MRI-targeted prostate biopsy: the next step forward!

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Abstract

Aim. For decades, the gold standard technique for diagnosing prostate cancer was the 10 to 12 core systematic transrectal or transperineal biopsy, under ultrasound guidance. Over the past years, an increased rate of false negative results and detection of clinically insignificant prostate cancer has been noted, resulting into overdiagnosis and overtreatment. The purpose of the current study was to evaluate the changes in diagnosis and management of prostate cancer brought by MRI-targeted prostate biopsy.

Methods. A critical review of literature was carried out using the Medline database through a PubMed search, 37 studies meeting the inclusion criteria: prospective studies published in the past 8 years with at least 100 patients per study, which used multiparametric magnetic resonance imaging as guidance for targeted biopsies.

Results. In-Bore MRI targeted biopsy and Fusion targeted biopsy outperform standard systematic biopsy both in terms of overall and clinically significant prostate cancer detection, and ensure a lower detection rate of insignificant prostate cancer, with fewer cores needed. In-Bore MRI targeted biopsy performs better than Fusion biopsy especially in cases of apical lesions.

Conclusion. Targeted biopsy is an emerging and developing technique which offers the needed improvements in diagnosing clinically significant prostate cancer and lowers the incidence of insignificant ones, providing a more accurate selection of the patients for active surveillance and focal therapies.

Keywords: Fusion targeted biopsy, In-Bore MRI targeted biopsy, multiparametric MRI, prostate cancer detection, systematic prostate biopsy, targeted prostate biopsy

Introduction

Prostate cancer (PCa) is the most frequent malignancy in male patients, being held accountable for 19% of diagnosed cancers in the American male population [1], with the third-highest mortality rate (10.1 deaths/100000 men) [2].

The former gold standard technique recommended by the European Association of Urology (EAU) for diagnosing PCa was represented by 10 to 12 core systematic transrectal or transperineal biopsy (SBx), under ultrasound guidance, performed whenever the digital rectal exam is positive or the PSA above the cutoff value [3]. However, basing the indication of systematic biopsies solely on these criteria has led over the past years to an increased rate of false negative results (22-30%) [4] and detection of clinically insignificant PCa, resulting into overdiagnosis and overtreatment [5]. Thus, a prior imaging evaluation is needed. In 2019, EAU recommended association of systematic biopsy with targeted biopsy from the suspect lesion

identified by multiparametric MRI [6].

The advance of technology and the availability of multiparametric magnetic resonance imaging (mpMRI) in daily practice expanded its use, not only for staging purposes, but also for diagnosis and therapeutic ones, offering the possibility of targeted biopsy. Currently, three modalities are employed:

A. Cognitive targeted biopsy (Cog-TBx): the radiologist marks the suspected lesion on the MRI, while the urologist performs the visually targeted biopsy using ultrasound guidance.

B. MRI-transrectal ultrasound (TRUS) Fusion targeted biopsy (Fus-Bx): a software overlays the MRI and ultrasound image in real time, with the annotations (lesions marking) being done by the operator.

C. In-Bore MRI targeted biopsy (IB-TBx): which is performed inside de MRI gantry, by the radiologist, using magnetic field compatible biopsy kit.

The purpose of the current study was to evaluate the changes in diagnosis and management of PCa, brought by MRI-targeted prostate biopsy.

Methods

A critical review of literature was carried out using the Medline database through a PubMed search. The searching protocol included the following terms: "prostate cancer", "transrectal biopsy", "MRI", "fusion". The inclusion criteria were: prospective trials or retrospective prospective acquired databases published during the last 8 years, use of mpMRI for guiding targeted biopsy and minimum 100 patients included per study (except for the in-bore MRI targeted biopsy, due to the limited number of studies).

Results

37 studies were selected, with characteristics detailed in table I. Thirty two of the 37 trials were single center while 5 were multicenter. Six reports included only patients with previous negative biopsies, 18 studies patients with no prior biopsy, while 11 of them included both patients with repeated or initial biopsy. Population characteristics may be observed in table II and cancer detection rates (CDR) in table III. Definition of clinically significant prostate cancer (csPCa) varies among the studies and it is detailed in table I.

Table I. Trials included in the current analysis.

No	Study	Year	Instit.	Pa. No.	Previous Neg. Biopsy	MRI Sequences	T	Endorectal Coil	Evaluation System	Biopsy Type	Access Type	Definition of csPCa
1	Wysock et al. (PROFUS TRIAL) [7]	2013	Single	125	No Prior/ Prior neg. biopsy/ AS	T1W, T2W, DWI, DCE	3T	Pelvic Coil	ESUR 2012	FUS-TBx, COG-TBx, SBx	Transrectal	GS ≥ 3+4
2	Tonttila et al. [8]	2015	Single	113	No prior biopsy	T1W, T2W, DCE, DWI, ADC	3T	Pelvic Coil	1-4 Likehood of cancer	Cog-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 4 mm or with > 2 abnormal cores
3	Pepe et al. [9]	2016	Single	200	Prior neg. biopsy	T2W, DCE, DWI, Spect.	3T	Pelvic Coil	PIRADS Score	TPM-Bx, Fus-TBx, Cog-TBx	Transperineal/ Transrectal	GS ≥ 6 with > 2 cores
4	Delongchamps et al. [10]	2013	Single	127	No prior biopsy	T2W, ADC, DCE	1.5T	Endorectal Coil	3 point Scale	SBx, Cog-TBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 5 mm
		2013	Single	131	No prior biopsy	T2W, ADC, DCE	1.5T	Endorectal Coil	3 point Scale	SBx, rigid Fus-TBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 5 mm
		2013	Single	133	No prior biopsy	T2W, ADC, DCE	1.5T	Endorectal Coil	3 point Scale	SBx, elastic Fus-TBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 5 mm
5	Kam et al. [11]	2017	Single	56	NA	T1W, T2W, DWI, DCE	1.5 T	Pelvic Coil	PIRADS	Cog-TBx, SBx	Transrectal	GS ≥ 3+4
		2017	Single	65	NA	T1W, T2W, DWI, DCE	1.5 T	Pelvic Coil	PIRADS	FUS-TBx, SBx	Transperineal	GS ≥ 3+4
6	Kaufmann et al. [12]	2014	Single	35	Prior negative biopsy	T2W, ADC, DCE	1.5T	Endorectal Coil	PIRADS Score	IB-TBx, SBx	Transrectal	GS pattern ≥ 4 or tertiary pattern 5, PSA > 10 ng/ml, PSAD > 0.15 ng/ml/cm³
7	Quentin et al.[13]	2014	Single	128	No prior biopsy	T2W, ADC, DCE	3T	Pelvic Coil	PIRADS Score	IB-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 4 mm
8	Pokorny et al. [14]	2014	Single	223	No prior biopsy	T2W, DCE, DWI	3T	Pelvic Coil	PIRADS v1	IB-TBx, SBx	Transrectal	very low volume GS 3+4 / low volume GS 6
9	Arsov et al. [15]	2015	Single	106	Prior negative biopsy	T1W, T2W, DWI, DCE	3 T	Pelvic Coil	Likert Scale	IB-TBx	Transrectal	GS ≥ 3+4
				104	Prior negative biopsy	T1W, T2W, DWI, DCE	3 T	Pelvic Coil	Likert Scale, PIRADS Score	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
10	Sonn et al.[16]	2013	Single	105	Prior negative biopsy	T2W, ADC, DCE	3T	Pelvic Coil	Image grade 1-5	SBx, Fus-TBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 4 mm
11	Kuru et al. [17]	2013	Single	347	No Prior/ Prior neg. biopsy	T1W, T2W, DCE, DWI, ADC	3 T	NA	Low-High Suspicion	TPM-Bx, Fus-TBx	Transperineal	GS ≥ 3+4
12	Rastinehad et al. [18]	2014	Single	105	No Prior/ Prior neg. biopsy	T2W, DWI, ADC, DCE	3 T	Pelvic Coil	NIH Risk System/ Likert Scale	SBx, Fus-TBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 50% or with > 2 abnormal cores

