Diagn Interv Radiol 2013; 19:411-417

INTERVENTIONAL RADIOLOGY
ORIGINAL ARTICLE

MRI-guided biopsy of the prostate: correlation between the cancer detection rate and the number of previous negative TRUS biopsies

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PURPOSE
We aimed to investigate prostate cancer detection rate of magnetic resonance imaging (MRI)-guided biopsy and to elucidate possible relations to the number of prior negative transrectal ultrasonography (TRUS)-guided biopsies.

MATERIALS AND METHODS
Eighty-seven consecutive patients (mean age, 65.0 years; mean prostate-specific antigen, 13.3 ng/mL) with at least one prior negative TRUS-guided biopsy and persistent suspicion of prostate cancer were included in this study. All patients underwent MRI-guided biopsy after a diagnostic multiparametric MRI examination at 1.5 Tesla. Specimens were immediately fixated and subsequently evaluated by an experienced uropathologist. Prostate cancer detection rates were calculated. Prostate cancer-positive and -negative cores were compared. Correlation between number of prior biopsies and presence of prostate cancer was evaluated.

RESULTS
Cancer detection rates for patients with one (n=24), two (n=25), three (n=18), and four or more (n=20) negative TRUS-guided biopsies were 29.2%, 40.0%, 66.7%, and 35.0%, respectively (P = 0.087). The median number of removed cores per patient was 3 (range, 1–8) without a significant difference between patients with and without cancer (P = 0.48). Thirty of 36 cancer patients were at intermediate or high risk according to the D´Amico clinical risk score. Eleven of 15 high risk cancers were localized in the transition zone (P = 0.002).

CONCLUSIONS
This study demonstrates high cancer detection rates of MRI-guided biopsy independent of the number of previous TRUS-guided biopsies and the number of taken prostate cores. MRI-guided biopsy therefore represents a less invasive and effective diagnostic tool for patients with prostate cancer suspicion and previous negative TRUS-guided biopsies.

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Received 5 February 2013; revision requested 18 February 2013; revision received 14 March 2013; accepted 24 March 2013.

Published online 25 July 2013.
DOI 10.5152/dir.2013.13055

Prostate cancer is the most prevalent cancer afflicting men in the Western world (1). Digital rectal examination and prostate-specific antigen (PSA) blood levels are the most common clinical tests used to screen for prostate cancer (2). Because several benign conditions, such as benign prostatic hyperplasia and prostatitis, can also elevate the PSA level, the PSA level blood test is not specific for cancer; therefore, the USA Preventive Task Force Service does not recommend this test for prostate cancer screening (3). Transrectal ultrasonography (TRUS)-guided biopsy is the best established standard for diagnosing prostate cancer. The European Prostate Cancer Detection Study (4) revealed a 22% cancer detection rate for patients undergoing initial TRUS-guided biopsy. In this study, an additional 123 patients, corresponding to 12% of the initial cohort, were diagnosed with prostate cancer after undergoing a second, third, or fourth repeat biopsy (4). The TRUS-guided biopsy technique is known to frequently overlook cancers in the anterior region of the prostate, where approximately 30% of cancers reside (5). Therefore, the false negative rate of TRUS-guided biopsies is a major concern. It is well known that cancer detection by TRUS-guided biopsy can be improved by increasing the number of removed cores and by contrast-enhanced-targeted biopsies (6–10).

Multiparametric magnetic resonance imaging (MRI) of the prostate has been shown to have a high sensitivity and specificity for detecting prostate cancer (11–14). Its accuracy in localizing prostate cancer was found to be superior to that of TRUS-guided biopsy in the prostate apex and transition zone (15, 16). MRI was also shown to be valuable prior to TRUS-guided biopsy and to improve prostate cancer detection compared to TRUS alone (17, 18). "In-bore" MRI-guided biopsy was recently introduced and has the advantage of enabling direct MRI-guided, targeted biopsies of suspicious areas rather than the traditional ultrasonography (US)-guided systematic biopsies (19, 20). Therefore, the MRI-guided biopsy technique provides an alternative to TRUS-guided biopsy in patients with abnormal PSA values (19, 20). The prostate cancer detection rate of TRUS-guided biopsy decreases with every rebiopsy and increases with the number of cores collected (4, 6, 8). This phenomenon is most likely due to the systematic biopsy approach of TRUS biopsies compared to a targeted biopsy technique, such as direct MRI-guided biopsy, which should not be affected by prior biopsies.

