ORIGINAL ARTICLE

Association of training level and outcome of software-based image fusion-guided targeted prostate biopsies

Niklas Westhoff[1] · Henning Haumann[1] · Maximilian Christian Kriegmair[1] · Jost von Hardenberg[1] · Johannes Budjan[2] · Stefan Porubsky[3] · Maurice Stephan Michel[1] · Patrick Honeck[1] · Manuel Ritter[1]

Abstract

Purpose The aim of this study was to assess the impact of experience on the outcome of image fusion-guided prostate biopsies performed by urologists working at a high-volume medical center.

Methods The first 210 consecutive fusion biopsies were analyzed following installation of the software-based biopsy platform Artemis™ (Eigen, USA). The impact of training was measured in terms of changes in prostate cancer detection rates and biopsy duration over time. We sought to identify a threshold of experience for urologists, which predicts higher detection rates of targeted biopsies. The influence of various factors on prostate cancer detection rates was evaluated using bi- and multivariate analysis.

Results Twenty-two urologists ($n = 9$ senior urologists, $n = 13$ urological residents) performed targeted biopsies followed by systematic 12-core biopsies. Overall, targeted biopsies yielded a positive result in 39.6% of 260 suspicious MRI lesions. A subgroup analysis of the six urologists who performed more than ten biopsies was then conducted, and their level of experience (i.e., performance of more than eight biopsies) was found to be associated with higher detection rates than those with less experience (49.0% and 23.0%, respectively; $p < 0.001$) in the targeted biopsies. Experience was likewise a significant and independent predictor of a cancer-positive targeted biopsy ($p = 0.002$). Experienced senior physicians did not outperform residents in their targeted biopsy results. Further, biopsy duration correlated negatively ($r = -0.5931$, $p < 0.001$) with the total number of biopsies performed for all subgroups during the period of assessment.

Conclusions Experience is an important predictor of the rate of detection in targeted biopsies using software-based biopsy platforms with semi-robotic assistance. Moreover, the performance of just a few procedures appears sufficient to increase biopsy effectiveness significantly. Lastly, supervision by experts is recommended during the training phase.

Keywords Biopsy · Fusion · Learning curve · Multiparametric MRI · Prostatic neoplasm

Introduction

A systematic, 10- to 12-core prostate biopsy is the gold standard for detection of prostate cancer. More than 1 million biopsies are performed every year in the US, making this one among the most common diagnostic procedures performed by urologists [1]. A simple, standardized procedure is necessary to yield reliable results. Previous studies

Patrick Honeck and Manuel Ritter contributed equally to this work.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00345-018-2605-z) contains supplementary material, which is available to authorized users.

✉ Niklas Westhoff
niklas.westhoff@medma.uni-heidelberg.de

1 Department of Urology, University Medical Center Mannheim, Medical Faculty Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim 68165, Germany

2 Institute of Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim, Medical Faculty Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim 68165, Germany

3 Institute of Pathology, University Medical Center Mannheim, Medical Faculty Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim 68165, Germany

of high-quality systematic biopsies have concluded that expertise is relatively unimportant for cancer detection [2, 3].

The introduction of targeted biopsies of tumor-suspicious intraprostatic lesions involving the fusion of preliminary multiparametric MRI (mpMRI) with transrectal ultrasound (TRUS) images has improved the detection rates of clinically significant cancers markedly in recent years [4–6]. Various fusion techniques are available, including cognitive image fusion, in-bore MRI fusion, and software-based biopsy platforms. Cognitive and software-based image fusion has gained greater acceptance than in-bore biopsy owing to its ability to detect cancer more quickly and at a lower cost.

Image fusion-guided biopsies are, however, more time-consuming than regular biopsies and may fail at any number of steps. Moreover, while the cognitive image fusion approach demands a sophisticated grasp of anatomy and skillful needle navigation to avoid deviations, software-based biopsy platforms that incorporate semi-robotic assistance may obviate such requirements. In any case, the targeted biopsy of small lesions constitutes a far more sophisticated approach than random sampling of the prostate gland.

The increasing use of these procedures calls for evaluation of the level of experience necessary to perform MRI/TRUS fusion-guided targeted biopsies with precision. Accordingly, we have assessed the effect of training on both cancer detection through targeted biopsy and on biopsy duration using the Artemis™ biopsy platform (Eigen, USA) and have evaluated the applicability in clinical routine.