Table I. Trials included in the current analysis (continuation).

No	Study	Year	Instit.	Pa. No.	Previous Neg. Biopsy	MRI Sequences	T	Endorectal Coil	Evaluation System	Biopsy Type	Access Type	Definition of csPCa
13	Panebianco et al. [19]	2014	Single	570	No prior biopsy	T2W, DCE, DWI	3 T	Endorectal/ Pelvic Coil	PIRADS Score	SBx	Transrectal	NA
				570	No prior biopsy	T2W, DCE, DWI	3 T	Endorectal/ Pelvic Coil	PIRADS Score	FUS-TBx, SBx	Transrectal	NA
14	Baco et al. [20]	2015	Single	175	No prior biopsy	T2W, DWI, ADC	1.5 T	Pelvic Coil	PIRADS Score	FUS-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 5 mm
15	Siddiqui et al.[21]	2015	Single	1003	No Prior/ Prior neg. biopsy	T2W, DWI, DCE, Spect.	3T	Endorectal/ Pelvic Coil	Low-High Suspicion	FUS-TBx, SBx	Transrectal	GS ≥ 3+4 with > 50% of core
16	de Gorski et al. [22]	2015	Single	232	No prior biopsy	T1W, T2W, DCE, DWI, ADC	1.5 T	Pelvic Coil	Likert Scale	SBx, Fus-TBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 4 mm
17	Radtke et al. [23]	2015	Single	294	No Prior/ Prior neg. biopsy	T2W, DCE, DWI	3T	Pelvic Coil	PIRADS Score	TPM-Bx, Fus-TBx	Transperineal	GS ≥ 3+4
18	Cash et al. [24]	2015	Single	408	No Prior/ Prior neg. biopsy	T2W, DWI	3T	No endorectal coil	PIRADS Score v1	FUS-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 4 mm
19	Mozer et al. [25]	2015	Single	152	No prior biopsy	T2W, DCE, DWI	1.5 T	Pelvic Coil	Likert Scale	FUS-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 4 mm
20	Peltier et al. [26]	2015	Single	110	No prior biopsy	T1W, T2W, DWI, DCE	3T	Endorectal/ Pelvic Coil	PIRADS	FUS-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 6 mm
21	Porpiglia et al.[27]	2016	Single	107	No prior biopsy	T2W, DCE, DWI	1.5 T	Endorectal Coil	PIRADS Score	SBx, Fus-TBx	Transperineal/ Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 5 mm
				105	No prior biopsy	T2W, DCE, DWI	1.5 T	Endorectal Coil	PIRADS Score	SBx	Transperineal/ Transrectal	GS ≥ 3+4 or GS 6 with MCL ≥ 5 mm
22	Zhang et al. [28]	2016	Single	224	No prior biopsy	T2W, DCE, DWI, ADC	3T	NA	PIRADS	FUS-TBx, SBx	Transperineal	GS ≥ 3+4 or GS 6 with MCL ≥ 50%
23	Mehralivand et al. [29]	2017	Single	339	No Prior/ Prior neg. biopsy	T2W, DWI, ADC, DCE	3T	Endorectal/ Pelvic Coil	PIRADS Score v2	FUS-TBx, SBx	Transrectal	ISUP ≥ 2
24	Hakozaki et al. [30]	2017	Single	177	No Prior/ Prior neg. biopsy/ AS	T2W, DCE, DWI	3T	NA	PIRADS	FUS-TBx, SBx	Transperineal	Epstein Criteria
25	Gordetsky et al. [31]	2017	Single	191	NA	T2W, DCE, DWI, ADC	NA	NA	PIRADS	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
26	Castellucci et al. [32]	2017	Single	168	No prior biopsy	T2W, DCE, DWI	1.5 T	Surface coil	PIRADS Score v1	Cog-TBx, SBx	Transrectal	GS ≥ 3+4
27	Mariotti et al. [33]	2017	Single	100	No Prior/ Prior neg. biopsy	T2W, DCE, DWI	3T	Surface coil	Likert	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
28	Boesen et al. [34]	2017	Single	289	Prior negative biopsy	T2W, DCE, DWI	3T	NA	PIRADS Score v1	FUS-TBx, SBx	Transrectal	GS ≥ 3+4; > 50% of core; ≥3 positive cores
29	Kasivisvanathan et al. [35]	2018	Multi	500	No prior biopsy	T2W, DCE, DWI	1.5T/ 3T	Endorectal or Pelvic Coil	PIRADS	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
30	Borkowetz et al. [36]	2018	Multi	214	No prior biopsy	T1W, T2W, DWI, DCE	3T	No endo-rectal coil	PIRADS v1 and v2	SBx, Fus-TBx	Transperineal	GS ≥ 3+4
31	Hofbauer et al. [37]	2018	Single	704	No Prior/ Prior neg. biopsy	T2W, DCE, DWI	3T	Pelvic Coil	PIRADS Score v2	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
32	Costa et al. [38]	2018	Single	103	No Prior/ Prior neg. biopsy	T2W, DCE, DWI	3T	Endorectal Coil	PIRADS Score v2	IB-Tx,	Transrectal	GS ≥ 3+4
				300	No Prior/ Prior neg. biopsy	T2W, DCE, DWI	3T	Endorectal Coil	PIRADS Score v2	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
33	Maxeiner et al. [39]	2018	Single	318	No prior biopsy	T2W, DCE, DWI	3T	Surface coil	PIRADS Score	FUS-TBx, SBx	Transrectal	GS ≥ 4+3 or MCCL ≥ 6MM
34	Wegelin et al. [40]	2018	Multi	79	Prior negative biopsy	T2W, DCE, DWI	3T	NA	PIRADS Score v2	FUS-TBx	Transperineal	GS ≥ 3+4
				78	Prior negative biopsy	T2W, DCE, DWI	3T	NA	PIRADS Score v2	Cog-TBx	Transrectal	GS ≥ 3+4
				77	Prior negative biopsy	T2W, DCE, DWI	3T	NA	PIRADS Score v2	IB-TBx	Transrectal	GS ≥ 3+4
35	van der Leest [41]	2019	Multi	626	No prior biopsy	T2W, DCE, DWI	3T	NA	PIRADS Score v2	IB-TBx, SBx	Transrectal	GS ≥ 3+4
36	Elkhoury et al. [42]	2019	Single	248	No prior biopsy	T2W, DCE, DWI	3T	Surface coil	PIRADS Score v2	FUS-TBx, SBx	Transrectal	GS ≥ 3+4
				248	No prior biopsy	T2W, DCE, DWI	3T	Surface coil	PIRADS Score v2	Cog-TBx, SBx	Transrectal	GS ≥ 3+4
37	Rouviere et al. [43]	2019	Multi	251	No prior biopsy	T2W, DCE, DWI	1.5T/ 3T	Surface/ endorectal coil	Likert score	Fus-TBx/Cog-TBx, SBx	Transrectal	GS ≥ 3+4 or GS 6 with ≥ 6mm