The aims of the present study were to determine the cancer detection rates of MRI-guided biopsy at 1.5 Tesla (T) and to investigate the possible effects of the number of previous TRUS-guided biopsies and of the number of tissue cores sampled. Hence, we analyzed consecutive patients after they underwent at least one negative TRUS-guided biopsy

and who had persistent prostate cancer suspicion due to their constantly elevated or increasing PSA values.

Materials and methods

Patients

Eighty-nine consecutive patients underwent MRI-guided biopsy in our clinic between January 2008 and December 2011. Only patients with at least one negative TRUS-guided biopsy were included in the study. Two patients underwent MRI-guided biopsy for their initial prostate biopsies and were subsequently excluded from the final study population, which consisted of 87 patients. All patients had at least one suspicious lesion on diagnostic endorectal (Medrad® Prostate eCoil™, Bayer Healthcare, Berlin, Germany) MRI examination (1.5 T, Magnetom Avanto or Sonata, Siemens Healthcare, Erlangen, Germany) before MRI-guided biopsy. Exclusion criteria included general contraindications to MRI such as cardiac pacemakers or metal clips, a diagnosis of claustrophobia, acute but also infections of the urinary tract, and decreased blood clotting parameters. All patients gave written informed consent prior to the examination. This study was approved by the local institutional review board of the Charité University Medicine Berlin.

MRI

Prebiopsy multiparametric MRI included an angulated axial T2-weighted turbo spin-echo (TSE) sequence (TR/TE, 4850 ms/85 ms; echo train length [ETL], 15; number of signals acquired, three; field of view [FOV], 160×160 mm), an angulated axial T1-weighted TSE sequence (TR, 691 ms; TE, 12 ms; ETL, three; number of signals acquired, two; FOV, 160×160 mm), and an angulated coronal T2-weighted TSE sequence (TR, 4000 ms; TE, 95 ms; ETL, 13; number of signals acquired, three; FOV, 200×200 mm). All sequences were performed with a 256×256 image matrix, a section thickness of 3.0 mm, an intersection gap of 0.6 mm, and 100% phase oversampling. Furthermore, multiparametric imaging included a multishot echoplanar diffusion-weighted sequence and three orthogonal diffusion gradients (TR, 3200 ms; TS, 59 ms; number of signals acquired, eight; FOV, 200×200 mm; image matrix, 164×164; section thickness, 3.6 mm; b values, 0, 100, 400, and 800 s/mm^2). In a subset of the patients, MR spectroscopy (54 patients) and dynamic contrast-enhanced imaging (60 patients) were performed. Confluent hypointense areas on T2-weighted images were classified as suspicious if the corresponding T1-weighted image was also homogeneously hypointense. Multiparametric data were evaluated together with T2-weighted images. Areas of low signal intensity in the apparent diffusion coefficient maps were classified as suspicious for cancer if morphologic imaging did not show the typical appearance of a hyperplastic nodule in the central gland. Dynamic contrast-enhanced imaging was evaluated using pharmacokinetic parameter maps (K^{trans} and k_{ep}) based on an open two-compartment model (21). An increase in the choline+creatinine-to-citrate ratio was regarded as indicative of cancer in MR spectroscopy (22).

MRI-guided biopsy

Patients with at least one suspicious lesion in the peripheral zone or central gland were considered for MRI-guided biopsy. Approval for the procedure was contingent upon normal blood clotting parameters at least one week before the scheduled biopsy. Prophylactic antibiotics were administered one day prior to MRI-guided biopsy and continued for three days after biopsy. MRI-guided biopsy was performed on a 1.5 T scanner (Magnetom Avanto or Sonata, Healthcare). Images were acquired using combined body and spine phased-array coils. The MRI-guided biopsy protocol was performed as described elsewhere (19). Briefly, patients were placed in the prone position. A needle guide marked with a Gd-chelate gel was inserted rectally and then connected to the arm of the biopsy device (Invivo International, Best, The Netherlands). To localize the lesions detected by prebiopsy diagnostic MRI, a three-dimensional T2-weighted TSE sequence (TR, 1500 ms; TE, 79 ms; number of excitations [NEX], 3; FOV, 240×240 mm; image matrix, 256×256; d, 0.9 mm) was acquired. The isotropic image voxels enabled the simulation of needle guide directions relative to the suspicious target area in the prostate for planning the optimal biopsy direction. The needle guide was directed at the suspicious lesions using the sagittal and oblique T2-weighted rapid acquisition with relaxation enhancement images (TR, ∞; TE, 79 ms; NEX, 2; FOV, 340×306 mm; image matrix, 320×288; d, 5 mm) oriented parallel to the needle guide. Biopsies were obtained using a semiautomatic MRI-compatible, core needle biopsy device (needle length, 15 mm; size, 18 G or 16 G) (Invivo International). Samples were immediately fixed in formaldehyde and processed using standard histopathological techniques. An experienced uropathologist evaluated the samples for prostate cancer.

