Post N Med 2016; XXIX(11): 836-840

©Borgis

*Szymon Kawecki[1], Mieszko Kozikowski[1], Jakub Dobruch[1, 2]

The role of multiparametric magnetic resonance imaging (mpMRI) in the diagnosis of prostate cancer

Znaczenie wieloparametrycznego rezonansu magnetycznego (mpMRI) w rozpoznawaniu raka gruczołu krokowego

[1]1st Unit of Didactics, Department of Urology, Centre of Postgraduate Medical Education, European Health Centre Otwock
Head of Department: Jakub Dobruch, MD, PhD
[2]2nd Unit of Didactics, Department of Urology, Centre of Postgraduate Medical Education, Professor W. Orłowski Independent Public Teaching Hospital, Warsaw
Head of Department: Jakub Dobruch, MD, PhD

Keywords

multiparametric magnetic resonance, prostate cancer, radical prostatectomy

Słowa kluczowe

wieloparametryczny rezonans magnetyczny, rak prostaty, prostatektomia radykalna

Conflict of interest
Konflikt interesów

None
Brak konfliktu interesów

Adres/address:

*Szymon Kawecki
Klinika Urologii CMKP
Europejskie Centrum Zdrowia Otwock
ul. Borowa 14/18, 05-400 Otwock
tel. 535-244-175
kaweckiszymon@gmail.com

Summary

Prostate cancer is the second most common neoplasm in men in Poland. Due to the complex pathophysiology and the course of disease, some imaging methods prove more effective than others in certain clinical stages of prostate cancer. Multiparametric magnetic resonance imaging provides complex information about morphology and functional changes in the prostate, therefore it is useful in many situations, where standard imaging methods are insufficient. The paper is a review of current imaging modalities in prostate cancer, with particular emphasis on the significance of multiparametric magnetic resonance imaging.

Streszczenie

Rak stercza jest drugim co do częstości nowotworem wśród mężczyzn w Polsce. Skomplikowana patofizjologia i przebieg choroby sprawiają, że niektóre metody obrazowania sprawdzają się lepiej od innych w poszczególnych stadiach klinicznych raka stercza. Wieloparametryczny rezonans magnetyczny dostarcza złożonej informacji na temat morfologii i zmian czynnościowych w sterczu, co powoduje, że jest on przydatny w wielu sytuacjach, w których standardowe metody obrazowania stają się niewystarczające. Praca stanowi przegląd aktualnych metod obrazowania raka stercza ze szczególnym naciskiem na znaczenie wieloparametrycznego rezonansu magnetycznego.

Prostate cancer (PCa) is one of the most common malignancies in men. The incidence of PCa varies among different countries, with the highest rates in Australia, New Zealand, Northern America, particularly among black males, and Western Europe (fig. 1). The lowest rates are reported in Asian countries. An estimated 1.1 million men worldwide were diagnosed with PCa in 2012, accounting for 15% of all malignancies diagnosed in men at that time (1). In Poland, prostate cancer is the second most common neoplasm after lung cancer. About 10,201 men were diagnosed with PCa in 2012 in Poland (2).

PCa primarily develops in the peripheral zone of the prostate (fig. 2).

Improved imaging methods for prostate scanning with enhanced biopsy accuracy for PCa diagnosis resulted in higher detection rates for tumours arising in the transition zone (TZ), located anterior to the urethra.

Initially, the cancer is limited to the prostate gland (organ-confined disease). However, with time it invades the periprostatic tissues (ECE – extraprostatic extension; locally advanced disease). Perineural invasion, i.e. tumour spread along a nerve, is a characteristic feature of PCa. Further development of PCa may result in the spread of cancer cells beyond the prostate gland, particularly to sites penetrated by the cavernous nerves, as well as lead to the invasion of the seminal vesicles as a result of cancer spread along the ejaculatory ducts, direct invasion of the seminal vesicles by the tumour itself or, least often, as a result of metastasis. The spread of cancer beyond the prostate gland can result in the invasion of the neck and the triangular region of the bladder. Ureteral invasion prevents the