Table II. Population characteristics of the trials included in our analysis.

No.	Study	Number of patients	Mean age	Mean PSA ng/ml	Prostate volume cc
1	Wysock et al. (PROFUS TRIAL) [7]	125	65 (56.3-71.0)	5.1 (3.5-7.31)	46 (31.0-62.5)
2	Tonttila et al. [8]	113	62.5 (56-67)	6.15 (4.0-10.7)	29.8 (23.5-44.3)
3	Pepe et al. [9]	200	61 (47-75)	8.6 (4.5-26)	NA
4	Delongchamps et al. [10]	127	62.7 ± 7.4	8.1 ± 3.7	53 ± 25
		131	64.6 ± 6.7	8.3 ± 4.1	55.7 ± 35.1
		133	64.5 ± 7.9	9 ± 3.9	58.3 ± 28.6
5	Kam et al. [11]	56	66.3 (45-80)	7.5 (1.3-18)	49.7 (13-125)
		65	65.0 (48-75)	7.3 (2.7-18)	55.2 (16-128)
6	Kaufmann et al. [12]	35	68 (55-75)	9.42 (4-25)	42 (20-66)
7	Quentin et al. [13]	128	67 (62-72)	6.7 (5.1-9)	47.5 (36-66.9)
8	Pokorny et al. [14]	223	63 (57-68)	5.3 (4.1-6.6)	41 (30-59)
9	Arsov et al. [15]	106	66 (60-71)	10 (7.8-14.9)	54 (40-77)
		104	68 (63-71)	10.8 (7.4-15.5-	60 (42-82)
10	Sonn et al. [16]	105	65 [59-70]	7.5 [5-11.2]	58 [39-82]
11	Kuru et al. [17]	347	65.3 (42-82)	9.85 (0.5-105)	48.7 (9-180)
12	Rastinehad et al. [18]	105	65.8 (42-87)	9.2 (0.6-62.0)	NA
13	Panebianco et al. [19]	570	64 (51-82)	NA	NA
		570	64 (51-82)	NA	NA
14	Baco et al. [20]	175	65 (59-69)	7.3 (5.5-9.9)	42 (30-59)
15	Siddiqui et al. [21]	1003	62.1 (7.5)	6.7 (4.4-10.7)	49 (36-71)
16	de Gorski et al. [22]	232	64 ± 6.4	6.5 ± 1.8	47 ± 24.3
17	Radtke et al. [23]	294	64 (60-71)	7.3 ±6.0	47.00 ± 37.5
18	Cash et al. [24]	408	67 (60-71)	9.33 (0.68-14.65)	50 (35-65)
19	Mozer et al. [25]	152	63 (59.3-67.5)	6 (5-7.9)	44 (30-55)
20	Peltier et al. [26]	110	65.1 (48.0-79.2)	8.4 (0.7-40)	49.3 (18-162)
21	Porpiglia et al. [27]	107	64 (58-70)	5.9 (4.8-7.5)	46.2 (34.5-71.6)
		105	66 (60-70)	6.7 (5.5-8.5)	45.7 (34.6-65.0)
22	Zhang et al. [28]	224	69 (40-85)	10.05 (3.61-78.39)	45.5 (22-77)
23	Mehralivand et al. [29]	339	64.1	6.47 (4.59-9.31)	55 (41-79)
24	Hakozaki et al. [30]	177	68.3 (48-89)	10.9 (1.65-218)	42.4 (11-134)
25	Gordetsky et al. [31]	191	63.3 ± 7.2	9.2 ± 9.6	NA
26	Castellucci et al. [32]	168	61.4 ± 7.60	8.3 ± 6.1	48.9 ± 6.7
27	Mariotti et al. [33]	100	62.5 (35-86)	5.3 (0.2-36.0)	48 (16.0-130.0)
28	Boesen et al. [34]	289	64 (59-67)	12 (8.3-19)	63 (46-87)
29	Kasivisvanathan et al.[35]	500	64.4	6.62 (5.14 - 9.35)	NA
30	Borkowetz et al. [36]	214	63 (40-75)	6.22 (1-49)	42 (8-270)
31	Hofbauer et al. [37]	704	68 (62-73)	7.93 (5.97-12.17)	51 (40-72)
32	Costa et al. [38]	103	64 ±7	8 ±4.1	55.4 ±24.5
		300	66 ±8	8.6 ±11.5	51.6 ±23.5
33	Maxeiner et al. [39]	318	68 (60-72)	7.14 (5.13-10.3)	47 (36-65)
34	Wegelin et al. [40]	79	64.6 ±6.9	11.6 ±9.0	45.4 ±14.4
		78	66.5 ±6.3	11.0 ±7.1	48.5 ±18.1
		77	66.0 ±5.9	11.0 ±9.4	48.3 ±20.2
35	van der Leest [41]	326	65 (59-68)	6.4 (4.6-8.2)	55 (41-77)
36	Elkhoury et al. [42]	248	65.5 ±7.7	6.2 ±4.6-8.2	NA
		248	65.5 ±7.7	6.2 ±4.6-8.2	NA
37	Rouviere et al. [43]	251	64 (59-68)	6.5 (5.6-9.6)	50 (38-63)