Patients and methods

Patient cohort

We assessed a series of patients who underwent MRI/TRUS fusion biopsy after implementation of the software-based Artemis™ biopsy platform (Eigen, USA). Between 2014 and 2016, a total of 239 patients had received a fusion biopsy owing either to primary cancer suspicion based on elevated PSA level and/or a digital rectal finding, or to the need for re-biopsy in the active surveillance of a confirmed cancer or in anticipation of focal therapy. Prior mpMRI had confirmed at least one tumor-suspicious lesion in all of the patients, except for two who were excluded from the analysis because they had received a control biopsy 12 months after focal high-intensity focused ultrasound (HIFU) therapy and mpMRI gave a normal result. Another 27 patients, whose MRI lesions were not

classified according to PI-RADS (Prostate Imaging and Reporting Data System) but only as "suspicious," were excluded, thereby yielding a total sample size of 210. All patients signed an informed consent form, thereby agreeing to participate in the intervention.

Multiparametric magnetic resonance imaging protocol

All patients received an mpMRI before their biopsies. Of these procedures, the in-house radiological department performed 71.9%. Image acquisition protocols included T2-weighted sequences in transverse, coronal, and sagittal orientation, diffusion-weighted imaging (with b-values of 50, 400, 800, and 2000s/mm^2), and dynamic contrast-enhanced T1-weighted perfusion sequences on either a Magnetom Skyra or Trio (Siemens Healthineers, Erlangen, Germany). Each mpMRI acquired by the in-house radiological department was read by two radiologists (for total of 18 radiologists), at least one of whom had more than 4 years' experience reading prostate MRIs. An mpMRI was administered to 28.1% of the patients at an external radiological institution. When reports and images were inconsistent, the results were then reviewed by the in-house radiologists. Lesions were defined according to PI-RADS version 1 or 2 depending on when the image was acquired.

MRI/TRUS fusion biopsy

All MRI/TRUS fusion biopsies were performed using the Artemis™ platform as previously described [7]. General anesthesia was administered to all but seven of the patients, the latter of whom had contraindications for or refused it and, therefore, received analgosedation or local anesthesia. Urologists segmented the prostate and the target in the ProFuse® software in consultation with radiologists. Each patient received a targeted biopsy of the suspicious lesion or lesions followed by a 12-core systematic biopsy according to the sites automatically preselected by the Artemis™ software. Both types of biopsy were performed by the same urologist. Biopsy cores were embedded separately according to consensus recommendations to allow for pathological assessment of all biopsy sites [8].

Proctors taught the entire procedure to physicians, who then practiced it once using a training mode and a prostate phantom. Next, the platform was introduced into clinical usage. The first ten biopsies were supervised by the proctor and subsequent biopsies by experienced users. From the second year of residency on and after becoming familiar with regular systematic biopsies, residents were introduced to fusion biopsies. In general, after two–three supervised biopsies, the senior urologists (those who had completed specialist training) and

residents alike were able to perform the procedures independently. An urologist continued to supervise the residents, but active intervention proved unnecessary.

Data collection and statistical analysis

We prospectively collected patients' demographic data (i.e., age, prostate-specific antigen [PSA] value, prostate volume, any previous biopsies, clinical stage) and their imaging and histopathological results. Targeted and systematic biopsy cores were evaluated separately. One biopsy core revealing cancer served to define either a targeted or systematic biopsy as positive. Detection rates were analyzed on a per-patient and per-lesion basis. Biopsy duration was assessed in terms of the time data that were saved on the biopsy device and were divided into planning (of TRUS image acquisition, segmentation, image fusion, and the biopsy itself) and sampling phases. To assess the effect of experience on the biopsy results, we selected a subgroup of 165 biopsies, of which at least ten had been performed by the same physician. Of the six physicians involved, four were senior urologists and two were residents. A partition test was employed to determine the threshold for the biopsies performed that optimally distinguished high from low detection rates, and all biopsies performed by an individual surgeon above this threshold were identified as high experience. We then compared the groups of patients and biopsy outcomes below and above the threshold using either a Chi-square test or a Fisher's exact test for qualitative parameters. The impact of biopsy experience on cancer detection rates was assessed through bivariate analysis and a multivariate logistic regression model. Spearman's coefficient was used to correlate the number of performed biopsies and their duration over time. The biopsy-related complication rate was assessed and stratified based on the clinicians' levels of experience. Statistical significance was assumed for p values < 0.05. Analyses were performed using JMP® (version 13.0.0, SAS Institute Inc., USA).

Results

Demographics

The first 210 MRI/TRUS fusion biopsies performed at the institution were included in the analysis. The patients' median age was 67 years (ranging from 45 to 84); their median PSA level was 8.3 ng/ml (ranging from 0.7 to 170). Of these patients, 37.6% were biopsy-naïve, most with an mpMRI indicated by their urologists or at their own request; 40.5% had a prior negative and 21.9% a prior positive biopsy. Their demographics are presented in Table 1.

MRI analysis and biopsy results

MRI analysis revealed a total of 260 lesions, with a median of 1 per patient (ranging from 1 to 3). The median maximum diameter of the index lesion was 12 mm (ranging from 5 to 45). Most of the lesions were classified as PI-RADS 3 and 4 (34.6% and 32.7%, respectively) (Table 1).

