

# Accuracy of MRI-Targeted in-Bore Prostate Biopsy According to the Gleason Score with Postprostatectomy Histopathologic Control—a Targeted Biopsy-Only Strategy with Limited Number of Cores

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### **Abbreviations**

ADC

apparent diffusion coefficient

DCE

dynamic contrast enhanced

DWI

diffusion-weighted imaging

MRI

magnetic resonance imaging

PI-RADS

prostate imaging–reporting and data system

**PSA** 

prostate-specific antigen

RP

radical prostatectomy

trueFISP

true fast imaging with steadystate precession

TRUS

transrectal ultrasound

Rationale and Objectives: Accuracy of ultrasound-guided biopsy and Gleason score is limited, and diagnosis of insignificant cancer with Gleason score ≤6 is frequent when extended biopsy schemes are used. We evaluated whether the magnetic resonance imaging (MRI)-targeted in-bore prostate biopsy correctly identifies the Gleason score of prostate cancer in histopathologic correlation after prostatectomy. Simultaneously a targeted concept is expected to keep down the rate of insignificant cancer.

Materials and Methods: We compared retrospectively the Gleason score of the MRI-targeted in-bore biopsy with prostatectomy specimens in 50 men with prostate cancer. Endorectal MRI included T2-weighted imaging, diffusion-weighted imaging, dynamic contrast-enhanced imaging, and spectroscopy. Lesions with a prostate imaging–reporting and data system (PI-RADS) score ≥3 were considered. Upgrading and downgrading of tumors was evaluated, and significant upgrading was defined as a shift in Gleason score from 6 to 7 or more.

**Results:** Gleason score was concordant in 66% of the patients, overall upgraded in 30% of patients, and downgraded in 4% of patients. Significant upgrading of the Gleason score from 6 to 7 occurred in eight patients; upgrading did not exceed one step in the Gleason score. After prostatectomy the Gleason score 6 was found in 20% of patients. The median number of cores obtained was 4 (range 2–6), and the median number of positive cores was 2 (range 1–4).

**Conclusions:** In-bore MRI-targeted biopsy offers good accuracy in the Gleason score with postprostatectomy histopathologic control when compared to the literature. A limited number of cores are sufficient to achieve these results. The fraction of insignificant cancer identified by targeted only-biopsy is low. Upgrading is restricted to one step in the Gleason score. Clinicians should be aware of positive findings in MRI and the biopsy technique used when assessing prostate biopsy results.

**Key Words:** Magnetic resonance imaging; interventional; prostatic neoplasms; prostate biopsy; neoplasm grading.

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Prostate cancer has become the most common cancer among men. Widespread use of prostate-specific antigen (PSA) screening has led to an increasing number of diagnoses and at the same time to an increasing detection rate of insignificant cancer. Prediction of cancer significance is predominantly based on the Gleason score. According to

the Consensus Conference on Gleason grading, the Gleason score combines the most frequent and the highest Gleason grade in biopsy and the most frequent and second most frequent Gleason grade in prostatectomy specimens (1).

Now there are alternative treatment options to radical prostatectomy (RP) such as radiation therapy or active surveillance. Appropriate treatment depends on preoperative tumor grading in biopsy specimens.

However, the significance of the Gleason score in transrectal ultrasound (TRUS)-guided biopsies is controversial for prognostic evaluation of prostate cancer. TRUS-guided biopsies comprise systematically distributed cores that are more or less blindly obtained. Tumors are often heterogenous, thus the Gleason score identified by biopsy may not reflect the Gleason score of the entire tumor.

The accuracy of TRUS-guided biopsies in Gleason grading compared to prostatectomy specimens has remained limited over the past years with a rate of 63% in a meta-analysis (2). Upgrading from transrectal prostate biopsy to higher Gleason scores in RP has been reported up to 60% (2-12). In clinical decision-making, the classification of low-grade and highgrade cancer plays an important role. Significant upgrading means a shift from insignificant to significant cancer. However, definitions of insignificant cancer are controversial and may represent the Gleason score <7 or ≤7a (=3 + 4). Biopsyrelated tumor grading may lead to undertreatment of patients, whereas downgrading after prostatectomy indicates the risk of overtreatment of patients (3,5). Upgrading the Gleason score after prostatectomy is related to aggressive tumors and higher risk for biochemical recurrence, so an optimization of biopsy strategies is required (4).

