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Comparison of complications rates between multiparametric magnetic resonance imaging-transrectal ultrasound (TRUS) fusion and systematic TRUS prostatic biopsies

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Abstract

Purpose: The aim of this study was to compare the complication rates between transrectal ultrasound (TRUS) systematic prostate biopsy and multiparametric magnetic resonance imaging (MRI)-TRUS fusion prostate biopsy techniques.

Materials and methods: This is a single-center retrospective study, institutional review board approved. Systematic TRUS and MRI-TRUS fusion prostate biopsy complication rates were compared in 967 men. A total of 319 patients were received systematic TRUS prostate biopsy and 648 patients underwent systematic TRUS + MRI-TRUS fusion prostate biopsy. Complications were divided into immediate (those that occurred during the hospital observation period) and late (those that occurred within 5 days after biopsy).

Results: Seventeen complications were observed in patients who received either a systematic prostate biopsy or MRI-TRUS fusion prostate biopsy. Severe complications were not observed in both groups. Among patients who underwent systematic prostate biopsy, 6 (1.9%) cases of complications were observed and between those who received MRI-TRUS fusion prostate biopsy 11 (1.7%) cases of complications after the procedure ($p = 0.873$) were observed, with no statistical difference between groups. Also, no statistical differences between early and late complication groups ($p > 0.999$) were observed.

Conclusions: The complication rates were low in both groups, with no critical clinical outcomes and no significant difference of complication rates between systematic TRUS prostate biopsy and MRI-TRUS fusion prostate biopsy techniques.

Key words: Prostatic neoplasms/diagnosis—Magnetic resonance, imaging/methods—Biopsy—Ultrasonography—Interventional

Transrectal ultrasound (TRUS) systematic prostate-guided biopsy is the usual urologic procedure indicated for patients with abnormal findings on digital rectal exams or with elevated levels of prostate-specific antigen (PSA) [1, 2]. Additionally, it is a fundamental tool for diagnosis and treatment planning in patients with suspected prostate cancer [3]. An accurate prostate biopsy is based on balancing the improved detection of clinically significant cancer while limiting the detection of insignificant lesions, in addition to good correlations with findings in surgical specimens, avoiding overdiagnosis and overtreatment [4]. Several strategies have been developed to achieve these goals, such as increasing the number of cores per biopsy (saturation biopsy), oversampling suspected areas on digital rectal examination or transrectal ultrasound [3, 4] and methods that use prostatic multiparametric magnetic resonance (MRI) information to obtain prostate biopsies such as In-Bore MRI-guided [5, 6] or MRI-TRUS fusion prostate biopsies [7].

MRI is an established method to detect clinically significant prostate cancer as it can combine multiple image sequences including high-resolution T2, diffusion-weighted and dynamic post-contrast images [3, 8]. Prostate MRI-TRUS fusion target-guided biopsy is a

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feasible and accurate method and is one of the most promising strategies [3, 9, 10] to sample suspicious lesions.

The complications observed in TRUS-guided prostate biopsy are generally minor and well tolerated and can include pain. Additionally, bleeding occurs in 10–84% of all cases; however, less than 1% of these cases require hospitalization [2]. While fever can be observed in up to 17.5% of all cases [11], infection requiring hospitalization ranges from 0 to 6.3% of cases [2]. Urinary retention ranges from 0.2 to 1.7% of all cases and is usually transient. Last, transient worsening of lower urinary tract symptoms (LUTS) is present in up to 25% of all cases [2]. Although many studies have evaluated the use of MRI-TRUS fusion prostate biopsy platforms in the detection of clinically significant prostate cancers [9, 12], there is a lack of information on possible additional complications related to this method.

The aim of this study was to compare the complication rates between systematic TRUS-guided prostate biopsy and systematic plus MRI-TRUS fusion combined prostate biopsy techniques.