Statistical analysis

Data are presented as absolute and relative frequencies for categorical variables, and as medians with the associated minimum and maximum values for continuous variables and count data. Comparisons between the groups were analyzed using the Wilcoxon rank sum test for continuous data and the chi-square test based on the Poisson regression for count data. For categorical data comparisons between the groups data were tested by Pearson's Chi-square test or the Fisher Freeman-Halton test. Correlation between the number of prior biopsies and the presence of prostate cancer was evaluated using the Spearman rank correlation coefficient. Two-sided *P* values less than 0.05 were considered to be statistically significant. The D'Amico clinical risk score, which accounts for the PSA and biopsy Gleason score, was determined for each patient with prostate cancer (23). Accordingly, patients were assigned to one of three risk groups: low (Gleason score of 6 and PSA level of up to 10 ng/mL), intermediate (Gleason score of 7 or PSA of 10–20 ng/mL), or high (Gleason score of ≥8 or PSA >20 ng/mL) (23). Calculations were performed using SAS 9.2 (SAS Institute Inc., Cary, North Carolina, USA).

Results

The final study population included 87 patients who had at least one negative TRUS-guided biopsy and persistent

suspicion of prostate cancer due to elevated or increasing PSA levels. The mediean age at biopsy was 66 years (range, 47–78 years). The median PSA value before MRI-guided biopsy was 10.1 ng/mL (range, 2.9–66.1 ng/mL) (Table 1). The median time span between diagnostic MRI and MRI-guided biopsy was 7 days (range, 1–416 days) and 21 days (range, 1–142 days) in patients with and without prostate cancer, respectively ($P = 0.52$).

In total, 302 cores were removed in 87 patients. The median number of removed cores per patient was 3 (range, 1–8) for the entire study population (Fig. 1). No significant difference was found in the number of cores between the patients with (median, 4; range, 1–7) and without prostate cancer (median, 3; range, 1–8) ($P = 0.4809$, Table 1).

Prostate cancer was diagnosed in 36 (42%) patients. Seventy-four (25%) of the 302 prostate cores were positive for cancer (Table 2). Peripheral and transition zone cancers were evident in 42 (57%) and 32 (43%) of the removed cores, respectively. The Gleason scores ranged from 6 (all 3+3) to 10 (Table 2). Gleason scores of 6, 7, and ≥8 were demonstrated in 39, 25, and 10 prostate cancer cores, respectively (Fig. 2). No significant difference was found in the Gleason score and the location of the cancer in either the peripheral or transition zone ($P = 0.0713$, Table 2, Fig. 2). According to the D´Amico clinical risk score, only five patients were in the low-risk group, 16 patients were in the intermediate-risk group, and 15 patients were in the high-risk group (Table 3). No significant difference was found between the risk groups with respect to the prebiopsy history ($P = 0.20$, Table 3 and Fig. 3). Cancer patients with the highest Gleason scores in the transition zone were more likely to belong to the high-risk group, which was statistically significant ($P = 0.002$; Table 3). Of the 36 patients with prostate cancer detected by MRI-guided biopsy, 17 (47%) patients had a Gleason grade of 7 or more (Table 4).

The patients had a median of two negative TRUS-guided biopsy sessions (range, 1–10) before MRI-guided biopsy without a significant difference between the patients with and without cancer ($P = 0.8268$, Table 1). Of the entire study population, prior to MRI-guided biopsy, 24 patients underwent one TRUS-guided biopsy, 25 patients underwent two TRUS-guided biopsies, 18 patients underwent three TRUS-guided biopsies, and 20 patients underwent four or more TRUS-guided biopsies (Fig. 3). No significant difference was found in the cancer detection rates between these groups. The

Table 1. Study population characteristics

	Total (n=87)	Patients with cancer (n=36)	Patients without cancer (n=51)	*P*
Age (years), *median (range)*	66 (47–78)	69 (47–78)	65 (48–77)	0.0048[a]
PSA (ng/mL), *median (range)*	10.1 (2.9–66.1)	13.2 (4.9–47.2)	8.3 (2.9–66.1)	0.0039[a]
Number of prior TRUS-guided biopsies, *median (range)*	2 (1–10)	3 (1–6)	2 (1–10)	0.8268[b]
Collected MRI-guided biopsy cores, *median (range)*	3 (1–8)	4 (1–7)	3 (1–8)	0.4809[b]
Total number of collected cores, *n (%)*	301	130 (43)	171 (57)	-
Number of cores with prostate cancer, *n (%)*	-	74 (56.5)	-	-

[a]Wilcoxon rank sum test; [b]Chi-square test based on Poisson regression.
MRI, magnetic resonance imaging; PSA, prostate specific antigen; SD, standard deviation; TRUS, transrectal ultrasonography.

