

# Multiparametric Magnetic Resonance Imaging in the Detection of Prostate Cancer

## Multiparametrische Magnetresonanztomografie zur Detektion des Prostatakarzinoms

### Authors

T. Durmus, A. Baur, B. Hamm

### Affiliation

Charité Universitätsmedizin Berlin, Department of Radiology, Berlin

### Key words

- prostate
- MR imaging
- imaging sequences
- neoplasms

received 15.11.2013

accepted 17.1.2014

### Bibliography

**DOI** <http://dx.doi.org/10.1055/s-0034-1365937>  
 Published online: 22.1.2014  
 Fortschr Röntgenstr 2014; 186: 238–246 © Georg Thieme  
 Verlag KG Stuttgart · New York ·  
 ISSN 1438-9029

### Correspondence

**Dr. Tahir Durmus**  
 Universitätsmedizin Berlin,  
 Charité Campus Mitte, Institut  
 für Radiologie  
 Chariteplatz 1  
 10117 Berlin  
 Tel.: ++ 49/30/4 50 62 73 74  
 Fax: ++ 49/30/4 50 52 79 11  
 Tahir.Durmus@charite.de

### Abstract



Prostate cancer is the most common malignancy in men, but only about 10% of patients die from that cancer. Recent studies suggest that not all patients benefit from a radical therapeutic approach. When prostate cancer is suspected, magnetic resonance imaging (MRI) can make an important contribution to cancer localization within the prostate. Many studies show that T2-weighted morphologic imaging should be supplemented by multiparametric MRI techniques including diffusion-weighted imaging, contrast-enhanced sequences, and MR spectroscopy. This approach detects aggressive prostate cancer with high sensitivity and specificity. The findings of multiparametric MRI additionally contribute information to the assessment of cancer aggressiveness. The use of these multiparametric MRI techniques will gain an increasing role in the clinical management of prostate cancer patients. They can help in establishing a definitive diagnosis with a minimum of invasiveness and may also contribute to optimal individualized treatment. This review article presents the different techniques of multiparametric MRI and discusses their contribution to the detection of prostate cancer. Moreover, this review outlines an objective approach to image interpretation and structured reporting of MRI findings using the PI-RADS criteria. The review concludes with an outline of approaches to prostate biopsy on the basis of MRI (transrectal ultrasound, direct MRI guidance of tissue sampling, and MRI-ultrasound fusion biopsy) and emerging future uses of MRI in the planning of focal treatment options and in the active surveillance of patients diagnosed with prostate cancer.

### Citation Format:

- ▶ Durmus T, Baur A, Hamm B. Multiparametric Magnetic Resonance Imaging in the Detection of Prostate Cancer. Fortschr Röntgenstr 2014; 186: 238–246

### Zusammenfassung



Das Prostatakarzinom ist der häufigste bösartige Tumor des Mannes; allerdings versterben nur ca. 10% der Patienten am Prostatakarzinom. Studien der letzten Jahre legen nahe, dass nicht jeder Patient von einer radikalen Therapie profitiert. Bei Verdacht auf Prostatakarzinom kann die MRT einen wichtigen Beitrag zur Tumordetektion leisten. Eine Vielzahl von Studien konnte zeigen, dass T2-gewichtete morphologische Bildgebung im Sinne einer multiparametrischen MRT durch diffusionsgewichtete, kontrastmittelgestützte und MR-spektroskopische Bildgebung ergänzt werden sollte. Insbesondere aggressive Karzinome können mit hoher Sensitivität und Spezifität entdeckt werden. Die multiparametrische MRT kann darüber hinaus einen Beitrag zur Aggressivitätsbeurteilung leisten. Die Anwendung dieser Techniken wird in den nächsten Jahren im Management von Patienten mit Prostatakarzinom eine zunehmende Bedeutung erlangen. Sie werden nicht nur dabei helfen, auf möglichst wenig invasive Art die endgültige Diagnose zu sichern, sondern möglicherweise auch die Wahl der für den individuellen Patienten optimal geeigneten Therapieoption beeinflussen. In der vorliegenden Arbeit werden die verschiedenen Techniken der multiparametrischen MRT sowie ihre Bedeutung hinsichtlich der Tumordetektion vorgestellt. Es werden die Objektivierung der Bildinterpretation, die strukturierte Befundung anhand der PI-RADS Kriterien sowie die Verfahren zur bioptischen Befundsicherung auf Basis der MRT (transrektaler Ultraschall, direkte MR-geführte Biopsie und

MRT-Ultraschall-Fusionsbiopsie) beleuchtet. Abschließend wird auf mögliche zukünftige Indikationen der MRT hinsichtlich der Planung fokaler Therapien und der aktiven Überwachung von Patienten mit gesichertem Prostatakarzinom eingegangen.

## Introduction

Prostate cancer is the most common malignancy in men, but only about 10% of patients die from that cancer. While the incidence rate in the last 30 years has increased four-fold, the mortality rate has decreased over the last 20 years [1]. This can be primarily attributed to the early detection of prostate cancer as a result of the common practice of testing the prostate-specific antigen (PSA) in the peripheral blood. Trendsetting studies indicate that the current diagnostic and therapeutic approach must be fundamentally rethought. Wilt et al. could not show a significant reduction in the mortality rate for patients with a localized tumor who underwent a radical prostatectomy compared to patients who were simply monitored [2]. In addition to possible postoperative complications, radical prostatectomy was associated with a significantly higher morbidity rate (incontinence, erectile dysfunction) [2]. Like radical prostatectomy, radiation therapy is also associated with significant side effects, such as loss of potency, in up to 50% of patients [3]. Although prostate cancer can be effectively treated in many cases by radical therapies in the case of early diagnosis, not all patients seem to benefit from such treatments. Therefore, new management strategies, such as active surveillance and watchful waiting, as well as organ-preserving focal therapy options are currently being evaluated in studies.

Selecting the most suitable diagnostic and therapeutic approach for the individual patient is a significant challenge. As a matter of fact, MRI with its multiparametric imaging is shaking the foundations of established diagnostic and therapeutic paradigms and is now being used for the planning of diagnostic punctures and radical treatments. In the future it will become increasingly important for patient stratification with regard to therapeutic approach and treatment monitoring [4].

The following provides an overview of the current status of multiparametric MRI of the prostate and an interpretation of relevant findings. The role of multiparametric MRI in the diagnosis of prostate cancer including systematic and targeted biopsy and its potential in conservative and minimally invasive treatments will also be discussed.