MRI-targeted biopsy

A. Cognitive MRI-targeted biopsy

The first method of performing targeted MRI guided biopsies to be employed in clinical practice was Cog-TBx. However, due to the increasing availability of MRI-TRUS fusion and in-bore systems, the number of trials that observed the 8-years inclusion criteria was limited.

Eight studies were selected for our analysis, presenting conflicting results: Wysock, Elkhoury and Castelucci [7,32,42] report superiority of standard systematic biopsy (SBx) compared to Cog-TBx in terms of overall cancer detection rate (CDR) in biopsy naïve patients, while Delongchamps et al. [10] concludes the opposite. Tonttila et al. [8] and Kam et al. [11] presented the non-inferiority of Cog-TBx compared to SBx. Also, Cog-TBx presents the lowest performance in PCa diagnosis when compared to FUS-TBx or IB-TBx, even though it is not statistically significant [40]. Despite these results, Cog-TBx has similar detection rates of csPCa with saturation biopsy, with statistically significant lower number of cores obtained [44]. Association of Cog-TBx with SBx presents higher accuracy for PCa and csPCa diagnosis when compared to each technique alone (SBx or Cog-TBx) [11,32,42].

All studies reported that targeted biopsy methods were significantly more efficient when compared to SBx regarding cancer core length/core and number of positive cores.

B. MRI/TRUS Fusion targeted biopsy

Fus-TBx combines the advantages of both Cog-TBx and IB-TBx, fusing the broad availability of Cog-TBx with real time visualization of the tumor by magnetic resonance imaging [45].

Twenty-nine of the studies compiled in our analysis compared TBx with the previously listed techniques. In 17 studies, the CDR were similar between the evaluated methods (TBx vs SBx, ± 5-10%), while 2 studies reported a statistically significant higher detection rate for Fus-TBx, with an improvement of at least 10%, compared to SBx [27,28]. Only one study favored SBx concerning cancer detection rate [23]. PROFUS Trial reported no statistically significant difference between Cog-TBx and Fus-TBx in terms of CDR, with the mention that FUS-TBx provided better histological specimens compared to visual targeting [7]. Several studies demonstrate that Fus-TBx combined with SBx outperforms both Fus-TBx and SBx alone [34,36,38,39,42,43].

Regarding CDR for csPCa, 20 studies showed higher prevalence of csPCa for the patients biopsied by Fus-TBx, in 8 of them the difference was statistically significant [18,21,25–28,34,35]. Even in a multicenter designed trial, Fus-TBx outperformed SBx for the diagnosis of csPCa [35], while the detection rate for is PCa was lower [21,28,31,33–35,39,42,43]. It is necessary to mention that the definition of csPCa varied significantly among the studies. Fus-TBx presents a high performance in reducing statistically significant the diagnosis rate of insignificant PCa compared to SBx [21,28,31,34,43].

Five studies reported upgrading rates when Fus-TBx was performed compared to SBx, varying between 7.58% and 35% (Table III). Siddiqui's trial of 1003 patients, the most exhaustive study published up to date, concluded that Fus-TBx increased the diagnostic rate of high-risk cancers up to 30% (p<0.001) and upgrading to intermediate or high-risk groups (p<0.001), compared to SBx [21].

In terms of diagnostic efficiency, Radtke et al. showed that even if saturation biopsy outruled Fus-TBx from the perspective of CDR, it still needs twice more cores to detect 1 GS ≥7 (7.4 cores vs 3.4 cores) [23]. On the other hand, PRECISION multicenter trial reported a statistical significant better performance of Fus-TBx for CDR and diagnostic efficiency, while similar efficiency was observed in several other trials [12,16,26].

C. In-Bore MRI targeted biopsy (IB-TBx)

In-Bore MRI targeted biopsy is considered to be the most precise method. In the present paper, we included 7 studies: 4 comparing IB-TBx to SBx while 3 IB-TBx to Fus-TBx. Transrectal approach was used in all evaluated studies.

The over-all CDR for PCa varied significantly from 37% to 69.9%, with some authors reporting better diagnosis rates for IB-TBx compared to SBx [12,14]. IB-TBx presented higher CDR compared to Fus-TBx or Cog-TBx, although not statistically significant [13,21,34].

Reviewing CDR for csPCa, all authors showed that IB-TBx has a higher efficiency, compared to standard randomized biopsy [12–15,38,41], but similar to the Fus-TBx [15]. Also, IB-TBx identifies a statistically significant lower percentage of insignificant PCa when compared to SBx [14,41], upgrading 7% to 32% of cases diagnosed as no cancer or low risk PCa by SBx [13,14,41]. It presents a 9-10% risk of missing csPCa [13,41], depending upon the lesion dimension and location [46].