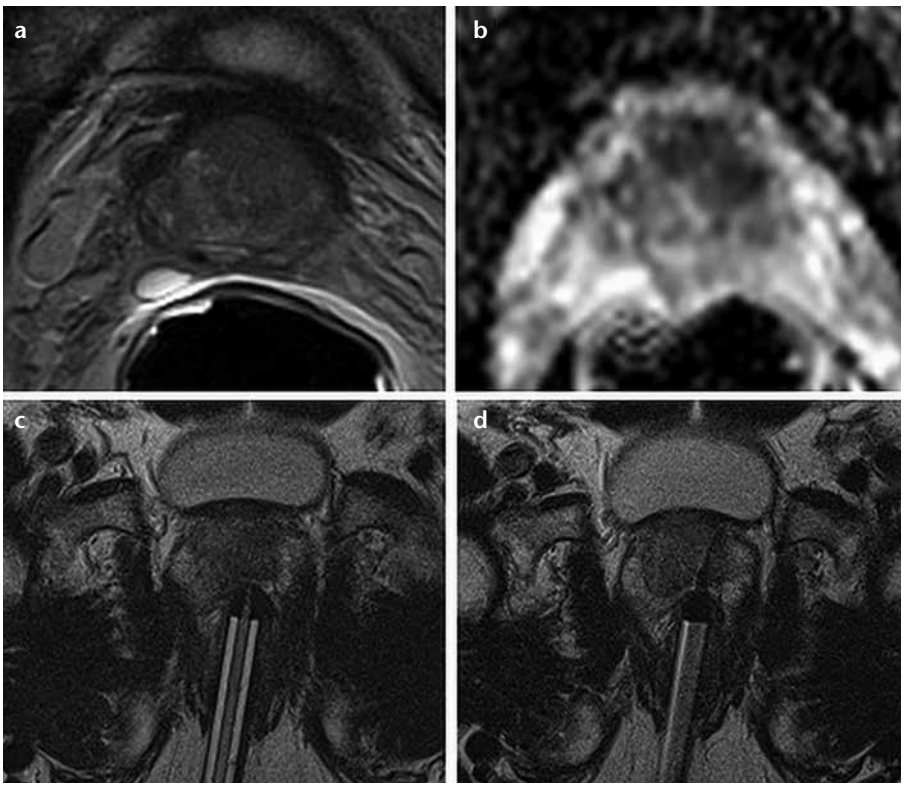

Figure 1. a–d. MRI in a patient with two negative TRUS-guided biopsies and a PSA value of 47.2 ng/mL. The axial T2-weighted image **(a)** shows a low-signal-intensity area in the left anterior aspect of the basal central gland with corresponding diffusion restriction demonstrated by a decreased signal in the axial apparent diffusion coefficient map **(b)**. Four days later, MRI-guided biopsy was performed. After orienting the needle guide towards the suspicious lesion **(c)**, biopsy was performed successfully **(d)**. Histology confirmed an adenocarcinoma of the prostate with a Gleason grade of 3+5.

Table 2. Prostate cancer-positive cores from the peripheral and transition zones with their associated Gleason grades

	Total (n=74)	Peripheral zone (n=42)	Transition zone (n=32)	*P*
Gleason 6, *n (%)*	39 (53)	21 (50)	18 (56)	
Gleason 7, *n (%)*	25 (34)	12 (29)	13 (41)	0.067
Gleason 8–10, *n (%)*	10 (14)	9 (21)	1 (3)	

Table 3. Clinical risk stratification according to the D´Amico clinical risk score of cancer-positive patients

		D´Amico clinical risk score			
	Total (n=36)	Low (n=5)	Moderate (n=16)	High (n=15)	*P*
Peripheral zone, *n (%)*	21 (58.3)	3 (14.3)	14 (66.7)	4 (19.0)	0.002[a]
Transition zone, *n (%)*	15 (41.7)	2 (13.3)	2 (13.3)	11 (73.3)	
Number of previous TRUS biopsies, *median (range)*	3 (1–6)	2 (1–6)	3 (1–6)	2 (1–4)	0.20[b]

[a]Fisher Freeman-Halton test; [b]Wilcoxon rank sum test.
TRUS, transrectal ultrasonography.