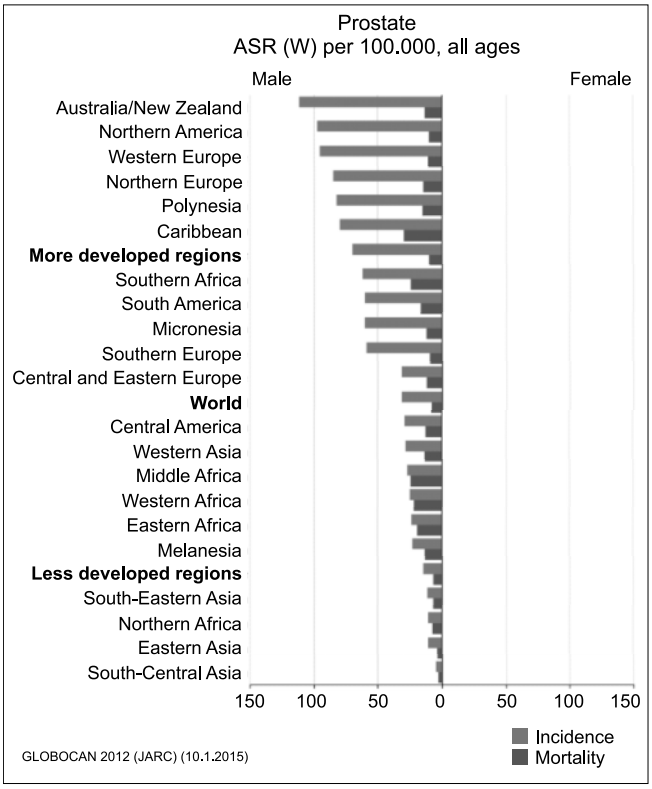

Fig. 1. Standardised incidence and mortality rates of prostate cancer in selected countries according to the Globocan database (WHO, 2012, www-dep.iarc.fr/globocan/globocan.html) (1)

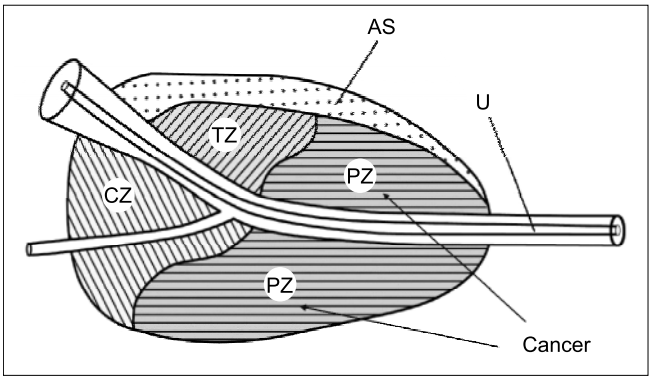

Fig. 2. The zonal structure of the prostate
AS – anterior commissure; TZ – transitional zone; CZ – central zone; PZ – peripheral zone; U – urethra (3)

urine flow from the upper urinary tract, causing hydronephrosis, which may lead to renal failure. Anterior rectal wall invasion is rare as this part is protected against invasion by a strong structure known as the Denonvilliers fascia. Significant local progression of the primary tumour is usually accompanied by the presence of lymph node and distant metastases, bone metastases in particular.

Prostate-confined cancer is usually asymptomatic or causes scarce, non-specific symptoms. In some cases, clinical consequences of significantly advanced cancer, e.g. pain in bones, anaemia and/or renal insufficiency, are the first manifestations of PCa.

Transrectal ultrasound guided TRU-CUT core biopsy (^{TRUS}TRU-CUT) of the prostate gland is the primary PCa diagnostic method. Indications for the TRU-CUT needle biopsy include abnormalities identified based on digital rectal examination (DRE), such as a nodular thickening in the prostatic parenchyma, generally increased prostate cohesion, asymmetry, blurred lateral boundaries and increased levels of serum prostate-specific antigen as well as lesions suspicious of PCa, which are detected by transrectal ultrasound (TRUS) or, recently increasingly often, by multiparametric magnetic resonance imaging (mpMRI). Prostate assessment based on DRE is very subjective and dependent on the experience of the examiner. TRUS-guided biopsy is superior in some respects when compared with DRE. It allows for an accurate determination of the size, boundaries and the internal structure of the prostate gland. Therefore, it is widely used for ^{TRUS}TRU-CUT. An hypoechoic area is a typical TRUS appearance of prostate cancer. Although about 50% of pathomorphologically confirmed prostate cancer foci are hypoechoic, the ultrasonographic pictures of poorly-differentiated cancers and cancers located outside the peripheral zone, where tumours most often develop, tend to vary (4, 5).

