ORIGINAL PAPER

Accuracy of 3 Tesla pelvic phased-array multiparametric MRI in diagnosing prostate cancer at repeat biopsy

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Summary
Introduction. Multiparametric pelvic magnetic resonance imaging (mpMRI) accuracy in prostate cancer (PCa) diagnosis was evaluated. Materials and Methods. From June 2011 to December 2013, 168 patients (median 65 years) with negative digital rectal examination underwent repeat transperineal saturation biopsy (SPBx; median 28 cores) for persistently high or increasing PSA values, PSA >10 ng/ml or PSA values between 4.1-10 o r 2.6-4 ng/ml with free/total PSA < 25% and < 20%, respectively. All patients underwent mpMRI using a 3.0 Tesla scanner equipped with surface 16 channels phased-array coil and lesions suspicious for PCa were submitted to additional targeted biopsies.
Results. A T1c PCa was found in 66 (39%) cases; SPBx and mpMRI-suspicious targeted biopsy diagnosed 60 (91%) and 52 (78.8%) cancers missing 6 (all of the anterior zone) and 14 cancers (12 and 2 of the lateral margins and anterior zone), respectively; in detail, mpMRI missed 12 (18.1%) PCa charaterized by microfocal (1 positive core with greatest percentage of cancer and Gleason score equal to 5% and 6, respectively) disease at risk for insignificant cancer. The diameter of the suspicious mpMRI lesion was directly correlated to the diagnosis of PCa with poor Gleason score (p < 0.05); detection rate of cancer for each suspicious mpMRI core was 35.3%. Diagnostic accuracy, sensitivity, specificity, positive and negative predictive value of mpMRI in diagnosing PCa was 75.7%, 82.5%, 71.8%, 78.9%, 87.9%, respectively.
Conclusion. Multiparametric pMRI improved SPBx accuracy in diagnosing significant anterior PCa; the diameter of mpMRI suspicious lesion resulted significantly predictive of aggressive cancers.

KEY WORDS: *Prostate cancer; Multiparametric MRI; Prostate targeted biopsy; Pelvic phased-array MRI..*

Submitted 12 January 2014; Accepted 31 October 2014

INTRODUCTION

Although extended (12-18 cores) and saturation biopsy (SPBx; > 20 cores) have been suggested (1, 2) to improve detection rate for *prostate cancer* (PCa), repeat prostate biopsy, still today, constitutes about 30% of the entire procedure with an estimated diagnosis of cancer equal to 20-40%. Therefore, the ideal biopsy scheme should perform targeted biopsies to diagnose only significant PCa, reducing the number of unnecessary procedures and false negative rate. In this light, *multiparametric magnetic resonance imaging* (mMRI) using pelvic phased-array coil (mpMRI) or endorectal coil (meMRI) has been proposed as a more accurate alternative in comparison with *transrectal ultrasound* (TRUS) to increase the detection rate for PCa, especially in case of repeat biopsy (3-16).
The accuracy of mpMRI in diagnosing PCa in men submitted to repeat biopsy was prospectively evaluated.
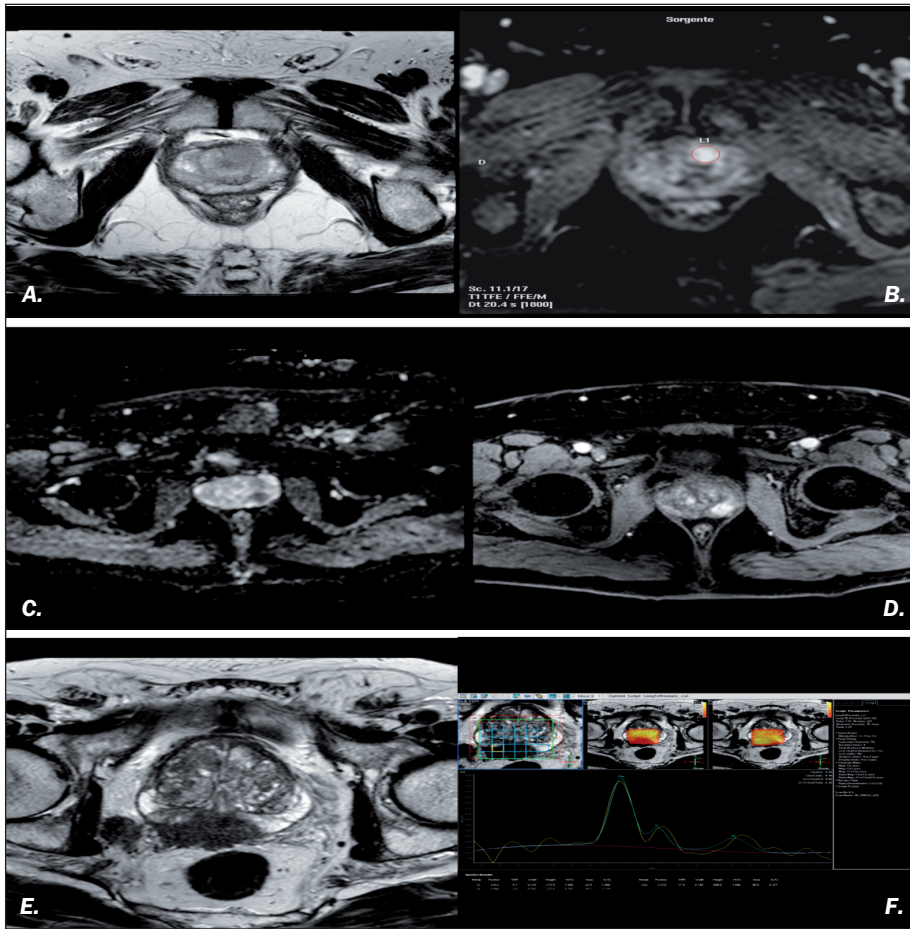
MATERIALS AND METHODS

