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UROGENITAL

Comparison of analgesic techniques in MRI-guided in-bore prostate biopsy

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Abstract

Objectives To evaluate different analgesic techniques in MRI-guided in-bore prostate biopsy (IB-GB) regarding the influence on patient procedural experience of pain.

Methods Two hundred fifty-two consecutive patients who had received an IB-GB either with intrarectal instillation of 2% lidocaine gel ($n = 126$, group A) or with periprostatic nerve block (PPNB) with 2% mepivacaine ($n = 126$, group B) were retrospectively included in this study. Pain scores were measured on a visual analog scale, the operating room time (ORT) was recorded for each biopsy and correlations between the parameters were analysed.

Results Pain scores for IB-GB were slightly lower in group B compared with group A (2.0 ± 1.9; 2.4 ± 1.7; $p = 0.02$). In group A, significantly more targeted biopsy cores were acquired (group B: 5.2 ± 1.1; group A: 5.6 ± 0.8; $p < 0.01$). ORT was comparable and not significantly different in both groups. There was only a weak correlation between pain scores and ORT in group B ($r_S = 0.22$; $p = 0.01$), but no correlation between pain scores and the number of biopsy cores or the prostate volume.

Conclusions Pain levels are generally low for MRI-guided in-bore biopsy using either PPNB or intrarectal instillation of lidocaine gel. A statistically significant, slightly lower pain score was documented for PPNB and might be preferred when the focus is analgesia. On the other hand, due to the minor difference and easier administration, intrarectal gel instillation seems to be a reasonable practice for standard analgesia for MRI-guided in-bore biopsy.

Key Points

- *Pain levels were low for MRI-guided in-bore biopsy using either PPNB or intrarectal instillation of lidocaine gel as analgesic method.*
- *PPNB prior to IB-GB resulted in a slightly lower pain score but required a higher effort.*
- *Intrarectal gel anaesthesia seems to be a reasonable practice for standard analgesia for IB-GB in an outpatient setting.*

Keywords Prostate cancer · Analgesics · Image-guided biopsy · Magnetic resonance–guided interventional procedures

Abbreviations

C-GB	Cognitive fusion–guided biopsy
EAU	European Association of Urology
FUS-GB	MRI/US fusion–guided prostate biopsy
IB-GB	MRI-guided in-bore prostate biopsy
IQR	Interquartile range
mpMRI	Multiparametric magnetic resonance imaging
ORT	Operating room time
PCa	Prostate cancer
PPNB	Periprostatic nerve block
PSA	Prostate-specific antigen
r_S	Spearman correlation coefficient
TRUS	Transrectal ultrasound-guided

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Introduction

Multiparametric prostate MRI (mpMRI) is developing towards a first-line investigation for prostate cancer diagnosis. Increasing detection of clinically significant prostate cancer–targeted MRI-guided biopsy is necessary when detecting suspicious lesions with mpMRI. Three different biopsy

techniques have been established: cognitive fusion–guided biopsy (C-GB), fusion MRI-ultrasound–guided biopsy (FUS-GB) and MRI-guided in-bore biopsy (IB-GB). While target re-identification in the ultrasound image has to be performed by the operator ("fusion in mind") in C-GB, FUS-GB uses software-based image co-registration. Both techniques can be easily combined with systematic biopsies (TRUS) within one biopsy session, and either a transrectal or a transperineal approach can be chosen using ultrasound for guidance. The European Association of Urology (EAU) guidelines recommend an ultrasound-guided periprostatic nerve block (PPNB) for TRUS-guided prostate biopsies [1]. Consequently, C-GB and FUS-GB usually are performed with ultrasound-guided PPNB, which can be administered immediately before the biopsy session. Intrarectal instillation of anaesthetic gel is mostly used for analgesia in IB-GB [2]. Performing a PPNB in the MRI operating room requires MR-compatible devices. Alternatively, PPNB has to be administered outside the MRI in advance. Nevertheless, the optimal analgesic technique for IB-GB has not been defined yet.

Materials and methods

Study population

One hundred twenty-six consecutive patients with IB-GB and prior intrarectal instillation of 2% lidocaine gel (group A) and 126 patients with IB-GB and prior periprostatic nerve block (PPNB) with 2% mepivacaine (group B) were analysed in this retrospective single-centre cohort study. A majority of patients in study group A were previously enrolled in a prospective randomised trial assessing the diagnostic efficacy of IB-GB and FUS-GB (ClinicalTrials.gov identifier: NCT02220517). All patients in study group B were previously enrolled in a prospective randomised trial assessing the diagnostic efficacy of IB-GB in comparison with TRUS-GB in biopsy-naïve men with elevated PSA (ClinicalTrials.gov identifier: NCT01553838). The results, especially the diagnostic performance of multiparametric prostate-MRI and MRI-guided biopsy of these prospective trials, have been reported earlier [3, 4] and are not part of this analysis. Patients in group A had at least one negative prior prostate biopsy, and persistently increased prostate-specific antigen (PSA) levels. Patients in group B were biopsy-naïve patients with likewise increased PSA levels. Written informed consent was obtained from all subjects. The trial was approved by our institutional review board.

