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ORIGINAL ARTICLE

Does 1.5 T mpMRI play a definite role in detection of clinically significant prostate cancer? Findings from a prospective study comparing blind 24-core saturation and targeted biopsies with a novel data remodeling model

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Abstract

Background Multiparametric-magnetic resonance imaging (mpMRI) can accurately detect high-grade and larger prostate cancers (PC).

Aims To evaluate the ability of 1.5 T magnetic field mpMRI-targeted Prostate Biopsies (PBx) in predicting PC in comparison with blind 24-core saturation PBx (sPBx).

Methods We prospectively collected data from patients undergoing transrectal sPBx and, if needed, targeted PBx of suspected lesions based on the 16-'region-of-interest' (ROI) PI-RADS graph. Data remodeling: for each 'target' (each suspected lesion at mpMRI), we identified all the 16 'ROIs' into which the lesion extended: these single 'ROIs' were identified as 'macro-targets'. For each 'ROI' and 'macro-target', we compared the mpMRI result with that of a saturation and targeted biopsy (if performed).

Results 1.5T mpMRI showed a PI-RADS value ≥ 3 in 101 patients (82.1%). We found a PC in 50 (40.6%). Negative-positive predictive values for mpMRI were 82–45%, respectively. Of the 22 patients with normal mpMRI, four had a PC, but none had a clinically significant cancer. After the data remodeling, we demonstrated the presence of PC in 228 'ROIs': (a) *only* in targeted biopsies in 15 'ROIs'/'macro-targets' (6.6%); (b) only in sPBx in 177 'ROIs' (77.6%); (c) in both targeted and sPBx in 36 'ROIs' (15.8%).

Discussion 81.8% of patients with normal 1.5T mpMRI were negative at PBx. Performing only targeted PBx may lead to lack of PC diagnosis in about 50% of patients.

Conclusions In patients with suspected PC and a previous negative PBx, a normal mpMRI may exclude a clinically significant PC, avoiding sPBx.

Keywords Multiparametric MRI · Prostate cancer · Prostate biopsy

Introduction

Two major concerns related to diagnosis of prostate cancer (PC) are overdiagnosis (and consequent overtreatment of indolent diseases) and the cost/benefit correlation of diagnostic techniques. The introduction of recent imaging techniques, such as multiparametric-magnetic resonance imaging (mpMRI), does provide much better visualization of the prostate compared with other imaging methods such as transrectal ultrasonography (TRUS), resulting in more accurate PC location and allowing image-guided targeted

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sampling to overcome the limitations of traditional 'blind' prostate biopsy (PBx) [1].

Several studies conclude that mpMRI may be useful not only in improving the detection of PC, but also and above all in helping PC management, identifying the biological aggressiveness of the cancer, and accurately staging the disease, both of which can facilitate selection of appropriate treatment [2].

It has been demonstrated that mpMRI can accurately detect high-grade and larger tumors, and that it is particularly useful in detecting clinically significant diseases [3, 4]: a recent review demonstrated that the rate of detection of clinically significant diseases ranges from 44 to 87% [5].

According to EAU guidelines, the first step recommended in the histologic diagnosis of PC is to perform 10–12 core PBx's, when > 12 cores are not significantly more conclusive [6]. This kind of PBx is also characterized by a high false-negative rate (20–30%) [7]. Consequently, about one-third of patients with persistent suspicion of PC after a first standard PBx with negative findings do have PC [8]. Patients with persistent suspicion of PC thus often undergo mpMRI and then targeted PBx procedures. Diagnostic accuracy is high, as documented in several studies [9]. mpMRI is sometimes performed before the first PBx, to improve the detection of clinically significant PC [10–12]. As recommended by EAU guidelines, mpMRI-targeted biopsies should be added to systematic ones, in the case of positive mpMRI. Due to the high risk that a tumor is either being missed or that its most aggressive part is not identified by mpMRI-targeted PBx, saturation biopsies (sPBx) must be added to targeted cores: however, this high number of cores may hit a small but not clinically significant cancer, contributing to overdetection and overtreatment.

There is a large body of evidence, suggesting that mpMRI-targeted PBx has a higher detection rate of detecting clinically significant PC when compared with systematic biopsy, although some concerns remain about the impact of the real cost-effective value of mpMRI [13]. There are only a few studies comparing saturation biopsies and mpMRI-targeted sampling in patients with a first negative standard PBx, but they do demonstrate that targeted biopsies can decrease the detection rate of PC, with a higher number of Gleason score 6's than sPBx can provide [14–16].

Most of the recently published studies have focused exclusively on the sensitivity of mpMRI-targeted biopsies or on the impact of various fusion techniques on diagnosing PC [13].