From June 2011 to December 2013, 168 patients, all of Caucasian origin and between the ages of 49 and 75 years (median 65 years), with negative digital rectal examination underwent SPBx (median 28, range: 6-35 cores) for persistent suspicion of PCa. The 168 patients enrolled in a prospective, monocentric and multi-departmental study were selected from a case-finding protocol for PCa detection (17) and had one single previous negative extended transperineal biopsy (18 cores) performed at least six months before (range: 6-20 months); the indications for repeat SPBx were: persistently high or increasing PSA value, PSA > 10 ng/ml or PSA values between 4.1-10 or 2.6-4 ng/ml with free/total PSA < 25% and < 20%, respectively.
All patients, provided a written informed consent, underwent mpMRI 3-10 days before undergoing the SPBx. All examinations were performed using a 3.0 Tesla scanner, (*ACHIEVA 3T; Philips Healthcare Best, the Netherlands*) equipped with surface 16 channels phased-array coil placed around the pelvic area with the patient in supine position; multiplanar turbo spin-echo *T2-weighted* (T2W), axial *diffusion weighted imaging* (DWI), axial *dynamic contrast enhanced* (DCE) and spectroscopy were performed for each patient (Figure 1). The criteria (14) for a positive lesion on T2W (Figure 1) were the presence of a circumscribed, low signal intensity lesion (hypointense); a posi-

Figure 1.
3 Tesla pelvic phased-array multiparametric MRI patterns in patients with prostate cancer.

- *T2-weighted (a) and DCE (b) MRI of an anterior nodular area.*
- *T2-weighted (c) and DCE (d) MRI of a peripheral nodular area (1 cm).*
- *Large (e) peripheral T2-weighted hypointense area with positive spectroscopy (f) that exceeded the surrounding tissue.*

cores) targeted TRUS guided-biopsies in addition to standard SPBx were performed. A probability (p) level of less than 0.05 was considered statistically significant.