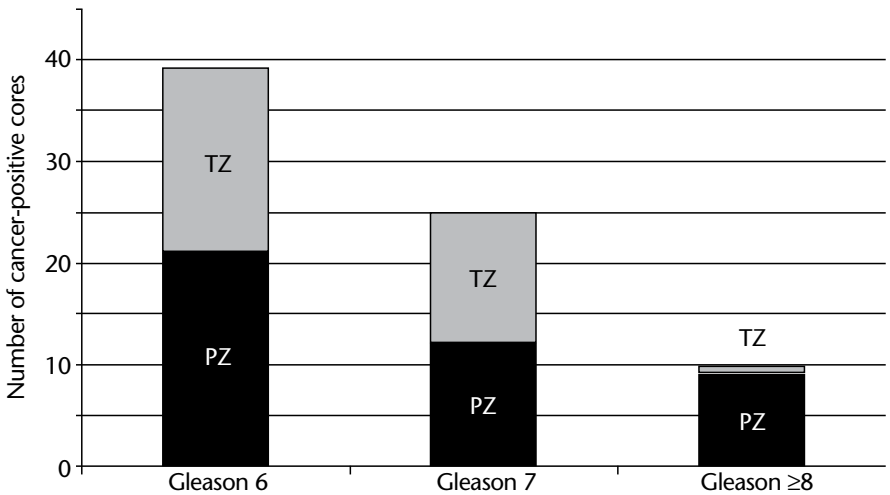

Figure 2. The number of peripheral (PZ) and transition zone (TZ) cancer cores vs. the Gleason score.

cancer detection rates for patients with one, two, three, and four or more negative TRUS-guided biopsies were 29.2%, 40.0%, 66.7%, and 35.0%, respectively (P = 0.087, Fig. 3, Table 4). Furthermore, no significant correlation was found between the number of TRUS-guided biopsies and the cancer detection rate (P = 0.29).

Discussion

TRUS is the most extensively studied and widely used imaging modality for guiding prostate biopsies. TRUS-guided biopsies are the gold standard for detecting prostate cancer. The old, standard 6-core TRUS-guided biopsy approach obtains mainly midlobar parasagittal cores and is not sufficient for detecting prostate cancer (24, 25). For TRUS-guided biopsies, higher detection rates can be achieved by increasing the number of core samples (6, 7, 26). Studies performed with a sampling of up to 21 cores by TRUS-guided biopsy yielded higher detection rates than biopsy regimens involving the removal of fewer cores (8). Cancer detection rates increase from 22.7% with the 6-core biopsy regimen to up to 31.3% with the 21-core biopsy regimen (8). The authors reported an almost linear increase in the detection rate with an increase in the core number, reflecting the systematic nature of biopsy sampling.

MRI-guided biopsy is an alternative method for patients with at least one negative TRUS-guided biopsy and persistent suspicion of prostate cancer. In MRI-guided biopsy, suspicious lesions of the prostate are localized in advance; in addition, targeted biopsies are collected under MRI guidance (19, 20, 27). Therefore, prostate cores are removed directly and only from the suspicious areas of the prostate rather than in a systematic fashion. In the present study, the targeted biopsy approach using MRI-guided biopsy resulted in a low number of removed cores (median, 3, range 1–8). Accordingly, our results are similar to those of other groups, who reported an average of 4 to 5 removed cores using MRI-guided biopsy at 1.5 T (28–30). However, the present study also demonstrates explicitly that no significant relationship exists between the number of removed cores and the detection of prostate cancer, underlining the targeted nature of MRI-guided biopsy. By only removing cores from suspicious areas, the MRI-guided biopsy technique achieves a high detection rate (42%). These findings support that MRI-guided biopsy is an effective and minimally invasive alternative for patients with continued suspicion of disease despite previous negative tests.

