https://doi.org/10.48047/AFJBS.6.2.2024.2354-2361

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Possible Role of Multi-Parametric Magnetic Resonance Imaging in Diagnosis of Prostate Cancer

Ibrahim M. Allam, Tarek A. Salem, Mohamed H. Ali, Mohammed M. Zaza

Department of Urology, Faculty of Medicine-Helwan University, Egypt

Corresponding author: Ibrahim M. Allam

Email: Hem.urology@gmail.com

Article History

Volume 6, Issue 2, Apr-Aug 2024

Received: 15 July 2024

Accepted: 1 August 2024

Published: 1 August 2024

doi: 10.48047/AFJBS.6.2.2024.2354-2361

Abstract: Background: Prostate cancer is the second most common cancer among males worldwide. The prostate cancer diagnostic pathway offers transrectal ultrasound-guided biopsy (TRUS-biopsy) in men who present with an elevated serum prostate specific antigen (PSA). As a result, many men without cancer undergo unnecessary biopsies, clinically insignificant cancers are often detected, & clinically significant cancers are sometimes missed. TRUS-biopsy also carries significant morbidity and can cause life-threatening sepsis. **Aim and objectives:** To evaluate if MP-MRI can be used as a triage test to decide which men with an elevated PSA might safely avoid unnecessary biopsy. **Subjects and methods**: This study was conducted in Badr university hospital and Nasr-City Health Insurance Hospital on 60 patients with clinical suspicion of prostate cancer. The duration of the study was 12 months. **Result:** The Multi-Parametric MRI findings recorded; 10% of patients had prostatitis, 65% had Prostatic cancer and 25% had BPH. Regarding TRUS biopsy findings, 60% of the patients were positive for cancer prostate, and 40% of the population were negative. The mean Serum prostate specific antigen PSA was 12.34 (ng/mL) with SD 5.11. The mp-MRI was able to correctly identify 33 out of 36 patients with Carcinoma (when the comparison is made with the Trus-biopsy). It could also exclude 18 out of 24 patients without carcinoma when compared to the biopsy. The Sensitivity of mp- MRI is 91.7 %, specificity is 75%, PVP = 84.6 % and PVN = 85.7%. There is moderate agreement between both techniques (k= 0.68). **Conclusion:** The usage of multiparametric MRI may increase the number diagnosis of clinically significant prostate cancer and reduce the unnecessary biopsies, which could in turn prevent overdiagnosis and overtreatment.

Keywords: Prostate specific antigen (PSA), Multi-Parametric Magnetic Resonance Imaging (MP-MRI), Transrectal ultrasound (TRUS) biopsy

Introduction

Prostate cancer is the second most common cancer among males worldwide **(1).** The prostate cancer diagnostic pathway offers transrectal ultrasound-guided biopsy (TRUS-biopsy) in men who present with an elevated serum prostate specific antigen (PSA). As a result, many men without cancer undergo unnecessary

biopsies, clinically insignificant cancers are often detected and clinically significant cancers are sometimes missed **(2)**. TRUS-biopsy also carries significant morbidity and can cause life-threatening sepsis **(3)**
The process of transrectal ultrasound guided (TRUS) prostate biopsy remains by far the most widely employed approach to prostate cancer diagnosis, it flaws as a standalone diagnostic strategy are increasingly apparent. TRUS-biopsy is an outlier in the diagnosis of cancer, with its lack of localization by visual or imaging cues, the unguided deployment of needles has led to considerable errors in the pathway for diagnosing men with a suspicion of prostate cancer **(4).** The ever criticized over-diagnosis of insignificant cancers along with their subsequent unnecessary treatment, the missed diagnosis of important cancers and the risk of 2-4% infection (some of which is life-threatening) all combine to make the current approach untenable **(5).**
A pathway with imaging as a triage test to decide which men with an elevated PSA go on to biopsy might both reduce unnecessary biopsy and improve diagnostic accuracy. Multi-Parametric Magnetic Resonance Imaging (MP-MRI) provides information on not just tissue anatomy but also tissue characteristics such as prostate volume, cellularity, and vascularity. There is some evidence that MP-MRI tends to detect higher risk disease and systematically overlooks low-risk disease **(6),** which makes it attractive as a potential triage test **(7).**
The aim of this study was to evaluate if MP-MRI can be used as a triage test to decide which men with an elevated PSA might safely avoid unnecessary biopsy.