RESULTS

All patients had negative TRUS; median PSA was 10.4 ng/ml (range: 3.7-45 ng/ml): 69 (41%) had PSA > 10 ng/ml, 92 (54.8%) between 4-10 ng/ml and 7 (4.2%) between 2.6-4 ng/ml, respectively.
Multiparametric pMRI was positive in 94 (56%) out of 168 patients (Table 1); in the patients submitted to mpMRI-suspicious targeted biopsy, 329 cores were performed; in 84 (89.3%) out of 94 the lesions were included in the SPBx scheme, on the contrary, in 10 (10.7%) cases, the suspicious areas were localized in the anterior zone (Figure 1a, 1b) near the bladder neck. None had significant complications from SPBx that needed hospital admission; moreover, the mpMRI procedure was well tolerated and successfully performed in all cases.
A T1c PCa was found in 66 (39%) out of 168 patients and normal parenchyma in the remaining 102 (61%). Clinical parameters, biopsy quantitative histology, Gleason score (GS) and mpMRI findings in the presence of PCa and normal parenchyma are listed in Table 1. SPBx scheme and mpMRI-suspicious targeted biopsy diagnosed 60 (91%) and 52 (78.8%) out of 66 PCa, respectively; in detail, SPBx and mpMRI missed 6 (all of the anterior zone) and 14 cancers (12 and 2 of the lateral margins and anterior zone) equal to 9% and 21.2% of the cases, respectively. In the presence and absence of PCa the nodular suspicious mpMRI lesions (Figure 1) had a median diameter equal to 12 mm (range = 5-32 mm) vs 6 mm (range = 5-13 mm), respectively; a cut-off of 10 mm resulted predictive of cancer in 22 out 27 patients (81.5% of the cases) with a false positive rate of 9.6%. In detail, mpMRI missed 12 (18.1%) PCa charaterized by microfocal biopsy disease (1 positive core with a greatest percentage of cancer and Gleason score equal to 5% and 6, respectively) (19) at risk for insignificant PCa (cancer volume < 0.5 ml and GS < 6) (20). Median nodular diameter on mpMRI was correlated to GS (GS 6 = 9 mm; GS 7 = 16 mm; GS 8 = 20 mm) showing a significantly difference between GS 6 vs GS 8 (p < 0.05). The detection rate of cancer for each core performing SPBx vs mpMRI targeted biopsy was 9.5% vs

tive lesion on DCE (Figure 1) was characterized by the presence of foci showing early and intense enhancement and rapid washout after power injection (3.0 ml/s) of gadobutrol 0.1 ml/kg (*Gadovist®; Bayer Schering Pharma, Germany*) followed by a 15 ml saline flush. A positive lesion on spectroscopy (Figure 1) was any area where the choline to citrato ratio was 3 or more standard deviations above the mean healthy value. Two radiologists (AF, GP) blinded to pre-imaging clinical parameters evaluated the MRI data separately and independently.
SPBx was performed transperineally using a tru-cut 18 gauge needle (*Bard; Covington, GA USA*) and a GE Logiq 500 PRO ecograph (*General Electric; Milwaukee, WI USA*) supplied with a biplanar transrectal probe (5-6.5 MHz) under sedation and antibiotic prophylaxis (18). To ensure that histopatological findings matched with MRI images the assessment of radiological images and SPBx scheme were performed dividing the prostate into 14 regions: apex, middle zone and base of posterior zone for each lobe beginning parasagittally to reach the outer edges of the gland (six regions for each lobe), anterior and transitional zone (15). In the presence of mpMRI lesions suspicious for cancer, 3-4 (median: median 3.5

Table 1.

Patients' characteristics.

Overall No of patients: 168	PCa 66 (39%)	GS 6 44	GS 7 18	GS 8 4	Normal parenchyma 102 (61%)
Median PSA ng/ml (range: 3.7-45)	10.6	12	10	16	10.3
Positive mpMRI	52 (78.8%)	30 (68.2%)	18 (100%)	4 (100%)	40 (39.2%)
Positive T2W (hypointense area)	52 (78.8%)	23 (52.2%)	18 (100%)	4 (100%)	40 (39.2%)
Positive DWI	51 (77.3%)	25 (56.8%)	18 (100%)	4 (100%)	37 (36.2%)
Positive DCE	52 (78.8%)	25 (56.8%)	18 (100%)	4 (100%)	36 (35.3%)
Positive spectroscopy	29 (43.4%)	2 (12.5%)	14 (77.8%)	4 (100%)	36 (35.3%)
Negative mpMRI	14 (21.2%)	14 (31.8%)	0	0	62 (60.8%)
GPC	40% (2-100%)	15% (1-60%)	85% (50-100%)	100%	- -
No. (%) of positive cores: 　SPBx 　mpMRI-suspicious biopsy	 7.5 (26.7%) 2.5 (62.6%)	 2.8 (9.7%) 1.3 (32.5%)	 12 (42.8%) 3 (75%)	 16 (57.1% 3.2 (80%)	 - -
Median diameter (mm) of mpMRI suspicious area < 10 mm > 10 mm	12 (5-25) 30 22	9 (5-16) 23 7	16 (9-32) 7 11	20 (18-25) 0 4	6 (5-13) 35 5

PSA: prostate specific antigen; PCa: prostate cancer; Gleason Score: GS; GPC: greatest percentage of cancer; SPBx: saturation prostate biopsy;
T2W: T2-weighted; DWI: diffusion-weighted imaging; DCE: dynamic contrast-enhanced.

