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ORIGINAL ARTICLE

A randomized controlled comparison between periprostatic nerve block and pelvic plexus block at the base and apex of 14-core prostate biopsies

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Abstract

Purpose To compare the pain control efficacies of the pelvic plexus block (PPB), periprostatic nerve block (PNB), and controls during a 14-core basal and apical core prostate biopsy.

Methods This randomized controlled study, performed between January 2015 and January 2016, included patients with an abnormal serum prostate-specific antigen (PSA > 3 ng/mL) level or a palpable nodule on digital rectal examination. The enrolled patients were randomized into three groups: Group 1, intrarectal local anesthesia (IRLA, 10 mL of 2% lidocaine jelly) and PPB with 3.0 mL of 2% lidocaine injected at the bilateral pelvic plexus; Group 2, IRLA and PNB with 3.0 mL of 2% lidocaine injected at both periprostatic nerves; and Group 3, only IRLA. Patients answered the visual analog scale (VAS) questionnaire at 6 time points.

Results This study consisted of 163 patients (Group 1 = 55, Group 2 = 55, and Group 3 = 53). Pain at the apical biopsy location was less in Groups 1 and 2 than in Group 3 ($p < 0.001$, $p < 0.001$) and between the two local anesthetic groups (PNB + IRLA vs PPB + IRLA). Group 2 patients reported less pain than Group 1 patients ($p = 0.022$). Pain during the basal core biopsy was significantly less in Groups 1 and 2 than in Group 3 ($p = 0.002$, $p < 0.001$), but there were no significant differences in pain control between the two methods (PNB + IRLA vs PPB + IRLA, $p = 0.054$) during basal core biopsy.

Conclusions PNB + IRLA is an effective local anesthetic method for reducing pain when performing apical biopsies compared with PPB + IRLA or IRLA alone.

Keywords Pelvic plexus · Prostate · Biopsy · Pain

Introduction

Prostate cancer is the most common malignancy, with the highest mortality among men from Western countries [1]. Screening for prostate-specific antigen (PSA) levels and digital rectal examination (DRE) with prostate biopsy enables early diagnosis of prostate cancer, and mortality due to prostate cancer is improved. In this era, transrectal ultrasonography (TRUS)-guided prostate biopsy is an essential procedure used for diagnosing prostate cancer [1, 2].

Although TRUS-guided prostate biopsy is an invasive procedure that requires penetration of the rectal wall, relatively few complications and low morbidity have been reported in urology outpatient clinics primarily [3, 4]. As prostate biopsy can cause very severe pain, it is important for clinicians to identify methods of reducing pain to increase patient acceptance of the biopsy procedure. Nash et al.

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reported that periprostatic nerve block (PNB) effectively reduces pain during biopsy [5] and it has been shown to be a very effective local anesthetic method in several studies [6]. PNB is the most common local anesthetic method used for prostate biopsy [7–9].

The pelvic plexus block (PPB) method is a local anesthetic method introduced by Wu et al. [10]. Recently, there have been a few prospective studies showing that PPB is more effective than PNB for pain control during prostate biopsies [11–13]. The theory behind the superiority of PNB over PPB is that it more effectively reduces apical pain in the prostate. This is achieved because PNB blocks the nerves in the proximal neurovascular bundle that innervate the superolateral and anterior parts of the prostate [13–15]. However, controversy still exists regarding the amount of pain reduction that can be achieved using the two methods, and no previous reports have compared the pain scores associated with basal and apical biopsies.

In this study, we tested the hypothesis that PPB + IRLA will be more effective than PPB + IRLA in controlling pain in apex biopsy. Therefore, we designed this study to compare the pain control efficacies of PPB, PNB, and controls during a 14-core basal and apical prostatic core biopsy.

Materials and methods

Study design and patient eligibility

This was a single-center, randomized controlled trial conducted after obtaining the approval and insight of the Gangneung Asan Hospital Institutional Review Board, Republic of Korea (IRB No. 2015-013). This study was performed at our hospital between January 2015 and January 2016.

Eligible participants were all adults over 18 years old who had an abnormal serum PSA level (PSA > 3 ng/mL) or a palpable nodule on DRE. Patients with a previous history of prostatitis, neurological disease-related pelvic pain, active urinary tract infection, anal disease, or lidocaine allergy were excluded.

