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ARTICLE

End-fire versus side-fire: a randomized controlled study of transrectal ultrasound guided biopsies for prostate cancer detection

Margaretha A. van der Slot[a], Joost A. P. Leijte[a], Deric K. E. van der Schoot[a], Eric H. G. M. Oomens[a] and Stijn Roemeling[b]

[a]Department of Urology, Amphia, Breda, The Netherlands; [b]Urology, University Medical Center Groningen (UMCG), Groningen, The Netherlands

ABSTRACT

Objectives: To compare prostate cancer detection rates between end-fire and side-fire ultrasound guided prostate biopsy techniques.

Methods: A prospective randomized controlled trial was performed in patients who underwent prostate biopsy between 2009 and 2014. Patients were randomly assigned to the end-fire or side fire biopsy groups and underwent transrectal ultrasound guided prostate biopsy. The overall prostate cancer detection rate was compared between the two probe configurations. Trial was registered at Clinical Trials.gov with identifier: NCT00851292.

Results: A total of 730 patients were included and randomized, 371 patients underwent prostate biopsy with side-fire probe and 359 patients with the end-fire probe. Prostate cancer detection rates were 52.4% in the end fire group and 45.6% in the side fire group ($p = .066$).

Conclusions: No significant difference was found in detection rate of prostate cancer between the end-fire and side-fire probe in transrectal ultrasound guided prostate biopsy, neither for detection rate of prostate cancer in the apex.

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KEYWORDS
Prostate cancer; prostate biopsy; probe configuration; biopsy technique

Introduction

The most common indication for performing prostate biopsy is the suspicion of prostate cancer, mostly based on an elevated PSA level and/or an abnormal DRE. Currently, prostate biopsies remain the standard of care to assess the presence, type and extension of prostate cancer. Transrectal ultrasound guided prostate biopsy is one of the standard of care for taking biopsies [1]. Biopsies can be performed using either an end-fire or side-fire biopsy technique. A side-fire probe has two planes of view, of which the sagittal view is used to visualize the needle tract for biopsy. The end fire probe has a single plane on the tip of the probe, biopsy can be performed in all sections, transverse, sagittal and oblique plane, by turning and rotating the probe (Figure 1) [2]. A retrospective study of Ching et al., observed a higher prostate cancer detection rate using the end-fire technique [3]. Another retrospective study of Raber et al., showed no significant difference between the both techniques in detection rates of prostate cancer [4]. The aim of this study was to evaluate the prostate cancer detection rate of the end-fire and side-fire techniques in a prospective randomized controlled trial.

Materials and methods

A randomized controlled trial was performed in Amphia Hospital, Breda, The Netherlands. This is a large regional training hospital. The procedures were performed in accordance with the ethical standards of the institutional committee of Amphia hospital. The trial was registered at Clinical Trials.gov (identifier: NCT00851292) and approved by the institutional committee of Amphia Hospital.

Population

Prostate biopsy was indicated by the treating urologist if the PSA level was high and/or digital rectal examination (DRE) was suspected for prostate cancer. Patients were included when they underwent prostate biopsy (initial, repeated and surveillance biopsies). DRE was performed in advance of the biopsy. Patients were informed about the trial by their urologist and were asked to provide informed consent. In case of protocol violation, a patient was excluded.

Randomization

The patients were randomized by a sealed-envelope procedure. A nurse opened the sealed envelope just before the prostate biopsies were performed. The same nurse ensured that the technique was applied and the study forms were completed correctly. The patient was not informed about which technique was used.

CONTACT Margaretha A. van der Slot mvanderslot@amphia.nl Department of Urology, Amphia, Langendijk 75, 4819 EV Breda, The Netherlands

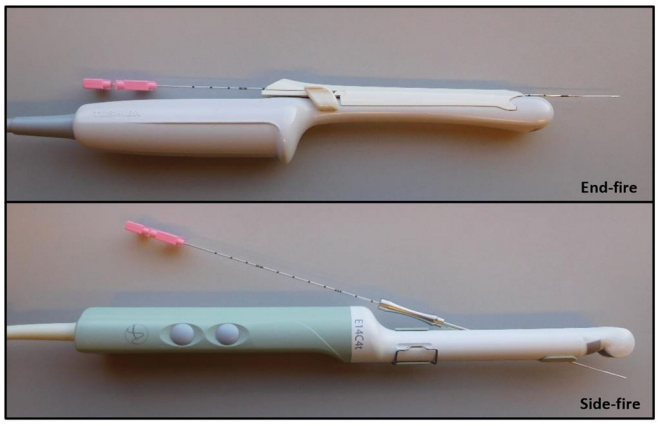

Figure 1. End- and side-fire probes.