## Multiparametric MRI of the prostate

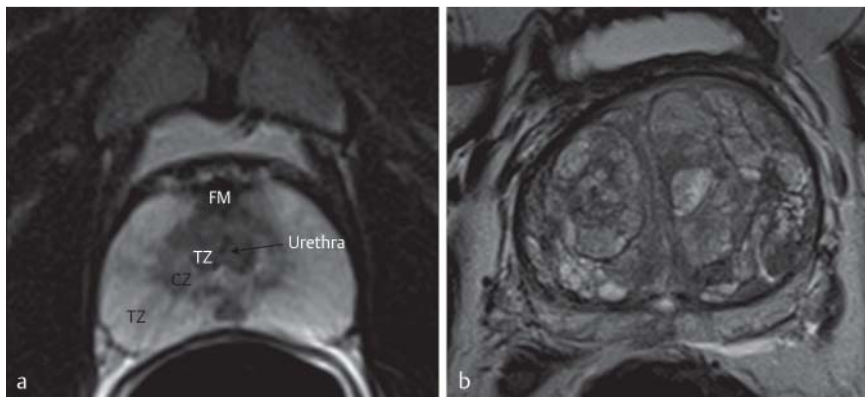
Due to its high soft tissue contrast, high resolution, and ability to simultaneously image functional parameters, MRI provides the best visualization of the prostate compared to other imaging methods. In the case of MRI scanners with a field strength of 1.5 T, it has proven to be advantageous to use a dedicated endorectal coil particularly for the local staging of prostate cancer [5]. In the case of MRI scanners with a field strength of 3 T and the associated higher signal-to-noise ratio, the image quality is so good even without an endorectal coil that the coil is not necessary for detection purposes. This should result in greater patient

acceptance and should further support the broader use of multiparametric MRI in the coming years.

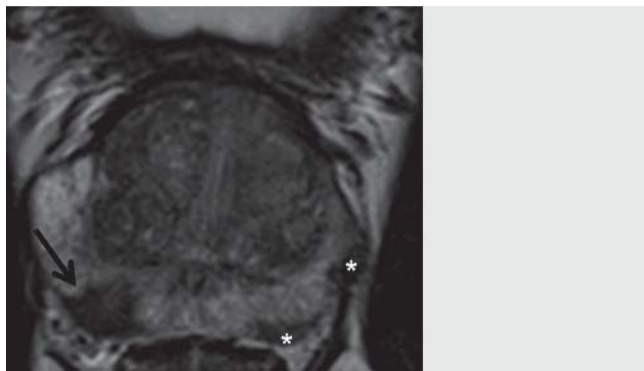
Multiparametric MRI refers to the combination of morphological sequences and functional imaging techniques. Standard T2-weighted (T2w) and T1-weighted (T1w) turbo-spin-echo sequences are used for visualization of the morphology while diffusion-weighted imaging (DWI), dynamic contrast-enhanced imaging (DCE) and MR spectroscopic imaging can be combined for the functional sequences.

## Morphological imaging (T2- and T1-weighted imaging)

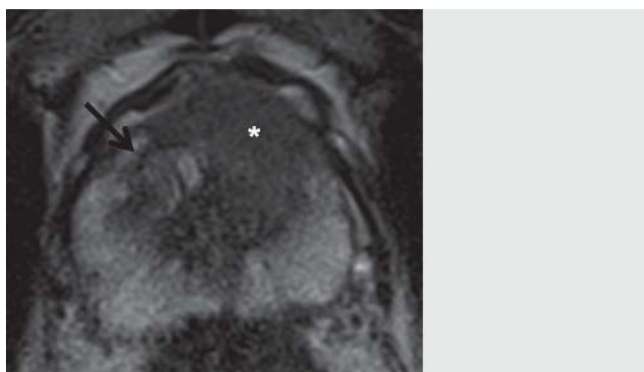
High-resolution axial T2-TSE is the backbone of every MR image of the prostate. This is typically supplemented by a sagittal and possibly a coronal T2-TSE sequence which facilitates evaluation of the seminal vesicle in particular. T2-weighted (T2w) imaging allows precise visualization of the zonal anatomy of the prostate with a peripheral and central zone and a transition zone (◉ Fig. 1a). Moreover, nodular, glandular, stromal, and cystic changes in benign prostate hyperplasia (BPH) can be reliably visualized (◉ Fig. 1b). Prostate carcinomas can be detected in T2w imaging on the basis of their low-signal, classic oval shape as well as their space-occupying nature once they reach a certain size (◉ Fig. 2, 3). The diagnostic accuracy of T2w imaging alone is highly variable according to the literature. This is primarily due to the differences in study design (e.g. prostatectomy versus biopsy as reference standard, type of reading, detection versus staging) and in the examined study population (e.g. patients with known prostate cancer versus patients after multiple biopsies). For T2w imaging without functional sequences, the sensitivity and specificity for prostate cancer are approximately 57–83% and 62–82% [6, 7]. The diagnostic limitations of T2w imaging alone are due to the often similar nature of regularly occurring acute and chronic inflammation of the prostate and hemorrhages, which also cause a hypointense pattern in T2w imaging. Prostatitis typically has a striated, slightly hypointense appearance and sometimes cannot be morphologically differentiated from prostate cancer in T2w imaging (◉ Fig. 4, 5). Hemorrhages have a very variable appearance in T2w imaging and can be detected in T1w imaging on the basis of their hyperintensity (◉ Fig. 6a, b). Bleeding is a regular occurrence after biopsy. Therefore, MRI of the prostate should not be performed until at least 6–8 weeks after biopsy to avoid unnecessary diagnostic impediments. However, hemorrhages can also persist for several months. Therefore, it is useful to know that bleeding can also serve as a diagnostic aid for detection. In a prostate that is hyperintense in T1w imaging due to post-biopsy hemorrhagic changes, hypointense island-like areas on the T1w images that correlate with areas that are hypointense on the T2w images can be an indication of prostate cancer (hemorrhage exclusion sign) [8]. It is presumed that the anticoagulative effect of the citrate which is highly concentrated in normal prostate tissue but is low in cancer tissue results in increased bleeding. Well vascularized and perfused cancer tissue is probably also a better site of degradation for bleeding residues than normal prostate tissue. With respect to a more exact diagnosis in the case of bleeding residues, diffusion-weighted imaging and MR spectroscopy have proven to be advantageous in



**Fig. 1** **a** Normal prostate of a 30-year-old man. The transition zone (TZ) is still highly localized around the urethra. It is surrounded by the central zone (CZ) in the basal segments and by fibromuscular tissue (FM). The majority of the prostate is comprised of the peripheral zone (PZ). **b** Nodular changes in benign prostate hyperplasia in an older patient enlarge the transitional zone with consecutive compression of the central zone and the peripheral zone.