Materials and methods

This is a single-center retrospective study, institutional review board (IRB) approved, with a waiver of informed consent. Data were obtained from an institutional database that included a total of 974 patients who were referred to receive prostate biopsies from July 2014 to June 2016. Patients received a prostate biopsy for clinical suspicion of prostate cancer by the patient's urologist (including high PSA levels, abnormalities on digital rectal examination or prior imaging studies with a suspicious lesion). A total of 319 patients were received systematic TRUS biopsies and 648 patients underwent MRI-TRUS fusion biopsies (Fig. 1). Seven patients did not respond to phone calls and were excluded. The median age of the patients in the systematic TRUS group was 62 years old (39–94 years old) and 62 years old (35–89 years old) in MRI-TRUS fusion group. The median prostate volume of the patients in the systematic TRUS group was 48 g (15–280 g) and 49 g (15–179 g) in the MRI-TRUS fusion ($p = 0.588$).

Biopsy procedure

According to the institutional protocol for prostate biopsy all patients underwent prophylactic antibiotic therapy with fluoroquinolones. This included one-week of ciprofloxacin treatment at 500 mg twice daily starting the night before the procedure. Additionally, rectal enemas were performed immediately before the procedure. Biopsies were performed under general anesthesia assisted by the anesthesiology staff.

The biopsies were performed with an automatic trucut biopsy gun with an 18G needle (Acecut-TSK Laboratory-Japan) using ultrasound equipment with endocavitary 4-9 MHz broadband curved array end-fire transducers and IU 22 Philips (Philips Healthcare, Andover, MA), Aplio 500 Platinum (Toshiba American Medical Systems, Tustin, CA) or Logiq E9 (GE Healthcare, Milwaukee, USA) devices. Systematic TRUS prostate biopsies initially obtained 14-fragments in a sextant pattern. This included 2 from the base (lateral and medial), 2 from the mid zone and 2 from the apex of the peripheral zone and one on each side of the transitional zone (Fig. 2). Additional cores of any suspicious areas observed on ultrasound were also obtained. MRI-TRUS fusion biopsies: all patients first underwent targeted biopsy generally consisting of at least 2 additional cores from each target, followed by systematic 14-core biopsies (a total of 16-24 fragments, as shown on scatter plots in Fig. 3) and were performed using one of the three different rigid registration software-based real-time mpMRI-TRUS fusion systems: Aplio 500 Smartfusion (Toshiba, Nasu, Japan), Logic E9 VNav (GE Healthcare, Milwaukee, USA) and MyLab 60 (Esaote, Florence, Italy). Each biopsy was performed by 1 out of 10 experienced interventional radiologists with 7–15 years of experience in TRUS biopsies and 4 years in targeted MRI-TRUS fusion biopsies, with a similar number of biopsies per radiologist. After the procedure, patients remained under observation and had their vital signs, pain, and bleeding monitored. Patient discharge criteria included the presence of clear spontaneous urination, no pain and no change of vital signs.

Assessment of complications

Complications were divided into immediate (those that occurred during the hospital observation period) and late (those that occurred within 5 days after biopsy). The evaluation of late complications was performed through telephone contact the following day and 5 days after the biopsy. If the patient remained asymptomatic, the evaluation protocol was ended. If the patient reported any change during a telephone call at day 1 or day 5, additional telephone calls were made at day 10 and day 15 to evaluate the maintenance of the symptoms in patients with grade 1 complications. In patients with complications graded 2–5, a telephone call within 30 days was performed. The evaluation of complications after the biopsy was performed using the standard questionnaire of the hospital and included the following information regarding each score. Patients were asked if there were any changes in symptoms after the biopsy (and if so, they should be described in detail). If there were none, patients were questioned about the presence of general malaise (subjective), pain (on a 10-point score), fever, hematuria, hematospermia,

