on the higher effectiveness of fusion biopsy when collecting more targeted cores [14, 15]. Patients with PI-RADS ≥3 were qualified for MRI-guided biopsy. Each patient was interviewed, including information on age, PSA, prostate volume, lesion size, PI-RADS v2, and DRE results. The duration of the biopsy, the total number of samples taken, and the number of samples taken from suspicious lesion were also noted. Eligible patients gave their informed consent to participate in our study.

We excluded patients with neurological disorders, who received anticoagulants and had no evaluable MRI reports.

The conducted study did not require the consent of the bioethics committee and was in accordance with the Declaration of Helsinki.

Table 1. *Summary of data on patients qualified for the study group*

Variable	1st Quartile	Median	3rd Quartile	Mean	SD
Age [years]	61.20	66.4	70.75	65.6	7.4
Prostate volume TRUS [mL]	35.00	50.0	63.00	52.7	24.9
PSA [ng/mL]	5.91	7.6	10.11	9.7	10.1
PSAD [ng/mL^2]	0.11	0.16	0.26	0.23	0.24
Biopsy time [min]	20.0	30.0	40.0	31.3	18.8
Lesion target diameter [mm]	9.0	14.0	16.0	13.5	6.0
Number of cores	12.0	14.0	16.0	13.7	3.0

TRUS – transrectal ultrasound; PSA – prostate-specific antigen; PSAD – ratio of PSA to prostate volume; SD- standard deviation

Statistical analysis

For statistical analysis, patients were divided into tertiles according to the date of biopsy (first tertile: 48 patients 12/11/2018–23/08/2019; second tertile: 48 patients 30/08/2019–18/06/2020; third tertile: 47 patients 24/06/2020-30/12/2021). The occurrence of association between tertiles in the values of PSA, DRE, ISUP grade, PI-RADS v2.1, and prostate volume were examined. The relationship between the number of taken cores, involved cores, as well as the duration of biopsy in individual tertiles were also checked.

Categorical variables were shown as percentages and frequencies. Continuous and ordinal data were summarized as median values with interquartile ranges (IQR).

Differences between more than two groups were determined using the Kruskal-Wallis H test. For the pairwise comparison between subgroups the Wilcoxon rank sum test (aka Mann-Whitney U test) was used. The p-values were FDR-corrected. The Cochran-Armitage test was used to assess the linear relationship (trend occurrence) between the proportions in individual categories. Fisher's exact test was used to evaluate the existence of a statistically significant relationship between two categorical variables. The measure of the interdependence effect for ordinal values analyzed with the Mann-Whitney U test was the Glass biserial correlation coefficient rg (with the interpretation of the effect analogous to Pearson's R, i.e.: 0.1 – weak effect; 0.3 – average effect; 0.5 – strong effect; 0.8 – very strong effect). A value of $p < 0.05$ was considered statistically significant.

All analyses were performed using R software package version 4.0.1 released on June 06, 2020 (R Foundation for Statistical Computing, Vienna, Austria, http://www.r-project.org).

RESULTS

We included 143 consecutive patients who underwent transrectal image-guided prostate biopsy. A total of 48% of them were biopsy naïve. The age of the patients ranged from 41 to 84 years and the median was 66.4 (IQR 61.2–70.75) years. For PSA, the median was 7.60 ng/mL (IQR 5.91–10.11). The median transrectal ultrasound (TRUS) volume was 50 mL (IQR 35–63), and the median ratio of PSA to prostate volume (PSAD) was 0.16 (IQR 0.11–0.26). All information on descriptive statistics was included in Table 1.

In total, 66% of patients had non-suspicious DRE. A further 134 (93%) people among the respondents were diagnosed with PI-RADS v2 ≥3 on MRI with a median target lesion diameter of 14 mm. Sixty-three patients were graded as ISUP 1 and 41 were classified as ISUP 2–5.

