Send Orders for Reprints to reprints@benthamscience.net

The Open Prostate Cancer Journal, **2014,** *7,* **1-6**

Open Access

A Comparison of Different Imaging Techniques for Localisation of Cancers in the Prostate

Sam Ladjevardi[1,*], Jan Weis[2], Jens Sörensen[2], Anna Tolf [3], Michael Häggman[1], Catrin von Below[3] and Håkan Jorulf[3]

[1]*Department of Urology, University Hospital, 751 85 Uppsala, Sweden*

[2]*Department of Radiology, Oncology and Radiation Science, University Hospital, 751 85 Uppsala, Sweden*

[3]*Department of Genetics and Pathology, University Hospital, 751 85 Uppsala, Sweden*

Abstract: The diagnostic accuracy of standard transrectal ultrasound-guided (TRUL) biopsy is limited due to the finite number of cores that can be obtained. It has been shown that the technique is not sufficiently reliable in defining the location and extent of prostatic cancer. The main aim of this study was to investigate the effectiveness of magnetic resonance imaging (MRI), and positron emission tomography (PET/CT) imaging techniques in pinpointing potential tumour lesions prior to prostate biopsy.

Material and methods. The study cohort consisted of 45 men with a raised prostate specific-antigen (PSA) level and/or suspected prostate cancer (PCa) at digital rectal examinations (DRE). Of the 45 patients, 23 had PCa detected with core needle biopsy (CNB). All had ^{11}C acetate PET/CT imaging. Ten of those 23 patients underwent radical prostatectomy (RP), of those ten patients, eight patients had MR spectroscopic imaging (MRSI) with 3 T and six had diffusion weighted imaging (DWI) with apparent diffusion coefficient calculation (MRI DWI ADC). CNB, PET/CT, 2D MRSI and ADC map results were compared with postoperative specimen histopathology.

Results. The sensitivity of CNB, PET/CT, MRSI and DWI ADC were 0.53, 0.55, 0.79 and 0.95, whereas the specificity of was 0.88, 0.87, 0.46 and 0.73, respectively.

Conclusion. MRI improves the PCa detection by defining the areas of interest for targeted CNB of the prostate and can reduce the number of biopsies required.

Keywords: Prostate cancer, Imaging technique, MRI, PET/CT.

INTRODUCTION

With the advent of prostate-specific antigen (PSA) screening, most PCa are now diagnosed at an early stage [1, 2]. The 10-year relative survival of men with well-differentiated PCa has been shown to be 100% regardless treatment [3]. The 5-year relative survival rate for all stages of PCa is 98%, which indicates that prostate tumours develop slowly and survival is hardly affected [4, 5].

In many patients PCa is multifocal. Thus, an imaging technique that non-invasively verifies the presence and extent of PCa may help in treatment strategy decisions in men with PCa. Such techniques include MRI, MRSI, and PET/CT imaging. These techniques could play an important role in the detection, localisation, and staging of PCa and may help guide management strategy [6].

*Address correspondence to this author at the Department of Urology, University Hospital, 751 85 Uppsala, Sweden; Tel: +46 18-611 00 00; Fax: +46 18-611 50 56; E-mail: sam.ladjevardi@surgsci.uu.se

At present the use of MRI in tumour detection is reserved for patients with elevated PSA levels where biopsy results are negative. PET/CT with ^{11}C acetate and other radiopharmaceuticals is mainly used for staging in primary disease in patients with high-grade tumours to evaluate the presence of metastatic disease or to localize the disease location in biochemical relapse after RP prior to radiotherapy (RT).

The main aim of this pilot study was to investigate the effectiveness of MRI, and PET/CT imaging techniques for targeting suspected tumour growth for guiding core biopsy.