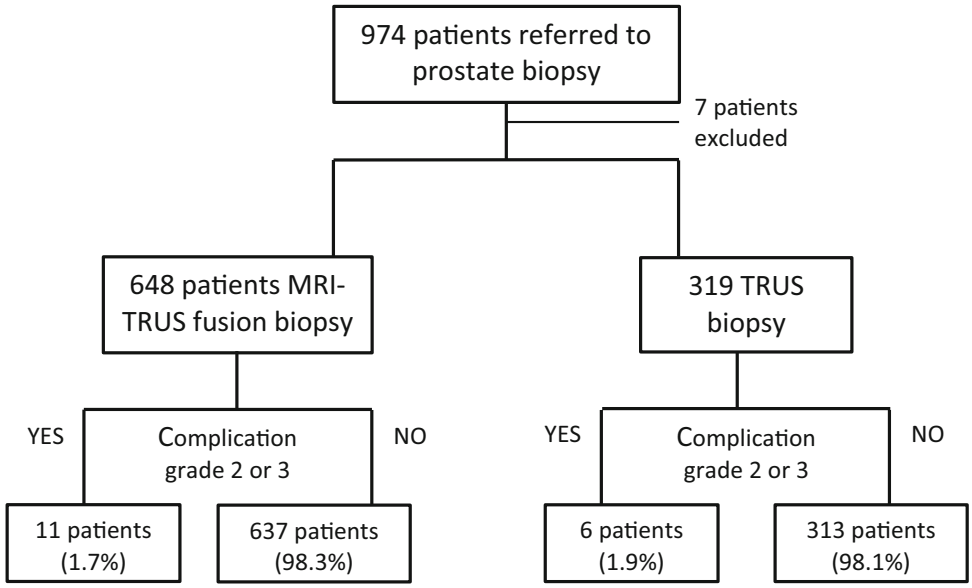

Fig. 1. Flowchart: study design.

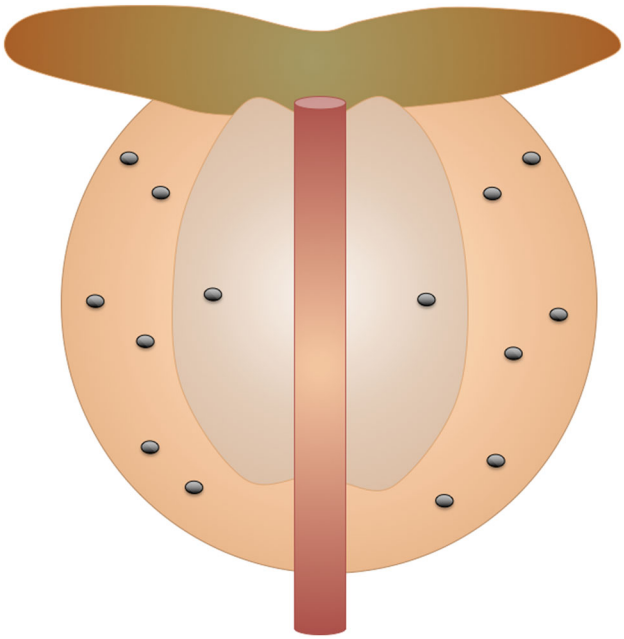

Fig. 2. 14-Fragments in a random biopsy pattern (coronal view, black dots represent systematic cores).

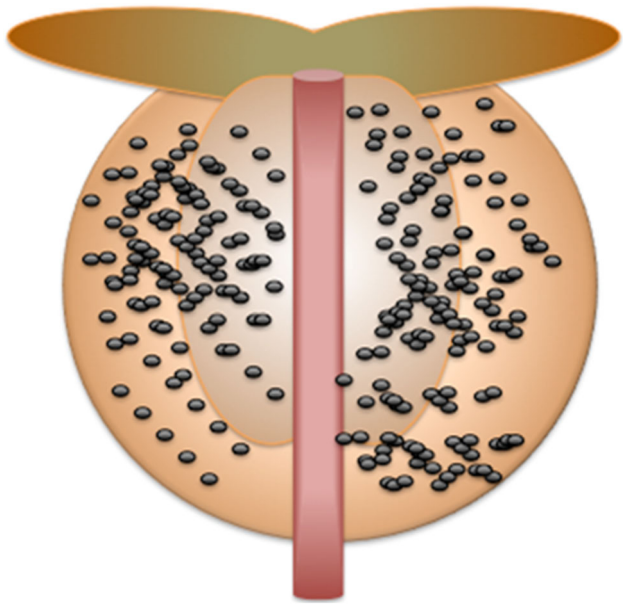

Fig. 3. Extrapolated scatter plot to mpMRI-TRUS targets in coronal view of prostate (black dots represent each target of mpMRI).

and the worsening of urinary retention (International Prostate Symptom Score- IPSS). Additionally, patients were questioned about the absence of rectal bleeding, streaks of blood with stool less than half the time, obvious blood with stool most of the time, and passes with only blood. The severity of complications was evaluated according to the National Institute of Health (NIH) terminology criteria [13] and was divided from grade 1–5 based on clinical descriptions of the severity of adverse events. Grade 1 complications (200 episodes) were excluded from the analysis.