Table 2. *False discovery rate-adjusted p-values for differences between tertiles of biopsy date for selected variables*

Variable	The p-value for the difference between tertiles		
	1st–2nd tertile	2nd–3rd tertile	1st–3rd tertile
PSA	p = 0.048	p = 0.176	p = 0.176
Biopsy time	p <0.001	p <0.001	p <0.001

PSA – prostate-specific antigen

Table 3. *Analysis of the percentage of cancer diagnoses based on a comparison of International Society of Urological Pathology grade group obtained in a systematic and targeted biopsy (per patient)*

ISUP (systematic+targeted)	Tertile of biopsy date (n, %)		
	1	2	3
ISUP grade group			
0–1	37 (77.1%)	30 (62.5%)	38 (80.9%)
2–5	11 (22.9%)	18 (37.5%)	9 (19.1%)

ISUP – International Society of Urological Pathology; n – number of patients

Table 4. *The degree of histological malignancy among the patients of the study group assessed on the basis of the analysis of targeted cores*

ISUP (targeted)	Tertile of biopsy date (n, %)		
	1	2	3
ISUP grade group			
0–1	39 (81.2%)	33 (68.8%)	39 (83%)
2–5	9 (18.8%)	15 (31.2%)	8 (17%)

ISUP – International Society of Urological Pathology; n – number of patients

The analysis of relationships between tertiles in terms of PSA values showed significant differences, ($p = 0.036$) however, further analysis showed a difference only between the first and second tertile ($p = 0.047$) with an upward trend (Table 2). There was no difference between tertiles for prostate volume ($p = 0.158$), lesion size ($p = 0.158$) and DRE test result ($p = 0.697$).

The analysis of the percentage of positive results was conducted by comparing the study group under the ISUP GG. The subjects were divided into two subgroups ISUP 0–1 and ISUP ≥2. Results of systematic (from the left and right lobes of the prostate) and targeted biopsy were compared between tertiles. This analysis showed no significant differences between the tested tertiles ($Z = 0.809$; $p = 0.687$) (Table 3). Additionally, biopsy results from targeted cores in individual tertiles was analyzed. In each of the examined tertiles, the percentage of patients with

ISUP 0–1 was the highest (first tertile: 81.2%; second tertile: 68.8%, third tertile: 83%). The greatest percentage of patients with ISUP ≥2 was recorded in the second tertile (31.2%). There was no trend between the tested tertiles (Z = 0.191; p = 0.848) (Table 4).

The duration of the biopsy, which in the third tertile was the shortest (median 20 min [IQR 15–23.75]), turned out to be statistically significant (p <0.001). Pairwise comparison showed relevant differences between first and second (p <0.001), second and third (p <0.001), and first and third (p <0.001) tertiles.

The difference between the tertiles in terms of the precision of the cancer detection was assessed using the ratio between the number of cores occupied by the cancer (involved) and the number of cores taken from the suspicious lesion (taken).

The involved/taken cores ratio increased with each tertile. In the first tertile, the median was 0 (IQR 0.00–0.75). In the second tertile the median was 0.5 (IQR 0.00–1.00) and in the third tertile the median was 0.85 (IQR 0.41–1.00). The greatest difference was between the first and third tertile (p = 0.002) (Figure 1).

Due to the fact that the number of samples taken from a suspicious lesion was increased during the study, an analysis of the change in the percentage of diagnoses due to the number of targeted biopsies was performed. For the purpose of the study, the group was divided into two subgroups (I <4 targeted cores; II ≥4 targeted cores). The distribution of ISUP values in groups I and II is shown on Figure 2. The analysis of the improvement in cancer diagnosis after increasing the number of specimens taken from a suspicious lesion with the Fisher's test allowed to obtain a result slightly exceeding the limit of statistical significance (p = 0.054). The obtained result prompted further analysis. The results obtained as ordinal variables were analyzed using the Mann-Whitney U test (W = 2333.5, p = 0.069) with the Glass biserial correlation coefficient (rg = 0.152 – weak effect).