MATERIAL AND METHODS

Forty-five men with an elevated PSA level and/or suspect PCa at DRE initially underwent TRUL- CNB (10 cores) from the determined areas, 5 on each side (Fig. **1**). The TRUL-CNB was performed by the same investigator. CNB confirmed PCa in 24 men. The Gleason Scores (GS) were between 5 and 10. Ten of those 24 patients with PCa

1876-8229/14

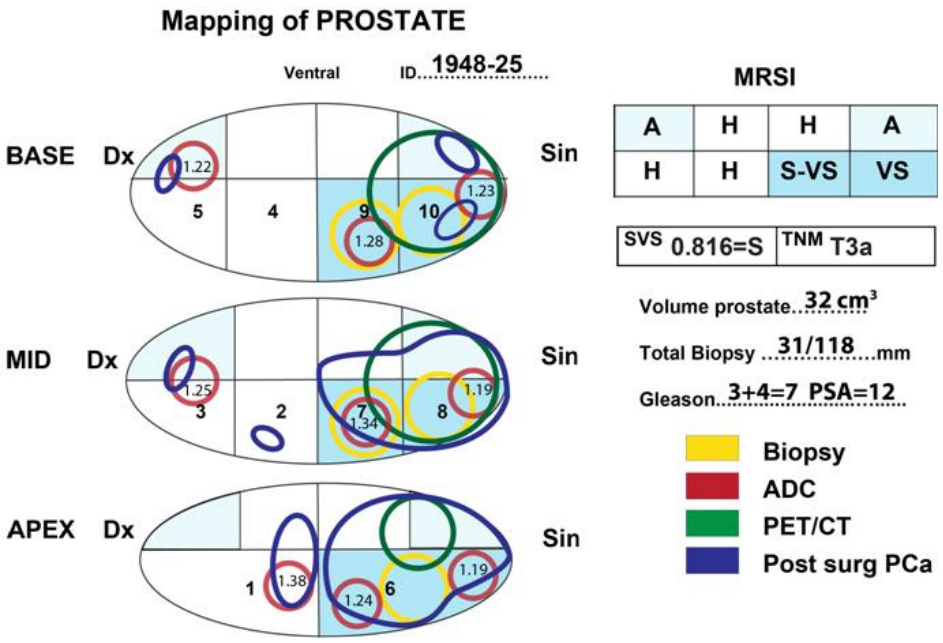

Fig. (1). Example of schematic based on mapping 1- 10 biopsy areas. Positive results from CNB (yellow), PET/CT ^{11}C acetate (green) SUV=7. MRI –DWI ADC maps (red areas) 1.19 – 1.38 x 10 $^{-3}$ mm²/s; 2D MRSI: H= Healthy; A = Ambiguous, ≥1-2 SD deviation from normal; S = Suspicious ≥ 2-3 SD; VS = Very Suspicious ≥3SD; S=single voxel MRSI (whole prostate volume). Dark blue = confirmed PCa at postoperative histology. Gleason 3+4, focal 3+2. TNM postoperative classification: small extra-capsular PCa Mid- Zone ventrolateral left side was not detected by imaging.

underwent RP and were included in the study. Two patients were treated with RT, and 11 patients were included into active surveillance (AS) program.

Ten patients who underwent RP with postoperative histology with 4 mm serial slice cuts for reference standard were compared with CNB, PETT/CT and multiparametric MRI (mpMRI) results (Fig. **1**).

The prostate was divided into 10 regions of interest (ROI) (Fig. **1**) according to a standardised CNB scheme: apex, middle zone (medial and lateral), and base (medial and lateral). Each region was quantitatively characterised by GS, ADC values, (Cho+PA+Cr)/Cit spectral intensity ratio, and by ^{11}C acetate uptake. The region was classified as PCa if GS was 6 or over and for ADC value was at least two standard deviations (SD) from the average healthy ratio for the periphery zon, and (Cho+PA+Cr)/Cit spectral to intensity ratio was from 2 SD over the average healthy ratio. For PET/CT examination, areas with a mean standard uptake value (SUV) 4 or over were classified as PCa.

One hundred estimates were determined for CNB and PET/CT imaging by the data from 10 patients who underwent RP. Due to initially incomplete technique, only 8 patients were included with 80 estimates from MRSI and 6 patients with 60 estimates for DWI with ADC maps (Table **2**).