Statistical analysis

Statistical analysis was performed using SPSS version 20.0 software. Groups were compared with Pearson's Chi-square or Fisher's test and Mann–Whitney test. Statistical significance was set at $p < 0.05$.

Results

The median number of cores obtained in systematic TRUS biopsy was 15 fragments (SD ± 2.57) with additional cores (based on suspicious findings in US) ranging

from 0 to 6 (mean 1.35 additional cores). In MRI-TRUS fusion prostate biopsy, the median was 18 cores (SD ± 2.38), with the number of additional cores varying between 0 and 12 (mean 3.77 additional cores). The most frequent sites of suspected targets in the fusion biopsies were in the middle third of the peripheral zone (n = 393; 50.6% of targets), followed by the apex of the peripheral zone (n = 159; 20.5%) (Fig. 2). In systematic TRUS biopsy, the most frequent target sites included the middle third of the peripheral zone (n = 71; 49.3% of targets), followed by the base of the peripheral zone (n = 32; 22.2%). Periurethral lesions in the transition zone represented 91 targets (14%) (Fig. 4 and 5) in fusion biopsies and 13 targets (4.1%) in systematic TRUS biopsies ($p < 0.001$). The presence of neoplasia in patients who received systematic TRUS biopsies was 59.3% (n = 189/319), whereas in patients who received MRI-TRUS fusion prostate biopsies it was 67.9% (n = 440/648), p = 0.012. When the histological grade of the biopsies was analyzed in the TRUS biopsy group, the distribution was 9.5% prostatic intraepithelial neoplasia (PIN) (n = 18), 3.2% atypical small acinar proliferation (ASAP) (n = 6), 23.7% Gleason 6 (n = 45), 44.2% Gleason 7 (n = 84), 8.4% Gleason 8 (n = 16), 10% Gleason 9 (n = 19), 0.5% Gleason 10 (n = 1), and 0.5% undifferentiated carcinoma (n = 1). In the group that received MRI-TRUS fusion biopsy, the results were 10% PIN (n = 44), 3.8% ASAP (n = 17), 18% Gleason 6 (n = 79), 51% Gleason 7 (n = 224), 9.5% Gleason 8 (n = 42), 7.5% Gleason 9 (n = 33), and 0.2% Gleason 10 (n = 1), p = 0.061.

A total of 17 (1.75%) complications grades 2 and 3 were observed in patients who received either systematic TRUS or MRI-TRUS fusion biopsies. Complications included prostatitis, urinary retention, hematuria, rectal bleeding, urethral bleeding, and orquiepididimitis (Table 1). Importantly, no sexual dysfunctions were observed and no patient with more than one complication was observed. Complications graded 4 or 5 were not observed in both groups. The mean follow-up was 8.23 days among the 967 patients. Six (1.9%) cases of complications were observed among patients who received systematic TRUS biopsy, and 11 (1.7%) cases of complications were observed in those who underwent MRI-TRUS fusion prostate biopsy (Table 2). No statistical significant difference was observed in the frequency of more severe complications in either method. The distribution of grade 3 complications was 7 out of 11 cases of complications in patients who underwent MRI-TRUS fusion biopsy, and 2 out of 6 cases in patients who received systematic TRUS biopsy, p = 0.335 (Table 3).

When early and late complications were compared, four (66.7%) early systematic TRUS biopsy complications and two (33.3%) late complications were observed. In MRI-TRUS fusion biopsies, six (54.5%) early complications and five (45.5%) late complications were observed, also with no statistical significance between groups ($p > 0.999$) (Table 4).