Pokorny et al. were the only ones to evaluate the two modalities from the perspective of sensitivity, specificity, positive negative predictive value, for each category IB-TBx outperforming SBx [14].

Regarding tumor features, IB-TBx presented higher efficacy in the number of biopsy cores needed to detect csPCa [14,15,41]. Average percentage of cancer core length was statistically higher for IB-TBx (p<0,001) [14], but the differences fade when Fus-TBx is associated with SBx [15].

Table III. Comparison of the performance of SB (Systematic Biopsy), Fus-TBx (Fusion Targeted Biopsy) and IB-TBx (In-Bore MRI Targeted Biopsy) in terms of overall CDR (cancer detection rate), csPCa (clinically significant Prostate Cancer), isPCa (clinically insignificant Prostate Cancer).

No	Study	S/M	Pa. No.	Type	PCa Overall CDR % (n/N)	PCa SBx % (n/N)	PCa TBx % (n/N)	PCa p value	csPCa Overall CDR % (n/N)	csPCa SBx % (n/N)	csPCa TBx % (n/N)	csPCa p Value	Upgrading % (n/N)	isPCa SBx % (n/N)	isPCa TBx % (n/N)	isPCa p value
1	Wysock et al. (PROFUS TRIAL) [7]	Single	125	FUS-TBx, COG-TBx, SBx	NA	55.2 (37/67)	40.3 (27/67)	NA	NA	32.8 (22/67)	32.8 (22/67)	NA	NA	22.4 (15/67)	7.5 (5/67)	NA
2	Tonttila et al. [8]	Single	113	Cog-TBx, SBx	NA	64 (34/53)	57 (34/60)	NA	NA	55 (29/53)	45 (27/60)	NA	NA	9.4 (5/53)	12 (7/60)	NA
3	Pepe et al. [9]	Single	200	TPM-Bx, Fus-TBx, Cog-TBx SBx	42.5 (85/200)	NA	NA	NA	30 (60/200)	98.3 (59/60)	93.3 (56/60)	NA	NA	NA	NA	NA
4	Delongchamps et al. [10]	Single	127	SBx, Cog-TBx	NA	43 (55/127)	67 (37/55)	NA	NA	33 (18/55)	45 (18/37)	0.6	NA	22	0	NA
		Single	131	SBx, rigid Fus-TBx	NA	46 (60/131)	76.6 (46/60)	NA	NA	NA	NA	NA	NA	25	9	NA
		Single	133	Fus-TBx SBx, elastic	NA	33 (44/133)	79.5 (35/44)	NA	NA	NA	NA	NA	NA	20	6	NA
5	Kam et al. [11]	Single	56	Cog-TBx, SBx	80 (46/56)	73 (41/56)	70 (39/56)	>0.05	64.28 (36/56)	58.92 (33/56)	57.14 (32/56)	NA	NA	NA	NA	NA
		Single	65	FUS-TBx, SBx	72 (47/65)	66 (43/65)	62 (41/65)	>0.05	50.76 (33/65)	43.09 (28/65)	44.61 (29/65)	NA	NA	NA	NA	NA
6	Kaufmann et al. [12]	Single	35	IB-TBx, SBx	46 (16/35)	23 (8/35)	46 (16/35)	<0.05	46 (16/35)	NA	46 (16/35)	NA	0	0	0	NA
7	Quentin et al. [13]	Single	128	IB-TBx, SBx	60.9 (78/128)	53.1 (68/128)	53.1 (68/128)	0.74	82.1 (64/78)	79.4 (54/68)	85.3 (58/68)	NA	10.9 (7/68)	NA	NA	NA
8	Pokorny et al. [14]	Single	223	IB-TBx, SBx	63.67 (142/223)	56.5 (126/223)	69.71 (99/142)	na	48.43 (108/223)	35.42 (79/223)	42 (93/223)	<0.0001	32 (35/108)*	21 (47/223)	3 (6/223)	<0.0001
9	Arsov et al. [15]	Single	106	IB-TBx	37 (39/106)	NA	37 (39/106)	0.7	29 (31/106)	NA	29 (31/106)	NA	NA	NA	NA	NA
10	Sonn et al.[16]	Single	104	FUS-TBx, SBx Fus-TBx	39 (41/108)	35 (36/104)	34 (35/104)	0.08	32 (33/104)	25 (26/104)	26 (27/104)	NA	NA	NA	NA	NA
		Single	105		34 (36/105)	27 (28/102)	24 (23/97)	NA	72 (26/36)	54 (21/28)	91 (21/23)	NA	25 (9/36)	NA	NA	NA
11	Kuru et al. [17]	Single	347	TPM-Bx	58 (200/347)	41.78 (145/347)	36.88 (128/347)	NA	73.5 (147/200)	50 (100/200)	52 (104/200)	NA	NA	NA	NA	NA
12	Rastinehad et al. [18]	Single	105	Fus-TBx SBx, Fus-TBx	62.8 (66/105)	48.57 (51/105)	50.47 (53/105)	<0.001	48.6 (51/105)	66.66 (34/51)	88.67 (53/57)	<0.001	34.84 (23/66)	33.33 (17/51)	11.33 (4/57)	NA
13	Panebianco et al. [19]	Single	570	SBx	37.71 (215/570)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Single	570	FUS-TBx, SBx Fus-TBx	71.92 (410/570)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
14	Baco et al. [20]	Single	175	FUS-TBx, SBx	56.57 (99/175)	54 (48/89)	59 (51/86)	0.4	46.85 (82/175)	49 (44/89)	38 (33/86)	0.2	NA	NA	NA	NA
15	Siddiqui et al. [21]	Single	1003	FUS-TBx, SBx	NA	46.75 (469/1003)	45.96 (461/1003)	NA	NA	26 (122/469)	37.5 (173/461)	<0.001	17 (167/1003)	55 (258/469)	46.2 (213/461)	0.002
16	de Gorski et al. [22]	Single	232	SBx, Fus-TBx	61.6 (143/232)	55.6 (129/232)	54.3 (126/232)	NA	48.7 (113/232)	39.2 (91/232)	44 (102/232)	NA	17.46 (22/126)	16.37 (38/232)	10.34 (24/232)	NA
17	Radtke et al. [23]	Single	294	TPM-Bx, Fus-TBx	51 (150/294)	45.91 (135/294)	38.09 (112/294)	0.001	57.3 (86/150)	45.3 (68/150)	50 (75/150)	NA	NA	44.66 (67/150)	24.66 (37/150)	NA
18	Cash et al. [24]	Single	408	FUS-TBx, SBx	56 (227/408)	NA	40.19 (164/408)	NA	45.58 (186/408)	NA	32.59 (133/408)	NA	NA	NA	NA	NA
19	Mozer et al. [25]	Single	152	SBx	NA	56.57 (86/152)	53.94 (82/152)	NA	NA	36.84 (56/152)	43.42 (66/152)	0.03	NA	19.7 (30/152)	10.52 (16/152)	NA
20	Peltier et al. [26]	Single	110	FUS-TBx, SBx	NA	45.45 (50/110)	51.81 (57/110)	NA	NA	29.09 (32/110)	45.45 (50/110)	0.0008	NA	16.36 (18/110)	5.45 (6/110)	NA