Clinical assessment of local tumour progression is based on DRE, TRUS, biopsy and, in some cases, computed tomography (CT) of the pelvis and/or mpMRI imaging. The mpMRI imaging technology is currently a method that most accurately reflects the structure of the prostate gland. This diagnostic method has been significantly improved in recent years. Currently, three-Tesla MRI scanners are available, which have better resolution of the obtained images, including dynamic contrast-enhanced images, compared to previous 1.5 Tesla MRI scanners. In addition to conventional morphology images, imaging using spectroscopy (magnetic resonance spectroscopic imaging – MRSI) and imaging based on water diffusion (diffusion-weighted MRI – DWMRI) have been introduced. Although collecting information obtained using all these technologies is very difficult, experience shows that combining at least two of them significantly improves the accuracy of evaluation, allowing for a final determination of the stage and the size of PCa. This information is useful in determining the extent of surgery (radical prostatectomy – RP) to minimise the risk of positive surgical margins (PSM) with the lowest possible impairment of quality of life.

MpMRI technology contributes to the improved diagnosis of PCa, which is of value for cancer patients at different stages of disease and in different clinical situations.

1. Localisation of PCa foci in patients with no abnormalities revealed by TRUS

As already mentioned, PCa tends to be isoechoic and thus invisible on TRUS. Only 60% of tumour foci are diagnosed based on transrectal ultrasonography (6). It was found based on the analysis of tissue material obtained during radical prostatectomy that mpMRI has a better PCa detection rate than TRUS, particularly in the case of tumours with Gleason score > 7 as well as

tumours located in the anterior portion of the prostate gland, where it is very difficult to collect specimens during ^{TRUS}TRU-CUT biopsy.

Data analysis of 175 patients after radical prostatectomy demonstrated that mpMRI detection rate for tumour size < 0.5 mL, 0.5-2.0 mL and > 2.0 mL is 21-29%, 43-54% and 67-75%, respectively, 63%, 82-88% and 97% for Gleason score <6, 80% for Gleason score 7, 93% and 100% for Gleason score > 8 (7). Another study assessed the value of mpMRI in men, whose first biopsy did not find PCa. mpMRI scans were performed in 265 men, followed by another biopsy. PCa was detected in 41% of patients, with clinically significant cancer according to Epstein's criteria in 87% of cases (8). Yuen et al. also investigated men after biopsy which failed to find PCa. The sensitivity, specificity, positive (PPV) and negative (NPV) predictive values as well as the accuracy of MRI, MRSI and the combination of MRI/MRSI in the detection of PCa were as follows: 57.1, 57.1 and 100.0% (sensitivity), 88.2, 82.4 and 70.6% (specificity), 66.7, 57.1 and 58.3% (PPV), 83.3, 82.1 and 100% (NPV) and 79.2, 75.0 and 79.2% (accuracy) (9). mpMRI is more effective than TRUS in detecting focal PCa. This method usually reveals abnormalities in patients with PCa volume > 0.5 mL and Gleason score > 6.

2. Assessment of local progression

Neurovascular bundles responsible for erection run along the posterolateral surface of the prostate. The apex of the prostate gland is adjacent to the external urethral sphincter responsible for urinary continence after radical prostatectomy. Therefore, the knowledge of PCa location and stage during RP is essential. So far, TRUS has been a widely used method to assess the local progression of PCa. However, it's effectiveness in detecting ECE is insufficient. mpMRI allows for detecting the involvement of neurovascular bundles, seminal vesicles and the rectum. Unfortunately, mpMRI assessment of the prostate gland, like other imaging techniques, is a macro-scale evaluation. Focal ECE still represents a diagnostic challenge (10). The estimated probability of periprostatic tissue involvement is 25% in patients with mpMRI revealing only segmental, smooth bulging of the outline of the prostatic capsule and up to 75% in patients with mpMRI showing "sharp" distortion of the prostate contours (11). The sensitivity, specificity and accuracy of 3-Tesla MRI in detecting ECE are 55.9, 82.2 and 73.9%, respectively (12). In another study, which included 70 patients with locally advanced PCa, mpMRI showed sensitivity, specificity, PPV and NPV for ECE detection of 94.7, 69, 93 and 75%, respectively (13). The superiority of mpMRI to TRUS in detecting extraprostatic PCa extension increases the chance to preserve the neurovascular bundles in patients undergoing radical prostatectomy. This may help minimise the impairment of life quality in patients after radical prostatectomy.