The 210 fusion biopsies were performed by 22 different urologists, 157 by 9 senior urologists and 53 by 13 residents. Their combined cancer detection rate for targeted and systematic biopsies was 64.3%. Targeted biopsy alone was positive for cancer in 47.6% of cases per patient and in 40.4% per lesion and detected more Gleason Score $3 + 4$ tumors than systematic 12-core biopsy. The latter was positive in 126 patients (60.0%) and detected more low-grade tumors than targeted biopsy. Additionally, systematic biopsy detected seven tumors with Gleason scores $\geq 4 + 3$ that were missed by targeted biopsy. Senior urologists detected slightly more cancers than residents in total (66.3% and 58.5%, respectively, $p = 0.499$) and by systematic biopsies (62.4% and 52.8%, respectively; $p = 0.599$), but the difference was not statistically significant. The detection rates of the targeted biopsies were almost identical on a per-lesion basis and higher on a per-patient basis for the residents than the senior urologists (50.9% and 46.5%, respectively; $p = 0.575$). These results are presented in Table 1.

Impact of experience on targeted biopsy

In the subgroup of 165 biopsies, the partition test for cancer detection revealed eight biopsies as the necessary threshold for experience. Thus, in the group of patients who received a biopsy from a physician who had previously performed at least this number, the detection rate of targeted biopsies on a per-lesion level was significantly higher than the rate for physicians with less experience (49.0% and 23.0%, respectively; $p < 0.001$). The threshold was the same for senior urologists and the supervised residents performing the fusion and systematic biopsies independently. Senior urologists performed more of the higher-experience group of biopsies ($p = 0.005$). Otherwise, no significant differences were found between the two groups with regard to age, PSA, digital rectal examination (DRE), prostate volume, prior biopsy status, PI-RADS scores, or the diameter of the index lesions (Table 2).

The impact of experience on the outcome of targeted biopsies was evaluated through bi- and multivariate analysis. The physicians' experience of at least eight biopsies was a significant factor in targeted biopsies positive for cancer in the bivariate analysis ($p < 0.001$) and an independent predictor in the logistic multivariate model (HR $= 3.32$, QI $= 1.55$–7.08, $p = 0.002$). Analysis of biopsy experience

Table 1 Patient characteristics, imaging and biopsy results of 210 patients with an MRI/TRUS fusion biopsy

Variable	$n = 210$ patients	
Patient characteristics		
Age, year (median, range)	67 (45–84)	
PSA, ng/ml (median, range)	8.3 (0.7–170)	
DRE suspicious	43 (32.3)	
Prostate volume, ml (median, range)	40 (10–118)	
Biopsy status (n, %)		
Biopsy-naïve	79 (37.6)	
Prior negative	85 (40.5)	
Prior positive	46 (21.9)	
MRI data		
MRI lesions, n (median, range)		
Total number of targets	260	
Number of targets per patient	1 (1–3)	
Median max. diameter index lesion, mm	12 (5–45)	
PI-RADS lesions (n, %)		
PI-RADS < 3	20 (7.7)	
PI-RADS 3	90 (34.6)	
PI-RADS 4	84 (32.3)	
PI-RADS 5	66 (25.4)	
Biopsy data		
Number of biopsies (n, %)		
Senior urologists	157 (74.8)	
Urological residents	53 (25.2)	
Targeted biopsy cores per lesion (median, range)	2 (1–6)	
Prostate cancer detection rate (n, %)		
Overall detection	135/210 (64.3)	
Senior urologists	104/157 (66.3)	
Urological residents	31/53 (58.5)	$p = 0.499$
Detection by targeted biopsy (per patient)	100/210 (47.6)	
Senior urologists	73/157 (46.5)	
Urological residents	27/53 (50.9)	$p = 0.575$
Detection by targeted biopsy (per lesion)	105/260 (40.4)	
Senior urologists	78/193 (40.4)	
Urological residents	27/67 (40.3)	$p = 0.655$
Detection by systematic biopsy	126/210 (60.0)	
Senior urologists	98/157 (62.4)	
Urological residents	28/53 (52.8)	$p = 0.599$
Highest Gleason Scores of positive biopsies		
3 + 3		
Targeted biopsy	30/135 (22.2)	
Systematic 12-core biopsy	54/135 (40.0)	
3 + 4		
Targeted biopsy	34/135 (25.2)	
Systematic 12-core biopsy	31/135 (23.0)	
4 + 3		
Targeted biopsy	27/135 (20.0)	
Systematic 12-core biopsy	32/135 (23.7)	
≥ 4 + 4		
Targeted biopsy	8/135 (5.9)	
Systematic 12-core biopsy	10/135 (7.4)	