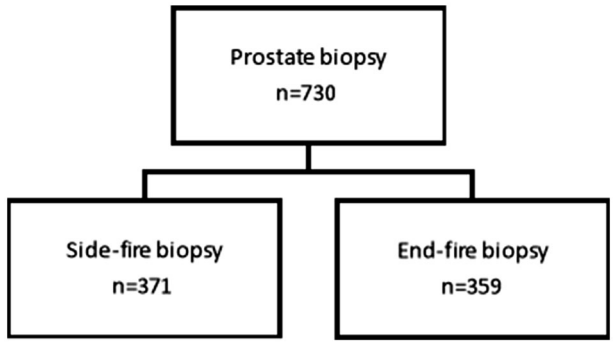

Figure 2. Study flow diagram.

Table 1. Patient characteristics.

Patient characteristics ($n = 730$)	Side-fire $n = 371$	End-fire $n = 359$
Mean age in years (SD)	65.6 (7.5)	66.1 (7.5)
Median PSA in ng-mL (interquartile range: IQR)	9.56 (7.1–14.7)	9.56 (6.9–15.0)
Median prostate volume in mL (interquartile range: IQR)	45.0 (33.0–60.2)	39.0 (29.0–58.0)
DRE abnormal (%)	125 (33.7%)	130 (36.2%)

Procedure

All patients received antibiotic prophylaxis. Local anesthesia was not applied. Anti-coagulants were discontinued before prostate biopsy. The biopsies were performed by six urologists and two residents in urology, all of whom were familiar with both biopsy techniques. The B-K Medical Pro Focus ultrasound scanner with a B-K medical type 8818 combined biplane and end-fire transrectal probe was used. The guide channels are angled at 0° to the transducer axis of the end-fire transrectal probe and 19° to the transducer axis of the side-fire probe. The angles are similar in all B-K transducers. The biopsies were performed with an 18 gauge needles and a Bard spring-loaded biopsy gun. The prostate volume was measured (length × height × width × π/6) and depending on the volume 8–12 cores were taken with patient in left side position. Eight cores were obtained if the prostate volume was less than 40 mL, 10 cores if the volume was 40–60 mL and 12 cores if the volume was more than 60 mL. The apex cores were stored in separate pathology containers. The interim analysis was done after inclusion of 345 patients and showed a smaller prostate volume in the end-fire probe group compared to the side-fire probe group, but not significant (p=.106). A difference in prostate volume between the two probes can lead to a difference in numbers of cores and prostate cancer detection. After the interim analysis, 10 cores were taken of the prostate, the number of cores conforms the EAU guidelines.

Sample size calculation

In the sample size calculation, an absolute difference of 10% in detection of prostate cancer was assumed as clinically relevant. With a power of 80% and α-level of 5% three different calculations (Kelsey, Fleiss and Fleiss with CC; 364, 362, 382, respectively per group) showed an average of 375 participants per group. Based on these numbers, sample size was aimed at inclusion of 800 patients.

Data analysis

The following variables were documented from every patient: age, (initial, repeat or surveillance) biopsy, PSA, DRE findings, prostate volume and number of biopsy cores. All patients were questioned about the complications and pain two weeks after biopsy, during follow-up visit. Pain was measured with a numbering rating scale from 0 to 10. The Gleason score, presence of prostate cancer in the apex cores and length of biopsy were collected from the pathology report. The microscopic length of biopsy was collected, if the microscopic length was not mentioned in the pathology report the estimated macroscopic length was collected. Statistical analyses were performed using SPSS version 24 for Windows (SPSS Inc., Chicago, IL). Outcomes in the groups were compared using the chi-square test, independent t-test and logistic regression. A p value of less than .05 was considered significant.