The aim of our study was to evaluate whether adding 1.5 T magnetic field mpMRI-targeted PBx improves PC detection in patients undergoing blind 24-core sPBx.

Methods

From January 2013 to December 2016, at the Urologic Clinic of the Padova University Hospital, we prospectively collected data from patients undergoing blind sPBx and, if needed, data from other targeted biopsies of suspected lesions reported at 1.5 T mpMRI for persistent suspected PC ('normal clinical practice').

We enrolled all patients who had already undergone a first 10/12-core PBx (according to prostate volume) with suspected PC due to PSA increase and/or positive digital rectal examination. We excluded all patients with records of more than one set of 10/12 core PBxs, or patients who had previously undergone TURP or other low urinary tract endoscopic procedures. All enrolled all the patients underwent 1.5 T mpMRI at the Department of Radiology of the Padova Hospital. Table 1 lists the parameters used during mpMRI.

All mpMRI were evaluated by two skilled radiologists (CSL-AL). Lesions with a PI-RADS score (version 1) of ≥ 3 were considered suspicious for PC. Findings identified by radiologists are shown in the PI-RADS scheme with 16 'Regions of Interest' ('ROIs') [Fig. 1a].

After mpMRI, all patients underwent transrectal TRUS-guided blind sPBx with one additional core for each mpMRI-suspected lesion. The procedure was performed by one of the skilled urologists with the patient in the lithotomic position, under local anesthesia (10 cc 2% lidocaine injected at the level of the apex and the vesico-prostatic angle, bilaterally) and light sedation (1–2 cc Fentanyl i.v.). A transrectal end-fire and side-fire US probe (Siemens BE9-4™) was used. A 18-gauge needle was used for tru-cut.

In view of the high level of skill of the urologists performing PBx (more than 700 cases each), targeted cores were taken using cognitive fusion, based on suspected lesions found on the 16-region PI-RADS graph. If a suspected lesion appeared at mpMRI, the operator performed first the target PBx and then the sPBx. Radiologists were present during the procedure and reviewed the cases prior to biopsy.

All cores were immediately stretched and placed in 24 labeled tissue cassettes between nylon sponges, without orientation of the specimens, as we previously described [17]. All slides were analysed by a single experienced uropathologist (MPG) using contemporary diagnostic criteria for HGPIN, ASAP, and PC.

Pathology assessment of the biopsy cores included core length, number and location of positive cores, percentage of cancer involvement in any positive core, presence of perineural invasion, and Gleason scores.

All data were reported according to the START recommendations [18].

Table 1 Parameters used during 1.5 T mpMRI

	Tirm axial pelvis	T1 axial pelvis	T2 axial pelvis	T2 sagittal	T2 axial	T2 coronal	DWI axial	VIBE axial
No. slices	40	40	40	30	23	23	18	1
Dist. factor (%)	20	20	20	10	10	10	0	20
Phase encoding	AP	AP	AP	AP	R > L	R > L	AP	R > L
Phase oversamp. (%)	0	0	0	50	80	80	0	70
FOV (mm)	380	380	380	180	180	180	260	260
FOV phase (%)	81	81	81	100	100	100	100	100
Thickness (mm)	5	5	5	3	3	3	3	3
TR (ms)	3060	520	2620	7000	7000	7000	4000	5.44
TE (ms)	55	8.6	120	110	108	112	91	1.98
TI	160	–						
Average		1	1	5	5	5	10	1
concatenations		4	1	1	1	1	1	1
Matrix	256×166	256×143	320×208	320×256	320×226	320×254	192×192	192×180
Phase resolution (%)	80	73	80	80	71	80	100	94
IPAT	2	2	2	2	2	2	2	2
B values							50-400-1000	
Aquisition time (min)	1.10	0.53	2.50	7.09	7.09	7.09	6.14	6.18
Voxel size (mm)	1.9×1.5×5	1.0×0.7×5	1.5×1.2×5	0.7×0.7×3	0.7×0.7×3	0.7×0.7×3	1.4×1.4×3	1.4×1.4×3