All MRI and PET/CT evaluations were blinded from the results of both pre- and postoperative histology results. Informed consent was obtained from all patients. The Local Ethics Committee approved the study protocol (EPN 2009/191) .Diagnostic and treatment details are shown in Tables **1** and **2**.

MRI

All measurements were performed with a 3 Tesla scanner (Achieva, Philips Medical Systems, Best, Netherlands) using a surface (cardiac) receiver coil. MRI was performed at 4 to 7 weeks after CNB. High-resolution axial, coronal and sagittal T2-weighted turbo spin-echo images were used for an anatomical overview of the prostate and surrounding tissues (effective TE 100 ms, TR 3028 ms, echo train length 21, field of view (FOV) 160 mm, acquisition pixel size 0.8x1 mm, slice thickness 3 mm, bandwidth/pixel 218 Hz, 3 averages). Maps of apparent diffusion coefficient (ADC) were acquired with five b values (0, 100, 200, 400, 500

Table 1. Clinical Parameters, CNB and PCa Volumes, mean and range. 10 Patients Included in the Study

Patient age (N = 10) 65 (50-75)	PSA ng/ml 9 (3.8 -13)
Gleason Score 6-8	Stage T2A-T2C
CNB volume mm³ 85 (72 -107)	No. CNB out of 10 3.8 (2 – 5) positive for PCa,
CNB PCa volume mm³ 13 (1.3-34)	CNB Ca/CNB 19 (1.1 – 25.3) volume %
Prostate volume from 32.2 (24 – 46.9) postop. sections, cm³	PCa volume from 4.3 (1.2 – 8.4) postop. sections, % of P 13.4 cm³ and % of P (3.6 – 23.5)

Table 2. Imaging Techniques and Initial CNB in Relation to Postoperative Histology of Specimen. Ten Parameters from each Examination: 60 Parameters for ADC Maps; 80 for MRSI; 100 for CNB and PET/CT Respectively

CNB, PET/CT, MRSI, ADC maps **Correlated to postoperative histology**				
	CNB	**PET/CT**	**MRSI**	**DWI ADC**
Patients (N)	10	10	8	6
Parameters (N)	100	100	80	60
Sensitivity	0.53	0.55	0.79	0.95
Specificity	0.88	0.87	0.46	0.73
Accuracy	0.64	0.67	0.69	0.87

s/mm^2) using a fat suppressed single-shot spin-echo echo-planar imaging sequence (FOV 200 mm, acquisition pixel size 1.8x1.8 mm, slice thickness 3 mm**,** effective TE 55 ms, TR 1650 ms, EPI factor 121, 6 averages, measurement time 5 min 20 sec). 2D MRSI was performed with the following parameters: PRESS, TR/TE 1400/140 ms, spectral band-width 2000 Hz, 1024 points, spectral matrix 16×16, nominal voxel size 10×10×20 mm^3, 3 acquisitions. The net measurement time was 14 min 7 sec. Spectra were considered ambiguous for cancer if the spectral intensity ratio of choline + polyamines + creatine to citrate (Cho+PA+Cr)/Cit) was > 1, but ≤ 2 standard deviations (SD) above the mean normal value. Spectra were designated possible cancer with a (Cho+PA+Cr)/Cit > 2, but ≤ 3 SD above the mean healthy ratio, and probable cancer if (Cho+PA+Cr)/Cit was > 3 SD above the average normal value [23].

PET/CT

Patients with verified PCa assigned for prostatectomy (N=10) and 10 of 13 patients with low-grade PCa scheduled for active surveillance were examined with Positron Emission Tomography and CT, (PET/CT ^{11}C acetate). Low dose (40mA) CT imaging was followed by dynamic PET imaging over the pelvic region.^{11}C-acetate was injected as a bolus intravenously and PET emission aquisition started simultaneously. PET image data from 5 to 10 minutes after injection were combined to form static images. The images were visually evaluated in fused mode with PET superimposed on CT. Hot spots within the prostatic gland were reported as potentially representing tumour growth.

Statistics

The ten parameters related to the schema for biopsy regions (Fig. **1**) were evaluated for each patient; positive for PCa (=1) and negative (=0) related to tumour localization from RP specimens.