It is assumed that Gleason undergrading may be attributed not only to tumor biology but also to sampling error in TRUS biopsy, as the cores are randomly distributed (10,13). Extended TRUS-guided biopsy schemes with at least 10–12 cores are recommended for standard care in the guidelines of the European Association of Urology. On the other hand, magnetic resonance imaging (MRI) diagnostic and MRI-targeted biopsy are proposed in negative prostate biopsies with persistent clinical signs (14).

Targeted biopsy may increase accuracy in Gleason tumor grading to better identify significant cancer. In this context, multiparametric MRI of the prostate involving functional parameters has shown high potential for tumor localization and for MRI-targeted biopsy (15). Particularly, diffusion-weighted imaging (DWI) and spectroscopy have shown a correlation to prostate cancer aggressiveness when used for direction of TRUS biopsies (16). Furthermore, MRI-targeted biopsy is presumed to decrease the diagnosis of insignificant prostate cancer (17).

Some techniques use additional MRI datasets for visual direction in TRUS or fusion software (18) with improved results. At the same time the number of cores is further increased compared to conventional TRUS biopsy.

Haffner et al. (19) suggested a targeted biopsy-only strategy instead of extended biopsy schemes to avoid unnecessary

prostate biopsies and to avoid potentially unnecessary diagnosis of insignificant prostate cancer.

Cancer detection rates depend heavily on patient selection. In contrast, comparing the Gleason score in biopsy with prostatectomy specimens reflects accuracy of the method and may better show the clinical impact of MRI in diagnostic of prostate cancer. There has been abundant research investigating the accuracy of Gleason score in TRUS biopsy (2–13,20–22). Evaluation of the accuracy of Gleason score in MRI fusion biopsy combined to TRUS biopsy (15,16,18,23,24) and particularly in MRI-targeted biopsy-only strategy (25) seems interesting in this context, but to date only a limited number of studies have been reported.

In a retrospective analysis, we evaluated Gleason scores of MRI-targeted in-bore prostate biopsy and Gleason scores of matched prostatectomy specimens to determine the accuracy of preoperative tumor grading by an MRI-targeted biopsy alone. Simultaneously a targeted concept with a reduced number of cores was expected to keep down the rate of insignificant cancer. Results are compared to data published for different biopsy techniques.

### MATERIALS AND METHODS

### **Patients**

Between November 2007 and May 2014, 177 patients underwent multiparametric MRI and MR-targeted in-bore biopsy because of suspected lesions. The institutional review board approved the study. Prostate cancer was found in 64 patients, 52 of these patients had surgery with RP. Two patients had to be excluded because of neoadjuvant therapy, thus data from 50 patients with proven cancer and histopathologic examination after RP were available for analysis (Fig 1).

# **Imaging**

Diagnostic MRI was performed on a 1.5 Tesla wide bore system (ESPREE; Siemens Healthcare, Erlangen, Germany) using an endorectal coil combined to a six-channel body array and an eight-channel spine coil. Our standard protocol fulfilling the requirements of Consensus Meeting on the Standardization of Prostate MRI (26) included T2-weighted imaging in three planes (slice thickness 3 mm), DWI, dynamic contrast-enhanced (DCE) imaging, and spectroscopy (Fig 2). DWI was performed using four b-values (0, 100, 800, and 1400 s/mm<sup>2</sup>), apparent diffusion coefficient was calculated from b = 0, 100, and 800 s/mm<sup>2</sup>, the additional b1400 s/mm<sup>2</sup> sequence was used for further visual interpretation. Volume interpolated gradient echo sequences with a temporal resolution of 8 seconds were used for DCE. Gadoteric acid was applied as contrast-media in a weight-adapted standard dose (0.1 mmol/kg body weight) with an injection rate of 3 mL/s. Postprocessing of DCE datasets was carried out on a syngo Multimodality Workplace with Tissue 4D (Siemens, Erlangen, Germany) with color-coded Ktrans