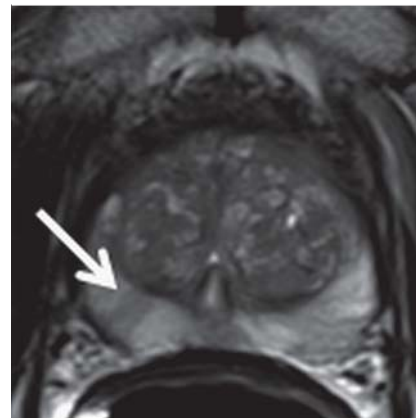


**Fig. 2** Prostate cancer of the peripheral zone: Axial T2 TSE with a hypointense lesion on the right side in the peripheral zone (arrow). After targeted biopsy under MRI guidance, an acinar prostate adenocarcinoma with a Gleason score of 3+4=7 was able to be detected. The additional smaller foci on the left side of the peripheral zone should also be mentioned (\*).

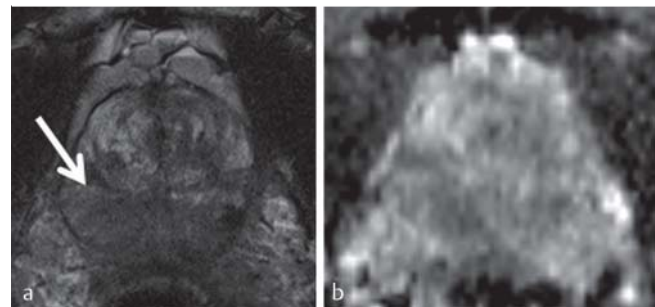


**Fig. 3** Prostate cancer of the transitional zone: Axial T2 TSE with homogeneously hypointense lesion ventral left paramedian (\*). While the benign hyperplastic nodule has a distinct hypointense border on the right in the transitional zone (arrow), the border around the focus is unclear (erased charcoal sign). There is a ventral protrusion in the contour of the cancer.

particular [9, 10]. At present, morphological imaging should normally be combined with at least two functional sequences in order to significantly increase the sensitivity and specificity of MRI [11–13]. These will be introduced in the following.



**Fig. 4** Prostatitis: Axial T2 TSE with slightly hypointense, striated changes on both sides diagnosed in histology as chronic prostatitis.

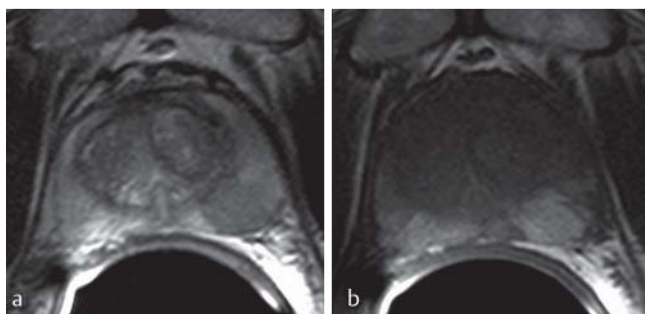


**Fig. 5** Granulomatous prostatitis. Axial T2 TSE **a** and corresponding ADC map **b** of a patient with PSA values between 6–8 ng/ml and three transrectal ultrasound-guided biopsies without detecting cancer. The extensive and partially significantly T2w hypointense changes (arrow) were able to be diagnosed as granulomatous prostatitis after targeted MRI-guided biopsy. The finding in T2w imaging would also be consistent with imaging of an advanced diffusely growing prostate cancer.

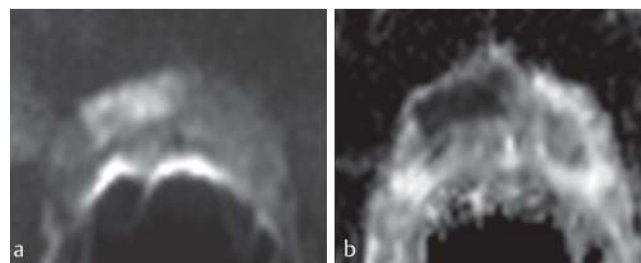
### Diffusion-weighted imaging

Diffusion-weighted imaging visualizes the Brownian molecular motion of water. It has become an important part of oncological imaging since malignant tumors are typically comprised of densely arranged cells whose numerous cell membranes limit this Brownian molecular motion [14]. Prostate cancers are thus visualized on highly diffusion-weighted images (typically upper b-values of 800–1000 s/mm<sup>2</sup> in prostate imaging) as areas with high signal intensity (► **Fig. 7a**). Diffusion coefficients (apparent diffu-





**Fig. 6** Post-puncture bleeding can be mistaken for prostate cancer in T2 imaging due to its hypointense appearance (**a**, axial T2 TSE). Hyperintense post-puncture hemorrhagic changes can be detected on both sides in the peripheral zone in the corresponding axial T1 TSE slice **b**.



**Fig. 7** **a** Axial DWI with a b-value of 1000 shows a lesion ventral right with a hyperintense signal. **b** This area has low signal intensity in the corresponding ADC map. With normal diffusion, the peripheral zone of the prostate has high signal intensity in the ADC and low signal intensity in the b-1000. After prostatectomy, an acinar prostate adenocarcinoma with a Gleason score of  $4 + 3 = 7$  was able to be diagnosed ventral right in the patient.

sion coefficient, ADC) can be calculated from the diffusion-weighted data. In the ADC maps, areas with normal diffusion can then be differentiated as having high signal intensity and those with diffusion restriction as having comparatively low signal intensity (► **Fig. 7b**). Most studies showed that DWI is a very useful addition to morphological imaging and can increase sensitivity in particular by 10–25% [15–17]. Since hyperplastic stromal nodules can have pronounced diffusion restriction in BPH, DWI must be evaluated together with morphological imaging (T2w) especially when assessing the central portions of the prostate gland [16].

Studies in recent years have increasingly examined the capabilities of DWI with respect to evaluating the aggressiveness of prostate cancer. It was able to be shown that the ADC value has a negative correlation with the Gleason score, i. e., low ADC values are seen primarily in high-grade aggressive prostate cancers [15, 18]. Results regarding the ability to differentiate low-grade tumors (Gleason score  $3 + 3 = 6$ ) and high-grade tumors (Gleason score  $> 4 + 3 = 7$ ) in the peripheral zone are very promising since they may be able to help to better determine patient risk potential [19, 20]. However since there can still be relevant overlapping of the ADC values in the different Gleason groups, additional studies are needed to implement this grading potential of diffusion-weighted imaging in the clinical routine. However, DWI will play an important role in differentiating patients with a low risk from those with a high risk and separating them with respect to management [21].