Table 2 Comparison of clinical, imaging and biopsy parameters between patients who received a biopsy by a urologist with lower or higher experience (cut-off eight performed biopsies)

Variable	Lower experience ($n=42$)	Higher experience ($n=123$)	p value
Age ≥ 67 years (n, %)	16 (38.1)	65 (52.9)	0.110
PSA ≥ 10, ng/ml (n, %)	10 (23.8)	44 (35.8)	0.185
DRE suspicious (n, %)	10 (23.8)	19 (15.5)	0.243
Prostate volume ≥ 40 ml (n, %)	17 (40.5)	48 (39.0)	0.857
Prior positive biopsy (n, %)	7 (16.7)	30 (24.4)	0.393
Prior negative biopsy (n, %)	16 (38.1)	52 (42.3)	0.718
PI-RADS 4 or 5 (n, %)	40 (65.6)	99 (69.2)	0.625
Max. target diameter index lesion ≥ 10 mm (median, range)	14 (33.3)	57 (46.4)	0.153
Senior urologist status	28 (66.7)	107 (87.0)	0.005
Prostate cancer detection rate by TB, per lesion (n, %)	14/61 (23.0)	70/143 (49.0)	< 0.001
Biopsy time, min (median, range)	20 (8–92)	14 (7–87)	< 0.001

treated as a continuous variable in another multivariate model of all biopsies performed by urologists with ≥ 2 completed biopsy procedures confirmed these results (HR = 0.98, QI = 0.96–1.00, $p = 0.049$) (Online Resource 1).

A suspicious DRE finding ($p < 0.001$), a PI-RADS score of 4 or 5 ($p = 0.038$), and an index lesion with a diameter ≥ 10 mm ($p = 0.015$) proved also to be significant and independent factors in both analyses (Table 3). Increasing age of patients had a significant impact on cancer detection in the bivariate ($p = 0.016$) but not the multivariate analysis ($p = 0.604$).

Given that biopsy duration represents an additional marker of the training effect, we assessed the duration overall

and of the planning and biopsy phases for 179 patients. For the remaining 31 patients, no complete duration data were recorded. Duration was found to decrease with increasing number of biopsies performed and was consistent across all groups of physicians and all biopsy phases, as illustrated in Fig. 1. In the group of biopsies below the threshold of eight, the median total duration was significantly longer compared with the group above the threshold (20 and 14 min., respectively; $p < 0.001$) (Table 2).

Overall, 35 biopsy-related adverse events (AEs) were reported in 33 patients (16.2%). The most frequent AE was mild rectal bleeding following a biopsy (45.7%). Physicians with lower experience (< 8 biopsies) encountered 14 AEs (40%), while those with higher experience encountered 21 (60%) ($p = 0.548$) (Online Resource 2).

Discussion

Image fusion-guided prostate biopsy is increasingly recommended under current guidelines for the diagnosis of prostate cancer [9, 10]. This procedure holds promise for improving detection of clinically significant cancers, not only after prior negative biopsies but also when cancer is first suspected [11]. It is also useful for patient selection and monitoring in active surveillance and focal therapy [12].

Owing to this development in routine diagnostics, urologists face tremendous demand for fusion biopsies, and they must choose among the techniques available. Recent evaluations of the cancer detection rates of various fusion biopsy techniques have favored software-based biopsy platforms, but too few studies have been conducted to allow for a definitive recommendation [13, 14]. Differences with regard to image registration, image fusion, biopsy tracking, and needle navigation complicate the choice of fusion biopsy technique, in which other factors may be at play. Beyond the acquisition costs, the clinical efficiency of a fusion technique in routine

Table 3 Bivariate analysis and multivariate logistic regression model for the prediction of a targeted biopsy positive for cancer