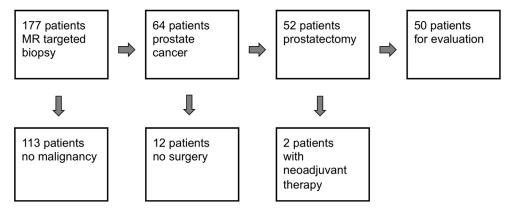
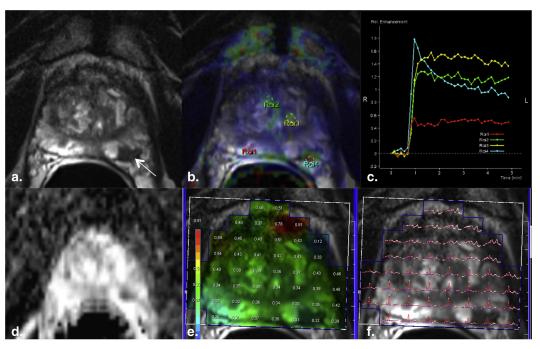


Figure 1. Flowchart of patient selection.



**Figure 2.** Multiparametric diagnostic imaging, prostate carcinoma in left peripheral zone (*arrow* in **a**) with Gleason score 7: **(a)** T2-weighted TSE axial, **(b)** pharmacokinetic analysis—color-coded ktrans fused to T2-weighted TSE, **(c)** perfusion curves of regions of interest in **(b)**, blue = highest peak in lesion left peripheral zone, **(d)** apparent diffusion coefficient map, and **(e** and **f)** spectroscopy analysis with citrate/ (creatine + choline) ratio. TSE, Turbo spin echo. Color version of figure is available online. (Color version of figure is available online.)

maps and curve evaluation according to the Tofts pharmacokinetic model (27).

Evaluation was performed by two MRI experienced radiologists, after introduction of the prostate imaging–reporting and data system (PI–RADS) (28) lesions with a score ≥3. Cases of the start-up phase were retrospectively reviewed, and all target lesions could be corresponded to a diagnostic score ≥PI–RADS 3.

# **Biopsy**

Biopsy was performed on the same 1.5 Tesla system in a second session allowing a detailed lesion detection according to the PI-RADS in the diagnostic imaging and an accurate biopsy planning. An adjustable needle guide was inserted

transrectally with the patient in supine position (Fig 3) lying on a biopsy positioning device (Invivo, Schwerin, Germany) with two six-channel body arrays. Landmarks were defined for navigation in an axial T2-weighted sequence in correlation to the preceding diagnostic MRI (Fig 4a). The needle guide was positioned under the control of sagittal and coronal true fast imaging with steady-state precession (Fig 4b and c) sequences (see biopsy protocol in Table 1). Thereby an iterative procedure was performed. After correct positioning of the guiding system an 18 G MR compatible needle fully automatic biopsy gun with a needle length of 150 or 175 mm (Invivo) was inserted. The number of cores obtained depended on the number of suspected lesions in the preceding diagnostics. In patients with lesions in only one side of the prostate, an additional core from the contralateral side was



**Figure 3.** Biopsy positioning device with adjustable needle guide, prepared for patient in the supine position, wide bore MR scanner. (Color version of figure is available online.)

taken. Each needle position was controlled carefully by fast T2-weighted imaging in axial and sagittal plane (Fig 4d and e) to exclude errors caused by patient movement and to confirm the position of the notch inside the lesion. If necessary a second core was obtained in the same lesion.

Of all 177 subjects, one experienced fever after the procedure with possible prostatitis. The correlation to the procedure was not certain because of a febrile infection of his family at the time. Moreover, no major complications occurred.

# Data Analysis

All biopsy specimens were examined in the same histopathologic institute. Histopathologic evaluation was performed according to the modifications of the Consensus Conference on Gleason grading of prostatic carcinoma (1). According to the site of surgery chosen by the patient, the prostatectomy specimens were assigned to different histopathologic institutes. The core with the highest Gleason score was selected in biopsy and the area with the highest Gleason score in prostatectomy specimen was selected for comparison. A tertiary pattern in RP specimens was not evaluated.

Upgrading was defined as a shift from one Gleason score to the next higher score, and downgrading was defined as a shift to the next lower score. Additionally, significant upgrading was evaluated from the group of low-grade tumor (Gleason score  $\leq$ 6) to a high-grade tumor (Gleason score  $\geq$ 7).