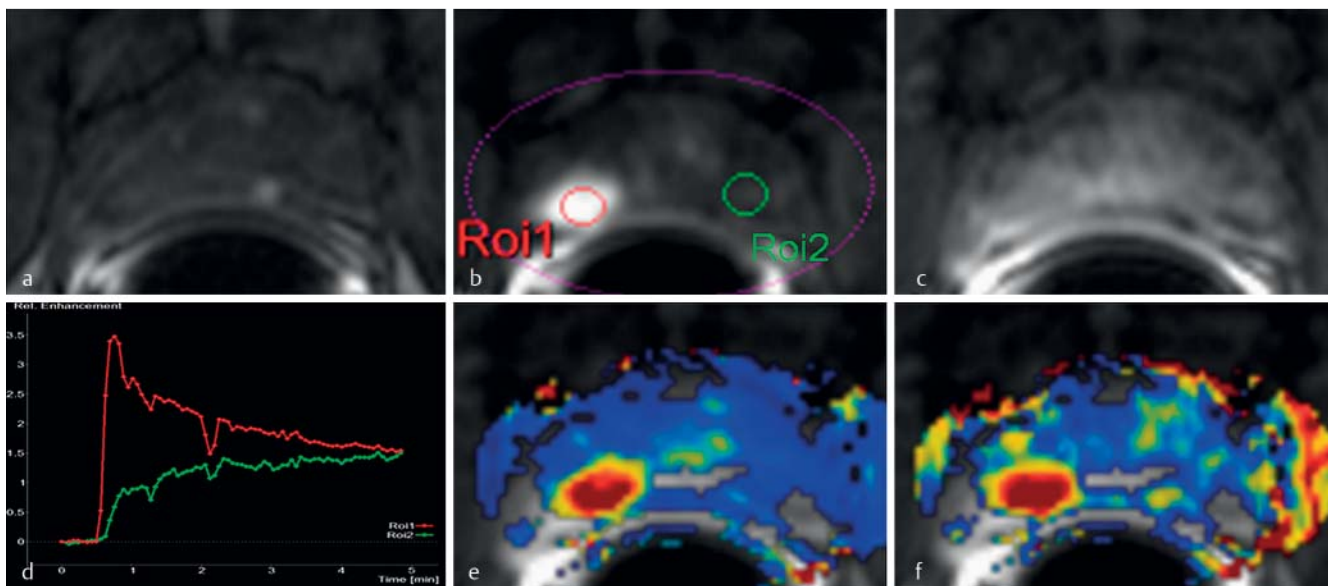
### Dynamic contrast-enhanced (DCE) MRI

Contrast-enhanced MRI sequences can be used to assess the vascularity and permeability of tissues. Gadolinium-containing extracellular T1w contrast agent is typically administered intravenously for this purpose [22]. Fast T1w gradient echo sequences with a temporal resolution of 4–10 seconds are primarily used in prostate imaging. Measurements should be performed over a period of up to approximately 5 minutes after contrast agent application [13]. The enhancement can be displayed in the form of curves over time thus helping to characterize tissues. Prostate cancers are characterized by fast wash-in (early peak enhancement) and fast wash-out compared to healthy tissue (type III

curve). Enhancement typically increases steadily (type I) in the given measurement time in cancer-free tissue, while a curve with a plateau (type II) occurs relatively frequently both in healthy tissue and in cancer tissue [22]. On the basis of enhancement curves, gadolinium concentrations in tissue and tissue transport constants in the direction of the tumor interstitium ( $K^{trans}$ ) and back in the direction of the blood plasma ( $k_{ep}$ ) can be calculated using suitable mathematical models (two-compartment Tofts model). Prostate cancers are characterized by an increase in the tissue transport constants which can be displayed using color coding in pharmacokinetic parameter maps (► **Fig. 8**) [23]. The currently available studies do not provide a clear conclusion regarding the improvement of prostate cancer detection via DCE. Some studies were able to show an improvement of the diagnostic accuracy of conventional MRI (T2w and T1w) when supplemented by DCE imaging [24, 25]. However, it is problematic in the case of DCE that hyperplastic nodules in BPH can enhance and wash out quickly like prostate carcinoma foci and  $K^{trans}$  and  $k_{ep}$  can be accordingly increased, thus limiting the sensitivity and specificity of DCE in the central portions of the prostate gland in particular [26, 27]. In addition, inflammation can often have greater vascularity and tissue permeability, which also limits the sensitivity and specificity of DCE for the detection of prostate cancer. However, it was able to be shown that the local staging of prostate cancer and the detection of local tumor relapses after definitive therapy can be significantly improved using dynamic T1w sequences with good temporal resolution [28, 29].

### MR spectroscopy

MR spectroscopy allows spatially resolved visualization of chemical substances in an organ. The healthy prostate gland produces an ample amount of a citrate-containing secretion, resulting in a high citrate content and a low choline level. In the case of prostate cancer, the choline level is significantly elevated and the citrate content is reduced due to the metaplastic processes of the cell membranes. The relationship between these two metabolites can therefore be used as a measure of malignancy [30]. MR spectroscopy increases the specificity of the MRI examination in particular,



**Fig. 8** a-c Axial T1 GRE unenhanced a. After contrast agent administration, an area with early enhancement is seen on the right in the peripheral zone (b, ROI1) with significant washout in the late-phase image c. The enhancement can be graphically shown as SI/time curve d. A type III curve (red) with early enhancement is a typical finding in the case of prostate

cancer, while healthy prostate tissue is characterized by a steady slow wash-in (type I, green). Parameter maps represent an alternative. High transport constants  $K_{trans}$  e and  $kep$  f can confirm suspicion of prostate cancer. In this example a minimally differentiated prostate adenocarcinoma with a Gleason score of  $4 + 5 = 9$  was diagnosed after prostatectomy.

but can also be used to evaluate tumor volume [31, 32]. The diagnostic accuracy of the morphological MRI examination can be increased by MR spectroscopy from 52% to 75% [10]. The basic requirement for good spectral resolution of the individual metabolites is a homogeneous magnetic field in the field of measurement and sufficient suppression of the fat and water signal during the measurement. In addition to sequence adjustments, this usually requires multiple shimming steps and saturation bands around the prostate to be manually adjusted to the individual prostate anatomy. Together with these preparations, MR spectroscopy at 1.5 T requires a measurement time of 13–20 minutes. Evaluation and interpretation are complex and often only possible after appropriate physical adjustments. Even if automatic segmentation algorithms are able to automatically detect the prostate in the near future thus minimizing measurement preparations, MR spectroscopy will remain limited in its daily use due to the significant time investment and the high level of physical-medical expertise required.