Biopsy procedure technique

The patients were placed in a standard left lateral decubitus position during the procedure. A transrectal probe (Prostate Biplane 8808e, BK Medical ApS, Herlev, Denmark) was used with the Flex Focus 1202 Ultrasound system (BK Medical ApS).

The nerve block procedure was based on established standards in the literature. The pelvic neurovascular plexuses of the patients in Group 1 were identified on the lateral side of the seminal vesicle using color Doppler sonography. The PNBs were induced by injecting 3 mL of 2% lidocaine on both sides (Supplementary Figure 2) [10–12]. Triangular echogenic neurovascular bundles, viewed at an angle from the prostate base to the proximal tip of the seminal vesicle in the sagittal view, were identified in patients in Group 2. These PPBs were then induced by injecting 3 mL of 2% lidocaine on both sides (Supplementary Figure 1) [13, 16, 17]. The patients in Group 3 underwent biopsy, with no procedures performed after the administration of IRLA. Five minutes after the anesthesia was administered according to the group allocations, a 14-core prostate biopsy (base, 4 cores; mid, 4 cores; apex, 4 cores; apex anterior, 2 cores) was performed. Two cores of the apex anterior according to the prostate biopsy protocol were biopsied at the more apical site where the peripheral zone was thinned to obtain sufficient anterior tissue of the prostate apex (Supplementary Figure 3) [18].

Nerve blocks (PPB and PNB) were performed using a 22 gauge, 160 mm Disposable Nerve Blockade Needle Metal Hub® (Hakko®, Tokyo, JAPAN). Pathologic examination was performed using an 18-gauge, 20-cm long, disposable core tissue biopsy needle with a sample notch length of 1.9 cm (BARD® MAGNUM®, Providence, NJ, USA).

Assessment of complications and pain

Patients were administered an intravenous injection of 1 g aztreonam (Mezactam®) as a prophylactic antibiotic 1 h before the procedure. The patients were observed for urinary retention, dysuria, and hematuria for about 2 h after the procedure and were prescribed ciprofloxacin 250 mg bid for 1 week upon discharge home. Patients were assessed regarding the occurrence of post-procedural complications, such as high-grade fever, hematuria, rectal bleeding, and urinary retention, via questionnaires and statements in the outpatient clinic after 7–14 days.

After 30 min, patients were asked for the degree of pain using the visual analog scale (VAS, 0 as no pain to 10 as worst pain) at six time points: VAS-1, probe insertion; VAS-2, local injection of anesthetics (PPB, PNB); VAS-3, TRUS; VAS-4, prostate biopsies (basal and middle); VAS-5, prostate biopsies (apex, apex anterior); and VAS-6, 30 min after the prostate biopsies.

End point, randomization, and blinding

Patients were randomly assigned to three groups. Randomization sequence was generated in a 1:1:1 allocation ratio using random blocks of 3 and 6 via the Stata software (Stata version 12.0, Stata Corporation, TX, USA). Patients included in this study did not know their allocation group. The intervention staff did not know how the patients had been randomized and performed the procedures according to the allocation results. The questionnaires on post-procedural pain were evaluated by another clinician who was not involved with the procedure and conducted the evaluations separately. The VAS-2 questionnaire contained items about the allocation of the control arm; hence, these questions were asked last. Data analysts analyzed the data according to the research design without any information about the allocation.

Sample size estimation and statistical analysis

We calculated that 54 patients per group were needed to detect a difference of 0.4 in pain scores, assuming a standard deviation of 2.0 among the three groups (PNB + IRLA vs PPB + IRLA vs IRLA). The number of patients estimated assumed an effect size of 0.45 with 80% power and a 5% probability of type 1 error using the one-way analysis of variance (ANOVA) test by G*Power (version 3.1.9.2, Franz Faul, University Kiel, Germany).

Patient characteristics were summarized using descriptive statistics. The mean values and standard deviation (SDs) were reported for age and body mass index (BMI), and the differences among the three groups were analyzed using one-way ANOVA. Median values and interquartile ranges (IQR) were used to report prostate volume and PSA, and the differences among the three groups were analyzed using the Kruskal–Wallis *H* test (Table 1).