# **RESULTS**

Table 2 shows patient characteristics. Patients were aged 47–80 years (median 66 years), and had a PSA in a range from 3.03 to 38.8 ng/mL (median 8 ng/mL). Prostate volume was measured between 20 and 79 mL (median 36.5 mL). PSA density was 0.09–0.90 ng/mL<sup>2</sup> (median 0.24 ng/mL<sup>2</sup>). Time between biopsy and surgery was 12–106 days (median

38.5 days). Under MR guidance 2–6 (median 4) cores were obtained in each patient, in 1–4 cores per patient (median 2) malignancy were shown. Tumor percentage of cores was between 3 and 100 (median 33%). Fifteen of 50 patients (30%) had TRUS-guided biopsy before, and nine of these 15 patients had more than one TRUS-guided biopsy before.

In 15 of 50 cases (30%) biopsy and prostatectomy specimens were evaluated both in the same institute.

Concordant Gleason score between the biopsy and prostatectomy specimens was achieved in 33 of 50 patients (66%), upgrading in the Gleason score was necessary in 15 of 50 patients (30%), and four of these 15 patients were patients with TRUS biopsy before. Downgrading occurred in two of 50 patients (4%). Upgrading of the Gleason score from 6 to 7 was found in eight of 18 patients (44%), and in no case upgrading did exceed one step in the Gleason score. The percentage of patients with prostatectomy grade of the Gleason score ≤6 was 10 of 50 patients (20%). Table 3 shows the detailed results.

### DISCUSSION

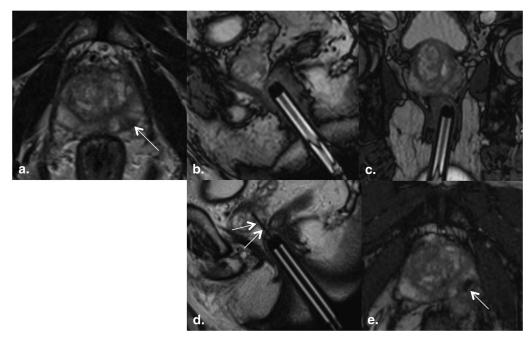
# **Overall Accuracy**

Our results show an accuracy of 66% for the Gleason score of in-bore MRI-targeted biopsies compared to matched prostatectomy specimens. Compared to data published for accuracy of the Gleason score in prostate biopsy (see Table 4) this is higher than most TRUS-related studies.

However, in 2005 the Gleason scoring system was modified for biopsies in the Consensus Conference of the International Society of Urological Pathology. The original system graded the tumor by listing the most common and second most common Gleason pattern in contrast to the modified system in which the most common and the highest grade is recorded (1). Accordingly, a better agreement of the Gleason score of needle biopsy and prostatectomy specimens is expected. Data from a large cohort of 7643 patients based on the updated Gleason system indicated an overall accuracy of 73% (5566/7643 patients). This was at the same time related to a high percentage of insignificant cancer (50% with Gleason score ≤6) (3).

Other recently published studies had an accuracy of 62% (4) and 44% (5).

It is widely expected that increasing the number of cores should overcome the sampling error and would increase the accuracy in Gleason scoring. Numao et al. presented an extraordinary accuracy of 92.3% in a 26-core prostate biopsy that contained a combination of transperineal 14-core biopsy and transrectal 12-core biopsy under spinal or general anesthesia. However, these results are only related to the presence or absence of Gleason 4/5 pattern and the procedure is markedly invasive (20). The median number of cores taken in our study was 4 (range 3–5) compared to at least sextant biopsies in TRUS-guided biopsies. An increase in accuracy of up to 57% could be seen with at least 10 cores (7). At the same time in 15% of



**Figure 4.** MRI-targeted biopsy of left peripheral zone lesion (*arrow* in **a**), prostate carcinoma with Gleason score 7 in biopsy and postoperative histology: (a) T2-weighted axial without endorectal coil, (b and c) trueFISP sagittal and coronal for navigation of needle holder, (d) BLADE sagittal for control of needle and notch position (*arrows*), and (e) trueFISP axial for verification of the needle position inside the lesion (*arrow*). MRI, magnetic resonance imaging; trueFISP, true fast imaging with steady-state precession.

the patients the Gleason score differed by more than one point. Another study found a higher accuracy only when differences of only one step in the Gleason score were ignored (6).