3. Diagnosis of PCa metastasis to lymph nodes and bones

Excision (open or laparoscopic lymphadenectomy) followed by histopathological evaluation is the most accurate method for the assessment of regional lymph nodes in patients with clinically organ-confined prostate cancer. Imaging techniques (CT and MRI), which can only show lymph node enlargement, not necessarily related to metastases (14), are of limited value due to their low sensitivity, which is evaluated in a broad range of between 0 to 70% (15-17).

The size of pelvic lymph nodes is assessed in the T1-weighted sequence of mpMRI. Analysing only the size of lymph nodes, the sensitivity of this technique is unsatisfactory. With a cut-off value of 10 mm, the sensitivity is less than 40% (18). Detection of small, microscopic PCa infiltrations in lymph nodes is even lower, up to 1% in patients with Gleason score < 8 and PSA < 20 ng/mL. Therefore, the role of mpMRI in patients with cancer with low risk of lymph node metastasis is limited.

The improvement in mpMRI imaging by the use of ultra-small superparamagnetic iron oxide particles (USPIO) has greatly enhanced detection rates for PCa lymph node metastases. The sensitivity and specificity in the detection of lymph node metastases in 80 patients after lymphadenectomy were 90.5 and 97%, respectively (19). Scintigraphy (20-23), which uses technetium bisphosphonates, so far the best available markers ensuring a great difference between the intensity of bone and soft tissue images, still remains the most sensitive method for detecting PCa bone metastases (24). This method detects bone metastases in at least 25% of patients, in whom no metastases are found using other techniques (25). Recent studies indicate that whole-body MRI and axial MRI may prove more sensitive than scintigraphy, X-ray and CT in detecting PCa bone metastases.

Positron emission tomography (PET/CT) using ^{11}C and ^{18}F tracers is another new technique for detecting lymph node metastases. A meta-analysis has shown that choline PET/CT detects pelvic lymph node metastases with sensitivity and specificity of 63% (51-66%) and 92% (89-94%), respectively (26). However, studies have shown that the sensitivity of this method is significantly lower in men before therapy. Therefore PET/CT is not used in the preliminary diagnosis of metastases, whereas it undoubtedly proves beneficial in patients diagnosed with biochemical recurrence, with sensitivity and specificity in metastasis detection of 85% (79-89%) and 88% (73-95%), respectively. However, the use of PET/CT only for detecting lymph node metastases is still limited by the low sensitivity of this method. There is a strong correlation between the diagnostic accuracy of PET/CT and PSA levels in men diagnosed with biochemical recurrence, therefore PET/CT scan is recommended for PSA values ≥ 1 ng/mL (27).

Promising results were also reported for 68Ga PSMA (prostate-specific membrane antigen) PET/CT. PSMA is a membrane antigen whose expression increases with increasing stage and aggressiveness of prostate cancer. This method produces positive findings in 40% of men assessed before the onset of therapy

and 76% of patients diagnosed with biochemical recurrence (28, 29). However, due to the limited availability, and thus scarce scientific reports, it is still regarded as an experimental technique.