Statistical analysis for sensitivity, specificity, and accuracy, (false positive and negative rates, positive and negative predictive values) were made for correlation of findings at CNB, PET/CT, MRSI, and MRI Diffusion weighted images (DWI) ADC map quantification with the postoperative histology, related to the10 prostate zones. Diagnostic parameters were calculated on a per-lesion and per-patient basis.

RESULTS

Clinical parameters, age, PSA level, CNB and PCa volumes are shown in Table **1**.

Cancer detection by CNB and by imaging (MRSI, MRI DWI ADC and PET/CT) of the ten prostate zones showed clear conformity between ADC maps and postoperative findings (Table **2**) with high accuracy (87%) and sensitivity (95%). Results of PET/CT alone (10 patients) may not provide confident information for targeting biopsy because of low resolution. Specificity of the method, however, is high (87%). ^{11}C Acetate signals from cancer with a high GS were generally high, while some tumours with a low GS were close to background and not readily visualised. Small extra-capsular cancer 1.5 to 2 mm in one of the patients could not be demonstrated by any of the imaging techniques (Fig. **1**).

The total CNB volume is only a small fraction of the prostate as calculated from this small patient cohort, mean about 1/400 considering shrinking of the prostate about 4 % after formalin fixation. The mean PCa cancer volume from CNB was 13 mm^3 corresponding to about 1/2800 part of the prostate volume, which furthermore indicate the need for targeted biopsy procedure.

The mean PCa volume in the RP group calculated from consecutive slices of the prostate (Table **2**), was 4,3 cm^3 (13.4%). The numbers of cores positive for PCa in the RP group (Table **2**) were 2 to 5 and GS 5 to 8. PCa volume in CNB was 1.3 – 34 mm^3; mean 13.2 mm^3 corresponding to mean 1/2800 part of the prostate volume, as calculated from the postoperative specimen. The number of PCa positive CNBs in the AS group was 1-2. The cancer volume in the CNB in this group was significantly lower than in the RP group: 0.3 – 13.0 mm^3, mean 2.7 mm^3, corresponding to 1/21000 of the total prostate volume. Gleason Scores for the AS group were 5 to 7. Two patients treated by radiotherapy had GS 7 and 10 (Table **2**). The cancer volume was higher in this group compared to RP and AS, 46.4 mm^3, range 4.3 – 89 mm.

DISCUSSION

The results of our prospective study shows that a combination of MRI DWI ADC quantification and MR spectroscopy may provide an improved imaging of the prostate for targeted biopsy. PET/CT alone may not provide confident information for targeting biopsy because of low resolution. However, the specificity of the method is high (87%).

Transrectal ultrasound-guided core needle biopsy is the method most commonly used in the histopathological diagnosis of PCa.

MR imaging and MR spectroscopy are not used as first-line investigations in PCa, but may be useful for targeting biopsy probes, especially in patients with PSA levels indicative of cancer but with negative biopsy results.

PCa is histologically a multifocal disease, and biopsy has limitations in identifying all cancer sites and grades. With a PSA cut-off level of 4.1 ng/mL, 82% of cancers in men younger than 60 years and 65% of cancers in men older than 60 years could be missed [7]. Ultrasound-guided transrectal biopsy is considered the method of choice for PCa detection and characterisation. However, when biopsy results were compared with sextant tumour localisation in the radical prostatectomy specimen, the positive predictive value of biopsy was 83.3% and the negative predictive value 36.4% [8]. In other studies, up to 30% of cancers were missed at sextant biopsy [9].

Clinical T staging is largely dependent on imaging findings. Compared to CT, US, and DRE, MR imaging has a higher accuracy in the assessment of uni- and bilobar disease (stage T2), extra-capsular extension and seminal vesicle invasion (stage T3), and invasion of adjacent structures (stage T4). The literature, however, shows a wide range (50%–92%) in the accuracy of local staging with MR imaging [10].