Nevertheless our results still show a higher accuracy with a reduced number of cores and in no case did the difference exceed one step in the Gleason score.

A combination of systematic biopsy and targeted biopsy by means of fusion of MRI with ultrasound showed an accuracy of 46% and 52% for each biopsy method alone and 72% for the combination of both in 54 patients. A mean of 18 cores was obtained and the fraction of insignificant cancer was low (13%), probably because of the study population in which only 54 of all 276 patients with a biopsy were elected for prostatectomy (18). Data of Baco et al. (23) indicated an accuracy of 80% by a combination of MRI fusion and random biopsies. However, the number of cores obtained was not specified and again the low fraction of insignificant cancer may be linked to a high percentage of men (67% of prostate cancer patients) with nonsurgery therapy. This fraction was 19% (12/64 patients) in the present study.

To the best of our knowledge, there is only one study evaluating in-bore MR-targeted biopsy for the Gleason score accuracy compared to prostatectomy specimens as the gold standard. Hambrock et al. (25) also performed a true-targeted biopsyonly strategy with a mean of three cores taken in 34 patients, highest Gleason grades were evaluated instead of the Gleason score, which may have favored the high accuracy of 88%. The fraction of insignificant cancer (35%) is relatively high compared to other studies with a targeted approach (18,23) and compared to

other contemporary TRUS studies (5,10). This may be because of the patient selection with previous negative TRUS biopsy.

# Upgrading

The rate of upgrading (30%) was much higher in our small population than downgrading (4%).

Our upgrading results are in the range of the meta-analysis of Cohen et al. (2) who reported 30%. Slightly better results with 29% were published using a median of eight cores (4) and with more than six cores (8), respectively. In both studies, a considerable proportion of the patients (12% and 14%, respectively) showed a shift of more than one Gleason point. In contrast, in our study, no patient exceeded one Gleason point.

Other results in the more recent literature reported an upgrading of up to 57% considering even extended biopsy schemes (2,5–7,9,10).

# Significant Upgrading

There are different classifications for significant upgrade, often reported as a shift in Gleason score from 6 to 7 or more, some authors consider the Gleason score 7 to be of intermediate significance (2). In a more contemporary definition, different prognostic grades are attributed to Gleason scores 7a (3 + 4) and 7b (4 + 3) (3,23).

Confining our findings to the classic definition as a shift in Gleason score from 6 to 7 or more, we found a significant upgrade in eight of 18 patients (44%).

**FABLE 1. MRI Protocol for MR-Targeted In-bore Prostate Biopsy** 

Objective	Sequence	Plane	TR/TE (msec)	Slice TR/TE (msec) Thickness (mm) Matrix	Matrix	FOV (mm)	FOV (mm) Voxel Size (mm)	Flip Angle	Time of Flip Angle Acquisitions PAT Acquisition	PAT	Time of Acquisition
Planning of slice orientation	trueFISP	Axial, coronal, 4.2/2.1 msec sagittal	4.2/2.1 msec	3.5	256 × 256	400 × 400	$256 \times 256 \ \ 400 \times 400 \ \ 1.6 \times 1.6 \times 3.5$	22	-	2	45 seconds
Define landmarks	T2-weighted Axial	Axial	4930/100	က	$205\times256$	200 × 200	$200\times200 1.0\times0.8\times3.0$		-		1:53 minutes
Navigation of needle holder	trueFISP	Sagittal and coronal	4.2/2.1	3.5	256 × 256	400 × 400	$256 \times 256  400 \times 400  1.6 \times 1.6 \times 1.6 \times 3.5$	25	-	0	27 seconds
(Fig 4b and c) Control of needle	BLADE	Sagittal	4260/138	ო	$320\times320$	420 × 420	$320 \times 320 \ \ 420 \times 420 \ \ 1.3 \times 1.3 \times 3$	148	-	7	34 seconds
Control of needle position (Fig 4e)	trueFISP	Axial	4.5/2.3	3.5	384 × 384	400 × 400	$384 \times 384 \ \ 400 \times 400 \ \ 1.0 \times 1.0 \times 3.5$	22	7	8	39 seconds

BLADE, proprietary name for periodically rotated overlapping parallel lines with enhanced reconstruction; FOV, field of view; MRI, magnetic resonance imaging; PAT, parallel imaging techilque; TE, echo time; TR, repetition time; trueFISP, true fast imaging with steady-state precession; TSE, turbo spin echo.