Results

Between March 2009 and October 2014, 730 patients were included and randomly assigned to the end or side fire probe group, respectively, 359 patients and 371 patients (Figure 2). In 356 (48.8%) patients, prostate cancer was found. The patient characteristics are described in Table 1.

A 6.8% higher prostate cancer detection rate was measured for end-fire probe compared to side-fire probe (Table 2). This result was not significantly different (p=.066). Compared to the side-fire probe, the use of an end-fire probe did not result in a higher apical detection of prostate cancer nor in difference in Gleason's patterns. It did however result in biopsy cores of a greater length. The prostate cancer detection rate did not significantly differ after the number of cores were changed from 8 to 12 cores to 10 cores (p=.689). No significant difference was found in prostate cancer detection rate between the two probes in the initial biopsy group (p=.276), neither in the repeat biopsy group (p=.222). In the surveillance biopsy group, prostate cancer

Table 2. Primary outcomes.

Primary outcomes	Side-fire ($n = 371$)	End-fire ($n = 359$)	p Value
Prostate cancer (%)	169 (45.6%)	188 (52.4%)	.066
Prostate cancer apex (%)	111 (29.9%)	118 (32.9%)	.390
Number of cores positive for prostate cancer (%)	23.7%	20.2%	.137
Gleason (%)			.247
6	88 (23.7%)	101 (28.1%)	
7	46 (12.4%)	44 (12.3%)	
≥8	35 (9.4%)	43 (12.0%)	
Mean length biopsy in mm (SD)	14.2 (3.52)	15.6 (3.98)	.000
Biopsy type			.587
Initial biopsy	285 (79.4%)	283 (76.3%)	
Repeat biopsy	71 (19.8%)	85 (22.9%)	
Surveillance biopsy	3 (0.8%)	3 (0.8%)	

Table 3. Univariate and multivariate analyses.

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio	p Value	Odds ratio	p Value
Age	1.065	.000	1.051	.000
Abnormal DRE	4.041	.000	3.238	.000
PSA	1.032	.000	1.023	.004
Prostate volume	0.980	.000	0.979	.000
Probe configuration	0.850	.334	0.912	.626

Table 4. Complications.

Complications	Side-fire probe	End-fire probe	p Value
Hematuria	148 (39.9%)	126 (35.1%)	.181
Fever	5 (1.3%)	6 (1.7%)	.720
Hematospermia	76 (20.5%)	61 (17.0%)	.227
Acute urine retention	0 (0%)	2 (0.6%)	.150
Rectal bleeding	68 (18.3%)	64 (17.8%)	.860
Hospital admission	0 (0%)	3 (0.8%)	.078
Pain (score 0–10)	3.72	3.60	.535

was detected only with the end-fire probe ($p = .014$), but this group had only six patients. Of the 392 patients with a PSA less than 10.0 ng/mL 164 (41.8%) had prostate cancer, the detection rate for the end-fire probe and side-fire probe were 44.6% and 39.2%, respectively ($p = .282$).

Univariate and multivariate analyses show that increased age, suspected DRE, increased PSA and decreased prostate volume significantly increased detection rate of prostate cancer (Table 3). In the multivariate analysis, the configuration of the probe was not associated with detection of prostate cancer.

As can be seen from Table 4, there was no significant difference in the incidence of complications between the end- and side-fire groups.

Discussion

In this randomized controlled trial, we compared the prostate cancer detection rate between the end-fire and side-fire probe in a Dutch teaching hospital between 2009 and 2014. Compared to the end-fire probe, more cancers were detected than with the use of the side-fire probe. However, this result was not significantly different ($p = .066$). Although the apex is assumed to be more difficult to reach with the side fire probe, in this study, no significant difference was found in detection rate of prostate cancer in the apex of the prostate between the two groups.