In the present study, we detailed the detection rates of prostate cancer in relation to the number of prior negative TRUS-guided biopsies, which is the first study of its kind. We found no significant effect from the number of prior negative TRUS-guided biopsies on the prostate cancer detection by MRI-guided biopsy. For TRUS-guided biopsies, the detection rate decreases with the number of biopsies performed; detection rates of 10%, 5%, and 4% have been reported for the first, second, and third rebiopsies, respectively (4). In fact, in the present study, the detection rates of MRI-guided biopsy were 29%, 40.0%, 66.7%, and 35.0% in the first,

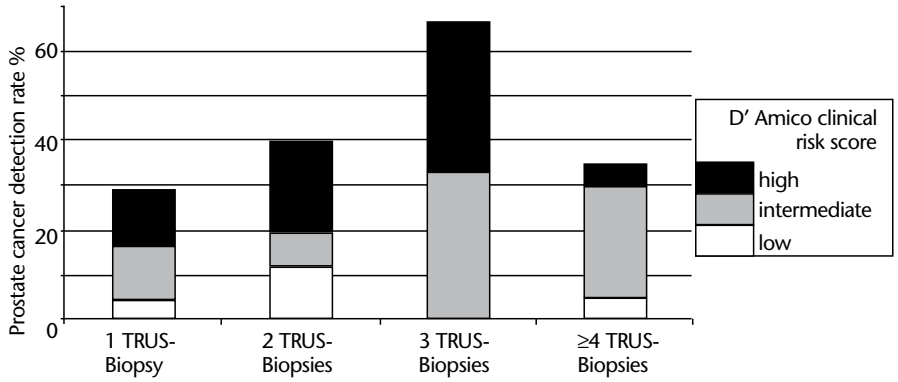

Figure 3. The prostate cancer detection rate (%) of MRI-guided biopsy was not significantly different between the groups ($P = 0.087$). Y-axis shows number of prior TRUS-guided biopsies. The majority of the patients were at an intermediate or high risk (31 of 36 cancer patients), and the groups did not have a significant difference in the number of negative TRUS-guided biopsies ($P = 0.20$). Even after three negative biopsies, 50% of patients detected by MRI-guided biopsy were at a high risk according to the D´Amico clinical risk score.

Table 4. Detection rate of prostate cancer with respect to number of previous TRUS-guided biopsies

	Number of of previous TRUS-guided biopsies				
	1	2	3	≥4	*P*
Total number, *n (% of whole study population)*	24 (27.6)	25 (28.8)	18 (20.1)	20 (23.0)	-
Detection rate, *n (% column)*	7 (29.2)	10 (40.0)	12 (66.7)	7 (35.0)	0.087
Gleason score, *n*					
6	3	5	6	5	0.7836
≥7	4	5	6	2	

second, third, and fourth or more rebiopsies, respectively. Unlike TRUS-guided biopsy, MRI-guided biopsy is a targeted biopsy technique, which likely explains the constant high detection rates of prostate cancer, which are independent of the number of previous negative TRUS biopsies and removed prostate cores. MRI-guided biopsy can be utilized as a primary or secondary rebiopsy technique because the available data imply that there are higher detection rates from one MRI-guided biopsy compared to TRUS-guided repeat biopsies, up to the third rebiopsy (4).

Only four 1.5 T MRI-guided biopsy studies, with a total of 176 patients, have been previously published (19, 28, 30, 31). The reported overall detection rates ranged between 42% and 55% with a high proportion of transition zone cancers, accounting for 35% of removed cores. Our results confirm these findings, demonstrating a high proportion of transition zone cancers (43% on a core basis and 42% on a patient basis). The high fraction of transition zone cancers detected by MRI and MRI-guided biopsy is likely due to a selection bias because cancers localized in the anterior part of the prostate are more likely to be missed using systematic TRUS-guided biopsy approaches (27, 32). This phenomenon is supported by our data; patients with a prostate cancer index lesion in the transition zone significantly more often belonged to the high risk group according to the D´Amico clinical risk score (Table 3). In this study, 19 patients had a low-grade prostate cancer with a Gleason score of 3+3=6. However, almost one in two cancer patients (n=17) in our study population had a more aggressive cancer with a Gleason score of 7 or higher. More importantly, according to the D´Amico clinical risk score, 31 of 36 patients were at intermediate or high risk (16 and 15 patients, respectively) but had a median of two or three prior negative systematic TRUS-guided biopsy sessions, which emphasizes the clinical benefit of MRI-guided biopsy for a high proportion of patients with aggressive prostate cancer.

The present study has some limitations. Because diagnostic MRI is necessary prior to MRI-guided biopsy, this study and others are limited by selection bias (33). All of the patients in our study had at least one suspicious lesion upon MRI. The sensitivity of prostate MRI depends on the Gleason score and tumor size, which in turn might be attributed to the preselection of clinically relevant cancers.