4. The search for recurrent PCa

The increasing serum levels of PSA in patients after radical therapy due to PCa are referred to as biochemical recurrence. Localisation of the primary tumour responsible for this increase is extremely important, particularly in men with PSA lower than 0.5 ng/mL. It is known that mpMRI limited to the morphological evaluation of the post-radical prostatectomy site and pelvic lymph nodes is insufficient for the detection of PCa recurrence. A recently published study assessed the role of DCE MRI in detecting recurrent PCa. The sensitivity and specificity were 84-88% and 89-100%, respectively. Unfortunately, the PSA levels in the assessed men were higher than 0.8 ng/mL (30). In another study, which used mpMRI in 88 patients after RP, local recurrence was found in 37% of patients with PSA levels exceeding 0.3 ng/mL and 13% of men with PSA levels below 0.3 ng/mL (31). The use of mpMRI for detecting early PCa recurrence after radical prostatectomy is limited, particularly in men with PSA levels below 0.5 ng/mL.

5. MRI-guided prostate biopsy

The analysis of mpMRI images can be time-consuming. Identification of abnormalities suggesting PCa requires the use of biopsy, which is usually TRUS-guided. Based on intuition, the operator determines the location of the primary tumour seen on mpMRI scans and collects biopsy samples. Such biopsy is associated with quite a considerable false-negative rate.

MRI-guided biopsy of the prostate has recently become available (^{MRI}TRU-CUT). Collection of samples during ^{MRI}TRU-CUT from regions suspected of PCa based on mpMRI in 265 men with previous TRU-CUT not revealing cancer allowed for detecting PCa in 41% of these patients, with most PCas (87%) considered clinically significant (8).

It is beyond doubt that ^{MRI}TRU-CUT allows for a reliable sample collection from regions previously considered abnormal based on mpMRI. This may reduce the number of cores collected from the prostate gland. However, the method is limited due to high costs.

MRI/TRUS image fusion is another method to verify mpMRI-revealed abnormalities. Owing to this method, the tissue material collected during ^{TRUS}TRU-CUT is sampled only from regions suspected in mpMRI. The biopsy is guided by a computer system.

CONCLUSIONS

Multiparametric magnetic resonance plays an important role in the diagnosis of prostate cancer. The analysis of PCa location helps in further planning of the extent of radical prostatectomy.