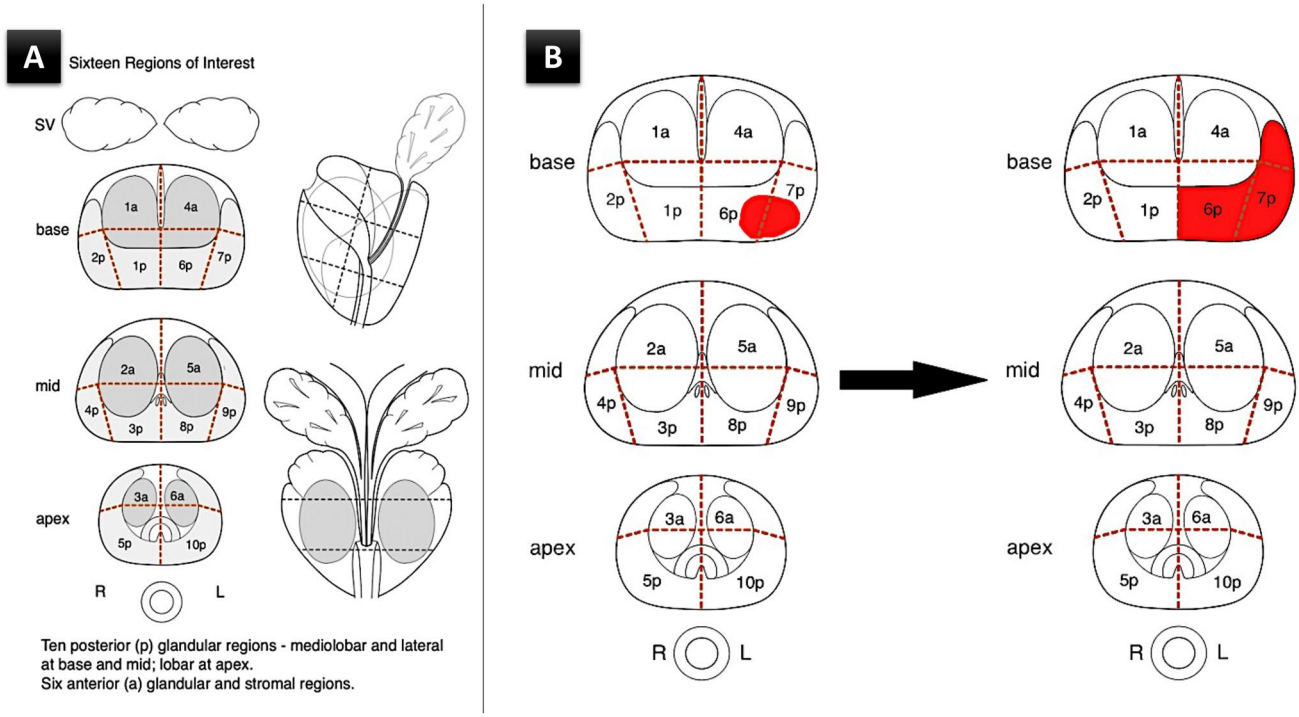

Fig. 1 **a** PI-RADS scheme with 16 'Regions of Interest'. **b** Example of data remodeling: the mpMRI lesion involving 'ROI' 6p and 7p is transformed in two 'macro-targets'

Power calculation

The minimum sample size was calculated using a statistical formula shown below:

$N = [Z^2PQ]/\delta$, where N = minimum sample size for a comparative study design [2]; Z = the standard normal deviation corresponding to 95% level of significance the value obtained from a normal distribution table is 1.96;

P = prevalence rates obtained from Fütterer [5] = 44–87% (= 0.44–0.87); δ = absolute precision, that is, value required (in percentage points) which in actual term describes the maximum difference between the population rate and the sample rate that can be tolerated; taken for this study to be 10% (0.1); DEFF = estimated design effect = 1.

The result was a minimum sample size from 43 to 94 patients, according to the different accuracy rates reported in the literature [5].

Definition

As clinically significant disease, we considered a PC found in more than two cores (or maximum cancer core invasion > 5 mm), or Gleason score > 6, according to the definition proposed by Ahmed et al. [19].

Data remodeling model

After a first evaluation of the correlation between mpMRI findings and PBx results, we analysed the biopsy results using the 16 'ROIs' of the map of the prostate as points of reference. For each 'ROI', we compared the mpMRI result with that of a saturation and targeted biopsy (if performed).

Table 2 lists the scheme used for sPBx and the corresponding 'ROI' of the PI-RADS scheme.

For this analysis, we had to perform a preliminary operation: for each 'target' (each suspected lesion at mpMRI evaluation), we identified all the 16 'ROIs' into which the lesion extended: these single 'ROIs' were identified as 'macro-targets'.

Although some cores (e.g., core 1) only sampled material from 'ROI' 5p, there were other single cores which sampled several 'ROIs', e.g., core 5 samples; 'ROIs' 1p, 2p, 3p, and 4p. Conversely, each single radiologic 'ROI' could be sampled or covered by several bioptic cores. For example, 'ROI' 2p was sampled by cores 2, 3, 4, 7, and 8.