Despite its high specificity in the identification of organ-confined disease and extra-capsular extension, owing to lower sensitivity and substantial inter-observer variability, the routine use of MR imaging in the local staging of PCa remains controversial. Increased experience in interpretation and a better understanding of morphologic criteria used to diagnose extra-prostatic disease are key factors if we are to further improve the role and accuracy of MR imaging in the staging of PCa. In one patient, minor extra-capsular extension was confirmed at postoperative histology of the specimen but was not detected by either method. PET/CT using ^{11}C acetate has mainly been used for localisation of PCa recurrence following PSA relapse after previous radical prostatectomy [11]. ^{11}C -acetate traces endogenous acetate and is incorporated into anabolic processes such as lipid membrane and protein formation associated with proliferative activity [12]. In this study, there was a high variability in tumour uptake. A number of prostate tumours were not distinctly visualised due to low uptake, while some had intense uptake. It is probable that the uptake pattern noted in this study is a reflection of the rate of cancer growth. This implies that PET/CT can be used to detect intra-prostatic cancer growth when there is high metabolic activity. More indolent tumours are not identified. Fusion of sequentially obtained PET/CT and contrast enhanced 1.5 Tesla MRI data for the location of prostate cancer related to sextant biopsy samples as method of reference has been reported [19]. However, resolution with this technique is lower compared to MRI at 3 Tesla.

The main goal of cancer care is to minimise risk and at the same time maximise the effectiveness of treatment. In order to avoid treatment-related risks and to achieve effective cancer control in men with PCa, location and extent of spread should be identified. The most reliable basis for treatment decision of men with prostate cancer is the combination of PSA level, GS and T stage [13]. Treatment decisions should also take into consideration the patient's age, co-morbidity and personal preferences.

The inclusion of MRI and/or MRSI findings in clinical nomograms may help to improve the prediction of cancer extent, thereby improving patient selection for therapy. Other advantages of improved cancer staging include a better stratification of patients in clinical trials, and the possibility of monitoring the progress of patients who select active surveillance. MRSI and MRI (diffusion weighted images and ADC maps) have shown great promise in distinguishing between indolent and aggressive disease [14-19]. For MRSI imaging and DW ADC numerical data, we used our own reference values when deviated 2 SD or over from our own developed normal values from healthy individuals [18]. Thus medium or low-grade cancers were not included in our calculations.

Though this study included only a small number of patients, MRI at 3Tesla using a surface coil seems to be a promising technique for indicating areas of interest for targeted biopsy of the prostate in cancer diagnosis, compared to standard 10 CNB. By using surface coil, a reasonable spatial resolution was achieved by T2-weighted images, DWI 1.8 x 1.8 x 3 mm for ADC maps, and 1 x 1 x 2 cm for 2D MRSI. It is evident that ADC anatomic mapping with numerical data has high potential for identification of aggressive tumour allowing for targeted biopsy and reducing the number of biopsies. It should be noted that endo-rectal receiver coil improves significantly the signal-to-noise ratio and thereby sensitivity of MR examinations [20]. This coil, however, was not available at our department at the time of this study.

The local cost for combined 2D MRSI, MRI diffusion weighted imaging and ADC maps is SEK 7000, (USD 1000). This should be compared with the cost for repeated biopsies needed in case of missed PCa at routine CNB against the ability to hit the most active cancer area if multifocal. The advantages of reducing the number of biopsies should be considered as well as the possibility to sustain for repeated biopsies in case no PCa is demonstrated at MRI investigation.

Standardized system for interpretation and characterization of PCa has been recommended [21] as it is used e.g for breast cancer diagnosis for the benefit of both research and clinical work. Clinically significant disease was defined as Gleason $\geq$4+3 and/or lesions $\geq$ 0.5 cc in volume. Recommendations include the use of at least 16 ROIs for minimal clinical practice, and 27 ROIs for optimal research

practice. European Society of Uro-Radiology (ESUR) has also developed guidelines for diagnostic mpMRI.

Reducing the number of ultrasound-guided CNB specimens is made possible by restricting biopsy to regions most likely to contain PCa with the highest GS (cancer area). To achieve this, a combination of information from MRSI and DWI ADC quantification together with ultrasound has been suggested [19, 22, 23].