### Structured interpretation and communication of MRI findings in the prostate (MR PI-RADS)

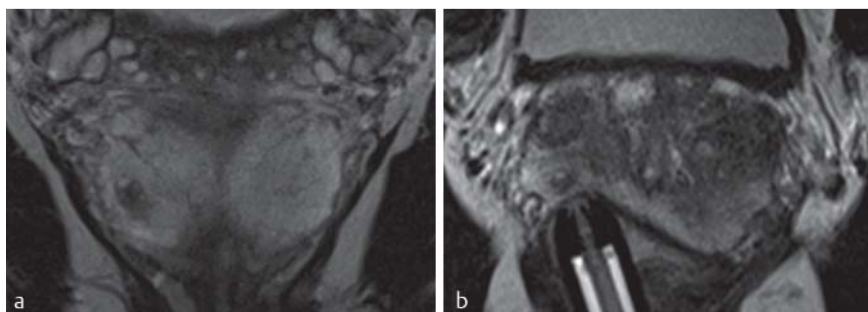
In 2012 the European Society of Urogenital Radiology (ESUR) created the Magnetic Resonance Prostate Imaging Reporting and Data System (MR PI-RADS) as part of its MRI guidelines for prostate imaging [13]. Based on the breast imaging reporting and data system (BI-RADS), a standardized method for reporting multiparametric MRI of the prostate for the detection of prostate cancer is proposed here. The goal was to standardize image interpretation and to simplify communication between the radiologist and colleagues in other departments.

Based on clearly defined criteria according to PI-RADS, every lesion suspicious for tumor within the prostate is assigned a point value between 1 and 5 for every sequence performed as part of multiparametric MRI (consisting of at least T2w, DWI, and DCE). Moreover, a total point value is calculated for every lesion suspicious for tumor [33]. Thus, a statement regarding the probability of the presence of a clinically significant prostate cancer should be possible: A point value of 1 means that a lesion is probably benign, while a point value of 5 indicates a high probability of malignancy. The development of PI-RADS and the criteria contained therein for the assignment of point values are based on published literature and an expert consensus. Since being published in February 2012, PI-RADS has been evaluated in multiple studies.

The point values of T2w, DWI, and DCE were added to form a total point value for lesions suspicious for tumor. Good and reproducible diagnostic accuracy was documented for the total point values calculated in this manner [33–37]. Standardization of image interpretation in research and the clinical routine is an important milestone that should accelerate the acceptance of multiparametric MRI in the coming years. The results of clinical studies should be easier to compare using PI-RADS. Moreover, PI-RADS makes it possible to formulate guidelines for diagnostic clarification and perhaps even for the treatment of prostate cancer. The present data indicates that a biopsy should be performed in the case of lesions with PI-RADS  $\geq 4$  while monitoring via MRI and PSA could be sufficient in lesions with PI-RADS  $\leq 3$ .

### MRI and prostate biopsy

The standard prostate biopsy is the transrectal ultrasound (TRUS)-guided systematic prostate biopsy. Urological stud-



**Fig. 9** **a** Patient with a negative ultrasound-guided biopsy in history and increasing PSA value; 12 ng/ml at the time of MRI. Coronal T2 TSE with lesion suspicious for cancer measuring a maximum of 5 × 7 mm in the peripheral zone. **b** Targeted biopsy under direct MRI guidance yielded a total sample length of 12 mm with 4 mm of an acinar prostate adenocarcinoma (Gleason score 3 + 3 = 6).

ies in particular have shown that the detection rate increases as expected with the number of samples so that approximately 6 samples are currently taken from each lateral lobe in accordance with the recommendations of the professional associations [38, 39]. However, the entire context of the diagnostic weaknesses of TRUS biopsy only becomes clear with MR imaging and visualization of prostate cancer [40]. The rate of carcinomas in the ventral portion of the prostate gland as well as in an extreme lateral position in the peripheral zone and on the apex of the gland is significant in patients with multiple negative ultrasound-guided biopsies. It was shown that patients with a diagnosis of prostate cancer in the ventral portions of the gland by direct MRI-guided biopsy have a higher clinical risk than those with a diagnosis of prostate cancer in the peripheral zone [41].

### Direct MRI-guided biopsies

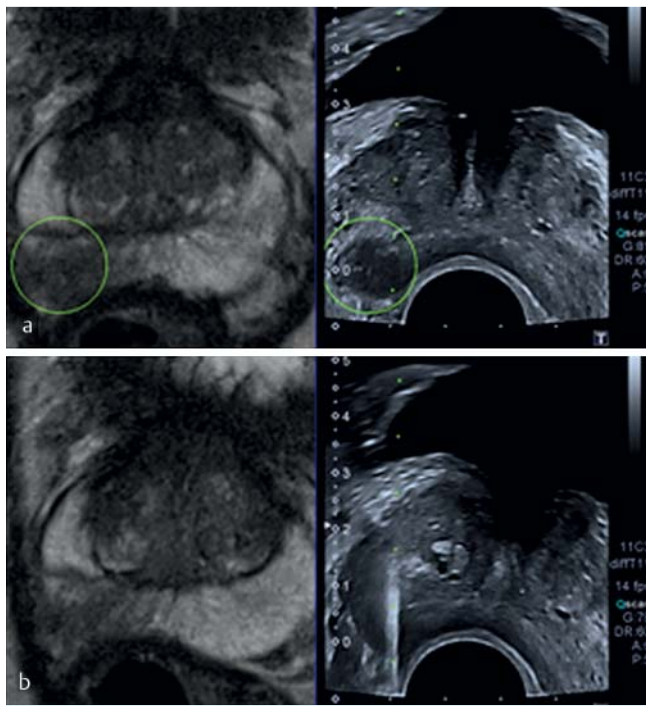
All direct MRI-guided biopsy techniques have in common that MRI is performed during the biopsy and the images are used to guide the biopsy needle. Therefore, the biopsy equipment must be MRI-compatible. MRI-guided biopsies should be performed on a 1.5 T or 3 T unit since exact visualization of the lesions during biopsy is of essential importance. Direct MRI-guided biopsies can be performed via transgluteal, transperineal, and transrectal access [41–43]. Transrectal biopsy is the most common and most accepted direct MRI-guided biopsy technique since there are no special requirements regarding anesthesia or sterility in contrast to the transperineal and transgluteal methods. Transrectal MRI-guided biopsy is typically performed after simply coating the rectal mucous membrane with a disinfecting and locally anesthetizing gel [44]. The patient is premedicated with antibiotics as in standard transrectal ultrasound-guided biopsies. Transrectal MRI-guided biopsy can be evaluated as the most exact prostate biopsy method on the basis of the present data (► Fig. 9): In populations with multiple negative systematic ultrasound-guided biopsies detection rates of 41–59% could be achieved with direct MRI-guided prostate biopsy with the majority of the tumors being classified as clinically relevant [41, 45–47]. As shown in ► Fig. 9, the targeted clarification of non-clinically relevant cancers is also important since this can resolve the diagnostic dilemma of an increasing PSA with a negative biopsy thus creating a foundation for noninvasive and minimally invasive strategies, such as active surveillance or focal therapy.