35.3%, respectively (p < 0.05). Diagnostic accuracy, sensitivity, specificity, positive and negative predictive value of multiparametric mpMRI in diagnosing was 75.7%, 82.5%, 71.8%, 78.9%, 87.9%, respectively.

DISCUSSION

Although TRUS imaging was enriched in recent years by the introduction of three-dimensional, computerized images and contrast media, which allow better characterization of intraparenchymal microvasculature (21), ultrasound accuracy is poor in performing targeted-biopsy (22, 23); therefore, SPBx still today remains the gold standard (2, 18) in case of repeat prostate biopsy. On the other hand, transrectal prostate biopsy, recently, has been associated with an increased risk of complications secondary to urinary tract infection and sepsis (1% of the cases), with the necessity for hospital admission in 2% of the cases (24); conversely, transperineal prostate biopsy demonstrated a better accuracy in comparison with transrectal approach in the diagnosis of anterior zone PCa (15, 25), resetting the risk of sepsis (26, 27).

In the last years, mMRI has gained growing importance in PCa diagnosis and staging using mpMRI or meMRI (3-16); recently, 3 Tesla MRI has been suggested in the re-evaluation of patients enrolled in active surveillance protocols (9), and is highly representative of the true GS (12, 14, 15) and predictive of significant PCa (11, 12, 15). The estimated sensitivity and specificity for PCa detection by MRI varies between 57% and 100% vs 44% and 96%, respectively (3); therefore, there is increasing interest in using MRI, especially in men with prior negative prostate biopsy and persistent suspicion of PCa. Multiparametric pMRI and eMRI have been introduced in clinical practice to detect suspicious areas which could be submitted to real-time MRI-guidance targeted-biopsy or translated into real-time MRI/TRUS imaging fusion to perform targeted biopsy (4, 7, 11, 16). *Pinto et al.* (4)

showed a greater detection rate of cancer for each core using MRI imaging/ultrasound fusion-guided biopsy in comparison with standard 12-core transrectal biopsy (20.6% vs 11.7%, respectively). *Franiel et al.* (5) and *Hambrock et al.* (6) in patients with previous negative biopsy submitted to MRI-guided biopsy demonstrated a detection rate for PCa of 39% and 59%, respectively; *Kuru et al.* (7), recently, evaluated the *Prostate Imaging Reporting and Data System* (PIRADS) in mpMRI based on single-core histology suggesting that PIRADS can be used as a decision-support system for targeting of suspicious lesions. Although eMRI had the best sensitivity and specificity in diagnosing and staging PCa, recently 3 Tesla pMRI demonstrated good accuracy in detecting areas suspicious for PCa and increasing diagnosis of cancer localized in the anterior zone of the gland (5, 15, 25). The use of mpMRI provides, in daily practice, more advantages in comparison with meMRI; in fact, its use is widespread in many general hospitals, it is easy to perform and it does not generate discomfort to the patient. In addition, whole-body MRI has been suggested as a one-step procedure for staging men with high-grade PCa (28).

In our series, mpMRI detected 52 out 66 PCa; in detail, mpMRI in comparison with SPBx diagnosed 4 significant cancer of the anterior zone missing 12 cancers characterized by microfocal biopsy histological disease (18) at risk for insignificant PCa (22). In addition, a correlation between mpMRI suspicious lesion diameter vs PCa diagnosis and tumour grade was found.

Some limitations and considerations of the present study deserve mention. Firstly, we do not know the true diagnostic accuracy of mpMRI in PCa diagnosis because the detection rate for cancer was compared with SPBx results. Secondly, we do not know if the false-positive rate (23.8% of the cases) of mpMRI was secondary to false-negative SPBx results or was biased because an MRI imaging/ultrasound fusion-guided biopsy, theoretically more accurate, was not performed. In conclusion, in case of repeat biop-

sy, mpMRI targeted biopsy improves diagnosis of anterior zone PCa missing cancers at risk for clinically insignificant disease; moreover, suspicious mpMRI lesions > 10 mm are highly predictive of aggressive PCa.

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