TABLE 2. Patient Characteristics			
Variable	Mean	Median	Range
Age (years)	66	66	47–80
PSA (ng/mL)	10.79	8	3.03-38.8
Prostate volume (mL)	40.5	36.5	20-79
PSA density (ng/mL <sup>2</sup> )	0.28	0.24	0.09-0.9
Time between biopsy and surgery (days)	39.78	38.5	12–106
Biopsy cores obtained per patient	3.96	4	2-6
Cores with tumor per patient	2.4	2	1–4
Tumor length per core (mm)	4.47	4	0.3-15
Tumor percentage per core (%)	39.8	33	3-100

PSA, prostate-specific antigen.

Although the rates of significant upgrading in TRUS-guided biopsies in the literature (20%–67%) are to some extent lower than our findings, all these studies included upgrading of the Gleason score from 5–6 to 8 and 9–10, whereas in our study we found only upgrading of one step to the next higher Gleason score. For the individual patient, this is of high importance. This is partly in line with the MRI fusion biopsy with an upgrading limited to one step reported by Le et al. (18).

The restricted upgrading and downgrading of one step in the Gleason score in our study may reflect a higher influence of subject error and borderline cases rather than undersampling in contrast to the TRUS-related studies reported in the literature. Furthermore, the proportion of patients with Gleason score 6 (20%) after prostatectomy was quite low in our small population. This would be in line with data published that MR-guided biopsy detected less insignificant cancer compared to TRUS biopsy (16,17). Nevertheless, more recent data based on the National Cancer Data Base indicated that percentage of patients with Gleason score 6 decreased from 2004 to 2011 from 57% to 42%. This may be attributable to the modified Gleason score (29). But this fraction is still in contrast to our findings with a fraction of 20% patients with Gleason score 6 and may reflect a different selection of patients by means of positive findings in MRI. We note that, in our small population, 30% of patients previously had a TRUS biopsy without findings of malignancy. This represents a different patient selection in contrast to the further in-bore MRI-targeted study of Hambrock et al. (25) as mentioned previously.

The sampling error in prostate biopsy is presumed to be responsible for upgrading in prostate biopsy. Thus, a less upgrading with an increasing number of biopsies is to be expected. This is confirmed in some TRUS-related studies (11,12,22). Capitanio et al. (22) evaluated only low-risk cancer with a biopsy core Gleason ≤6 and reported an upgrading of 48% with 10–12 cores obtained, whereas taking 13–18 and 19–24 cores reduced the upgrading to 32% and 24%, respectively. Nevertheless Chun et al. (30) evaluated 4789 patients and this study failed to show a difference in grade agreement or upgrading between the entire cohort (mean number of cores 8) and a subgroup of 1682 men with ≥10 cores.

TABLE 3. Distribution of Biopsy and Prostatectomy Gleason Grades

		Prostate	ectomy Grades (% o	f Biopsy Grades)		
Biopsy Grades	5	6	7	8	9	Total
6	1 (6%)	9 (50%)	8 (44%)	_	_	18
7	_	_	19 (79%)	5 (21%)	_	24
8	_	_	1 (20%)	2 (40%)	2 (40%)	5
9	_	_	_	_	3 (100%)	3
Total	1	9	28	7	5	50

Concordant Gleason scores are set in bold.

Our findings with an overall upgrading of 30% suggest that extended schemes may become redundant in terms of targeted biopsies.

# **Downgrading**

Overall 4% of our patients were downgraded. This is quite low compared to data published for TRUS biopsies between 5% and 23.9% (2,4–6,8–10,30). Downgrading from biopsy to prostatectomy may be because of tertiary patterns that contain less than 5% of the tissue. Thus, a higher Gleason pattern found in biopsy may be assessed as tertiary pattern after RP. This would explain the very low rate of downgrading referred by Hambrock et al. with 1% for TRUS biopsy and 0% for in-bore MRI-targeted biopsy. In this study, the highest Gleason grades are evaluated presumably including tertiary patterns. In the present study, tertiary patterns are not reported.