Table III. Comparison of the performance of SB (Systematic Biopsy), Fus-TBx (Fusion Targeted Biopsy) and IB-TBx (In-Bore MRI Targeted Biopsy) in terms of overall CDR (cancer detection rate), csPCa (clinically significant Prostate Cancer), isPCa (clinically insignificant Prostate Cancer) (continuation).

No	Study	S/M	Pa. No.	Type	PCa Overall CDR % (n/N)	PCa SBx % (n/N)	PCa TBx % (n/N)	PCa p value	csPCa Overall CDR % (n/N)	csPCa SBx % (n/N)	csPCa TBx % (n/N)	csPCa p Value	Upgrading % (n/N)	isPCa SBx % (n/N)	isPCa TBx % (n/N)	is PCa p value
21	Porpiglia et al. [27]	Single	107	SBx, Fus-TBx	50.5 (54/107)	19.2 (5/26)	60.5 (49/81)	<0.001	43.9 (47/107)	3.8 (1/26)	56.8 (46/81)	<0.001	NA	15.4 (4/26)	3.7 (4/81)	
		Single	105	SBx	29.5 (31/105)	29.5 (31/105)	NA	<0.001	18.1 (19/105)	18.1 (19/105)	NA	<0.001	NA	11.4 (12/31)	NA	NA
22	Zhang et al. [28]	Single	224	FUS-TBx, SBx	NA	34.82 (78/224)	44.20 (99/224)	0.001	NA	21.875 (49/224)	33.48 (75/224)	<0.001	7.58 (17/224)	12.94 (29/224)	10.71 (24/224)	0.005
23	Mehralivand et al. [29]	Single	339	FUS-TBx, SBx	47 (346/737)	NA	NA	NA	32 (237/737)	NA	NA	NA	NA	NA	NA	NA
24	Hakozaki et al.[30]	Single	177	FUS-TBx, SBx	65.3 (116/177)	58.7 (104/177)	49.7 (88/177)	>0.05	63.3 (112/177)	57.1 (101/177)	48 (85/177)	>0.05	NA	NA	NA	NA
25	Gordetsky et al. [31]	Single	191	FUS-TBx, SBx	56 (107/191)	41.4 (79/191)	49.2 (94/191)	0.15	NA	23.56 (45/191)	24.6 (47/191)	NA	NA	25.65 (49/191)	16.75 (32/191)	0.04
26	Castellucci et al. [32]	Single	168	Cog-TBx, SBx	41.1 (69/168)	35.7 (60/168)	28.6 (48/168)	NA	24.4 (41/168)	19.26 (33/168)	17.85 (30/168)	NA	NA	16.07 (27/168)	10.7 (18/168)	NA
27	Mariotti et al. [33]	Single	100	FUS-TBx, SBx	62 (62/100)	56 (56/100)	53 (53/100)	0.29	50 (50/100)	40 (40/100)	44 (44/100)	0.29	NA	16 (16/100)	9 (9/100)	NA
28	Boesen et al. [34]	Single	289	FUS-TBx, SBx	44.29 (128/289)	37.37 (108/289)	33.21 (96/289)	NA	30.4 (88/289)	20.41 (59/289)	26.9 (78/289)	0.004	11.41 (33/289)	16.95 (49/289)	6.22 (18/289)	0.004
29	Kasivisvanathan et al. [35]	Multi	500	FUS-TBx, SBx	NA	47.98 (119/248)	46.82 (118/252)		NA	26 (64/248)	38 (95/252)	0.005	NA	22 (55/248)	9 (23/252)	<0.001
30	Borkowetz et al. [36]	Multi	214	SBx, Fus-TBx	52 (111/214)	43 (91/214)	47 (100/214)	0.15	44 (94/214)	35 (74/214)	38 (81/214)	0.296	NA	7.94 (17/214)	8.87 (19/214)	NA
31	Hofbauer et al. [37]	Single	704	FUS-TBx, SBx	74 (521/704)	NA	63 (446/704)	NA	54 (380/704)	NA	45 (317/704)	NA	NA	NA	NA	NA
32	Costa et al. [38]	Single	103	IB-Tx	69.9 (72/103)	NA	69.9 (72/103)	NA	61 (63/103)	NA	61 (63/103)	<0.0001	NA	NA	NA	NA
		Single	300	FUS-TBx, SBx	64.66 (194/300)	NA	64.66 (194/300)	NA	47 (141/300)	NA	47 (141/300)	<0.0001	NA	NA	NA	NA
33	Maxeiner et al[39]	Single	318	FUS-TBx, SBx	77 (245/318)	69.8 (222/318)	66.7 (213/318)	NA	61.3 (195/318)	45.59 (145/318)	51.2 (163/318)	NA	NA	24.21 (77/318)	15.72 (50/318)	NA
34	Wegelin et al. [40]	Multi	79	FUS-TBx	NA	NA	49.4	0.4	NA	NA	34.2	>0.9	NA	NA	63.8	NA
		Multi	78	Cog-TBx	NA	NA	43.6	0.4	NA	NA	33.3	>0.9	NA	NA	66.7	NA
		Multi	77	IB-TBx	NA	NA	54.5	0.4	NA	NA	32.5	>0.9	NA	NA	63.5	NA
35	van der Leest [41]	Multi	326	IB-TBx, SBx	54 (338/626)	48 (301/626)	39 (247/626)	NA	32 (200/626)	23.3 (146/626)	25.4 (159/626)	0.17	7 (21/317)	25 (155/626)	14.1 (88/626)	0.0001
36	Elkhoury et al. [42]	Single	248	FUS-TBx, SBx	70.2 (174/248)	62.1 (154/248)	62.1 (154/248)	NA	NA	60.4 (150/248)	54 (134/248)	NA	NA	18.54 (46/248)	17.33 (43/248)	NA
		Single	248	Cog-TBx, SBx	70.2 (174/248)	62.1 (154/248)	46.8 (116/248)	NA	NA	60.4 (150/248)	46.77 (116/248)	NA	NA	18.54 (46/248)	15.3 (38/248)	NA
37	Rouviere et al. [43]	Multi	251	Fus-TBx/ Cog-TBx, SBx	64.14 (161/251)	52.19 (131/251)	41.4 (104/251)	NA	42 (105/251)	32.66 (82/251)	35.83 (90/251)	0.26	9.2 (5.9-13.4)	19.52 (49/251)	5.57 (14/251)	<0.0001