Patients and Methods

Type of the study: A prospective interventional study
Study setting: A hospital-based study, conducted at Badr university hospital and Nasr-City Health Insurance Hospital.
Sample size: The attendance rate of suspected prostate cancer with PSA > 4 ng/ml is 5 cases/ month so the total number of cases is (60 patients) as a comprehensive sample.
Timeline: The duration of the study was 12 months.
Study patients:
Inclusion criteria:
-Men who had never had a prostate biopsy with clinical suspicion that they might have prostate cancer and they had been advised to have a prostate biopsy including (Suspicious digital rectal examination and elevated serum PSA over than 4 ng/mL in two different tests).
-Age of 40 years or more.
- No contraindication for general or spinal anaesthesia.
-No contraindication for MP-MRI.
-Agree to give written informed consent.

Exclusion criteria:
Patients were excluded if they:
-1-Use 5-alpha-reductase inhibitors at time of recruitment or during the previous 6 months,
-Had previous history of prostate biopsy, prostate surgery, or treatment for prostate cancer (interventions for benign prostatic hyperplasia or bladder outflow obstruction are acceptable);
-Had evidence of a urinary tract infection or history of acute prostatitis within the last 3 months,
-Had any contraindication to MRI (eg, claustrophobia, pacemaker, estimated glomerular filtration rate ≤50); any medical condition precluding procedures; or previous history of hip replacement surgery, metallic hip replacement, or extensive pelvic orthopedic metal work,
-Had a bleeding disorder.
Procedure: From each patient the following data was collected upon admission
2.3.1. Initial assessment:

Complete full history taking, including personal history (Name, age and occupation), Present history, Past history of any disease (DM and Hypertension), Family history of prostate cancer.

2.3.2. Clinical examination focusing on:

- General examination: Vital signs (Blood pressure, Temperature, Heart rate, Respiratory rate), Signs as (Pallor, Cyanosis, Jaundice, and Lymph node enlargement).
- Prostate examination: To assess the size and check for bumps, soft or hard spots, and other abnormalities.

All enrolled patients were subjected to MP-MRI then TRUS biopsy.

Test 1: MP-MRI (index test)

Patients received first a standardized MP-MRI, compliant with European Society of Uro-Radiology guidelines, with 1·5 Tesla magnetic field strength and a pelvic phased-array coil. T1-weighted, T2-weighted, diffusion-weighted and dynamic gadolinium contrast-enhanced imaging sequences were acquired.

Tests 2: TRUS biopsy:

After the MP-MRI examination was done successfully, prostate biopsy procedure was done within one month of the imaging study. Biopsy was guided by trans-rectal ultrasound, under local, general, or spinal anesthesia.

In the standard test (TRUS-biopsy), core biopsies were taken as per international standards, with each core identified and processed separately. The TRUS-biopsy samples were sent for pathological examination by an expert pathologist.

Technique:

Biopsies were taken in the longitudinal plane using a biopsy attachment as guidance for an 18-gauge needle driven by a spring-loaded Biopsy gun.

A pre-examination enema was given to all patients, as well as prophylactic antibiotic treatment with 400 mg of norfloxacin twice daily for 3 days.' The first dose was given 1 hour before the examination.

Hypoechoic and hyperechoic lesions, regardless of the degree of definition, as well as irregular echogenicity in combination with an indistinct border between the peripheral and transition zones (the surgical capsule), were considered suspicious for malignancy.