|	Bivariate analysis			Multivariate analysis		
	HR	95% CI	p	HR	95% CI	p
Targeted biopsy positive for cancer						
Age ≥ 67 years	2.0	(1.14–3.52)	0.016	1.49	(0.62–2.27)	0.604
PSA ≥ 10 ng/ml	1.64	(0.91–2.96)	0.102			
DRE suspicious	4.4	(1.97–9.81)	< 0.001	4.85	(1.99–11.80)	< 0.001
Prostate volume ≥ 40 cm^3	0.67	(0.37–1.21)	0.187			
Prior positive prostate biopsy	0.83	(0.42–1.65)	0.6			
Prior negative prostate biopsy	1.69	(0.96–2.98)	0.071			
PI-RADS 4 or 5	2.63	(1.38–5.01)	0.003	2.13	(1.04–4.35)	0.038
Max. target diameter index lesion ≥ 10 mm	2.38	(1.32–4.3)	0.004	2.24	(1.17–4.27)	0.015
Senior urologist status	1.15	(0.56–2.35)	0.702			
Experience: ≥ 8 fusion biopsies	3.22	(1.63–6.36)	< 0.001	3.32	(1.55–7.08)	0.002
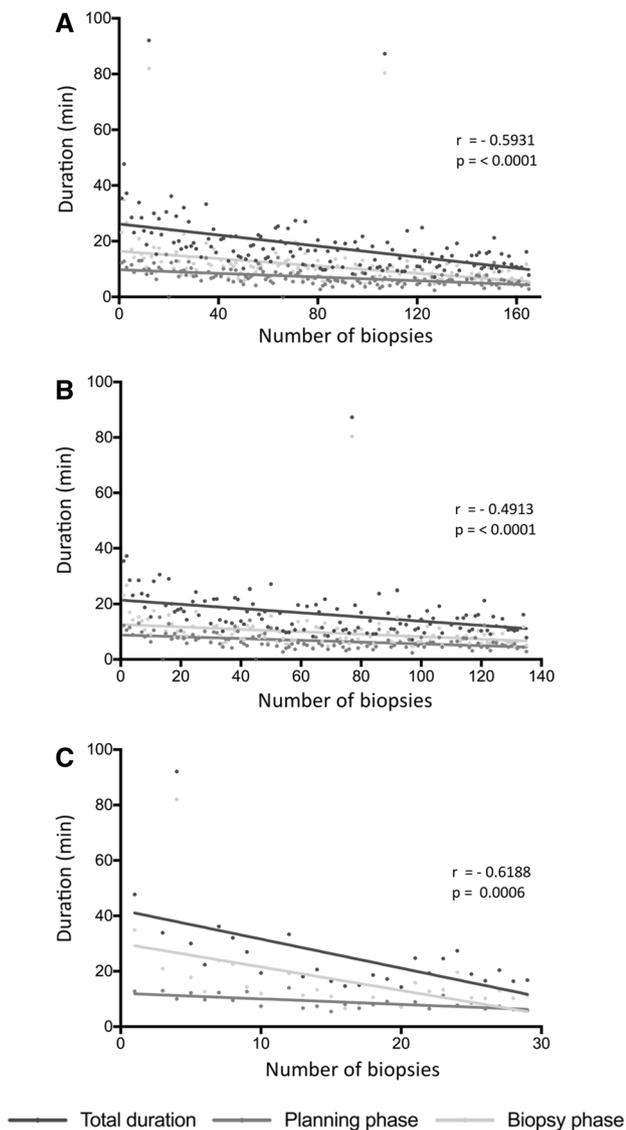
Fig. 1 Total biopsy duration, duration of planning and biopsy phase decreased with an increasing number of performed biopsies for **a** all surgeons, **b** senior urologists and **c** urological residents. Spearman's correlation coefficient of total biopsy duration and number of performed biopsies is displayed

workflows is also crucial. Efficiency can be indicated by reliable detection rates and short procedure durations, even when biopsies are performed by users with varying levels of training. In this study, we assessed the impact of training level on efficiency using the software-based and semi-robotically assisted biopsy platform Artemis™ within the first 2 years after its implementation at a high-volume medical center. With this platform, the procedure can be performed under highly standardized conditions using automated image registration and elastic image fusion that correct for deformations of the prostate during TRUS [15]. In addition, the

semi-robotic arm on which the TRUS probe is mounted ensures needle guidance accuracy [16].

In investigating the potential effect of training, we first assessed whether cancer detection rates changed over time. The overall detection rate for a combined targeted and systematic biopsy (64.3%) was similar to that reported for large series [17, 18]. The automatic preselection of sites by the Artemis™ software together with urologists' tendency to position a systematic core near a known suspicious lesion may explain the high detection rate of the systematic approach alone (60.0%). The detection rate of targeted biopsies on a per-target basis increased as more were performed until a physician reached the threshold of eight biopsies in this series (49.0% for those over the threshold and 23.0% for those under it, $p < 0.001$). This threshold was, therefore, determined to represent the experience necessary for reliable targeted biopsy results; during the first seven procedures, an unsupervised physician was more likely to miss cancers. To assess the informative value of this threshold further, we first compared biopsies performed after and before a physician reached the threshold and evaluated biopsy experience and potential co-predictors through bi- and multivariate analysis. The most important finding in this regard was that biopsy experience remained as a significant predictor in the bi- and multivariate analysis. Experience was also confirmed as a significant independent predictor in a linear multivariate regression model of all biopsies performed by urologists with more than one previous biopsy to exclude a potential bias by cut-offs ($n = 202$).