A single biopsy performed on a target lesion encompassing two or more defined 'ROIs' of the prostate was considered to contain multiple discrete biopsy samples. This single core contains material from multiple radiological 'ROI'. This sample was then considered as if it was multiple discrete samples, and the result from the single core was then attributed to all 'ROIs' involved in the radiological image.

For example, in Fig. 1b, the lesion identified by mpMRI involves 'ROI' 6p and 7p. If a single sample encompassing both 'ROIs' is taken from this lesion; and if a cancer is identified, both 'ROIs' were considered to be neoplastic.

To summarize, all areas identified by the radiological map, e.g., 2p, 3p, 4p., etc., were considered as 'ROIs'. Suspected lesions encompassing two or more 'ROIs' were identified as 'macro-targets'.

Table 2 Scheme used for sPBx and the corresponding 'ROI' of the PI-RADS scheme

Core no.	Site	Corresponding 'ROI' of PI-RADS scheme
1	Peri-apex right	5p
2	Anterior-lateral right	2p–4p
3	Intermediate lateral right	2p–4p
4	Posterior right	2p–4p
5	Postero-lateral right	1p–2p–3p–4p
6	Apex right	5p
7	Anterior para-median right	2p–4p
8	Intermediate para-median right	2p–4p
9	Posterior para-median right	2p–4p
10	Postero-medial right	1p–3p
11	Transitional right	1a–2a–3a
12	Transitional anterior right	1a–2a–3a
13	Peri-apex left	10p
14	Anterior-lateral left	7p–9p
15	Intermediate lateral left	7p–9p
16	Posterior left	7p–9p
17	Postero-lateral left	6p–7p–8p–9p
18	Apex left	10p
19	Anterior para-median left	7p–9p
20	Intermediate para-median left	7p–9p
21	Posterior para-median left	7p–9p
22	Postero-medial left	6p–8p
23	Transitional left	4a–5a–6a
24	Transitional anterior left	4a–5a–6a

Table 3 Demographic data of patients

Characteristics	Value
Age (median, IQR)	62 (57–68) years
Familiarity	
Negative	113
Positive	10
Digital rectal examination	
Negative	112
Positive	11
Prostate volume at TRUS (mean, range)	54.59 (20–149) cc
PSA (median, IQR)	6.27 (4.75–8.9) ng/ml
PSA free/total (median, IQR)	17 (11–24) %

Legenda: *IQR* interquartile range

Results

A total number of 123 patients were prospectively collected. Their demographic characteristics are listed in Table 3.

Patients

1.5T mpMRI showed a PI-RADS value of ≥ 3 in 101 patients (82.1%). We found a PC in 50 patients (40.6%).

The distribution of patients according to mpMRI and results of PBx are reported in Table 4.

Considering all patients with negative sPBx (73 cases), mpMRI was normal in 24.7% (18/73), with 75.3% (55/73) of false positives. Negative and positive predictive values were 82 and 45%, respectively.

Considering the cases with suspected mpMRI (101 patients) [Fig. 2a], the biopsies were negative at both sPBx and targeted samplings in 55 (54.4%), whereas 46 patients (45.5%) had a PC. Among the latter, PC was found:

on targeted biopsies in 28 patients (60.9%);

on saturation biopsies in 46 patients (100%).

With only targeted PBx, we would have non-diagnosed 18 patients with PC (39.1%).

Clinically significant PC

Of the 22 patients with normal mpMRI, four received a diagnosis of PC, but none had a clinically significant cancer. Consequently, there were no patients (0%) with normal mpMRI with a clinically significant PC.

Globally, we found a clinically significant PC in only 54% of patients with a cancer (27/50): all were suspected at mpMRI. Of the 23 patients with a not clinically significant neoplasm, mpMRI was normal or suspected in 4 and 19 cases, respectively. Consequently, the negative and positive predictive value of mpMRI in diagnosing a clinically significant PC was 100% e 26.7%, respectively.

Lesions

Overall, mpMRI identified a total number of 159 suspected lesions (mean 1.57/patient). Of these, only 33 (20.75%) were found to be positive for PC (corresponding to the total of 28 patients diagnosed as affected by PC).

Focusing now on the 16 'ROIs' of the prostate map, we subdivided all the glands into a total of 1968 'ROIs' (= 16 'ROIs' × 123 patients). mpMRI revealed a total of 230 suspected 'macro-targets'. Table A1 (Appendix) shows the distribution of single suspected lesions identified with mpMRI in the various 'ROIs'.

Considering all the PBx performed, cancer was found in 224 'ROIs', as shown in Table 5.

Table 4 Distribution of patients according to mpMRI and results of PBx

		Result of PBx		
		Normal	Cancer	
mpMRI	Normal	18	4	22
	Suspected	55	46	101
Total		73	50	123

Targeted biopsies

Of these 230 suspected 'macro-targets', 51 (43.5%) were positive for PC at biopsy. Table A2 (Appendix) lists the specific distribution of these positive cores diagnosed by a targeted PBx.