Depending on the size of the gland, 12 systematic biopsy samples were taken. specimens were taken from each lobe at the apex (AP), at the middle close to the midline (M/M), at the middle but further laterally (M/L), and at the base portion of the gland (BP). When the longitudinal length exceeded 4 cm, one biopsy sample was taken from the anterior parts of the transition zone (TZ) of each lobe. These biopsy samples were located close to the midline, and the needle was advanced at least 1 cm into the prostatic tissue before the gun was fired. Additional samples were obtained from lesions suspicious for prostate cancer when not included in the sampling using the systematic pattern.

Statistical Analysis:

All data were collected, tabulated, and statistically analyzed using statistical package of special science SPSS version 22 as follow:

- Editing and coding, Data entry in computer, Quantitative data were expressed as mean ± SD (standard deviation), Qualitative data were expressed as frequencies and relative percentage.
- Kappa agreement (k) was used to detect the degree of agreement between each two techniques and its analysis was according to its value: 0 – 0.20: none, 0.21 – 0.39: minimal, 0.40 – 0.59: weak, 0.60 – 0.79: moderate, 0.80 – 0.90: strong, above 0.90: perfect agreement.
- The validity of the Mp-MRI was assessed in terms of sensitivity, specificity, predictive value positive, predictive value negative and accuracy.

Table (1): Demographic data and history among the studied group.

	Patients (N=60)
	Mean ± SD
Age (years)	66.8± 11.32
	No. (%)
Past medical history of urologic disease	20 (33.33%)
Past surgical history of urologic disease	16 (26.67%)
History of smoking	51 (85 %)
Family history of Prostate cancer	18 (30%)

Regarding Demographic data, the mean age was 66.8 years with SD 11.32. 33.33% of the population had a past medical history of urologic disease, 26.67% had past surgical history of urologic disease and one third of patients had a family history of prostate cancer. Most of the patients were smoking.

Table (2): Vital data among the studied group.

Regarding vital data**,** the mean SBP was 124.3 (mmHg) with SD 8.65, the mean DBP was 78.13(mmHg) with SD 10.38, the mean pulse was 99.41 with SD 13.35, the mean temperature was 37.03 with SD 0.38, the mean respiratory rate was 14.95 **(**breaths per min**)** with SD 2.45 and the mean of oxygen saturation was 96.38 %with 2.31.