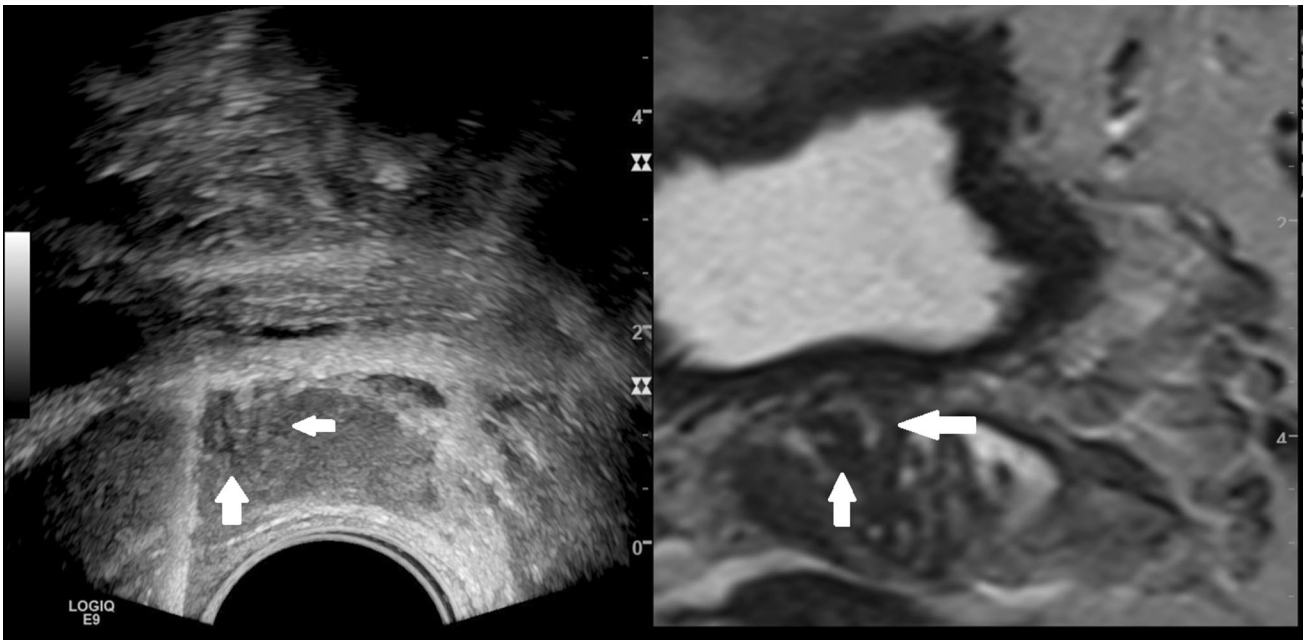

Fig. 4. Suspected area that insinuates in base of the right seminal vesicle (white arrows). Patient was received biopsy (14-fragments TRUS systematic biopsy and 6 additional targeted MRI-TRUS fusion cores). Presented no complications after the procedure.