The number of higher PI-RADS scores of 4 and 5 did not differ significantly in the groups below or above the threshold (65.6% and 69.2%, respectively) and was also shown to be significant for the targeted biopsy outcome ($p = 0.038$). The association of higher MRI risk scores with positive biopsy results has been demonstrated before and must be considered as an important factor in cancer detection [17, 19, 20]. In addition, the senior urologists performed far more of the biopsies beyond the threshold than the residents (107/123 and 28/42, respectively; $p = 0.005$). Senior urologists naturally have more experience with standard prostate biopsies that potentially enhances their anatomical and technical understanding. Their higher detection rates overall and for systematic biopsies specifically compared with residents are consistent with this assumption. However, a senior urologist's experience was not a significant predictor of the outcome of targeted biopsies ($p = 0.702$). This finding was supported by the fact that the experience threshold was the same for senior urologists and residents (again, eight biopsies) and the lower detection rate of the former on a per-patient level (45.9% and 50.9%, respectively). The detection rate on a per-lesion basis was similar (40.3% and 40.4%, respectively), with senior urologists detecting cancer in more than one lesion in five of the patients. More frequent consensus

discussions between residents and radiologists regarding the correct target definition prior to biopsy is a possible explanation for this finding. Further, for legal reasons, residents were supervised by senior urologists when performing the biopsies, and this could have affected the results, though in fact the latter did not feel the need to correct the former after a short training period of two or three biopsies.

Beyond biopsy experience and higher PI-RADS scores, suspicious DRE findings and index lesions with maximum diameters of ≥ 10 mm also predicted a positive targeted biopsy. These findings indicate that larger tumors are more likely to be identified by a targeted biopsy than smaller ones, as shown previously [21, 22]. Moreover, age is a known predictor of prostate cancer, as was confirmed by the bivariate analysis.

As a second indicator of training level, we investigated the duration of the procedure in detail by extracting the time required for TRUS image acquisition, contouring, image fusion, and mapping out the procedure before the first biopsy core was obtained (the planning phase) and for taking the biopsies (the biopsy phase). The duration decreased continually for both phases for both the senior urologists and the residents. Thus, for the first biopsies, the total procedure duration was longer for residents (around 40 min), but it decreased within the study period to that for senior urologists (around 15 min).

Further, biopsy-related AEs were independent of the number of biopsies performed by a single physician, indicating that complications were not related to experience.

Two recent studies have described the effect of urologists' experience on MRI/TRUS fusion biopsies. Thus, Calio et al. reported on a large series of fusion biopsies performed by a single urologist in fusion biopsy-naïve men for which the mpMRIs were read by two experienced radiologists. A research fusion biopsy platform was used for the first 6 years of their study and the UroNav (Invivo, USA) platform for the last three. These researchers assessed a cohort of the first 230 biopsies as a learning period during which targeted biopsies gave results similar to systematic biopsies in terms of detecting clinically significant cancers. After gaining more experience, detection rates of clinically significant cancers (those $\geq$ Gleason score $3 + 4$) by targeted biopsy increased whereas detection of indolent (Gleason score $3 + 3$) tumors decreased. These low detection rates of targeted compared with systematic biopsies early on are consistent with our results using a cohort of approximately the same size [23]. Compared with this series, in our cohort, targeted biopsy performed better overall, and an appropriate experience level was reached earlier. Our use of the biopsy platform Artemis™ with semi-robotic assistance and an automated image fusion could explain these results, especially when measured against an early-generation research platform. In addition,

the composition of the population differed between the two series in terms of previous biopsy status.

In another study, a smaller series of 126 patients, all of whom were biopsy naïve or previously negative, received fusion biopsies with rigid image fusion using the Hitachi Ascendus®. For one novice using this technique, the learning curve reached a plateau after 63 biopsies, while biopsy duration decreased constantly. The Hitachi biopsy device may require more experience because it relies on freehand technique; the observed slow learning curve for the first 42 biopsies and acceleration up to 63 remains unexplained [24].

The present study has some limitations, first owing to its focus on a single medical center. The large number of urologists who performed the biopsies may also have influenced the detection rates. The aim here, however, was to measure the impact of training on fusion biopsies in a typical clinical setting that demanded efficient workflows and consistency across users. We only focused on the six urologists there who had performed the most biopsies. However, analysis of these various users of the biopsy device could have avoided potential limitations of the evaluation of a single-user learning curve, which was the approach taken in previous studies [23, 24]. The eight-biopsy threshold should not be considered as absolute but rather as an indication of the brief institutional training period required for use of a software-based, robotic-assisted biopsy device. In this study, we focused on urologists' training; past trials have reported steep learning curves even for radiologists who specialize in MRI interpretation and for pathologists [25–27]. Future trials could include various types of fusion biopsies and various platforms for evaluating training effects. In any case, enhancement of any learning effects will require close collaboration among institutions.