Mean values and SDs were reported for VAS at the time of the procedure. The *p* values reported in VAS-1 were calculated using Student's *t* test, and the *p* values for VAS-2 through VAS-6 were estimated by one-way ANOVA testing. The pain scores for Group 3 were calculated by one-way ANOVA testing. The post hoc analysis included *p* values obtained using the Mann–Whitney *U* test according to the study design (Table 2).

Complication rates were analyzed using the Chi-squared test or Fisher's exact test, as appropriate. A *p* value less than 0.05 was considered statistically significant. Statistical

Table 1 Baseline characteristics of the patients according to group allocation

Variables	Group 1 (IRLA + PPB), $n=55$	Group 2 (IRLA + PNB), $n=55$	Group 3 (IRLA), $n=53$	*p*
Age, years	68.3 ± 10.4	69.0 ± 7.6	67.4 ± 8.4	0.331
Prostate volume, mL	31.9 (27.1; 45.1)	37.7 (28.5; 52.1)	31.6 (25.8; 39.8)	0.068
PSA, ng/mL	6.0 (4.3; 8.6)	6.0 (4.3; 10.9)	5.9 (4.0;8.2)	0.908
BMI, kg/m^2	24.2 ± 2.9	25.0 ± 3.1	24.1 ± 2.8	0.089
Palpable nodule	5 (9.1%)	3 (5.5%)	3 (5.7%)	0.736
Prostate cancer	26 (47.3%)	25 (45.5%)	23 (43.4%)	0.921

Values are given as mean ± standard deviation for each group for age and BMI. Values are presented as numbers and percentages for palpable nodules and prostate cancer. Values are presented as medians and interquartile ranges for prostate volume, PSA

BMI body mass index, *IRLA* intrarectal local anesthesia, *PNB* periprostatic nerve block, *PPB* pelvic plexus block, *PSA* prostate-specific antigen

Table 2 Mean comparison of the VAS scores according to group allocation

Time point	Group 1 (IRLA + PPB), $n=55$	Group 2 (IRLA + PNB), $n=55$	Group 3 (IRLA), $n=53$	*p* value*	*p* value**		
					Group 2 vs 1	Group 3 vs 1	Group 3 vs 2
VAS-1	2.6 ± 1.6	1.8 ± 1.4		0.002			
VAS-2	1.9 ± 1.4	1.7 ± 1.3	2.3 ± 1.6	0.167			
VAS-3	1.7 ± 1.4	1.5 ± 1.2	1.5 ± 1.0	0.741			
VAS-4	3.0 ± 1.9	2.4 ± 1.9	3.3 ± 1.7	0.005	0.054	0.002	< 0.001
VAS-5	3.6 ± 2.3	2.8 ± 2.1	4.8 ± 2.0	< 0.001	0.022	< 0.001	< 0.001
VAS-6	0.6 ± 0.8	1.0 ± 1.2	0.9 ± 1.3	0.318			

Values are presented as mean ± standard deviation for each group

VAS visual analog scale, *VAS-1* block, *VAS-2* probe insertion, *VAS-3* TRUS, *VAS-4* basal biopsy, *VAS-5* apical biopsy, *VAS-6* 30 min after biopsy, *IRLA* intrarectal local anesthesia, *PPB* pelvic plexus block, *PNB* periprostatic nerve block, *ANOVA* analysis of variance

*One-way ANOVA

**Mann–Whitney *U* test

results were generated using SPSS software (IBM SPSS Statistics for Windows, Version 20.0. IBM Corp., Armonk, NY, USA).

Results

In this study, of 182 patients evaluated for eligibility, 168 patients were enrolled and randomized. Among these patients, 163 patients (Group 1 (PPB + IRLA): $n = 55$; Group 2 (PNB + IRLA): $n = 55$; Group 3 (IRLA): $n = 53$) completed the study and were included in the analysis (Fig. 1).

Patients' mean age, prostate volume, PSA, and BMI parameters were comparable among the three groups. There was no significant difference in the proportion of patients with palpable nodules, and the cancer detection rate was not different among the three groups (Table 1).