Fisher's exact test showed an association between the tertiles in relation to the PI-RADS v2 (p = 0.003), however, a more thorough analysis showed a trend only in the case of Pi-RADS 3 vs. other (p = 0.005). Other levels of PI-RADS v2 advancement in relation to the entire study group did not show any trends, however, the abundance of the group has a significant impact on the obtained results.

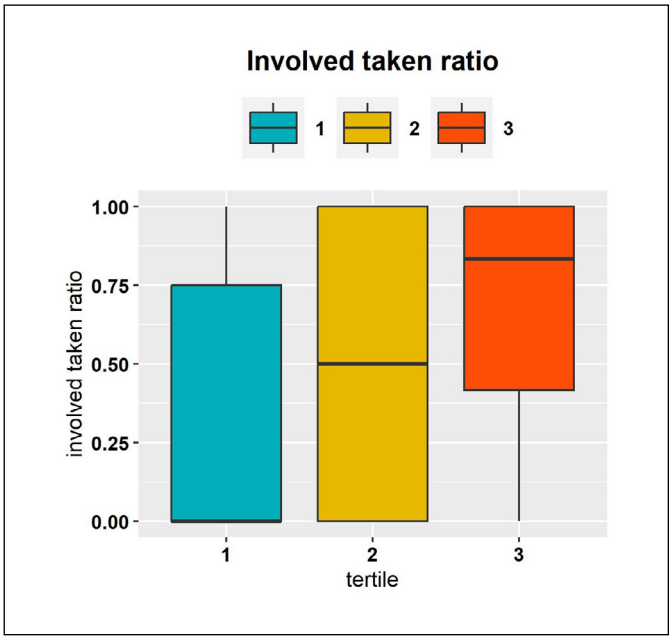

Figure 1. *Involved/taken cores ratios in the tertiles of biopsy date.*

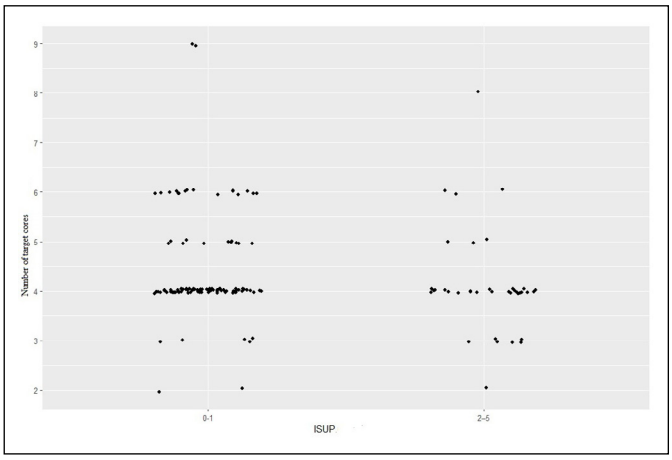

Figure 2. *The distribution of International Society of Urological Pathology (ISUP) values in subgroups I and II (I <4 targeted cores; II ≥4 targeted cores).*

DISCUSSION

The main aim of this study was to assess whether the precision of biopsy increases with the operator's experience. The results obtained in the course of the study made it possible to confirm the initial research hypothesis.

In the initial phase of the study, the group was divided into tertiles, and then the occurrence of dependencies between individual tertiles was examined in relation to the examined variables. There were significant differences only in PSA value (p = 0.036), unlike the lesion size (p = 0.158), DRE (p = 0.697), and ISUP (p = 0.399). As the PSA value increases, the probability of collecting involved cores during biopsy increases. The lesion

size, DRE and ISUP grade do not influence on the evaluation of the operator's precision. There are studies in the literature showing the influence of the PSA value and the size of the lesion on the detectability of the tumor, which may affect the distorted assessment of the operator's ability improvement over time [16, 17].