BIBLIOGRAPHY

1. GLOBOCAN 2012: Estimated cancer incidence, Mortality and Prevalence Worldwide in 2012; http://globocan.iarc.fr/.
2. Didkowska J, Wojciechowska U, Tarkowski W et al.: Nowotwory złośliwe w Polsce w 2003 roku. Centrum Onkologii – Instytut im. M. Skłodowskiej-Curie. Krajowy Rejestr Nowotworów, Warszawa 2006.
3. McNeal JE: The prostate and prostatic urethra: a morphologic synthesis. J Urol 1972; 107: 1008-1016.
4. Ahmed MM, Oesterling JE: Presentation and diagnosis. [In:] Hamdy FC, Basler JW, Neal DE, Catalona WJ (eds.): Management of urologic malignancies. Churchill Livingstone, London 2002: 139-150.
5. Borówka A, Chłosta P, Antoniewicz A et al.: Ultrasonografia w urologii. Ultrasonografia przezodbytnicza stercza – aspekty kliniczne i praktyczne. Ultrasonografia 2004; 16: 17-28.
6. Smith JA Jr, Scardino PT, Resnick MI et al.: Transrectal ultrasound versus digital rectal examination for the staging of carcinoma of the prostate: results of a prospective, multi-institutional trial. J Urol 1997; 157: 902-906.
7. 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.
8. Hoeks CM, Schouten MG, Bomers JG et al.: Three-Tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. Eur Urol 2012; 62: 902-909.
9. Yuen JS, Thng CH, Tan PH et al.: Endorectal magnetic resonance imaging and spectroscopy for the detection of tumor foci in men with prior negative transrectal ultrasound prostate biopsy. J Urol 2004; 171: 1482-1486.
10. Tacikowska M: Ocena skuteczności badania MR w przedoperacyjnym określeniu stopnia zaawansowania raka gruczołu krokowego w korelacji z transrektalnym badaniem ultrasonograficznym. Nowotwory 2000; 50: 357-361.
11. Schnall MD, Connick T, Hayes CE et al.: MR imaging of the pelvis with an endorectal-external multicoil array. J Magn Reson Imaging 1992; 2: 229-232.
12. Park BH, Jeon HG, Jeong BC et al.: Influence of magnetic resonance imaging in the decision to preserve or resect neurovascular bundles at robotic assisted laparoscopic radical prostatectomy. J Urol 2014; 192: 82-88.
13. Xylinas E, Yates DR, Renard-Penna R et al.: Role of pelvic phased array magnetic resonance imaging in staging of prostate cancer specifically in patients diagnosed with clinically locally advanced tumours by digital rectal examination. World J Urol 2013; 31: 881-886.
14. Tiguert R, Gheiler EL, Tefilli MV et al.: Lymph node size does not correlate with the presence of prostate cancer metastasis. Urology 1999; 53: 367-371.
15. May F, Treumann T, Dettmar P et al.: Limited value of endorectal magnetic resonance imaging and transrectal ultrasonography in the staging of clinically localized prostate cancer. BJU Int 2001; 87: 66-69.
16. Golimbu M, Morales P, Al-Askari S, Shulman Y: CAT scanning in staging of prostatic cancer. Urology 1981; 18: 305-308.
17. Hricak H, Dooms GC, Jeffrey RB et al.: Prostatic carcinoma: staging by clinical assessment, CT, and MR imaging. Radiology 1987; 162: 331-336.
18. Abuzallouf S, Dayes I, Lukka H: Baseline staging of newly diagnosed prostate cancer: a summary of the literature. J Urol 2004; 171: 2122-2127.
19. Harisinghani MG, Barentsz J, Hahn PF et al.: Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. N Engl J Med 2003; 348: 2491-2499.
20. McGregor B, Tulloch AG, Quinlan MF, Lovegrove F: The role of bone scanning in the assessment of prostatic carcinoma. Br J Urol 1978; 50: 178-181.
21. O'Donoghue EP, Constable AR, Sherwood T et al.: Bone scanning and plasma phosphatases in carcinoma of the prostate. Br J Urol 1978; 50: 172-177.
22. Gerber G, Chodak GW: Assessment of value of routine bone scans in patients with newly diagnosed prostate cancer. Urology 1991; 37: 418-422.
23. Terris MK, Klonecke AS, McDougall IR, Stamey TA: Utilization of bone scans in conjunction with prostate-specific antigen levels in the surveillance for recurrence of adenocarcinoma after radical prostatectomy. J Nucl Med 1991; 32: 1713-1737.
24. Buell U, Kleinhans E, Zorn-Bopp E et al.: A comparison of bone imaging with Tc-99m DPD and Tc-99m MDP: concise communication. J Nucl Med 1982; 23: 214-217.

25. Paulson DF, the Uro-Oncology Research Group of current staging procedures in assessing disease extent of prostatic adenocarcinoma. J Urol 1979; 121: 300-302.
26. Umbehr MH, Muntener M, Hany T et al.: The role of 11C-choline and 18F-fluorocholine positron emission tomography (PET) and PET/CT in prostate cancer: a systematic review and meta-analysis. Eur Urol 2013; 64: 106-117.
27. Heidenreich A, Bastian PJ, Bellmunt J et al.: EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration-resistant prostate cancer. Eur Urol 2014; 65: 467-479.
28. Evangelista L, Briganti A, Fanti S et al.: New Clinical Indications for (18) F/(11)C-choline, New Tracers for Positron Emission Tomography and a Promising Hybrid Device for Prostate Cancer Staging: A Systematic Review of the Literature. Eur Urol 2016; 70: 161-175.
29. Perera M, Papa N, Christidis D et al.: Sensitivity, Specificity, and Predictors of Positive 68Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol 2016 Jun 27. pii: S0302-2838(16)30293-7.
30. Cirillo S, Petracchini M, Scotti L et al.: Endorectal magnetic resonance imaging at 1.5 Tesla to assess local recurrence following radical prostatectomy using T2-weighted and contrast-enhanced imaging. Eur Radiol 2009; 19: 761-769.
31. Liauw SL, Pitroda SP, Eggener SE et al.: Evaluation of the prostate bed for local recurrence after radical prostatectomy using endorectal magnetic resonance imaging. Int J Radiat Oncol Biol Phys 2013; 85: 378-384.

received/otrzymano: 12.10.2016
accepted/zaakceptowano: 03.11.2016