Pain at the time of local anesthesia (VAS-1) was found to be less severe in Group 2 than in Group 1 ($p = 0.002$). The pain in basal core biopsies was significantly less severe in Groups 1 and 2 than in Group 3 (Table 2; Supplementary Figure 4; $p = 0.002$; $p < 0.001$). However, there was no significant difference in pain of basal core biopsies between the PPB + IRLA and PNB + IRLA methods ($p = 0.054$). The pain due to the apical biopsies was less severe in anesthetic Groups 1 and 2 than in Group 3 (Table 2; Supplementary Figure 4; $p < 0.001$; $p < 0.001$). Between the two local anesthetic groups, the patients in Group 2 reported less pain than those in Group 1 ($p = 0.022$; Table 2; Supplementary Figure 4).

Among the post-procedural complications, hematuria developed in 25 patients (45.5%) in Group 1, 26 patients (47.3%) in Group 2, and 29 patients (54.7%) in Group 3. Rectal bleeding occurred in less than 10% of patients in each group, and urinary retention occurred in 2 patients in Group 2 and 1 patient in Group 3. There was no significant difference in the incidence of complications among the three groups (Supplementary Table 1).

Discussion

Given the results of this randomized controlled study, PNB was a more effective local anesthetic method of reducing pain than PPB when obtaining the apex cores during a 14-core prostate biopsy. To our knowledge, this is the first study to evaluate pain control efficacy at a specific prostate biopsy site according to successful reports of two local anesthetic methods (PPB + IRLA, PNB + IRLA) with control (IRLA) (Supplementary Figures 1, 2) [7–9, 11–13]. This study is a well-followed-up study in which 90% of the eligibility-assessed patients participated in the study and

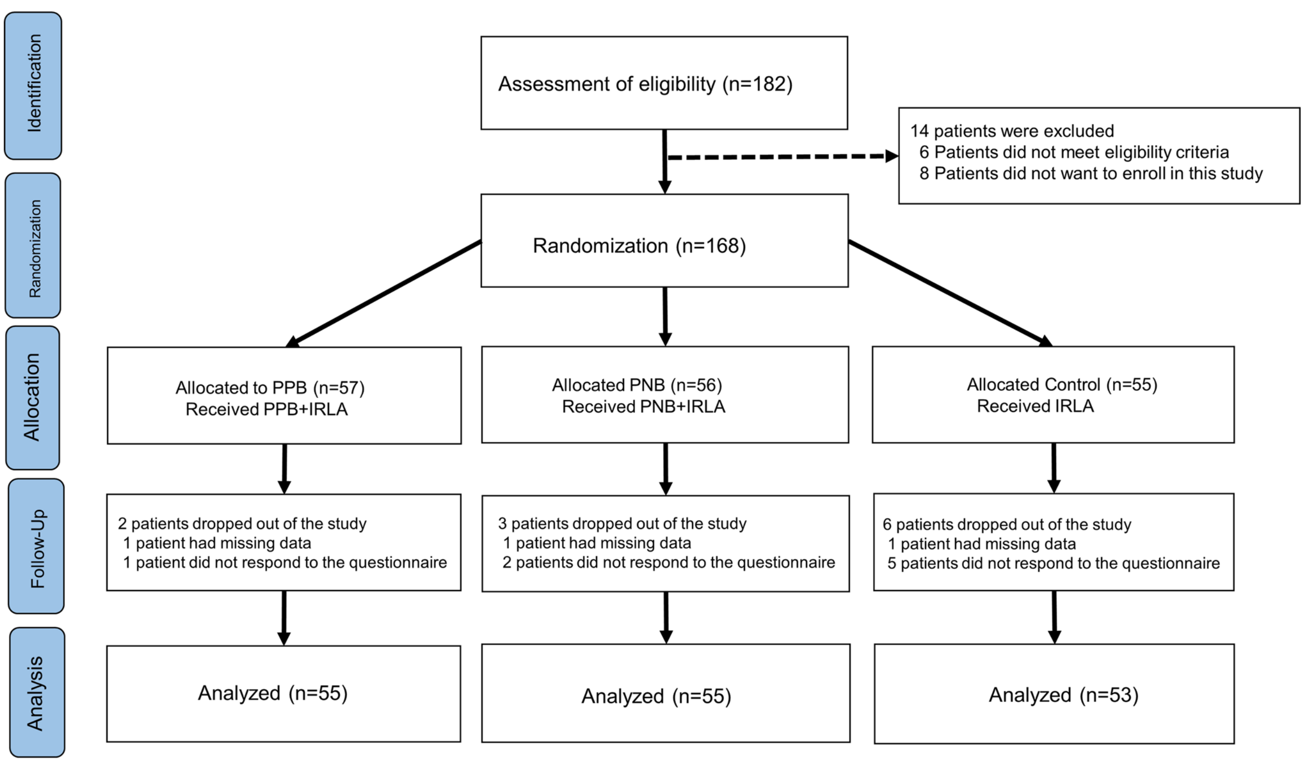

Fig. 1 Flow diagram of the study

more than 90% of the enrolled patients were included in the analysis.