Saturation biopsies

Focusing now on cases in which mpMRI identified one or more suspected areas, considering only the blind saturation biopsies, we found a PC in 213 'ROIs'. Table A3 (Appendix) lists the distribution of positive cores diagnosed by sPBx in the various 'ROIs'.

Saturation and targeted biopsies

Overall, we demonstrated the presence of PC in 228 'ROIs':

only in targeted biopsies in 15 'ROIs'/'macro-targets' (6.6%);

only in saturation biopsies in 177 'ROIs' (77.6%);

in both targeted and saturation biopsies in 36 'ROIs' (15.8%).

Figure 2b shows the subdivision of single positive 'ROIs' according to the different approach (targeted versus sPBx).

Figure 3 shows the spatial distribution of the 228 'ROIs' positive for PC, according to the type of biopsy performed.

Discussion

Analysis of our data showed that 81.8% of patients (18/22) with normal mpMRI were negative at PBx, whereas a PC was found in 18.2%, confirming the high negative predictive value of this imaging technique, already noted in the literature [20]. However, the most interesting finding was that all patients with a normal mpMRI were also negative for a clinically significant PC at blind sPBx. From the viewpoint of clinical practice, this result indicates that sPBx could be avoided in the case of a normal mpMRI. In addition, comparing the results of targeted and saturation biopsies in cases of suspected mpMRI, targeted samplings identified patients with PC: nevertheless, these patients (100%) could have been identified by the 24-core blind sPBx alone.

Consequently, the contribution of mpMRI in identifying patients with PC was nil (!). In fact, focusing on the 'macro-targets' identified by mpMRI, the advantage