# **Number and Quality of Positive Cores**

The biopsy mode may be essential for the quality of the cores as the MR compatible needle has special specifications. The histopathologic quality of the biopsy specimens was shown to be comparable for MR compatible needles and ferromagnetic needles (31).

The number of positive cores in our patients (median 2, range 1–4) is in line with a median of 2 (range 1–16) in the study of Epstein et al. (3), but is achieved with a median of four cores obtained (range 1–6) compared to at least 10 core sampling. These results are supported by the MRI fusion study of Le et al. (18) who report a higher percentage of positive cores in the targeted approach compared to the mapping biopsy (42% vs. 20%).

The tumor percentage of our cores was 39.8%/33% (mean/median). This matches the results of MR-targeted biopsies of Jung et al. (32) with a higher percentage of 37% (mean  $\pm$  8%) compared to 13% in TRUS biopsies, but is less than the findings of Pokorny et al. (33) with 60.6% for MR-targeted biopsies compared to 32.9% in TRUS biopsies.

In our study, we aimed to improve accuracy using a targeted approach with fewer biopsies. The reduced number of biopsies is presumed to be related to fewer complications. Naughton et al. showed fewer complications such as hematu-

ria, hematochezia, and hematospermia in 6-core biopsy compared to 12-core TRUS-guided biopsies. Nevertheless these differences were not significant (34). To our knowledge there are no data for complications in MR-guided biopsies using 3–5 cores compared to standard 12-core ultrasound-guided biopsies. MR guidance is expensive and time consuming. On the other hand, a reduced number of cores involve in less procedure time and fewer biopsy cores reduce the costs of histopathologic evaluations.

Clinicians should take the biopsy technique into consideration when assessing the clinical significance of the number of positive cores and tumor percentage.

### Limitations

The main limitation of this retrospective study is the small study population.

Biopsies were evaluated in a single institute, but because of patients' choice of the site of surgery, in 70% the prostatectomy specimens were examined in a histopathologic institute different to the institute where the biopsy was analyzed. Because of error or borderline results, the Gleason score evaluation has a subjective nature in some respects. Interobserver agreement is reported only 70% in the literature (35,36).

A tertiary pattern in RP specimens was not considered despite there could be an influence of tertiary patterns on the results (37). The higher accuracy of Gleason score in MR biopsy reported by Hambrock et al. (25) may be because of included tertiary patterns as mentioned previously.

The restriction of our investigation to available prostatectomy data comprises a possible selection bias excluding tumors deemed low grade in biopsy. Nevertheless, the fraction of patients with nonsurgery therapy is quite low. Long-term follow-up of patients without findings in MRI who potentially were not referred to standard TRUS biopsy is missing. However, this limitation is common to the previously cited studies related to accuracy in biopsies.

Whether higher accuracy of targeted biopsies is able to compensate for less cores obtained in a targeted only-biopsy strategy has to be evaluated in further studies.

In our study, consecutive patients were recruited, 15 of 50 patients (30%) had preceding negative TRUS biopsy, the remaining 70% had not had previous biopsy, so patient