The PNB, since its introduction by Nash et al. in 1996, is the most widely used method for local anesthesia during a prostate biopsy [5, 19]. In this study, as in previous studies, the PNB method was also the most effective pain control method applied to specific sites during prostate biopsies. They indicated that the optimal bibasilar injection sites in the parasagittal longitudinal view were at the echogenic angle of the prostate base and the seminal vesicle (Supplementary Figure 2). The efficacy of prostatic biopsies using this method has been studied since then. PNB is known to be a highly effective local anesthetic method for use in prostate biopsies and is effective for pain relief [7–9]. In a recent meta-analytic review, Yan et al. [20] concluded that the combination of PNB and IRLA was the most effective method of controlling pain.

The first description of the current PPB was by Wu et al. [10]. They randomized patients and performed grayscale ultrasound-guided injections of 5 mL of 1% lidocaine on the lateral side of the seminal vesicle and found no reduction in pain in the lidocaine-injected patients. However, Akpinar et al. [11], in a prospective randomized study, reported that 2 mL of 2% lidocaine injected under color Doppler ultrasound guidance was more effective than PNB. Jindal et al. [13] and Cantiello et al. [12] reported that injecting local anesthetics in the neurovascular bundle (pelvic plexus) is a more effective method for pain relief than PNB.

Theoretically, PPB is more advantageous than PNB when anesthetizing a large proportion of the prostate by blocking nerve fibers that supply the superolateral and anterior parts of the prostate. The pain caused by stimulation of the prostate gland originates from the S2 to S5 nerve roots, starting from the caudal root. It is initiated through the sympathetic ganglia, prostate, and pelvic plexus [14, 15]. In PNB, anesthetics penetrate the nerves around the prostate only. On the basis of the anatomical structure, PPB can block all prostate nerve fibers derived primarily from the pelvic plexus [13].

In our study, the PPB method was found to be associated with more pain than that on using the PNB method during the VAS-1 phase (Table 2). The application of a local anesthetic during the puncture of the rectum for PPB is painful because the needle penetrates the distal part of the dentate line. This area is very sensitive to pain because it contains a somatic nerve branch of the inferior rectal nerve, which originates in the pudendal canal [21]. After puncturing the rectal wall, the needle should travel a longer distance to effectively perform PPB, which results in more pain because of the deep penetration of the needle. Pain with local anesthesia may cause the patient to move involuntarily during the process [22]. Angular misalignment caused by patient movement under local anesthesia is likely to be more significant during PPB because of the aforementioned longer distance from the rectal wall puncture site to the neurovascular bundle [23]. When performing PPB using a longitudinal TRUS view, it is important to understand the anatomy of the seminal vesicles and bladder spatially. These structures are indirect anatomical markers that are not closely attached to the pelvic plexus. Investigators should find the vascularity associated with the pelvic plexus using color Doppler TRUS. However, in PNB, the puncture site is an echogenic point that is easily identifiable on grayscale TRUS by visualizing the angle between the seminal vesicle and prostate and using it as an anatomical landmark to directly aid in the anesthetic process. PPB is more difficult to perform than PNB when performed by individuals with the same level of proficiency (Supplementary Figures 1, 2).

In this study, performing an additional anterior biopsy compensated for the disadvantages of the conventional TRUS-guided biopsy protocol (12 cores), which sometimes fails to detect prostate cancer localized to the anterior prostate apex (Supplementary Figure 3) [18]. However, obtaining anterior tissue of the prostate apex by TRUS-guided prostate biopsy is a painful procedure. Transperineal prostate biopsy is generally more painful than TRUS-guided prostate biopsy [24], but it is an effective method with a high cancer detection rate, especially for anterior localized prostate cancer [25]. Because this method does not involve penetration into the distal dentate line of the rectal wall, it does not cause severe pain when obtaining anterior tissue of the prostate apex [21]. Thus, transperineal prostate biopsy may be considered a less painful alternative method to the prostate biopsy protocol performed in this study.