One concern regarding MRI-guided biopsy is the cost effectiveness compared to the less expensive TRUS-guided biopsy procedure. MRI-guided biopsy is not currently the primary biopsy technique for patients with elevated PSA values and suspicion of cancer; however, MRI-guided biopsy should be considered as a rebiopsy technique in patients with the aforementioned diagnostic dilemma of persistent cancer suspicion despite a negative primary biopsy. Furthermore, the present study indicates that MRI-guided biopsy may be more suitable as a first line rebiopsy technique than a TRUS-guided saturation biopsy because it is less invasive and has a high detection rate. However, two issues need to be addressed in future studies: 1) determining the optimal and most cost-effective time point for referring patients for MRI-guided biopsy and 2) whether MRI-guided biopsy is indeed more expensive than TRUS when factoring in the differences in the detection rates as well as the avoidance of unnecessary TRUS-guided biopsies (33). Part of the solution may be to utilize MRI in routine, diagnostic imaging for patients with suspected prostate cancer. Combining MRI and real time TRUS-guided biopsy using fusion techniques in selected patients might prove to be an effective diagnostic strategy for optimizing diagnostic accuracy and cost-effectiveness (34). A recently introduced real-time MRI/US fusion technique has been reported to yield promising prostate cancer detection rates of up to 34% (35). Notably, however, MRI was conducted at 3 T in that study, which might have improved the diagnostic accuracy of the

multiparametric MRI and MRI-guided biopsy compared to MRI and biopsy collection performed at 1.5 T. Indeed, MRI-guided biopsy detection rates at 3 T are up to 59% (29). Prospective randomized head-to-head comparisons of MRI-guided biopsy and MRI/US fusion biopsy should be conducted in the future with respect to prostate cancer detection rates, Gleason up- and downgrading and the complications and cost-effectiveness of methods.

In conclusion, the present study demonstrates that MRI-guided biopsy has a constant, high cancer detection rate independent of the number of previous negative TRUS biopsy sessions as well as the number of removed prostate cores. Assuming that MRI-guided biopsy provides an accurate diagnosis in a high proportion of patients while being less invasive than repeated TRUS-guided biopsies, this technique is an attractive alternative diagnostic tool for the selected group of patients who have at least one negative prior TRUS-guided biopsy and persistent suspicion of prostate cancer.