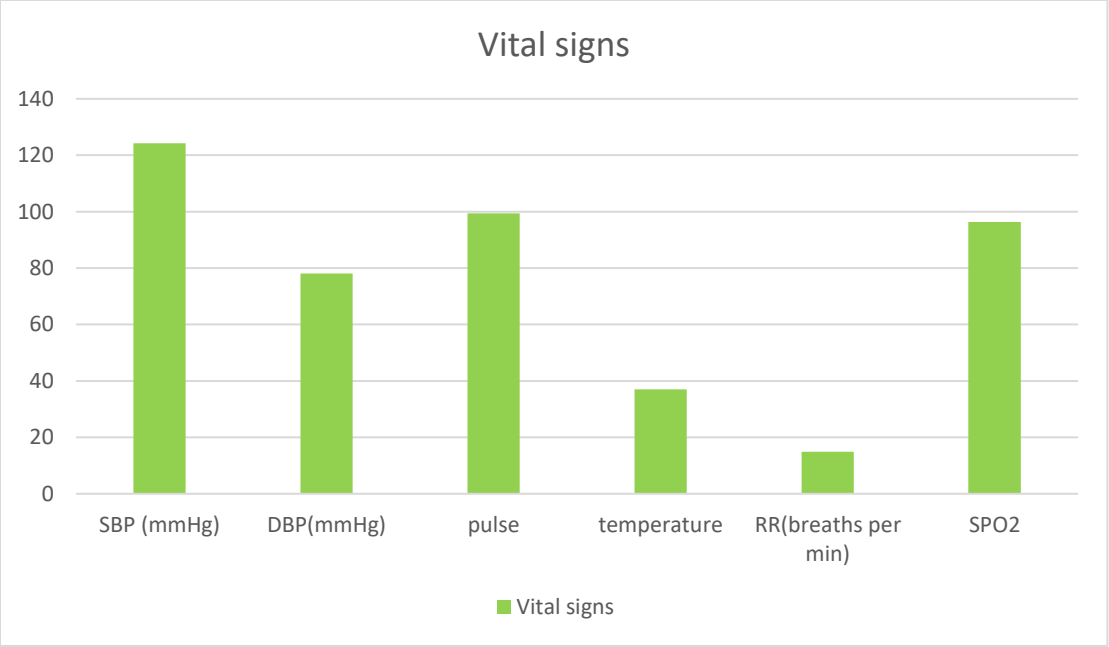

Fig (1): Vital data among the studied group.

Table (2): Serum prostate specific antigen among the studied group.

	Patients (N=60) **Mean ± SD**
PSA (ng/mL)	12.34±5.11

The mean serum prostate specific antigen PSA was 12.34 (ng/mL) with SD 5.11.
Regarding Multi-Parametric MRI finding among the studied group. 10% of patients had prostatitis, 65% had Prostatic cancer and 25% had BPH.

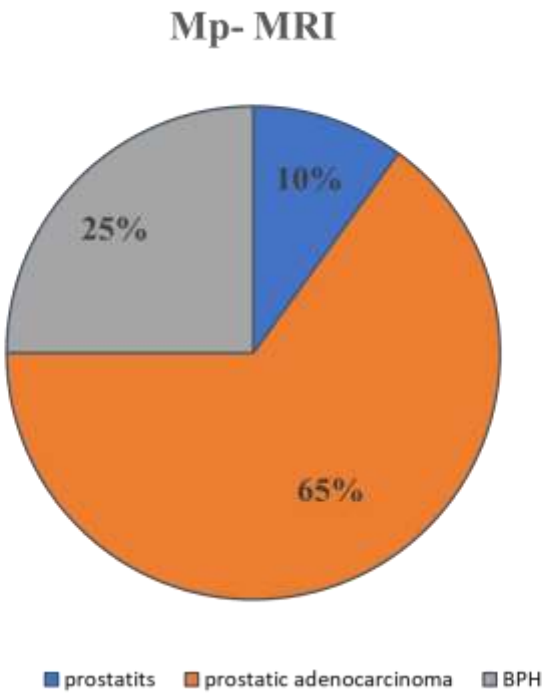

Fig (2): Multi-Parametric MRI finding among the studied group.

Table (3): TRUS biopsy finding among the studied group.

	Patients (N=60)
Positive for cancer prostate	36(60%)
Negative for cancer prostate	24(40%)

Regarding TRUS biopsy finding between the studied group. 60% of the patients were positive for cancer prostate, and 40% of the population were negative.

Table (4): Validity of Mp-MRI in diagnosis of prostate cancer in comparison to Trus- Biopsy:

mpMRI	Biopsy		Total	P	K
	Positive	Negative			
Positive	33	6	39	< 0.001	0.68
Negative	3	18	21		
Total	36	24	60		
Sensitivity= 91.7%			Specificity:75 %		
Predictive value positive: 84.6 %			Predictive value negative: 85.7%		
Accuracy: 85 %					

This table shows that MRI is able to correctly identify 33 out of 36 patients with Carcinoma (when the comparison is made with the Trus-biopsy). It can also exclude 18 out of 24 patients without carcinoma when compared to the biopsy. Sensitivity of 91.7 %, specificity of 75%, PVP of 84.6 % and PVN of 85.7% There is moderate agreement between both techniques (k= 0.68).