### MRI/ultrasound fusion biopsy

A multiparametric MRI scan is performed prior to every targeted biopsy to identify lesions that are suspicious for carcinoma and to evaluate whether targeted biopsy techniques are suitable. A possibility to improve reporting would be to create a drawing of the location of the suspicious focus in addition to the written findings. This drawing can then be used during a planned biopsy to perform a greater number of biopsies in certain regions of the prostate. The procedure is similar for cognitive fusion in which ultrasound-guided biopsy is performed immediately after viewing the MRI scan. The objective here is to evaluate the regions suspicious on MRI in a targeted manner and to identify focal lesions on the B-mode image [48]. The prostate must be viewed in both modalities on the same (or at least comparable) image plane. Otherwise, it is extremely difficult to recognize complex structures in the prostate. Navigation is facilitated by detection of the urethra, prominent hyperplastic nodules, or cysts. Peuch et al. were able to detect 15% more clinically relevant cancers per TRUS biopsy in their study by viewing the MRI images immediately prior to biopsy [48]. However, the cognitive fusion can be expected to be highly examiner-dependent. Therefore, software-based fusion of MRI datasets with ultrasound images would be desirable. Software on the latest ultrasound devices can fuse previously imported MRI datasets three-dimensionally and in real time with the B-mode image of an ultrasound examination. An electromagnetic unit that is coupled to the ultrasound probe and can track the movements of the probe is positioned next to the patient table during the biopsy for this purpose [48, 49]. By selecting individual reference points on the MRI images and the B-mode image, the MRI images are adjusted and moved in parallel with the ultrasound scan (► Fig. 10). This makes it possible to use the ultrasound probe to navigate to and biopsy lesions evaluated as suspicious for cancer in the preceding multiparametric MRI scan [48]. Software-supported 3D real-time fusion is currently under intense evaluation. Multiple workgroups were already able to document a significantly higher detection rate of clinically relevant prostate cancers compared to systematic ultrasound-guided biopsy [49–51].

To date, the different direct MRI-guided biopsy techniques and MRI/ultrasound fusion biopsy have not been evaluated in a direct comparison with respect to MRI preparation and examination time, cost, and diagnostic accuracy. However, the possibility of software-based fusion of MRI and ultrasound images in real time is a milestone in the bioptic diag-





**Fig. 10** **a** MRI-ultrasound 3D fusion in real time. After the MRI images (right T2 TSE axial) are imported, freely selectable reference points are selected in the T2 image and B-mode image. **a** Based on this information, the two datasets are combined by software so that the T2 image is adjusted in accordance with the movement of the ultrasound probe so that as shown in this example it is possible to navigate to the lesion suspicious for tumor in the right peripheral zone. **b** After the lesion is precisely targeted, it can be biopsied under ultrasound guidance.

nosis of prostate cancer and will probably be used more widely in coming years.

### MRI for active surveillance

Not all patients with prostate cancer benefit from radical surgery or radiation therapy, in particular under consideration of possible peri- and post-therapeutic complications including incontinence and erectile dysfunction [2]. In particular patients with low-grade prostate cancer (Gleason  $\leq 6$ ) can benefit from surveillance and watchful waiting. Multiparametric MRI can play a significant role in identifying suitable patients [52]. In the case of patients under surveillance, multiparametric MRI can help in the follow-up period to detect paraclinical parameters, such as PSA value and results of a rebiopsy, as well as any tumor progress and to initiate appropriate treatment. Such progress can be detected on the basis of an increase in size but in the future also on the basis of changes in functional sequences like DWI and DCE in terms of dedifferentiation. MRI could also significantly reduce the number of necessary rebiopsies, thus making management less invasive for patients. To date, multiparametric MRI has not been an integral part of diagnostic algorithms of large prospective studies for examining morbidity and mortality among patients under watchful waiting or active surveillance. However, the role of multiparametric MRI is being explicitly examined in studies currently in progress

regarding this topic. Corresponding evidence-based data can therefore be expected in the near future.

### MRI and minimally invasive therapies

A number of minimally invasive, focal, organ-preserving methods have been used in recent years as further alternatives to the radical treatment of prostate cancer. The goal of these methods is to ablate tumor tissue within the prostate while maintaining tumor-free areas of the prostate gland and preserving the periprostatic tissue and structures. These procedures seek to avoid typical peri- and postoperative complications. From the histopathological processing of prostatectomy specimens, it is known that prostate cancer is usually multifocal. However, a so-called “index lesion”, a tumor focus that is significant on the basis of size and differentiation (Gleason score), seems to be decisive for patient prognosis also in these patients [53]. The goal of a minimally invasive treatment must therefore not necessarily be to achieve tumor-free status but to ablate significant tumor foci. Imaging per multiparametric MRI makes it possible to determine the exact location of relevant tumor foci in order to thus guide focal therapies as in diagnostic biopsies [54]. The methods used to date for the prostate include cryotherapy, high-intensity focused ultrasound, and laser-induced thermoablation [55]. Other methods, such as irreversible electroporation (IRE), are currently being evaluated in studies [56]. Significant tumor foci that are generally accessible for ablation can be identified via multiparametric MRI. Moreover, MRI will become increasingly important in the image-guided use of locally ablative procedures [54, 55]. The PSA value remains a valuable marker for follow-up evaluation and for detecting relapses. The exact role that multiparametric MRI will play in treatment monitoring after minimally invasive therapy and as an instrument in long-term follow-up must be examined in the coming years.

### References

- 1 Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin* 2012; 62: 10–29. DOI: 10.3322/caac.20138
- 2 Wilt TJ, Brawer MK, Jones KM et al. Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 2012; 367: 203–213. DOI: 10.1056/NEJMoa1113162
- 3 Zelefsky MJ, Chan H, Hunt M et al. Long-term outcome of high dose intensity modulated radiation therapy for patients with clinically localized prostate cancer. *J Urol* 2006; 176: 1415–1419. DOI: S0022-5347(06)01371-1 [pii] 10.1016/j.juro.2006.06.002
- 4 Padhani AR. Integrating multiparametric prostate MRI into clinical practice. *Cancer Imaging* 2011; 11: S27–S37. DOI: 10.1102/1470-7330.2011.9007
- 5 Beyersdorff D, Darsow U, Stephan C et al. MRI of prostate cancer using three different coil systems: image quality, tumor detection, and staging. *Fortschr Röntgenstr* 2003; 175: 799–805. DOI: 10.1055/s-2003-39929
- 6 Nakashima J, Tanimoto A, Imai Y et al. Endorectal MRI for prediction of tumor site, tumor size, and local extension of prostate cancer. *Urology* 2004; 64: 101–105. DOI: 10.1016/j.urology.2004.02.036 S0090429504003231 [pii]
- 7 Beyersdorff D, Taupitz M, Winkelmann B et al. Patients with a history of elevated prostate-specific antigen levels and negative transrectal US-guided quadrant or sextant biopsy results: value of MR imaging. *Radiology* 2002; 224: 701–706