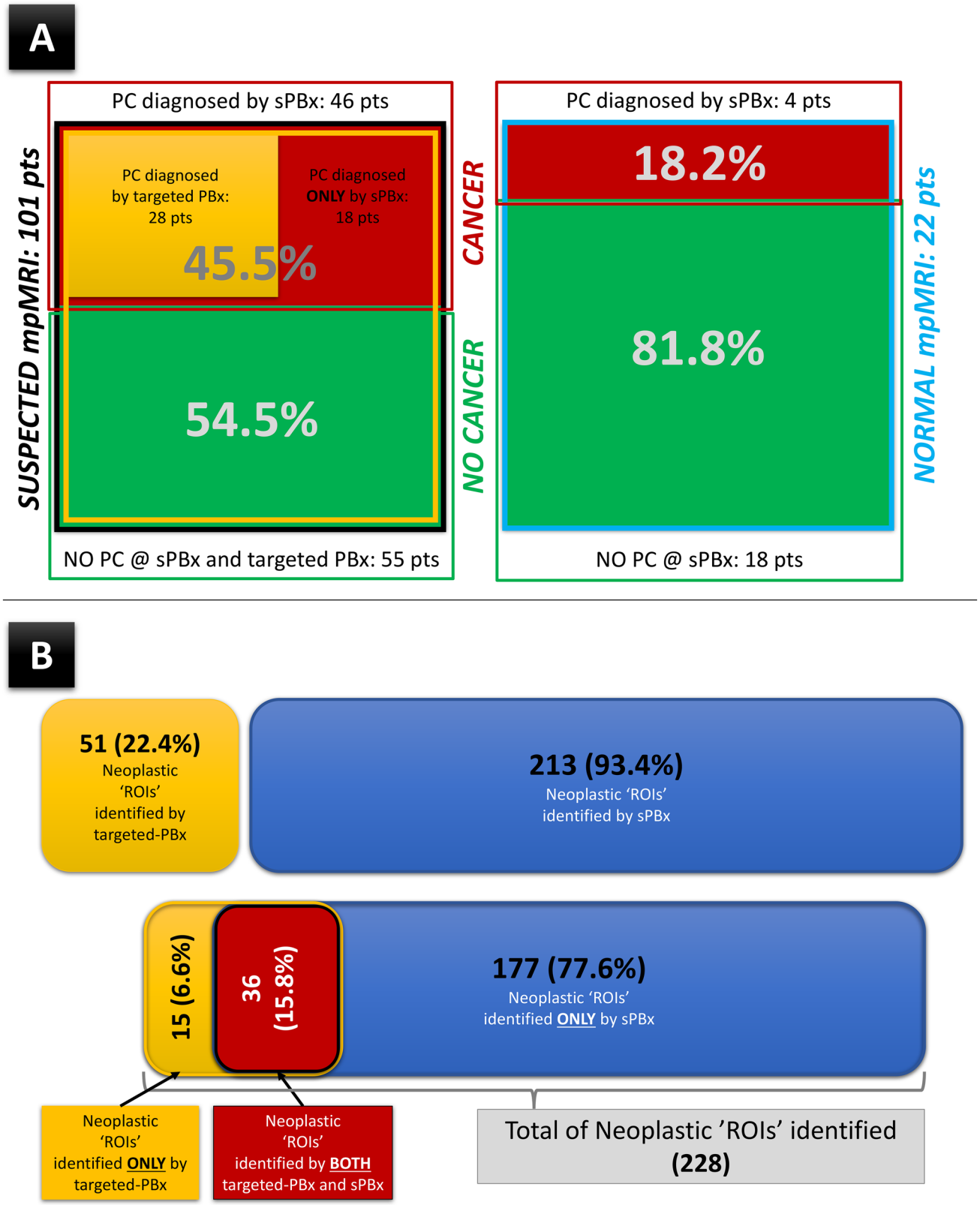

Fig. 2 **a** Subdivision of negative (green) and positive (red) cores in the group of suspected (left box) and negative (right box) mpMRI, according to sPBx and targeted PBx (yellow). **b** Schematic subdivision of single positive 'ROIs' according to the different approach (targeted versus sPBx)

Table 5 Distribution of 'ROIs' according to mpMRI and results of PBx

		Result of PBx		
		Normal	Cancer	
mpMRI	Normal	1556	182	1738
	Suspected	188	42	230
Total of 'ROIs'		1744	224	1968

of targeted biopsies was limited, revealing cancer in only 6.6% of the 'macro-targets' in the total of neoplastic 'ROIs'.

These findings are not easy to compare with other reported studies on this topic, because most of them involved a 12-core scheme for saturation biopsies: our 24-core scheme performs better, but is not the standard PBx approach used in the current practice [17, 21].

Another peculiarity of our work is that, whereas studies reported in the literature often compare only targeted PBx with sPBx (frequently defined by a 12-core PBx), thus demonstrating that the false-negative rate for sPBx is 20–24%, we compared sPBx with sPBx + targeted biopsies [22].

A recent publication by Hansen et al. analysed the role of mpMRI in patients who underwent targeted and 24-core sPBx, confirming the low probability of finding a significant PC when the mpMPRI is negative, but stressing the role of PSA density in selecting patients as candidates for active surveillance [23].

With our novel data remodeling method, we demonstrate that a 24-core sPBx can identify all significant PC, whereas targeted PBxs alone would not be able to identifiy 77.6% of 'ROIs' resulting positive for PC at sPBx.

These findings do not differ greatly from those in the literature, in which the few studies comparing patients undergoing saturation with targeted biopsies confirmed the better diagnostic power of a larger sampling. A recent prospective randomized study by Porpiglia et al. did, in fact, demonstrate that, in patients with suspected PC, prebiopsy mpMRI allows greater numbers of PCs (both significant and not significant) to be detected, compared with 12-core PBx [20]. Obviously, these results cannot be compared with our findings, not only because the above-mentioned authors performed mpMRI in biopsy-naïve patients, but also because they used a 12-core PBx. Nevertheless, our study also seems to confirm the possibility that patients with suspected PC but, with normal mpMRI, could avoid PBx.

This seems to be a very interesting point when evaluating the high costs of both mpMRI and repeated PBx—not only from the economic viewpoint, but also considering the risk of post-PBx complications and the impact of overdiagnosis and overtreatment. Moreover, because the cost-effectiveness of different diagnostic strategies is highly