Discussion

The present study aimed to test if MP-MRI can be used as a triage test to decide which men with an elevated PSA might safely avoid unnecessary biopsy. The study was conducted in Badr University Hospital and Nasr-City Health Insurance Hospital.

The mean age of patients was 66.8 years with SD 11.32, which was similar to the results of Thompson et al., (2014) [8] who reported a mean age of patients (62.4) years his prospective study on men older than 40 years with abnormal prostate specific antigen/digital rectal examination, aimed to determine the accuracy of multiparametric MRI for detecting significant prostate cancer before diagnostic biopsy in men with abnormal PSA/digital rectal examination.

Close also to Arumainayagam et al., (2013) [9] who aimed to evaluate the diagnostic performance of multiparametric (MP) magnetic resonance (MR) imaging for prostate cancer detection by using transperineal template prostate mapping (TTPM) biopsies as the reference standard and to determine the potential ability of MP-MR imaging to identify clinically significant prostate cancer. Their study included 64 men with mean age, 62 years [range, 40–76]; mean prostate-specific antigen, 8.2 ng/mL [8.2 μg/L] [range, 2.1–43 ng/mL]).

Aligning also with Ahmed et al., (2017) [10], who aimed to investigate whether MP-MRI could discriminate between men with and without clinically significant prostate cancer based on template prostate mapping biopsy (TPM-biopsy) as a reference test. TPM-biopsy was able to accurately characterize disease status in men at risk by sampling the entire prostate every 5 mm. They also aimed to compare the accuracy of MP-MRI with that of TRUS-biopsy. Their patient's age was close to our patients age (64 years).

Regarding our findings for serum prostate specific antigen among the studied group. The mean PSA was 12.34 (ng/mL) with SD 5.11 which was slightly higher than Arumainayagam et al., (2013) [9] who demonstrated that the mean PSA of his studied patients was 8.2 ng/mL [8.2 μg/L] [range, 2.1–43 ng/mL]). And, higher than Thompson et al., (2014) [8] who demonstrated that the mean of PSA was 5.6 (ng/mL).

Mp-MRI was able to correctly identify 33 out of 36 patients with Carcinoma (when the comparison is made with the Trus-biopsy). It could also exclude 18 out of 24 patients without carcinoma when compared to the biopsy, with sensitivity of 91.7 %, specificity of 75%, PVP of 84.6 % and PVN of 85.7%. There is moderate agreement between both techniques (k= 0.68).

Close to these results a recent systematic review from Europe by Moldovan et al., (2017) [11] reported a mpMRI negative predictive value (NPV) of 82.4% (range 69.0–92.4%) for overall CaP and 88.1% (range 85.7–92.3%) for csCaP. However, the authors discuss that the NPV is highly dependent on the overall prevalence of the cancer where NPV decreases as prevalence increases, and on the definition of csCaP.

Ahmed et al., in 2017, [10] in the Prostate MRI Imaging Study (PROMIS) study from the United Kingdom analyzed 576 men who reported that sensitivity of MP-MRI for clinically significant cancer was 93% (95% CI

88–96%) and negative predictive value 89% (83–94%). Specificity of MP-MRI was 41% (36–46%) with positive predictive value 51% (46–56%). 158 (27%) of 576 men had a negative MP-MRI, of whom 17 had clinically significant cancer on Template Prostate Mapping biopsy (TPM-biopsy). MP-MRI was more accurate than TRUS-biopsy in terms of both sensitivity (93% vs 48%) and negative predictive value (89% vs 74%). TRUS-biopsy showed better specificity (41% vs 96%, p<0·0001) and positive predictive value (51% vs 90%, p<0·0001). They concluded that mpMRI was more sensitive but less specific than TRUS biopsy for the detection of Constitute of Clinically Significant Prostate Cancer (Cs CaP).