Then, the duration of the biopsy was analyzed for inter-tertile differences. The obtained result ($p < 0.001$) was satisfactory because it confirmed the initial hypothesis. The duration of the procedure was significantly shorter with each tertile. This allows us to confirm the increase in the operator's skills over time. Similar results were obtained by several researchers in other research centers. Mager et al. indicated a significant increase in operator skills over time. The duration and detection of cancer in 126 fusion biopsies were studied. The division into tertiles was made, and the results were compared between the groups. As the operator gained experience with each tertile, the duration of the biopsy was shortened [18]. The data contained in the available literature indicate that the urologists' learning curve significantly affects the precision of the performed procedure [11, 19].

Other statistically significant inter-tertile differences obtained in our study are the number of samples taken from suspicious lesion ($p < 0.001$) and the number of involved cores taken from suspicious lesion ($p < 0.001$). Unfortunately, this result is not reliable because, over time, a decision was made to increase the number of samples taken from the lesion from <4 to ≥ 4. This decision was dictated by the desire to achieve greater accuracy in terms of tumor detection [14, 15]. The obtained result does not directly indicate the improvement of the operator's precision during the procedure, however, it shows the increase in his experience and the ability to modify the method in order to improve the detection. It indicates an increase in the level of expertise of the urologist. In order to be able to assess the impact of the studied variables, the study should be repeated, taking the same number of samples during the analysis.

The change in the number of samples taken from a suspicious lesion made it necessary to analyze the improvement in cancer detection as a result of increasing the number of targeted biopsies. Initially, the result was borderline statistically significant ($p = 0.054$), however, a more detailed analysis showed no correlation ($p = 0.069$). This result is inconsistent with the data contained in the available literature. However, it indicates that in our study a change in the number of taken cores (targeted) should not significantly affect the results obtained. There are scientific publications on the impact of the number of collected cores on the detection of prostate cancer, it has been shown that their increase correlates with the improvement in detection [14, 15, 20, 21].

The difference between the tertiles for the detected change in PI-RADS v2 3–5 was significant ($p = 0.003$). However, further statistical analysis showed differences only in the comparison of patients with PI-RADS 3 ($p = 0.005$) with the rest of the patients. However, it should be taken into account that the abundance of the group has a significant impact on the obtained results. The compared subgroups were heterogenous in terms of numerous, which makes it difficult to assess the impact of this variable to influence of the skill and precision of the operator in the detection of the tumor. A similar conclusion was presented in the available literature [22].

Differences between tertiles in relation to the variable involved/taken ratio were assessed. The result ($p = 0.002$) indicated the presence of significant differences, in particular between the first and the third tertile. The involved/taken ratio was the greatest in the third tertile. It is one of the most reliable results, as it does not depend on the number of taken cores, which was variable in our study. This result indicates the improvement of the operator's ability and precision related to the increase in the number of performed prostate fusion biopsy procedures. Similar results are contained in the available literature, where the development of the operator's abilities and the learning curve were analyzed [18, 23, 24]. However, the analysis of cancer diagnoses per patient did not show this relationship ($p = 0.687$). This result may be related to the chronological division into tertiles to which patients were assigned regardless of health status, PSA or PI-RADS value.

The assessment of the operator's ability and precision is difficult due to several factors affecting the course of the procedure, such as technological changes, the surgical team, the operator's characteristics, and even his physical and mental health [25]. In the course of the study, factors related to the equipment and the surgical team were eliminated, however, the physical and mental health of the operator remained and was included in the work limitations, impossible to remove. Limitations include the fact that it was a single-center study. It should also be mentioned that in the course of the study, the number of samples taken from the core was increased from 2-3 to min. 4. This change may affect the reliability of the results obtained.

CONCLUSIONS

The abilities and precision of the operator increase with the increase in the number of procedures performed. The biopsy time is shortened, proving that the urologist's skills have increased. But most importantly, as experience is gained, the detection of PCa during the procedure improves.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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