Past studies presented conflicting results about the influence of the probe in prostate cancer detection rate [2–4]. Two studies showed that the probe configuration did not affect the prostate cancer detection rate and are in line with our study [4,5]. The study of Raber et al. is a large retrospective study and had no significant differences in detection of prostate cancer between the end fire-probe and side-fire probe, respectively, 38.0% and 36.5% [4]. In this study, the end fire probe was associated with more pain during the biopsy probably due to the larger tip of the probe. In our study, no difference was found between the two probes in neither pain, nor complications. One prospective study compared the detection rate between the probe configurations and found no significant difference. This study of Rom et al. included 297 patients and found a prostate cancer detection rate 34.3% for end-fire probe and 34.4% for side-fire probe [5].

Two large retrospective studies suggested an improved detection rate of prostate cancer using an end-fire probe [2,3]. In the study of Paul et al., no significant difference was found in overall detection of prostate cancer between end-fire and side-fire probes [2]. In this study, sextant biopsy was performed regardless of the volume of the prostate; the cores were taken at the base, center and apex on both sides. In our study, the amount of cores was depending on the volume of the prostate and after interim analysis 10 cores were taken. The other retrospective study of Ching et al. did show a significant difference of overall prostate cancer detection between the probe configurations [3]. In the end-fire group, the prostate cancer detection rate was 45.8% compared to 38.5% in the side-fire group. However, there was a significantly higher rate of abnormal DRE in the end-fire group and possibly influencing results. The multivariate analysis showed also no significant difference of prostate cancer detection rate between the probe configurations.

We found a difference in the length of the biopsy cores between the two techniques, with a mean core length of 151.0 mm in the end-fire and 138.0 mm in the side-fire group. The length of biopsy has not been described in the abovementioned studies [2–5]. A possible explanation could be that the end fire probe has a better sampling of the prostate. Shorter biopsy length is also related with underestimation of the Gleason score [6,7]. In our study, no significant difference was found in Gleason score between the end- and side-fire groups.

In our study, the median prostate volume was 45.0 mL in the side-fire group and 39.0 mL in the end-fire group.

According to the CONSORT, any differences in baseline characteristics are the result of chance rather than bias [8]. To our knowledge, no studies examined the difference in prostate volume between the probe configurations. The prospective study of Rom et al. included 297 patients and found no significant difference in prostate volume between the groups [5].

As expected, our uni- and multivariate analyses showed that prostate cancer detection rate was associated with age, abnormal DRE, prostate volume and PSA in our univariate and multivariate analyses. These parameters are predictors for prostate cancer and also used in the European Randomized Study of Screening for Prostate Cancer risk calculators [9]. A decreased prostate volume was associated with increased detection rate of prostate cancer, despite the number of biopsy cores depended on the prostate volume. Other studies confirm this relation between prostate volume and cancer detection rates [4,10,11].

The use of MRI in detection of prostate cancer has a rapidly increasing role. Last year, the EAU guideline suggested an MRI of the prostate in patient with negative biopsies and a continuing suspicion of harboring prostate cancer. The current EAU guideline recommends to perform MRI before biopsy, also in biopsy-naïve patients [1]. Several studies show the use of MRI, in biopsy-naïve patients, leads to an improved detection rate of mainly significant prostate cancer [12–14]. In case of a suspicious lesion on MRI, targeted biopsies using TRUS/MRI fusion techniques are increasingly used. Most ultrasound/MRI fusion-systems use an end-fire probe configuration.

A limitation of our study is the amount of included patients, the calculated power of 800 patients was not reached. After inclusion of 730 patients, no significant difference was seen in prostate cancer detection rate between the two probes. This analysis suggested that no significant difference would be seen if the calculated power was reached. To our knowledge, this study is the largest randomized controlled trial which compared detection rate of prostate cancer in the end-fire and side-fire probe.

In conclusion, this randomized controlled trial showed no significant difference in prostate cancer detection rate between the use of an end fire probe versus a side fire probe. This holds also true for the apical detection and the amount of complications. We did find a significant difference in mean length of the biopsy cores; however, this did not result in better detection rates.

Trial registry

Clinicaltrials.gov name: The BIOPRES Trial: Transrectal BIOpsies of the PRostate: End Versus Side-firing (BIOPRES) Identifier: NCT00851292.

Geolocation information

Amphia, Langendijk 75, 4819 EV Breda, Netherlands.

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Margaretha A. van der Slot http://orcid.org/0000-0002-7304-7542

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