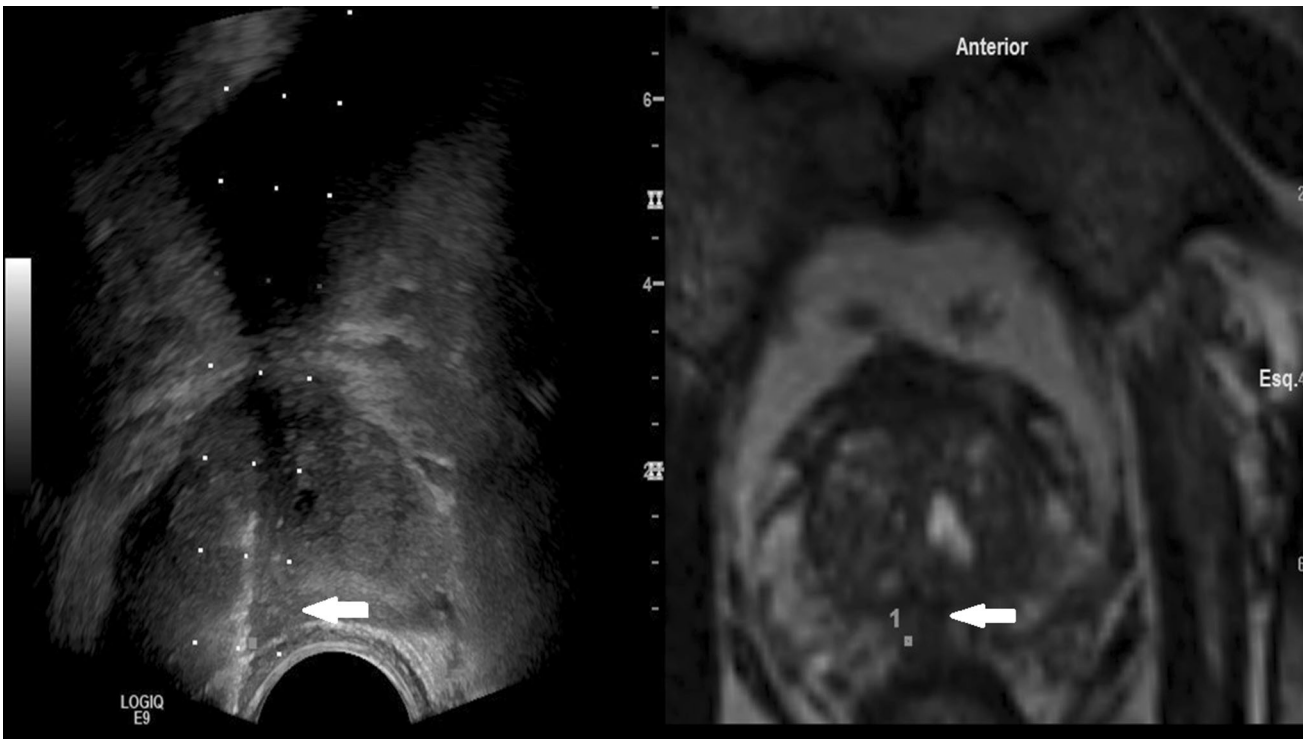

Fig. 5. Periurethral suspected area in the middle third in the right lobe of the prostate (white arrows). Patient was received biopsy (14-fragments TRUS systematic biopsy and 2 additional targeted MRI-TRUS fusion cores). Presented hematuria with spontaneous remission after the procedure.

Table 1. Distribution of complications among patients undergoing prostate biopsy

Patient	Complication	Grade	Technique	Treatment
1	Urinary retention	2	MRI-TRUS	Bladder catheterization (1 episode)
2	Prostatitis	3	MRI-TRUS	Hospitalization for 3 days and intravenous antibiotic therapy for 14 days (day-hospital after discharge)
3	Hematuria	3	MRI-TRUS	Hospitalization + hydration and bladder catheter irrigation for 1 day
4	Hematuria	2	MRI-TRUS	Hydration and bladder catheter irrigation for 12 h
5	Prostatitis	3	MRI-TRUS	Hospitalization and intravenous antibiotic therapy
6	Rectal bleeding	2	TRUS	30-min rectal compression
7	Urethral bleeding	3	MRI-TRUS	Indwelling bladder catheterization (1 day)
8	Urinary retention	2	MRI-TRUS	Bladder catheterization (1 episode)
9	Prostatitis	3	MRI-TRUS	Hospitalization and intravenous antibiotic therapy for 13 days
10	Prostatitis	3	MRI-TRUS	Hospitalization and intravenous antibiotic therapy
11	Orquiepididimitis	2	TRUS	Day hospital intravenous antibiotic therapy
12	Urinary retention	2	MRI-TRUS	Bladder catheterization (1 episode)
13	Urinary retention	3	TRUS	Indwelling bladder catheterization (10 days)
14	Prostatitis	3	TRUS	Hospitalization and intravenous antibiotic therapy for 13 days
15	Urinary retention	2	TRUS	Indwelling bladder catheterization (15 days)
16	Prostatitis	3	MRI-TRUS	Hospitalization and intravenous antibiotic therapy for 7 days
17	Rectal bleeding	2	TRUS	Hospitalization for 3 days