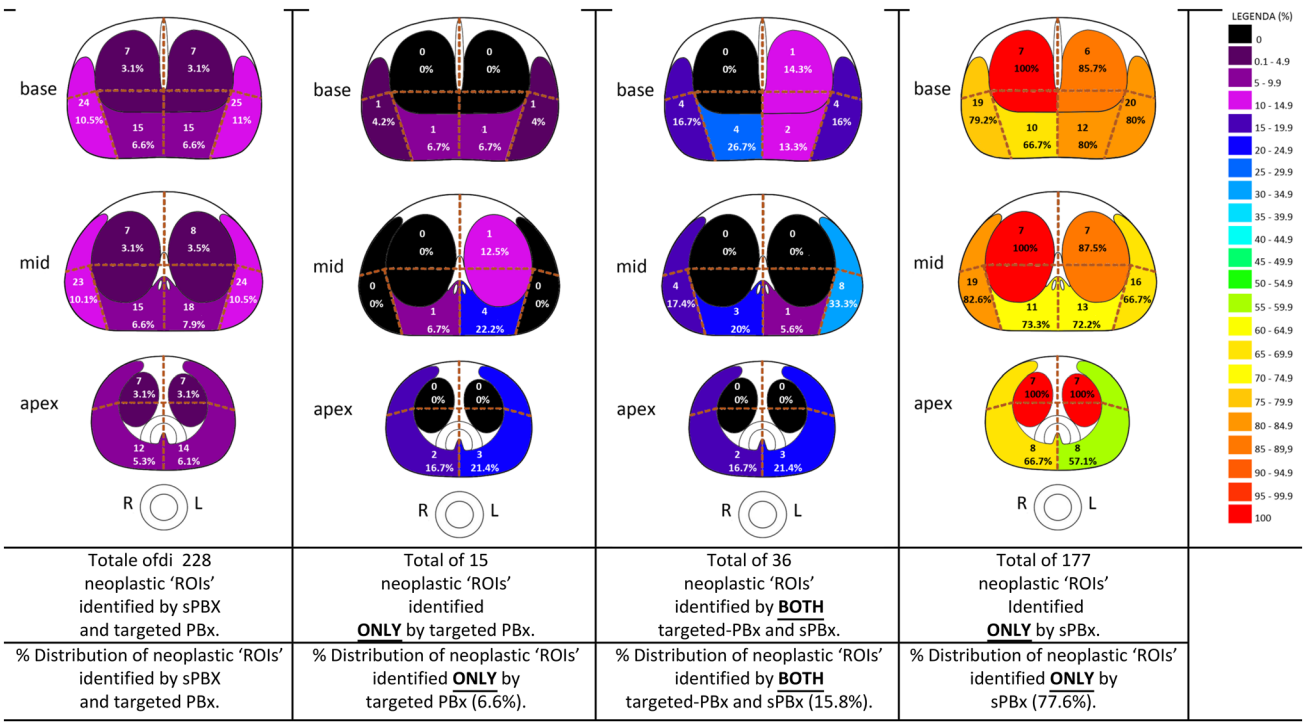

Fig. 3 Spatial distribution of the 228 'ROIs' positive for PC, according to the type of biopsy performed

sensitive to a number of key parameters, further prospective studies are needed to understand if 1.5T mpMRI could play a definite cost-effective role in detecting PC [24].

Our study has several limitations: (a) the sample size is low, which does not allow practical definitive conclusions; (b) we used a 1.5 T mpMRI, instead of a 3.0 T; (c) no external evaluation of the mpMRI images was made to reduce bias due only to internal interpretation, although two skilled radiologists examined the images; (d) PI-RADS version 1 was used to identify suspected areas (the introduction of version 2 was 2 years after the start of our study); (e) a cognitive fusion technique was used instead of a software method, although a recent meta-analysis shows that cognitive fusion does not show inferior results to MRI-fusion techniques for detection of both all PC and significant PC [25]. In general, another limitation is represented by the reproducibility attained by a single-center study, which cannot be compared with results from a multicenter study.

The strengths of this works are: (a) the results are reported according to START recommendations; (b) the results of blind saturation (24-core scheme) and targeted PBx are compared; (c) a novel datum remodeling method is introduced, through interpretation of single 'ROIs' the prostate, allowing a better interpretation of the effect of the 24-core sPBx scheme.

In conclusion, our study confirmed that a normal 1.5T mpMRI in patients with suspected PC and a previous negative PBx may exclude a clinically significant PC, avoiding sPBx, its possible complications, and the risk of both overdiagnosis and overtreatment.

Targeted samplings after mpMRI do not seem to be better at identifying clinically significant PC in comparison with blind 24-core sPBx. Performing only targeted PBx may lead to lack of PC diagnosis in about 50% of patients.

This work is only a pilot study, useful for justifying continued research, to solve limitations and improve targets. Further evaluations with 3T mpMRI are needed to confirm these findings, and for better selection of patients requiring repeated biopsies, also in view of the costs of both mpMRI and sPBx.

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Compliance with ethical standards