Acknowledgements

The authors thank Bettina Herwig for proofreading the manuscript and Dr. Carsten Schwenke for statistical assistance.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin 2010; 60:277–300. [CrossRef]
2. Farwell WR, Linder JA, Jha AK. Trends in prostate-specific antigen testing from 1995 through 2004. Arch Intern Med 2007; 167:2497–2502. [CrossRef]
3. Moyer VA. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012; 157:120–134. [CrossRef]
4. Djavan B, Ravery V, Zlotta A, et al. Prospective evaluation of prostate cancer detected on biopsies 1, 2, 3 and 4: when should we stop? J Urol 2001; 166:1679–1683. [CrossRef]
5. Bouye S, Potiron E, Puech P, Leroy X, Lemaitre L, Villers A. Transition zone and anterior stromal prostate cancers: zone of origin and intraprostatic patterns of spread at histopathology. Prostate 2009; 69:105–113. [CrossRef]
6. 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; 45:444–449. [CrossRef]
7. Pepe P, Aragona F. Prostate needle biopsy: 12 vs. 18 cores -- is it necessary? Urol Int 2005; 74:19–22. [CrossRef]
8. 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. [CrossRef]
9. Heijmink SW, Barentsz JO. Contrast-enhanced versus systematic transrectal ultrasound-guided prostate cancer detection: an overview of techniques and a systematic review. Eur J Radiol 2007; 63:310–316. [CrossRef]
10. Hong YM, Lai FC, Chon CH, McNeal JE, Presti JC Jr. Impact of prior biopsy scheme on pathologic features of cancers detected on repeat biopsies. Urol Oncol 2004; 22:7–10. [CrossRef]
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. [CrossRef]
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. [CrossRef]
13. Turkbey B, Bernardo M, Merino MJ, Wood BJ, Pinto PA, Choyke PL. MRI of localized prostate cancer: coming of age in the PSA era. Diagn Interv Radiol 2012; 18:34–45.
14. Iwazawa J, Mitani T, Sassa S, Ohue S. Prostate cancer detection with MRI: is dynamic contrast-enhanced imaging necessary in addition to diffusion-weighted imaging? Diagn Interv Radiol 2011; 17:243–248.
15. 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. [CrossRef]
16. Mullerad M, Hricak H, Kuroiwa K, et al. Comparison of endorectal magnetic resonance imaging, guided prostate biopsy and digital rectal examination in the preoperative anatomical localization of prostate cancer. J Urol 2005; 174:2158–2163. [CrossRef]
17. Kumar V, Jagannathan NR, Kumar R, et al. Transrectal ultrasound-guided biopsy of prostate voxels identified as suspicious of malignancy on three-dimensional (1)H MR spectroscopic imaging in patients with abnormal digital rectal examination or raised prostate specific antigen level of 4-10 ng/ml. NMR Biomed 2007; 20:11–20. [CrossRef]
18. Yagci AB, Ozari N, Aybek Z, Duzcan E. The value of diffusion-weighted MRI for prostate cancer detection and localization. Diagn Interv Radiol 2011; 17:130–134.
19. Beyersdorff D, Winkel A, Hamm B, Lenk S, Loening SA, Taupitz M. MR imaging-guided prostate biopsy with a closed MR unit at 1.5 T: initial results. Radiology 2005; 234:576–581. [CrossRef]
20. Hambrock T, Futterer JJ, Huisman HJ, et al. Thirty-two-channel coil 3T magnetic resonance-guided biopsies of prostate tumor suspicious regions identified on multimodality 3T magnetic resonance imaging: technique and feasibility. Invest Radiol 2008; 43:686–694. [CrossRef]
21. Tofts PS, Kermode AG. Measurement of the blood-brain barrier permeability and leakage space using dynamic MR imaging. 1. Fundamental concepts. Magn Reson Med 1991; 17:357–367. [CrossRef]
22. Kurhanewicz J, Vigneron DB, Hricak H, Narayan P, Carroll P, Nelson SJ. Three-dimensional H-1 MR spectroscopic imaging of the in situ human prostate with high (0.24-0.7-cm^3) spatial resolution. Radiology 1996; 198:795–805.
23. D'Amico AV, Moul J, Carroll PR, Sun L, Lubeck D, Chen MH. Cancer-specific mortality after surgery or radiation for patients with clinically localized prostate cancer managed during the prostate-specific antigen era. J Clin Oncol 2003; 21:2163–2172. [CrossRef]
24. Norberg M, Egevad L, Holmberg L, Sparen P, Norlen BJ, Busch C. The sextant protocol for ultrasound-guided core biopsies of the prostate underestimates the presence of cancer. Urology 1997; 50:562–566. [CrossRef]
25. Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. J Urol 1997; 157:199–202. [CrossRef]
26. Taylor JA 3rd, Gancarczyk KJ, Fant GV, McLeod DG. Increasing the number of core samples taken at prostate needle biopsy enhances the detection of clinically significant prostate cancer. Urology 2002; 60:841–845. [CrossRef]
27. Park BK, Lee HM, Kim CK, Choi HY, Park JW. Lesion localization in patients with a previous negative transrectal ultrasound biopsy and persistently elevated prostate specific antigen level using diffusion-weighted imaging at three Tesla before rebiopsy. Invest Radiol 2008; 43:789–793. [CrossRef]
28. Anastasiadis AG, Lichy MP, Nagele U, et al. MRI-guided biopsy of the prostate increases diagnostic performance in men with elevated or increasing PSA levels after previous negative TRUS biopsies. Eur Urol 2006; 50:738–739. [CrossRef]
29. Hambrock 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. [CrossRef]

30. 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. [CrossRef]
31. Engelhard K, Hollenbach HP, Kiefer B, Winkel A, Goeb K, Engehausen D. Prostate biopsy in the supine position in a standard 1.5-T scanner under real time MR-imaging control using a MR-compatible endorectal biopsy device. Eur Radiol 2006; 16:1237–1243. [CrossRef]
32. Deliveliotis C, Varkarakis J, Albanis S, Argyropoulos V, Skolarikos A. Biopsies of the transitional zone of the prostate. Should it be done on a routine basis, when and why? Urol Int 2002; 68:113–117. [CrossRef]
33. Scheidler J, Weores I, Brinkschmidt C, et al. Diagnosis of prostate cancer in patients with persistently elevated PSA and tumor-negative biopsy in ambulatory care: performance of MR imaging in a multi-reader environment. Rofo 2012; 184:130–135. [CrossRef]
34. Singh AK, Kruecker J, Xu S, et al. Initial clinical experience with real-time transrectal ultrasonography-magnetic resonance imaging fusion-guided prostate biopsy. BJU Int 2008; 101:841–845. [CrossRef]
35. 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. Rofo 2013; 185:428–433.