Also, we were aligned with Thompson et al. (2014) [8] who demonstrated that multiparametric magnetic resonance imaging was positive in 66% of patients, 61% had prostate cancer and 30% to 41% had significant prostate cancer. For significant cancer sensitivity was 93% to 96%, specificity was 47% to 53%, and negative and positive predictive values were 92% to 96% and 43% to 57%, respectively.

Thompson et al. (2016) [12] who aimed to assess the accuracy of multiparametric magnetic resonance imaging for significant prostate cancer detection before diagnostic biopsy in men with an abnormal prostate specific antigen/digital rectal examination reported that: out of the 388 men who were enrolled in the study 344 were analyzed. Multiparametric magnetic resonance imaging was positive in 77.0% of patients, 62.5% had prostate cancer and 41.6% had significant prostate cancer. The detection of significant prostate cancer by multiparametric magnetic resonance imaging had a sensitivity of 96%, specificity of 36%, negative predictive value of 92% and positive predictive value of 52%. Adding Prostate Imaging Reporting and Data System (PI-RADS) to the multivariate model, including prostate specific antigen, digital rectal examination, prostate volume and age, improved the area under curve (AUC) from 0.776 to 0.879 (p <0.001). Anatomical concordance analysis showed a low mismatch between the magnetic resonance imaging positive regions and biopsy positive regions (4 [2.9%]), and the significant prostate cancer area in the radical prostatectomy specimen (3.3%).

Another study by Branger et al. (2017) [13] compared the radical prostatectomy outcome against the preoperative negative mp-MRI and found 60.4% overall unfavorable pathology after surgery and concluded that a negative MRI could not assure absence of clinically significant cancer.

This study was Also in line with, Komai et al., (2013) [14] aimed to clarify the diagnostic ability of multiparametric magnetic resonance imaging to reveal anterior cancer missed by transrectal 12-core prostate biopsy based on the results of 3-dimensional 26-core prostate biopsy, which is a combination of transrectal 12-core and transperineal 14-core biopsies. Their study included 324 patients. The authors found that the overall cancer detection rate on 3-dimensional 26-core prostate biopsy was 39% (128 of 324 cases), of which 28% (36 of 128) were transrectal 12-core negative cancers. An anterior lesion on prebiopsy multiparametric magnetic resonance imaging was identified in 20% of men overall (65 of 324). Of men with and without an anterior lesion on imaging 40% (26 of 65) and 3.8% (10 of 259), respectively, had transrectal 12-core negative cancer. Significant transrectal 12-core negative cancer was observed in 0.4% (1 of 259 men) without an anterior lesion on imaging. Prebiopsy multiparametric magnetic resonance imaging revealed an anterior lesion in 92% of cases (11 of 12) of significant transrectal 12-core negative cancer. They also concluded that prebiopsy multiparametric magnetic resonance imaging has the potential to efficiently select men who could advantageously undergo anterior samplings, in addition to transrectal 12-core prostate biopsy.

Arumainayagam et al., (2013) [9] also reported that results of their study indicated that MP-MR imaging has a high negative predictive value to rule out clinically significant prostate cancer and may potentially have clinical use in diagnostic pathways of men at risk, and this agrees with Bjurlin et al., (2014) [15] who concluded that use of magnetic resonance imaging for targeting prostate biopsies has the potential to reduce the sampling error associated with conventional biopsy by providing better disease localization and sampling.

Conclusion:

There is common agreement in literature that the usage of multiparametric MRI may increase the number diagnosis of clinically significant prostate cancer and reduce of unnecessary biopsies (NPV of mpMRI for clinically significant cancer), which could in turn prevent overdiagnosis and overtreatment.
MP-MRI can be safely used as an imaging test for prostate cancer evaluation and is now being routinely used in many practices to assist tumor detection, biopsy guidance, and treatment planning. Nonetheless, continued technical optimization and further prospective investigations are anticipated prior to its widespread adoption.