Discussion

1. TBx impact on diagnosis and treatment management

Treatment options for non-metastatic PCa include active surveillance, focal therapy, radiation therapy and radical prostatectomy. The therapeutic decision is mainly based on the histopathological examination, provided by the prostate biopsy, randomized or targeted. Multiparametric MRI provides improved diagnosis rate for csPC and staging information, which are the basis for an informed treatment choice and future planning in case of surgical treatment or focal therapies [19].

A. TBx and prostate cancer diagnosis

• Malignant vs. benign

The cumulative risk of prostate cancer diagnosis increases with each repeated biopsy (68% after four biopsies), with 38% of patients requiring a second biopsy after 5 years from the first systematic biopsy [47]. This risk may be lowered by mpMRI and targeted biopsy, taking into consideration that in our analysis TBx outperformed SBx in the majority of studies. Moreover, there is no study to present a statistically significant higher CDR for the SBx, while it was observed that both in high level single institutions and multicenter (PRECISION, FUTURE) trials it is possible to achieve a higher cancer detection rate by TBx. Association of the two biopsy techniques may overcome the current limitations of targeted biopsy by improving both overall PCa and csPCa cancer detection rates. Dell'Oglio et al. emphasized the importance of systematic biopsy to limit the missed csPCa cases by targeted biopsy [48].

Multiparametric MRI (mpMRI) and the subsequent TBx need further improvement, due to a small percentage of prostate cancers being missed with these methods, while properly detected in SBx cases [14,35].

To conclude, even if Cog-TBx is the only available option, mpMRI should be performed prior to the biopsy, to increase the accuracy of diagnosis.

• CsPCa vs isPCa

Assessing the patient in the correct risk category is mandatory in order to decide further treatment. The most important limitation encountered in daily practice is the high inter-studies variability regarding the definition of csPCa (Table I). However, TBx offers more accurate diagnosis of csPCa, especially when Fus-TBx or IB-TBx are performed (Table III) [14,27,28]. Moreover, TBx presents lower detection rate of low risk PCa compared to SBx (Table III).

Cribriform and intraductal prostate carcinoma are included in the clinically significant prostate cancers group, having an aggressive evolution. There are conflicting results in terms of mpMRI performance of identifying these lesions and which biopsy type is more adequate [41,42]. The latest trial to address the issue demonstrated that Fus-TBx significantly outperformed SBx [50].

• Location of the lesion

Lesion localization is an important factor to be taken into consideration, being proved that in case of previous negative biopsy there is a higher probability that the lesion is located in the anterior region of the prostate, which also harbors more frequently csPCa [51]. In a retrospective analysis of 499 patients, half of the 241 anterior lesions identified on mpMRI were positive for PCa, Fus-TBx outperforming SBx in diagnosing PCa located anteriorly (p=0.001) [52].

On the other hand, there are differences between the targeted and systematic biopsies in reaching different prostate zones. Both TBx and SBx may miss apical lesions [46]. IB-TBx potentially misses more csPCa located in dorsolateral and apical segments of the prostate, while SBx tends to miss csPCa in the anterior, anterior midprostate and anterior apex [46].

• Limitations

Despite the fact that the initial mpMRI does not identify any lesion, in up to 26% of patients csPCa may still be present [53]. Standardization and improvement of mpMRI interpretation (PI-RADS v2, v2.1) increased the negative predictive value of mpMRI, up to 82.4% for overall cancer and 88.1% for csPCa [54]. A negative TBx cannot exclude the presence of csPCa, as 46% of the highly suspicious lesions described on MRI can harbor csPCa [55], while repeated Fus-TBx reveals clinically significant discordance with the initial TBx in more than half of the cases [56].

Two possible reasons may explain the percentage of misdiagnosis for targeted biopsy, as reported by Cash et al: firstly, the inaccurate PIRADS Score classification, inexperienced readers having a tendency of reporting higher initial PIRADS score, in up to 39% of lesions [24]. Secondly, TBx failure may be due to prostate movement/deformation by the transrectal ultrasound probe, patient movement, incorrect image registration or mismatch of image planes, but no significant differences were shown by elastic registration or real-time sensor based image registration platforms [57].

The accuracy of three-dimensional MRI/US registration associates a mean target error of 2.4-2.5 mm [58]. An in-vivo experiment showed that in daily practice, co-registration error may be up to 5.6 mm, with the highest errors encountered at the apex of the gland [59]. Despite higher csPCa detection rate when elastic registration was performed, it was not statistically significant different to the rigid one [60]. The skills required to perform TBx improve in time as revealed in a cohort of 1330 patients that underwent Fus-TBx when csPCa detection rate raised by 26%, between the initial and last 190 cases [56].

Moreover, Halstuch et al. showed that larger prostates and right sided biopsy may significantly induce a needle tip deflection, which may account for targeted biopsy error [61]. Despite that prostate volume alters

the accuracy of the biopsy, it was observed that Fus-TBx performs better than SBx in larger prostates [22]. In the multivariate analysis, Mozer et al. reported that the probability for detecting csPCa increased in cases of lower volume prostates and larger MRI lesions [25].