Previous studies have shown that approximately 3–4% of patients are at risk for serious complications after biopsy procedures, such as sepsis, requiring hospitalization [3, 4]. In our study, 163 patients received 1 g of aztreonam (Mezactam®) intravenously and ciprofloxacin 250 mg orally twice daily for 1 week as a prophylactic antimicrobial regimen. None of our study patients experienced complications such as sepsis requiring hospitalization or intervention.

This study has several limitations. The local anesthetic procedures were performed by two urologists. There could have been variability in patients' pain thresholds because of differences in procedural expertise. The total of 14-core prostate biopsies performed (with an extra 2 cores taken from the anterior apex) were likely to cause more severe pain in the apex than in the setting of the more widely used 10- to 12-core biopsy.

Conclusions

PNB + IRLA was a more effective local anesthetic method for reducing the pain in apical prostatic biopsies than PPB + IRLA or IRLA alone. More research is needed to evaluate pain control in specific prostate areas of the prostate according to the methods of local anesthesia.

Author contribution SJK: data management, data analysis, manuscript writing/editing. JL: data collection, data analysis. DHA: data collection data analysis. CP: data analysis. JHL: project development. HGK: manuscript writing/editing. JYP: project development, manuscript editing.

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Eastham J (2017) Prostate cancer screening. Investig Clin Urol 58:217–219. https://doi.org/10.4111/icu.2017.58.4.217
2. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, Mason M, Matveev V, Wiegel T, Zattoni F, Mottet N (2014) EAU guidelines on prostate cancer. part 1: screening, diagnosis, and local treatment with curative intent—update 2013. Eur Urol 65:124–137. https://doi.org/10.1016/j.eururo.2013.09.046
3. Akduman B, Akduman D, Tokgoz H, Erol B, Turker T, Ayoglu F, Mungan NA (2011) Long-term fluoroquinolone use before the prostate biopsy may increase the risk of sepsis caused by resistant microorganisms. Urology 78:250–255. https://doi.org/10.1016/j.urology.2011.02.065
4. Gaylis F, Nasseri R, Fink L, Calabrese R, Dato P, Cohen E (2016) Prostate biopsy complications: a dual analysis. Urology 93:135–140. https://doi.org/10.1016/j.urology.2016.03.035
5. Nash PA, Bruce JE, Indudhara R, Shinohara K (1996) Transrectal ultrasound guided prostatic nerve blockade eases systematic needle biopsy of the prostate. J Urol 155:607–609. https://doi.org/10.1016/S0022-5347(01)66464-4
6. Li M, Wang Z, Li H, Yang J, Rao K, Wang T, Wang S, Liu J (2017) Local anesthesia for transrectal ultrasound-guided biopsy of the prostate: a meta-analysis. Sci Rep 7:40421. https://doi.org/10.1038/srep40421
7. Adamakis I, Mitropoulos D, Haritopoulos K, Alamanis C, Stravodimos K, Giannopoulos A (2004) Pain during transrectal ultrasonography guided prostate biopsy: a randomized prospective trial comparing periprostatic infiltration with lidocaine with the intrarectal instillation of lidocaine-prilocain cream. World J Urol 22:281–284. https://doi.org/10.1007/s00345-003-0386-4
8. Alavi AS, Soloway MS, Vaidya A, Lynne CM, Gheiler EL (2001) Local anesthesia for ultrasound guided prostate biopsy: a prospective randomized trial comparing 2 methods. J Urol 166:1343–1345. https://doi.org/10.1016/S0022-5347(05)65765-5
9. Autorino R, De Sio M, Di Lorenzo G, Damiano R, Perdona S, Cindolo L, D'Armiento M (2005) How to decrease pain during transrectal ultrasound guided prostate biopsy: a look at the literature. J Urol 174:2091–2097. https://doi.org/10.1097/01.ju.0000181212.51025.06