Analgesic techniques

Immediately before the IG-GB, two different analgesic techniques were used. Patients in group A received a local intrarectal instillation of 12 ml of 2% lidocaine gel (Instillagel®, FARCO-PHARMA) in the MR operating room by a uro-radiologist. Patients in group B received a TRUS-guided PPNB with 10 ml of 2% mepivacaine (Scandicain®, AstraZeneca) outside the MR operating room. The PPNB was applied by a urologist (at least 3 years of experience in TRUS-guided prostate biopsy) with a 22-gauge spinal needle, using a Sonoace X8 ultrasound scanner (Samsung Medison) with an end fire 3D 3D4-9ES TRUS probe for guidance.

MRI-guided in-bore biopsy

Each patient received oral antibiotic prophylaxis for 5 days (daily 500 mg of levofloxacin) starting 2 days before biopsy. Coagulation parameters were routinely checked at least 1 week before the biopsy. MRI-guided in-bore biopsies were performed in prone position by an experienced uro-radiologist (at least 4 years of experience) using a 3-T scanner with a six-channel, phased-array body coil (Magnetom Trio; Siemens Healthineers). A needle guide was inserted transrectally proximal to the prostate gland and connected to the biopsy device (DynaTRIM; Invivo Corporation). For biopsy planning, T2-weighted HASTE axial (TR 2000 ms, TE 76 ms, FOV 28 cm, voxel size 1.4 × 1.1 × 3.0 mm) and sagittal (TR 2000 ms, TE 76 ms, FOV 28 cm, voxel size 1.4 × 1.1 × 3.0 mm) images were obtained. DynaCAD software (Invivo Corporation) was used for targeting of the suspicious lesions. All lesions were correlated on ADC maps before performing the biopsy to ensure the targeting of the lesion centre. Biopsies were performed with an MRI-compatible 18-gauge, fully automatic biopsy gun (needle length 150 or 175 mm, Invivo Corporation). After needle placement, a needle-in control scan was obtained in axial and coronal orientation: T2-weighted HASTE (TR, 1600 ms; TE, 96 ms; FOV, 38 cm; voxel size, 1.5 × 1.2 × 4.0 mm; acquisition time, 32 s) to verify the correct needle position. By default, two cores were taken from each lesion. Only in cases of inaccurate needle placement was a third biopsy core acquired. A total of no more than eight cores of up to three intraprostatic lesions were taken.

Pain score and operating room time (ORT)

A visual analog scale (VAS) was used to access the patients' pain from 0 to 10 (0 defined as no pain and 10 defined as maximal pain) immediately after the biopsy session still in the operating room. ORT was defined as the time between patient entry and exit of the operating room. In group B, PPNB was carried out before the biopsy procedure outside the operation room and, thus, was not included in the ORT. Pain scores and ORT were correlated with baseline characteristics (prostate volume, age and number of biopsy cores).

Statistical analysis

Statistical analysis was performed using IBM® SPSS® Statistics 21 (IBM) for Windows. For comparison of variables, the Mann-Whitney *U* test was used. The Spearman product-moment correlation was performed to determine the association between pain scores in relation to ORT, prostate volume and number of biopsy cores.

Results

Baseline characteristics

The patients' age and prostate volume were not significantly different between groups A and B. PSA levels were significantly higher in group A. Baseline characteristics are presented in Table 1.

Biopsy cores, pain score and ORT

In total, 711 targeted biopsy cores out of 351 lesions (97 patients with three lesions, 28 with two and one patient with four lesions; median 3, IQR 3–3) were obtained in group A: 4 to 8 cores per patient. Out of nine lesions, an additional third core was obtained to verify the optimal hit of the lesion. In group B, 660 targeted biopsy cores out of 323 lesions (80 patients with three lesions, 37 with two and 9 patients with one lesion; median 3, IQR 2–3) were taken: 2 to 6 cores per patient; 16 lesions with an additional third biopsy core. There were no punctures without following issue sample. Pain scores were slightly but significantly higher in patients receiving intrarectal lidocaine gel analgesia (VAS 2.4 ± 1.7) compared with patients with periprostatic nerve block (VAS 2.0 ± 1.9). The amount of time in the operating room (ORT) for both groups was nearly the same. Detailed values of biopsy cores, pain score and ORT are shown in Table 2.