In conclusion, this study confirms the importance of experience for those who perform MRI/TRUS fusion biopsies. It also demonstrates that a software-based and semi-robotically assisted biopsy platform requires only a relatively brief institutional training period. To ensure that no cancers are missed, supervision of trainees by an experienced user is recommended. The procedure includes more steps and is generally more complex than systematic biopsies, but its overall duration is appropriate. The fact that urologists with various levels of experience achieved comparable detection rates using the procedure demonstrates the ease with which it can be implemented in clinical settings.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest to disclose.

Ethical approval This study was approved by the institutional ethical review board (2018-878R-MA).

References

1. Loeb S, Carter HB, Berndt SI, Ricker W, Schaeffer EM (2011) Complications after prostate biopsy: data from SEER-Medicare. J Urol 186(5):1830–1834. https://doi.org/10.1016/j.juro.2011.06.057
2. Karam JA, Shulman MJ, Benaim EA (2004) Impact of training level of urology residents on the detection of prostate cancer on TRUS biopsy. Prostate Cancer Prostatic Dis 7(1):38–40. https://doi.org/10.1038/sj.pcan.4500695
3. Benchikh El Fegoun A, El Atat R, Choudat L, El Helou E, Hermieu JF, Dominique S, Hupertan V, Ravery V (2013) The learning curve of transrectal ultrasound-guided prostate biopsies: implications for training programs. Urology 81(1):12–15. https://doi.org/10.1016/j.urology.2012.06.084
4. Bjurlin MA, Mendhiratta N, Wysock JS, Taneja SS (2016) Multiparametric MRI and targeted prostate biopsy: improvements in cancer detection, localization, and risk assessment. Cent Eur J Urol 69(1):9–18. https://doi.org/10.5173/ceju.2016.734
5. Woo S, Suh CH, Kim SY, Cho JY, Kim SH (2017) Diagnostic performance of prostate imaging reporting and data system version 2 for detection of prostate cancer: a systematic review and diagnostic meta-analysis. Eur Urol 72(2):177–188. https://doi.org/10.1016/j.eururo.2017.01.042
6. de Rooij M, Hamoen EH, Futterer JJ, Barentsz JO, Rovers MM (2014) Accuracy of multiparametric MRI for prostate cancer detection: a meta-analysis. Am J Roentgenol 202(2):343–351. https://doi.org/10.2214/AJR.13.11046
7. Sonn GA, Natarajan S, Margolis DJ, MacAiran M, Lieu P, Huang J, Dorey FJ, Marks LS (2013) Targeted biopsy in the detection of prostate cancer using an office based magnetic resonance ultrasound fusion device. J Urol 189(1):86–91. https://doi.org/10.1016/j.juro.2012.08.095
8. van der Kwast TH, Lopes C, Santonja C, Pihl CG, Neetens I, Martikainen P, Di Lollo S, Bubendorf L, Hoedemaeker RF, Members of the pathology committee of the European Randomised Study of Screening for Prostate C (2003) Guidelines for processing and reporting of prostatic needle biopsies. J Clin Pathol 56(5):336–340
9. Deutsche Gesellschaft für Urologie e.V. (DGU) (2018) Interdisziplinäre Leitlinie der Qualität S3 zur Früherkennung, Diagnose und Therapie der verschiedenen Stadien des Prostatakarzinoms. Available from: http://www.awmf.org/uploads/tx_szleitlinien/043-022OLl_S3_Prostatakarzinom_2018-04.pdf. Accessed 08 Apr 2018
10. European Association of Urology (EAU) (2017) Guidelines on prostate cancer. Available from: http://uroweb.org/guideline/prostate-cancer/. Accessed 08 April 2018
11. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, Collaco-Moraes Y, Ward K, Hindley RG, Freeman A, Kirkham AP, Oldroyd R, Parker C, Emberton M, Group Ps (2017) Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 389(10071):815–822. https://doi.org/10.1016/S0140-6736(16)32401-1
12. Elkhoury FF, Simopoulos DN, Marks LS (2018) Targeted Prostate Biopsy in the Era of Active Surveillance. Urology 112:12–19. https://doi.org/10.1016/j.urology.2017.09.007
13. Wegelin O, van Melick HH, Hooft L, Bosch JL, Reitsma HB, Barentsz JO, Somford DM (2016) Comparing three different techniques for magnetic resonance imaging-targeted prostate biopsies: a systematic review of in-bore versus magnetic resonance imaging-transrectal ultrasound fusion versus cognitive registration. Is there a preferred technique? Eur Urol. https://doi.org/10.1016/j.eururo.2016.07.041
14. Wysock JS, Rosenkrantz AB, Huang WC, Stifelman MD, Lepor H, Deng FM, Melamed J, Taneja SS (2014) A prospective, blinded comparison of magnetic resonance (MR) imaging-ultrasound fusion and visual estimation in the performance of MR-targeted prostate biopsy: the PROFUS trial. Eur Urol 66(2):343–351. https://doi.org/10.1016/j.eururo.2013.10.048
15. Natarajan S, Marks LS, Margolis DJ, Huang J, Macairan ML, Lieu P, Fenster A (2011) Clinical application of a 3D ultrasound-guided prostate biopsy system. Urol Oncol 29(3):334–342. https://doi.org/10.1016/j.urolonc.2011.02.014
16. Sonn GA, Margolis DJ, Marks LS (2014) Target detection: magnetic resonance imaging-ultrasound fusion-guided prostate biopsy. Urol Oncol 32(6):903–911. https://doi.org/10.1016/j.urolonc.2013.08.006
17. Filson CP, Natarajan S, Margolis DJ, Huang J, Lieu P, Dorey FJ, Reiter RE, Marks LS (2016) Prostate cancer detection with magnetic resonance-ultrasound fusion biopsy: the role of systematic and targeted biopsies. Cancer 122(6):884–892. https://doi.org/10.1002/cncr.29874
18. Baco E, Rud E, Eri LM, Moen G, Vlatkovic L, Svindland A, Eggesbo HB, Ukimura O (2016) A randomized controlled trial to assess and compare the outcomes of two-core prostate biopsy guided by fused magnetic resonance and transrectal ultrasound images and traditional 12-core systematic biopsy. Eur Urol 69(1):149–156. https://doi.org/10.1016/j.eururo.2015.03.041
19. Meng X, Rosenkrantz AB, Mendhiratta N, Fenstermaker M, Huang R, Wysock JS, Bjurlin MA, Marshall S, Deng FM, Zhou M, Melamed J, Huang WC, Lepor H, Taneja SS (2016) Relationship between prebiopsy multiparametric magnetic resonance imaging (MRI), biopsy indication, and MRI-ultrasound fusion-targeted prostate biopsy outcomes. Eur Urol 69(3):512–517. https://doi.org/10.1016/j.eururo.2015.06.005
20. Delongchamps NB, Lefevre A, Bouazza N, Beuvon F, Legman P, Cornud F (2015) Detection of significant prostate cancer with magnetic resonance targeted biopsies–should transrectal ultrasound-magnetic resonance imaging fusion guided biopsies alone be a standard of care? J Urol 193(4):1198–1204. https://doi.org/10.1016/j.juro.2014.11.002
21. Martorana E, Pirola GM, Scialpi M, Micali S, Iseppi A, Bonetti LR, Kaleci S, Torricelli P, Bianchi G (2017) Lesion volume predicts prostate cancer risk and aggressiveness: validation of its value alone and matched with prostate imaging reporting and data system score. BJU Int 120(1):92–103. https://doi.org/10.1111/bju.13649
22. Okotie OT, Roehl KA, Han M, Loeb S, Gashti SN, Catalona WJ (2007) Characteristics of prostate cancer detected by digital rectal examination only. Urology 70(6):1117–1120. https://doi.org/10.1016/j.urology.2007.07.019
23. Calio B, Sidana A, Sugano D, Gaur S, Jain A, Maruf M, Xu S, Yan P, Kruecker J, Merino M, Choyke P, Turkbey B, Wood B, Pinto P (2017) Changes in prostate cancer detection rate of MRI-TRUS fusion vs systematic biopsy over time: evidence of a learning curve. Prostate Cancer Prostatic Dis. https://doi.org/10.1038/pcan.2017.34
24. Mager R, Brandt MP, Borgmann H, Gust KM, Haferkamp A, Kurosch M (2017) From novice to expert: analyzing the learning