10. Wu CL, Carter HB, Naqibuddin M, Fleisher LA (2001) Effect of local anesthetics on patient recovery after transrectal biopsy. Urology 57:925–929. https://doi.org/10.1016/S0090-4295(01)00930-X
11. Akpinar H, Tufek I, Atug F, Esen EH, Kural AR (2009) Doppler ultrasonography-guided pelvic plexus block before systematic needle biopsy of the prostate: a prospective randomized study. Urology 74:267–271.e261. https://doi.org/10.1016/j.urology.2009.01.082
12. Cantiello F, Cicione A, Autorino R, Cosentino C, Amato F, Damiano R (2012) Pelvic plexus block is more effective than periprostatic nerve block for pain control during office transrectal ultrasound guided prostate biopsy: a single center, prospective, randomized, double arm study. J Urol 188:417–422. https://doi.org/10.1016/j.juro.2012.04.003
13. Jindal T, Mukherjee S, Sinha RK, Kamal MR, Ghosh N, Saha B, Mitra N, Sharma PK, Mandal SN, Karmakar D (2015) Transrectal ultrasonography (TRUS)-guided pelvic plexus block to reduce pain during prostate biopsy: a randomised controlled trial. BJU Int 115:892–896. https://doi.org/10.1111/bju.12872
14. Hollabaugh RS Jr, Dmochowski RR, Steiner MS (1997) Neuroanatomy of the male rhabdosphincter. Urology 49:426–434. https://doi.org/10.1016/s0090-4295(96)00497-9
15. Stirling BN, Shockley KF, Carothers GG, Maatman TJ (2002) Pain perception during transrectal ultrasound guided prostate needle biopsy: an objective analysis of local anesthesia use. Prostate Cancer Prostatic Dis 5:209–211. https://doi.org/10.1038/sj.pcan.4500598
16. Berger AP, Frauscher F, Halpern EJ, Spranger R, Steiner H, Bartsch G, Horninger W (2003) Periprostatic administration of local anesthesia during transrectal ultrasound-guided biopsy of the prostate: a randomized, double-blind, placebo-controlled study. Urology 61:585–588. https://doi.org/10.1016/S0090-4295(02)02406-8
17. Stirling BN, Shockley KF, Carothers GG, Maatman TJ (2002) Comparison of local anesthesia techniques during transrectal ultrasound-guided biopsies. Urology 60:89–92. https://doi.org/10.1016/S0090-4295(02)01671-0
18. Moussa AS, Meshref A, Schoenfield L, Masoud A, Abdel-Rahman S, Li J, Flazoura S, Magi-Galluzzi C, Fergany A, Fareed K, Jones JS (2010) Importance of additional "extreme" anterior apical needle biopsies in the initial detection of prostate cancer. Urology 75:1034–1039. https://doi.org/10.1016/j.urology.2009.11.008
19. Soloway MS, Obek C (2000) Periprostatic local anesthesia before ultrasound guided prostate biopsy. J Urol 163:172–173. https://doi.org/10.1016/S0022-5347(05)67997-9
20. Yan P, Wang XY, Huang W, Zhang Y (2016) Local anesthesia for pain control during transrectal ultrasound-guided prostate biopsy: a systematic review and meta-analysis. J Pain Res 9:787–796. https://doi.org/10.2147/jpr.S117451
21. Bastide C, Lechevallier E, Eghazarian C, Ortega JC, Coulange C (2003) Tolerance of pain during transrectal ultrasound-guided biopsy of the prostate: risk factors. Prostate Cancer Prostatic Dis 6:239–241. https://doi.org/10.1038/sj.pcan.4500664
22. Ochiai A, Babaian RJ (2004) Update on prostate biopsy technique. Curr Opin Urol 14:157–162
23. Bjurlin MA, Carter HB, Schellhammer P, Cookson MS, Gomella LG, Troyer D, Wheeler TM, Schlossberg S, Penson DF, Taneja SS (2013) Optimization of initial prostate biopsy in clinical practice: sampling, labeling and specimen processing. J Urol 189:2039–2046. https://doi.org/10.1016/j.juro.2013.02.072
24. Guo LH, Wu R, Xu HX, Xu JM, Wu J, Wang S, Bo XW, Liu BJ (2015) Comparison between ultrasound guided transperineal and transrectal prostate biopsy: a prospective, randomized, and

controlled trial. Sci Rep 5:16089. https://doi.org/10.1038/srep16089
25. Pepe P, Aragona F (2014) Prostate biopsy: results and advantages of the transperineal approach—twenty-year experience of a single center. World J Urol 32:373–377. https://doi.org/10.1007/s00345-013-1108-1