Discussion

The gold standard to diagnose suspected prostate cancer is still conventional sextant-extended random prostate biopsy. Its limitations, however, are increasingly evident when compared to new strategies, specifically when a target is chosen based on MRI information [14]. Repeating biopsy procedures should be avoided as it involves additional costs, risks and an increase in patient anxiety [14]. A recent Consensus Statement by the American Urological Association (AUA) and Society of Abdominal Radiology (SAR) recognizes that MRI targeted cores appear to be superior to detect clinically significant prostate cancer over standardized biopsies in

Table 2. TRUS versus MRI-TRUS fusion prostate biopsies: complication (Chi-square test)

	MRI-TRUS fusion prostate biopsies				Total		*p*
	No		Yes				
	n	%	*N*	%	*N*	%	
Complication							0.837
No	313	98.1	637	98.3	950	98.2	
Yes	6	1.9	11	1.7	17	1.8	
Total	319	100	648	100	967	100	

Table 3. TRUS versus MRI-TRUS fusion prostate biopsies: adverse event grade (Fisher exact test)

	MRI-TRUS fusion prostate biopsies				Total		*p*
	No		Yes				
	n	%	*N*	%	*n*	%	
Adverse event grade (2–5)							0.335
2	4	66.7	4	36.4	8	47.1	
3	2	33.3	7	63.6	9	52.9	
Total	6	100	11	100	17	100	

Table 4. TRUS versus MRI-TRUS fusion prostate biopsies: complication (early/late) Fisher exact test

	MRI-TRUS fusion prostate biopsies				Total		*p*
	No		Yes				
	n	%	*N*	%	*n*	%	
Complication (early/late)							>0.999*
Early	4	66.7	6	54.5	10	58.8	
Late	2	33.3	5	45.5	7	41.2	
Total	6	100	11	100	17	100	

patients with at least one previous random biopsy [15]. Fusion biopsies also seem to be a potential screening test in patients with high PSA levels and can avoid unnecessary biopsies [16]. They can become the standard of care in the near future. MRI-TRUS fusion prostate biopsies require a learning curve that could be related to higher rates of complications. So far, the literature is scarce regarding if this new strategy leads to an increase in the rate of complications and which factors could be associated with it.

In the present study, the complication rates of systematic TRUS and MRI-TRUS fusion prostate biopsies were compared and no significant differences between the two procedures were observed. The complication rates in both techniques were very low (1.7% in MRI-TRUS versus 1.9% in TRUS) and were mostly grades 2 and 3, with no cases of complications grades 4 and 5.

When comparing early and late complication rates, also no significant difference between systematic TRUS and MRI-TRUS fusion prostate biopsies were observed, suggesting that both procedures are safe and MRI-TRUS fusion prostate biopsies did not increase the rate of adverse events.

In a recent literature review, Borghesi et al. [17] analyzed the rates of complications of prostate biopsies in different studies regardless of the access used (either transrectal or transperineal) and if the procedure was performed with or without image fusion. He concluded that after a prostate biopsy the most frequent complication was bleeding (hematuria and hematospermia); however, it was generally minor and self-limited, regardless of the biopsy approach. Other studies included small samples and/or a short follow-up [17] and none compared the rate of complications and associated factors between systematic TRUS biopsies and MRI-TRUS fusion prostate biopsies performed by the same physicians.

The present study has some limitations. First, it was a retrospective non-randomized study with patients that may have had clinical characteristics which led urologists to request MRI prior to the biopsies that were not accounted for in the present study. Another limitation was

the lack of uniformity of criteria for prostate biopsy indications such as high PSA levels, abnormalities on digital rectal examination, or MRI imaging findings prior to the biopsy. Other factors that could affect complication rates (e.g., diabetes) also were not compared between both groups.

This study inserts the knowledge that increasing the use of fusion biopsies will not lead to higher rates of complications. Complication rates related to systematic TRUS-guided prostate biopsies and MRI-TRUS fusion biopsies were very low in the present study, with no significant differences between both groups. Despite a higher incidence of cores close to the prostatic urethra, the MRI-TRUS fusion prostate biopsy is not related to a significant increase of adverse events.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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