curve for MRI-transrectal ultrasonography fusion-guided transrectal prostate biopsy. Int Urol Nephrol 49(9):1537–1544. https://doi.org/10.1007/s11255-017-1642-7

25. Gaziev G, Wadhwa K, Barrett T, Koo BC, Gallagher FA, Serrao E, Frey J, Seidenader J, Carmona L, Warren A, Gnanapragasam V, Doble A, Kastner C (2016) Defining the learning curve for multiparametric magnetic resonance imaging (MRI) of the prostate using MRI-transrectal ultrasonography (TRUS) fusion-guided transperineal prostate biopsies as a validation tool. BJU Int 117(1):80–86. https://doi.org/10.1111/bju.12892

26. Rosenkrantz AB, Ayoola A, Hoffman D, Khasgiwala A, Prabhu V, Smereka P, Somberg M, Taneja SS (2017) The learning curve in prostate MRI Interpretation: self-directed learning versus continual reader feedback. Am J Roentgenol 208(3):W92–W100. https://doi.org/10.2214/AJR.16.16876

27. Shah MD, Parwani AV, Zynger DL (2017) Impact of the pathologist on prostate biopsy diagnosis and immunohistochemical stain usage within a single institution. Am J Clin Pathol 148(6):494–501. https://doi.org/10.1093/ajcp/aqx103