B. TBx and prostate cancer treatment
• PCa grading

Prostate cancer staging and grading are essential for the choice between active surveillance, focal therapy or radical therapy. Despite the PCa multifocality, in up 97.5% of cases the index tumor is the one with the largest volume [53], and several studies reported MRI detection rate around 92% [57,58]. MRI performance in identifying index tumors >0.5 mL varied among 86%-92% [53,63].

SBx is responsible for up to 30% of Gleason Score (GS) incorrect classification [64]. Performing saturation biopsy does not significantly improve rate of correct GS [65], while the associated risks of the procedure are well-known. There is better correlation between the GS of biopsy and prostatectomy specimen when Fus-TBx is performed compared to SBx, both in terms of primary and secondary Gleason grade pattern [66].

From the perspective of GS down-grading, Porpiglia et al. reported in a retrospective analysis of 683 cases, that up to one-third of the patients diagnosed by SBx with Gleason 8 were down-graded. Down-grading has a strong impact on the chosen therapy, a tendency to recommend radiation therapy with long-term androgen deprivation for patients with GS 8 or higher has been observed [66].

• Active surveillance (AS) selection and reevaluation

MpMRI is a useful tool in selecting patients for AS due to the high negative predictive value for csPCa [67]. mpMRI provides additional information compared to other imagistic examination. Firstly, it evaluates the extraprostatic extension (EPE), being observed that in those with extraprostatic extension the risk of csPCa is 12 times higher, therefore a more aggressive option is chosen [68]. Secondly, targeted biopsy based on mpMRI reclassified up 10% of patients considered eligible for AS based on SBx [69], with Fus-TBx upgrading up to 24% of SBx results [70].

Multiparametric MRI can play a role in the reevaluation of patients under AS, with the possibility to avoid re-biopsy in patients with PIRADS ≤ 3 lesions and no sign of extra-prostatic extension [68]. PIRADS score is an independent predictor of csPCa in patients benefiting from AS [71]. However, in case of repeated negative mpMRI, biopsy cannot be ruled out because a low risk of csPCa still persists [68]. TBx performs better in the follow-up evaluation of patients under AS compared with SBx [65,68].

• MRI/TRUS Fusion impact on focal therapy

MRI/TRUS Fusion technology not only guides the biopsy, but also focal therapies. MRI/TRUS Fusion technology meets the precision requirement, providing more accessible environment to perform the focal therapy in comparison with the MRI gantry.

Despite an initial pilot study with a 100% recurrence free rate at four weeks after the MRI/TRUS Fusion HIFU [73], another prospective trial with double the number of patients and 12 month reevaluation landmark revealed a recurrence rate of 40% and established that the technique needs further evaluation and improvement [74].

Other focal therapies used were MRI/TRUS Fusion focal cryotherapy, which showed no evident imagistic recurrence, not leaving the possibility of bioptic reevaluation [75], and MRI/TRUS Fusion focal laser ablation which in the pilot study presented no recurrence at the six month rebiopsy [76].

C. TBx cost-effectiveness

The associated higher costs for targeted biopsy (mpMRI, biopsy platform, materials) represent the main argument against its wide employment [77]. PROMIS Trial suggested that mpMRI prior to biopsy has several advantages with possible impact into the healthcare costs, such as avoiding prostate biopsy in up to a quarter of patients, for those with no MRI or low score PIRADS lesion [78]. As shown by our analysis, TBx lowers clinically insignificant cancer diagnosis rate, which will decrease the overtreatment observed and its associated side-effects. A higher detection of clinically significant PCa, from the initial biopsy lowers the number of further necessary investigation with patients benefitting from the correct treatment from the beginning [78]. PRECISION Trial showed that the number of patients with persistent PCa suspicion who needed further investigation was 5 times higher for those who were evaluated by SBx [35].

Venderick et al. performed a computer simulation for biopsy naïve population, which showed that fusion biopsy is cost-effective in the context of two different healthcare systems [79]. Another similar study based on the PROMIS Trial data, showed the same cost-effectiveness of using mpMRI and TBx [80].

2. Future improvement directions

mpMRI interpretation training and reproducibility is crucial in establishing TBx as standard of care. PROMIS and PRECISION Trials supported the collaboration with experienced radiologists, who also benefitted from training in the pilot phase of the study [35,78]. The key to achieve higher sensibility and specificity regarding mpMRI diagnosis of csPCa lies within the improvement brought by PIRADS v2 and v2.1, associated with efficient training for the radiologist. Also, the performance in terms of CDR is correlated with the learning curve [37].

Collaboration between radiologists and urologists is essential. In our analysis in 21 out of the 37 studies, TBx was performed solely by the urologist. It is observed that the definition of TBx between the two specialists may differ

in up to 23% cases, with urologists identifying more lesions and with larger volumes in disagreement with PIRADS criteria [81]. A pilot study using a mpMRI case-based ibook for urologists demonstrated a statistically significant improvement in mean score test after book review (37% to 57%, p=0.0039) [82]. Therefore, urologist training in mpMRI reading is essential to overcome errors such as lesion choice, target lesion dimensions [81].

Having in mind the persistent low number of csPCa missed by mpMRI and TBx, it is necessary to improve the existent technology by better identification and visualization of suspect lesions using MRI spectroscopy and in vivo metabolic changes observed in prostate cancer [83]. Better performance is needed in terms of higher accuracy when performing registration of the ultrasonography and MRI, which may be acquired using co-registrations markers such as fiducial ones, visible on MRI and US, guiding both biopsy and focal therapy [59].

There are further studies needed in order to evaluate whether factors such as PIRADS score, prostate dimension, number of lesions, location and dimension, anatomic particularities and technique biases can influence the urologist into choosing the right targeted biopsy technique for the patient.

Conclusion

Targeted biopsy is an emerging and developing technique which offers the needed improvements in diagnosing clinically significant prostate cancer and lowers the incidence of insignificant one, providing more accurate selection of the patients for active surveillance and focal therapies. No significant differences between the MRI targeting techniques have been observed, the key for an accurate diagnosis being the individualization of the biopsy technique according to the particularities of each patient.

Acknowledgement

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