Additionally, possible correlations between pain score and the number of biopsy cores, ORT and prostate volume were analysed in both groups (Table 3). Neither in patients with intrarectal lidocaine gel analgesia nor in patients with periprostatic nerve block were pain scores significantly correlated to the number of biopsy cores. We could demonstrate a weak correlation between pain scores and ORT for patients with PPNB. Prostate volume did not significantly correlate to pain scores.

Discussion

This study demonstrated that pain levels during MRI-guided IB-GB were generally low. The PPNB prior to the biopsy enabled a slightly further reduction of pain scores compared with local gel anaesthesia.

MRI-guided prostate biopsy techniques enable higher detection rates of clinically significant prostate cancer compared with systematic biopsy in patients with suspicion for prostate cancer [5]. The MRI-guided in-bore biopsy is the only

Table 1 Baseline characteristics

	Group A	Group B	*T* test
	MRI-guided in-bore biopsy with intrarectal lidocaine gel	MRI-guided in-bore biopsy with PPNB	
Number of subjects	126	126	
Prior biopsies	Yes	No	
Age (year)			0.8
Mean ± SD	66 ± 7.1	66 ± 8.1	
Median	67	67	
Range	47–79	45–82	
PSA (ng/ml)			**< 0.01**
Mean ± SD	13 ± 9.3	8.8 ± 8.7	
Median	10.3	6.7	
Range	4.1–61	4.1–93	
Interquartile range	7.2–15	5.1–9.1	
Prostate volume (cc)			0.6
Mean ± SD	58 ± 32	55 ± 28	
Median	48	48	
Range	16–204	14–156	
Interquartile range	35–72	36–68	

PPNB periprostatic nerve block; *PSA* prostate-specific antigen

Values in bold indicate p value < 0.05

Table 2 Pain score, operating room time (ORT) and number of biopsy cores in MRI-guided in-bore biopsy with intrarectal lidocaine gel (Group A) or periprostatic nerve block (*PPNB*, Group B)

	Group A	Group B	*p* value
	MRI-guided in-bore biopsy with intrarectal lidocaine gel	MRI-guided in-bore biopsy with PPNB	
Pain score Mean ± SD (range)	**2.4 ± 1.7 (0–7)**	**2.0 ± 1.9 (0–8)**	**0.02**
ORT (min) Mean ± SD (range)	42 ± 10 (20–70)	39 ± 10 (20–65)	0.08
Biopsy cores Mean ± SD (range)	**5.6 ± 0.8 (4–8)**	**5.2 ± 1.1 (2–6)**	**< 0.01**

Values in bold indicate p value < 0.05

technique which enables a direct MRI-controlled documentation of the needle position within the suspected intraprostatic lesion.

Analgesic techniques for IB-GB harbour certain limitations. A PPNB prior to MRI requires a trained operator (urologist or radiologist), an ultrasound device for targeted instillation of the local analgesia and additional time. Thus, PPNB increases to the personnel effort, material expense, and the costs of the interventions. Applying the PPNB in the operating room with a MR-compatible needle would further extend the procedural time and the material expense. Because of these limitations, transrectal IB-GB is typically performed with local gel analgesia [2]. This is in concordance with the current recommendations of the working group on uro-radiology and urogenital diagnosis which have been established by the German Radiological Society [6]. Fischbach et al described a freehand transgluteal IB-GB approach using a local anaesthetic with a mean pain score of 3 [7]. Penzkofer and colleagues described a transperineal IB-GB approach using a benzodiazepine (2–5 mg of midazolam hydrochloride), an opioid (50–300 μg of fentanyl citrate) and a local anaesthetic (2% sodium bicarbonate–buffered lidocaine, 10–20 ml per session) with an MR-compatible device resulting in a mean pain score of 1 [8]. When using analgesic drugs or general anaesthetic, subsequent patient monitoring dependent on the half-life needs to be taken into account for an outpatient setting.

PPNB is recommended as the standard of care in TRUS-guided systematic biopsy by the EAU guidelines [1]. Several studies have shown a significant pain reduction with PPNB compared with local gel anaesthesia in TRUS-guided biopsy [9–11]. In these studies, pain levels differ at least by 1 point on the visual analog scale. Adamakis reported a pain score of 4.8 with local gel anaesthesia, compared with 2.5 with PPNB, Rodriguez a score of 2.8 compared with 1.7 and Song a score of 5.5 compared with 3.6, respectively. Higher average pain scores compared with our results may be caused, among other reasons, by the higher number of biopsy cores in these studies. Stirling and colleagues could not show a significant difference in the local aesthesia group compared with the PPNB group in a prospective randomised trial when asking how uncomfortable the whole procedure was (score 2.2 vs. 3.0). They showed a slight advantage for PPNB when asking only for the biopsy procedure while initial probe injection was rated more painful compared with local anaesthesia [12]. In a prospective study, García et al could demonstrate that oral benzodiazepines could reduce pain in TRUS biopsy compared with the control group, but not as effective as PPNB [13]. In our study, we detected only a minor difference of 0.4 points on the pain score in favour of PPNB. However, comparing the absolute pain levels for TRUS-guided biopsy and IB-GB, pain levels in IB-GB are generally low in this study, independent of the analgesia used.