- 8 Barrett T, Vargas HA, Akin O et al. Value of the hemorrhage exclusion sign on T1-weighted prostate MR images for the detection of prostate cancer. *Radiology* 2012; 263: 751–757. DOI: 10.1148/radiol.12112100
- 9 Rosenkrantz AB, Kopec M, Kong X et al. Prostate cancer vs. post-biopsy hemorrhage: diagnosis with T2- and diffusion-weighted imaging. *J Magn Reson Imaging* 2010; 31: 1387–1394. DOI: 10.1002/jmri.22172
- 10 Kaji Y, Kurhanewicz J, Hricak H et al. Localizing prostate cancer in the presence of postbiopsy changes on MR images: role of proton MR spectroscopic imaging. *Radiology* 1998; 206: 785–790. DOI: 10.1148/radiology.206.3.9494502
- 11 Franiel T, Stephan C, Erbersdobler A et al. Areas suspicious for prostate cancer: MR-guided biopsy in patients with at least one transrectal US-guided biopsy with a negative finding—multiparametric MR imaging for detection and biopsy planning. *Radiology* 2011; 259: 162–172. DOI: radiol.10101251 [pii] 10.1148/radiol.10101251
- 12 Turkbey B, Pinto PA, Mani H et al. Prostate cancer: value of multiparametric MR imaging at 3 T for detection – histopathologic correlation. *Radiology* 2010; 255: 89–99. DOI: 255/1/89 [pii] 10.1148/radiol.09090475
- 13 Barentsz JO, Richenberg J, Clements R et al. ESUR prostate MR guidelines 2012. *Eur Radiol* 2012; 22: 746–757. DOI: 10.1007/s00330-011-2377-y
- 14 Turkbey B, Aras O, Karabulut N et al. Diffusion-weighted MRI for detecting and monitoring cancer: a review of current applications in body imaging. *Diagn Interv Radiol* 2012; 18: 46–59. DOI: 10.4261/1305-3825.DIR.4708-11.2
- 15 Yagci AB, Ozari N, Aybek Z et al. The value of diffusion-weighted MRI for prostate cancer detection and localization. *Diagn Interv Radiol* 2011; 17: 130–134. DOI: 10.4261/1305-3825.DIR.3399-10.1
- 16 Haider MA, van der Kwast TH, Tanguay J et al. Combined T2-weighted and diffusion-weighted MRI for localization of prostate cancer. *Am J Roentgenol* 2007; 189: 323–328. DOI: 189/2/323 [pii] 10.2214/AmJRoentgenol.07.2211
- 17 Kim CK, Park BK, Lee HM et al. Value of diffusion-weighted imaging for the prediction of prostate cancer location at 3T using a phased-array coil: preliminary results. *Invest Radiol* 2007; 42: 842–847. DOI: 10.1097/RLI.0b013e3181461d21 00004424-200712000-00007 [pii]
- 18 Oto A, Yang C, Kayhan A et al. Diffusion-weighted and dynamic contrast-enhanced MRI of prostate cancer: correlation of quantitative MR parameters with Gleason score and tumor angiogenesis. *Am J Roentgenol* 2011; 197: 1382–1390. DOI: 10.2214/ajr.11.6861
- 19 Turkbey B, Shah VP, Pang Y et al. Is apparent diffusion coefficient associated with clinical risk scores for prostate cancers that are visible on 3-T MR images? *Radiology* 2011; 258: 488–495. DOI: radiol.10100667 [pii] 10.1148/radiol.10100667
- 20 Hambrook T, Somford DM, Huisman HJ et al. Relationship between apparent diffusion coefficients at 3.0-T MR imaging and Gleason grade in peripheral zone prostate cancer. *Radiology* 2011; 259: 453–461. DOI: 10.1148/radiol.11091409
- 21 Turkbey B, Bernardo M, Merino MJ et al. MRI of localized prostate cancer: coming of age in the PSA era. *Diagn Interv Radiol* 2012; 18: 34–45. DOI: 10.4261/1305-3825.DIR.4478-11.1
- 22 Durmus T, Vollnberg B, Schwenke C et al. Dynamic Contrast Enhanced MRI of the Prostate: Comparison of Gadobutrol and Gd-DTPA. *Fortschr Röntgenstr* 2013; 185: 862–868. DOI: 10.1055/s-0033-1335892
- 23 Franiel T, Hamm B, Hricak H. Dynamic contrast-enhanced magnetic resonance imaging and pharmacokinetic models in prostate cancer. *Eur Radiol* 2011; 21: 616–626. DOI: 10.1007/s00330-010-2037-7
- 24 Ocak I, Bernardo M, Metzger G et al. Dynamic contrast-enhanced MRI of prostate cancer at 3 T: a study of pharmacokinetic parameters. *Am J Roentgenol* 2007; 189: 849. DOI: 189/4/849 [pii] 10.2214/AmJRoentgenol.06.1329
- 25 Kozlowski P, Chang SD, Jones EC et al. Combined diffusion-weighted and dynamic contrast-enhanced MRI for prostate cancer diagnosis – correlation with biopsy and histopathology. *J Magn Reson Imaging* 2006; 24: 108–113. DOI: 10.1002/jmri.20626
- 26 Noworolski SM, Vigneron DB, Chen AP et al. Dynamic contrast-enhanced MRI and MR diffusion imaging to distinguish between glandular and stromal prostatic tissues. *Magn Reson Imaging* 2008; 26: 1071–1080. DOI: 10.1016/j.mri.2008.01.033 S0730-725X(08)00057-X [pii]
- 27 Delongchamps NB, Rouanne M, Flam T et al. Multiparametric magnetic resonance imaging for the detection and localization of prostate cancer: combination of T2-weighted, dynamic contrast-enhanced and diffusion-weighted imaging. *BJU Int* 2011; 107: 1411–1418. DOI: 10.1111/j.1464-410X.2010.09808.x
- 28 Bloch BN, Furman-Haran E, Helbich TH et al. Prostate cancer: accurate determination of extracapsular extension with high-spatial-resolution dynamic contrast-enhanced and T2-weighted MR imaging – initial results. *Radiology* 2007; 245: 176–185. DOI: 2451061502 [pii] 10.1148/radiol.2451061502
- 29 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. DOI: 10.1007/s00330-008-1174-8
- 30 Scheenen TW, Futterer J, Weiland E et al. Discriminating cancer from noncancer tissue in the prostate by 3-dimensional proton magnetic resonance spectroscopic imaging: a prospective multicenter validation study. *Invest Radiol* 2011; 46: 25–33
- 31 Turkbey B, Mani H, Shah V et al. Multiparametric 3T prostate magnetic resonance imaging to detect cancer: histopathological correlation using prostatectomy specimens processed in customized magnetic resonance imaging based molds. *J Urol* 2011; 186: 1818–1824. DOI: 10.1016/j.juro.2011.07.013 S0022-5347(11)04362-X [pii]