TABLE 4. Data Published for an Accuracy of Gleason Score in Prostate Biopsy

Study	n Patients	Time Period	Biopsy Technique	Number of Cores Obtained	Accuracy	Upgrading	Significant Upgrading (Gleason Score 6 to >7 or More)	Downgrading	Prevalence of Gleason score ≤6
Capitanio et al. (22)	301	2001–2007	TRUS	 18 (Median)			32%		
Capitalilo et al. (22)	Only Gleason score ≤6	2001-2001	11100	To (Median)		_	<b>02</b> /0	_	_
Chun et al. (8)	2982	1992-2004	TRUS	6–12	56%	29%	37%	14%	47%
Chung et al. (10)	247	2006-2011	TRUS	≥12	57%	35%	42%	8%	30%
Cohen et al. (2) own data	2890	1982–2007	TRUS	_	58%	36%	46%	5%	40%
Cohen et al. (2) meta-analysis	14,839	1973–2007	TRUS	_	63%	30%	38%	7%	47%
Corcoran et al. (4)	1629	1995-2010	TRUS	8 (Median)	62%	29%	41%	10%	17%
Corcoran et al. (13)	684	2003-2008	TRUS	10, 3-30 (Median, range)	_	_	67%	_	_
	Only Gleason score 6, 7								
Divrik et al. (7)	206	1998–2005	TRUS	11, 10-14 (Median, range)	57%	34%	_	10%	50%
	186	1998-2005	TRUS	6-9 (Sextant biopsy)	41%	38%	_	22%	46%
Epstein et al. (3)	7643	2002-2010	TRUS	≥10	73%*	19%*	36%	8%*	50%
Fanning et al. (9)	206	2003-2008	TRUS	≥12	52%*	36%*	52%	12%	31%
Freedland et al. (12)	1113	1996-2006	TRUS	10, 6-40 (Median, range)	62%	27%	32%	11%	53%
Gofrit et al. (21)	448	2003-2006	TRUS	≥8	_	_	20%	_	_
	Only Gleason score 6								
Kahl et al. (6)	185	1999–2003	TRUS	24, 13-33 (Mean, range)	20%	57%	_	24%	42%
	55	1997–2001	TRUS	9 (Mean, ≤12)	24%	60%	_	16%	37%
Numao et al. (20)	143	2002–2006	TRUS + transperineal	26	92%	_	26%	_	20%
Richstone et al. (11)	4035	1983–2003	TRUS	6, 2-39 (Median, range)	66%*	30%	36%	6%	49%
Sfoungaristos et al. (5)	271	2005–2010	TRUS	11–13 (Mean, different groups)	44%	42%	64%	14%	31%
Arsov et al. (15)	8	2010–2011	TRUS + MRI visually directed	11 (Median)	63%	37%	25%	0%	0%
Baco et al. (23)	128	2010–2013	TRUS + MRI fusion	Targeted cores 2, 1–4 per lesion (median, range) + mapping biopsies (number not specified)	80%*	16%	30%	14%	20%
Hambrock et al. (25)	64	2006-2009	TRUS	10	55%	44%	56%	1%	28%
( - 7	34		MRI in-bore	3, 1-5 (Median, range)	88%	12%	8%	0%	35%

Labanaris et al. (24)	70	2004–2009	2004-2009 TRUS + MRI	3-6	%06	%6	%6	1%	I
Le et al. (18)	54	2010–2013	visually directed TRUS + MRI	18, 15-20 (Mean, range)	72%	7%	I	20%	13%
	54	2010-2013	fusion combined	12	20%	%68	ı	11%	
	54		MRI fusion	6, 4-8 (Mean, range)	21%	31%	I	11%	
Zhang et al. (16)	40 (48 Tumors		TRUS 12-core	12-18	%22	13%	29%	2%	29%
	in 40 patients)		versus TRUS +						
			MRI visually						
			directed						
Own data	50	2007–2014	MRI in-bore	4, 2–6 (Median, range)	%99	30%	44%	4%	20%

MRI, magnetic resonance imaging; TRUS, transrectal ultrasound. \*Rates adjusted to Gleason score 5-9 if data were given.

selection was not directed to bigger or smaller tumor sizes. The sample size was not sufficient for a separate analysis of both groups. Nevertheless, comparison of our results regarding MR-guided biopsies to other results in the literature regarding TRUS or MRI biopsy with different status of preceding biopsies remains crucial.

Biopsy strategy has to be evaluated further with respect to upgrading and the presence of insignificant cancer with long-term follow-up.

# **CONCLUSIONS**

In-bore MRI-targeted biopsy offers a good accuracy in Gleason score with postprostatectomy histopathologic control when compared to the literature. Furthermore, a limited number of cores, compared to data published for TRUS and MRI fusion biopsies, are sufficient in achieving these results. The fraction of insignificant cancer identified by targeted only-biopsy is low. Upgrading is restricted to one step in the Gleason score. Clinicians should be aware of positive findings in MRI and the biopsy technique used when assessing the clinical significance of the number of positive cores, tumor, and biopsy Gleason grades.

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