Since both cognitive fusion-guided biopsy (C-GB) and fusion MRI-ultrasound–guided biopsy (FUS-GB) uses the ultrasound device for targeting, a PPNB can easily be added for both techniques. Comparing different techniques, we have previously published that FUS-GB with PPNB caused slightly

Table 3 Correlation of pain scores with number of biopsy cores, operating room time (ORT) and prostate volume in both study groups with different analgesic techniques (intrarectal lidocaine gel vs. periprostatic nerve block, *PPNB*)

		Group A	Group B
		MRI-guided in-bore biopsy with intrarectal lidocaine gel	MRI-guided in-bore biopsy with PPNB
Correlation of pain score (r_S) with	Number of biopsy cores	0.11 ($p = 0.21$)	− 0.09 ($p = 0.32$)
	ORT	0.10 ($p = 0.25$)	**0.22 ($p = 0.01$)**
	Prostate volume	0.16 ($p = 0.07$)	0.03 ($p = 0.72$)

Values in bold indicate p value < 0.05. r_S Spearman correlation coefficient

less pain compared with IB-GB with local gel analgesia [14]. However, currently pain levels are low and comparable for both techniques which may be due to further increase of experience and clinical routine.

The operating room time for both groups was not significantly different and in accordance with the literature. A median biopsy time of 24 to 63 min has been reported for IB-GB [15]. The required time strongly depends on the number of suspicious lesions on prostate-MRI and the number of obtained biopsy cores. Development of robotic biopsy techniques as e.g. the MR-compatible remote-controlled manipulator might reduce the time-consuming process of needle placement, which also might reduce patients' pain sensation [16].

The number of biopsy cores should have an influence on patient pain levels. Normally, IB-GB is restricted to targeted biopsies only. Both C-GB and FUS-GB can be easily combined with a systematic biopsy. Following the Prostate Imaging – Reporting and Data System (PI-RADS) v2 recommendation, no more than four lesions with the highest likelihood of clinically significant cancer should be described in multiparametric prostate MRI [17]. In the literature, mostly two biopsy cores per lesion are obtained in IB-GB [15]. Nevertheless, we could demonstrate earlier that the benefit of a second biopsy core is minor regarding the detection rate assuming that the primary biopsy was sufficient [18]. In this study, significant fewer biopsy cores were taken in the PPNB group. Although this might explain less pain in the PPNB group, the correlation coefficients between biopsy cores and pain did not reach statistical significance.

Our study has some limitations. First, patients in the PPNB group were biopsy-naïve and patients with local gel anaesthesia had at least one prior negative ultrasound-guided biopsy. The experience of a prior biopsy might influence sensation of pain in the following biopsy procedure. Nevertheless, it remains unclear if a prior biopsy will increase or decrease the pain score. Second, the analysis of the procedural duration was limited to the documented operating room time, while the amount of time for the PPNB before biopsy was not included.

Conclusions

MRI-guided in-bore biopsy was performed with low pain levels using either PPNB or intrarectal instillation of lidocaine gel as analgesic method. A prior PPNB resulted in a statistically significant slightly lower pain score. Taking the higher effort and pre-biopsy workflow challenge of PPNB into account, gel anaesthesia might be well reasonable for standard analgesia for MRI-guided in-bore biopsy. Further prospective controlled randomised studies are requested focussing on analgesic techniques for MRI-guided in-bore biopsy.

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Compliance with ethical standards

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Statistics and biometry One of the authors has significant statistical expertise.

No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Some study subjects or cohorts have been previously reported:

Some patients in study group A were previously enrolled in a prospective randomised trial assessing the diagnostic efficacy of IB-GB and FUS-GB (ClinicalTrials.gov identifier: NCT02220517; Arsov C, Rabenalt R, Blondin D, et al (2015) Eur Urol).

Patients in study group B were previously enrolled in a prospective randomised trial assessing the diagnostic efficacy of IB-GB in comparison with TRUS-GB in biopsy-naïve men with elevated PSA (ClinicalTrials.gov identifier: NCT01553838; Quentin M, Blondin D, Arsov C, et al (2014) J Urol).

Methodology
- retrospective
- diagnostic or prognostic study
- performed at one institution

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