References:

1. Torre, L., Siegel, R., Ward, E., Jemal, A. (2016). Global cancer incidence and mortality rates and trends—an update. Cancer Epidemiol Biomarkers Prev. 25:16–27.
2. Caverly, T., Hayward, R., Reamer, E., et al. (2017). Presentation of Benefits and Harms in US Cancer Screening and Prevention Guidelines: Systematic Review. J Natl Cancer Inst. 108: djv436.
3. Abraham, N., Mendhiratta, N., Taneja, S. (2015). Patterns of repeat prostate biopsy in contemporary clinical practice. J Urol. 193: 1178-1184.
4. Loeb, S., Vellekoop, A., Ahmed, H., et al. (2013). Systematic review of complications of prostate biopsy. Eur Urol. 64: 876-892.
5. Grey, A., & Ahmed, H. (2017). The PROMIS trial – time for multi-parametric MRI before a first prostate biopsy. Urology News. 21 (3). https://www.urologynews.uk.com/media/7897/uroma17-promis-new.pdf.
6. Turkbey, B., Brown, A., Sankineni, S., Wood, B., Pinto, P., Choyke, P. (2016). Multiparametric prostate magnetic resonance imaging in the evaluation of prostate cancer. CA Cancer J Clin. 66(4): 326–336.
7. Valerio, M., Donaldson, I., Emberton, M. et al. (2015). Detection of clinically significant prostate cancer using magnetic resonance imaging-ultrasound fusion targeted biopsy: a systematic review. Eur Urol 68:8–19.
8. Thompson, J., Moses, D., Shnier, R., Brenner, P., Delprado, W., Ponsky, L. & Stricker, P. (2014). Multiparametric magnetic resonance imaging guided diagnostic biopsy detects significant prostate cancer and could reduce unnecessary biopsies and over detection: a prospective study. The Journal of urology, 192(1), 67-74.
9. Arumainayagam, N., Ahmed, H., Moore, C., Freeman, A., Allen, C., Sohaib, S., Emberton, M. (2013). Multiparametric MR imaging for detection of clinically significant prostate cancer: a validation cohort study with transperineal template prostate mapping as the reference standard. Radiology, 268(3), 761-769.
10. Ahmed, H., Bosaily, A., Brown, L., Gabe, R., Kaplan, R., Parmar, M., Emberton, M. (2017). Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. The Lancet, 389(10071), 815-822.
11. Moldovan, P., Van den Broeck, T., Sylvester, R., Marconi, L., Bellmunt, J., van den Bergh, R., Rouvière, O. (2017). What is the negative predictive value of multiparametric magnetic resonance imaging in excluding prostate cancer at biopsy? A systematic review and meta-analysis from the European Association of Urology Prostate Cancer Guidelines Panel. European urology, 72(2), 250-266.
12. Thompson, J., Van Leeuwen, P., Moses, D., Shnier, R., Brenner, P., Delprado, W., Stricker, P. (2016). The diagnostic performance of multiparametric magnetic resonance imaging to detect significant prostate cancer. The Journal of urology, 195(5), 1428-1435.
13. Branger, N., Maubon, T., Traumann, M., Thomassin-Piana, J., Brandone, N., Taix, S, Walz, J. (2017). Is negative multiparametric magnetic resonance imaging really able to exclude significant prostate cancer? The real-life experience. Bju international, 119(3), 449-455.
14. Komai, Y., Numao, N., Yoshida, S., Matsuoka, Y., Nakanishi, Y., Ishii, C., Kihara, K. (2013). High diagnostic ability of multiparametric magnetic resonance imaging to detect anterior prostate cancer missed by transrectal 12-core biopsy. The Journal of urology, 190(3), 867-873.
15. Bjurlin, M., Meng, X., Le Nobin, J., Wysock, J., Lepor, H., Rosenkrantz, A., Taneja, S. (2014). Optimization of prostate biopsy: the role of magnetic resonance imaging targeted biopsy in detection, localization and risk assessment. The Journal of urology, 192(3), 648-658.