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

Statement on the welfare of animals This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Bratan F, Niaf E, Melodelima C et al (2013) Influence of imaging and histological factors on prostate cancer detection and localisation on multiparametric MRI: a prospective study. Eur Radiol 23:2019–2029
2. Mendhiratta N, Rosenkrantz AB, Meng X et al (2015) Magnetic resonance imaging-ultrasound fusion targeted prostate biopsy in a consecutive cohort of men with no previous biopsy: reduction of over detection through improved risk stratification. J Urol 194:1601–1606
3. Hoeks CM, Barentsz JO, Hambrock T et al (2011) Prostate cancer: multiparametric MR imaging for detection, localization, and staging. Radiology 261:46–66
4. Pokorny MR, de Rooij M, Duncan E et al (2014) Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. Eur Urol 66:22–29
5. Fütterer JJ, Briganti A, De Visschere P et al (2015) Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. Eur Urol 68:1045–1053
6. Cornford P, Bellmunt J, Bolla M et al (2017) EAU-ESTRO SIOG Guidelines on prostate cancer. Part II: Treatment of Relapsing, Metastatic, and Castration-Resistant Prostate Cancer. Eur Urol 71:630–642
7. Djavan B, Ravery V, Zlotta A et al (2001) Prospective evaluation of prostate cancer detected on biopsies 1, 2, 3 and 4: when should we stop? J Urol 166:1679–1683
8. Serefoglu EC, Altinova S, Ugras NS et al (2013) How reliable is 12-core prostate biopsy procedure in the detection of prostate cancer? Can Urol Assoc J 7:E293-298. https://doi.org/10.5489/cuaj.11224
9. Panebianco V, Barchetti F, Sciarra A et al (2015) Multiparametric magnetic resonance imaging vs. standard care in men being evaluated for prostate cancer: a randomized study. (17.e1-7.) Urol Oncol 33:7.e1–17.e7
10. Tonttila PP, Lantto J, Pääkkö E et al (2016) Prebiopsy multiparametric magnetic resonance imaging for prostate cancer diagnosis in biopsy-naïve men with suspected prostate cancer based on elevated prostate-specific antigen values: results from a randomized prospective blinded controlled trial. Eur Urol 69:419–425
11. Mozer P, Roupret M, Le Cossec C et al (2015) First round of targeted biopsies with magnetic resonance imaging/ultrasound fusion images compared to conventional ultrasound-guided transrectal biopsies for the diagnosis of localised prostate cancer. BJU Int 115:50–57
12. Delongchamps NB, Peyromaure M, Schull A et al (2013) Prebiopsy magnetic resonance imaging and prostate cancer detection: comparison of random and targeted biopsies. J Urol 189:493–499
13. Siddiqui MM, Rais-Bahrami S, Turkbey B et al (2015) Comparison of MR/ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 313:390–397
14. van Hove A, Savoie PH, Maurin C et al (2014) Comparison of image-guided targeted biopsies versus systematic randomized

biopsies in the detection of prostate cancer: a systematic literature review of well-designed studies. World J Urol 32:847–858
15. Pepe P, Garufi A, Priolo G et al (2013) Prostate cancer detection at repeat biopsy: can pelvic phased-array multiparametric MRI replace saturation biopsy? Anticancer Res 33:1195–1199
16. Radtke JP, Kuru TH, Boxler S et al (2015) Comparative analysis of transperineal template saturation prostate biopsy versus magnetic resonance imaging targeted biopsy with magnetic resonance imaging-ultrasound fusion guidance. J Urol 193:87–94
17. Abdollah F, Novara G, Briganti A et al (2011) Trans-rectal versus trans-perineal saturation rebiopsy of the prostate: is there a difference in cancer detection. Rate? Urology 77:921–925
18. Moore CM, Kasivisvanathan V, Eggener S et al (2013) START Consortium. Standards of reporting for MRI-targeted biopsy studies (START) of the prostate: recommendations from an International Working Group. Eur Urol 64:544–552
19. Ahmed HU, Hu Y, Carter T et al (2011) Characterizing clinically significant prostate cancer using template prostate mapping biopsy. J Urol 186:458–464
20. Porpiglia F, Manfredi M, Mele F et al (2017) Diagnostic pathway with multiparametric magnetic resonance imaging versus standard pathway: results from a randomized prospective study in biopsy-naïve patients with suspected prostate cancer. Eur Urol 72:282–288
21. Scattoni V, Raber M, Capitanio U et al (2011) The optimal rebiopsy prostatic scheme depends on patient clinical characteristics: results of a recursive partitioning analysis based on a 24-core systematic scheme. Eur Urol 60:834–841
22. Lane BR, Zippe CD, Abouassaly R et al (2008) Saturation technique does not decrease cancer detection during followup after initial prostate biopsy. J Urol 179:1746–1750
23. Hansen NL, Barrett T, Koo B et al (2017) The influence of prostate-specific antigen density on positive and negative predictive values of multiparametric magnetic resonance imaging to detect Gleason score 7–10 prostate cancer in a repeat biopsy setting. BJU 119:724–730
24. Mowatt G, Scotland G, Boachie C et al (2013) The diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostateabnormalities for biopsy: a systematic review and economic evaluation. Health Technol Assess 17:vii–xix. https://doi.org/10.3310/hta17200
25. Schoots IG, Roobol MJ, Nieboer D et al (2015) Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol 68:438–450