- 32 Coakley FV, Kurhanewicz J, Lu Y et al. Prostate cancer tumor volume: measurement with endorectal MR and MR spectroscopic imaging. *Radiology* 2002; 223: 91–97
- 33 Rothke M, Blondin D, Schlemmer HP et al. PI-RADS-Klassifikation: Strukturiertes Befundungsschema für die MRT der Prostata. *Fortschr Röntgenstr* 2013; 185: 253–261. DOI: 10.1055/s-0032-1330270
- 34 Portalez D, Mozer P, Cornud F et al. Validation of the European Society of Urogenital Radiology scoring system for prostate cancer diagnosis on multiparametric magnetic resonance imaging in a cohort of repeat biopsy patients. *Eur Urol* 2012; 62: 986–996. DOI: 10.1016/j.eururo.2012.06.044 S0302-2838(12)00757-9 [pii]
- 35 Schimmoller L, Quentin M, Arsov C et al. Inter-reader agreement of the ESUR score for prostate MRI using in-bore MRI-guided biopsies as the reference standard. *Eur Radiol* 2013; DOI: 10.1007/s00330-013-2922-y
- 36 Rosenkrantz AB, Kim S, Lim RP et al. Prostate Cancer Localization Using Multiparametric MR Imaging: Comparison of Prostate Imaging Reporting and Data System (PI-RADS) and Likert Scales. *Radiology* 2013; DOI: radiol.13122233 [pii] 10.1148/radiol.13122233
- 37 Quentin M, Schimmoller L, Arsov C et al. 3-T in-bore MR-guided prostate biopsy based on a scoring system for target lesions characterization. *Acta Radiol* 2013; DOI: 0284185113492972 [pii] 10.1177/0284185113492972
- 38 de la Taille A, Antiphon P, Salomon L et al. Prospective evaluation of a 21-sample needle biopsy procedure designed to improve the prostate cancer detection rate. *Urology* 2003; 61: 1181–1186. DOI: S0090429503001080 [pii]
- 39 Eskicorapci SY, Baydar DE, Akbal C et al. An extended 10-core transrectal ultrasonography guided prostate biopsy protocol improves the detection of prostate cancer. *Eur Urol* 2004; 45: 444–448; discussion 448–449. DOI: 10.1016/j.eururo.2003.11.024 S0302283803006353 [pii]
- 40 Wefer AE, Hricak H, Vigneron DB et al. Sextant localization of prostate cancer: comparison of sextant biopsy, magnetic resonance imaging and magnetic resonance spectroscopic imaging with step section histology. *J Urol* 2000; 164: 400–404. DOI: S0022-5347(05)67370-3 [pii]
- 41 Durmus T, Reichelt U, Huppertz A et al. MRI-guided biopsy of the prostate: correlation between the cancer detection rate and the number of previous negative TRUS biopsies. *Diagn Interv Radiol* 2013; 19: 411–417. DOI: 10.5152/dir.2013.13055
- 42 Bodelle B, Naguib NN, Schulz B et al. 1.5-T magnetic resonance-guided transgluteal biopsies of the prostate in patients with clinically suspected prostate cancer: technique and feasibility. *Invest Radiol* 2013; 48: 458–463. DOI: 10.1097/RLI.0b013e31827c394b
- 43 Wolter K, Decker G, Willinek WA. Transperineal MR-guided stereotactic prostate biopsy utilizing a commercially available anorectal biopsy device. *Fortschr Röntgenstr* 2013; 185: 116–120. DOI: 10.1055/s-0032-1330549
- 44 Beyersdorff D, Winkel A, Hamm B et al. MR imaging-guided prostate biopsy with a closed MR unit at 1.5 T: initial results. *Radiology* 2005; 234: 576–581. DOI: 10.1148/radiol.2342031887
- 45 Hambrook T, Somford DM, Hoeks C et al. Magnetic resonance imaging guided prostate biopsy in men with repeat negative biopsies and increased prostate specific antigen. *J Urol* 2010; 183: 520–527. DOI: S0022-5347(09)02657-3 [pii] 10.1016/j.juro.2009.10.022
- 46 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. DOI: 10.1016/j.eururo.2012.01.047 S0302-2838(12)00123-6 [pii]
- 47 *Roethke M, Anastasiadis AG, Lichy M et al.* MRI-guided prostate biopsy detects clinically significant cancer: analysis of a cohort of 100 patients after previous negative TRUS biopsy. *World J Urol* 2012; 30: 213–218. DOI: 10.1007/s00345-011-0675-2
- 48 *Puech P, Rouviere 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. DOI: 10.1148/radiol.13121501 radiol.13121501 [pii]
- 49 *Durmus T, Stephan C, Grigoryev M et al.* Detection of prostate cancer by real-time MR/ultrasound fusion-guided biopsy: 3T MRI and state of the art sonography. *Fortschr Röntgenstr* 2013; 185: 428–433. DOI: 10.1055/s-0032-1330704
- 50 *Sonn GA, Chang E, Natarajan S et al.* Value of Targeted Prostate Biopsy Using Magnetic Resonance-Ultrasound Fusion in Men with Prior Negative Biopsy and Elevated Prostate-specific Antigen. *Eur Urol* 2013; DOI: S0302-2838(13)00249-2 [pii] 10.1016/j.eururo.2013.03.025
- 51 *Walton-Diaz A, Hoang AN, Turkbey B et al.* Can MR-US Fusion Biopsy Improve Cancer Detection in Enlarged Prostates? *J Urol* 2013; DOI: S0022-5347(13)04619-3 [pii] 10.1016/j.juro.2013.05.118
- 52 *Lees K, Durve M, Parker C.* Active surveillance in prostate cancer. *Current Opinion in Urology* 2012; 22: 210–215. DOI: 10.1097/MOU.0b013e328351dc47
- 53 *Wise AM, Stamey TA, McNeal JE et al.* Morphologic and clinical significance of multifocal prostate cancers in radical prostatectomy specimens. *Urology* 2002; 60: 264–269. DOI: S0090429502017284 [pii]
- 54 *de la Rosette J, Ahmed H, Barentsz J et al.* Focal therapy in prostate cancer-report from a consensus panel. *Journal of endourology/Endourological Society* 2010; 24: 775–780. DOI: 10.1089/end.2009.0596
- 55 *Bomers JG, Sedelaar JP, Barentsz JO et al.* MRI-guided interventions for the treatment of prostate cancer. *Am J Roentgenol* 2012; 199: 714–720. DOI: 199/4/714 [pii] 10.2214/Am J Roentgenol.12.8725
- 56 *van den Bos W, Muller BG, de la Rosette JJ.* A randomized controlled trial on focal therapy for localized prostate carcinoma: hemiablation versus complete ablation with irreversible electroporation. *Journal of endourology/Endourological Society* 2013; 27: 262–264. DOI: 10.1089/end.2013.1568