Franiel *et al*. [26] demonstrated with targeted ultrasound-guided biopsy after multiparametric 1.5-T ^{1}H-MRTS spectroscopy and apparent diffusion-weighted (DW) and contrast-enhanced MR imaging, increased cancer-positive rates in 21 of 54 patients who had a median of two prior negative TRUS-guided biopsies. T2W imaging + MRSI detection rate was 81%; MRSI DWI ADC quantification detection rate 91%, and a negative result was found in15 % of cases.

A biopsy simulation study [24] demonstrated poor performance of standard TRUS biopsy for detecting clinically important cancer and only marginal improvement by additional cores, and the template prostate mapping (TPM) was the optimal technique.

The detection rate for mpMRI for transperineal fused MRI/US targeted biopsy using a cognitive registration technique for clinically significant prostate cancer has been reported [25]. MRI targeted biopsy and template guided CNB showed in 103 (57%), and in 113 of the 182 men (62%) and clinically insignificant cancer in 17 (9.3%) and 31 (17 %) respectively. They found multiparametric MRI (mpMRI) had encouraging rates of detection of clinically significant cancer, while also decreasing the detection rate of clinically insignificant cancer. This was achieved with fewer biopsy cores than for systematic template guided biopsy

In literature search by Moore CM *et al.* [26], fifty unique records corresponding to 16 discrete patient populations comparing MR-targeted biopsy with a standard transrectal approach were found. When MRI was applied to all biopsy naive men, 62% had MRI abnormalities. In patients subjected to targeted biopsy, PCa was detected in 66%. They concluded that MRI-guided biopsy detects clinically significant cancer in numbers equivalent to standard biopsy. This is achieved using fewer biopsies in fewer men, with reduction in the diagnosis of clinically insignificant cancer. They concluded there is a need for a robust multicenter trial of targeted biopsies.

This study was intended as a pilot study to explore imaging techniques in cancer of the prostate. Results of the study must be interpreted with care because only a small number of patients were included. Nevertheless, the results of this study are comparable with other studies using mpMRI techniques. We compared the results of mpMRI to those of ultrasonography and postoperative specimen histology from 10 patients who underwent radical prostatectomy. We could thus be certain that changes seen on MRI were due to cancer. To our knowledge this study is the first to compare different radiographic techniques for the imaging of PCa. The results of this study indicate that mpMRI, specifically DWI with ADC maps may be useful in targeting biopsy probes, especially in patients with PSA levels indicative of cancer but with negative results from previous biopsies.

Patients with negative biopsy results were neither examined with MRI nor PET scanner and it is therefore difficult to say whether these patients had PCa despite negative findings or not. This is one of the weaknesses of the study. Another weakness is that the results of MRI imaging was not used to guide the second round of biopsies for patients included in the active surveillance arm, who are usually followed-up with a second set of biopsies after three months.

CONCLUSION

We present a method that may be used for further studies aimed at improving targeted biopsy. Reduction of biopsy complications is of great importance. This may be achieved by reducing the number of biopsies by concentrating on areas suspected of PCa as seen on MRI. We suggest standardized ROI´s and evaluation of the grade of malignancy related to SD values for the respective imaging methods. Numerical data for ADC anatomic mapping has the potential for targeted biopsy of aggressive tumour of the prostate. Though with lower resolution, this may be combined with MRI spectroscopic imaging.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

ACKNOWLEDGEMENTS

This study was partly funded by the Percy Falk Foundation.

REFERENCES

[1] Galper SL, Chen MH, Catalona WJ, Roehl KA, Richie JP, D'Amico A. Evidence to support a continued stage migration and decrease in prostate cancer specific mortality. J Urol 2006; 175(3 Pt 1): 907-12.

[2] Makarov DV, Trock BJ, Humphreys EB, *et al*. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. Urology 2007; 69(6):1095-101.

[3] Ladjevardi S, Sandblom G, Berglund A, Varenhorst E. Tumour grade, treatment, and relative survival in a population-based cohort of men with potentially curable prostate cancer. Eur Urol 2010; 57(4): 631-8.

[4] Johansson JE, Holmberg L, Johansson S, *et al*. Fifteen-year survival in prostate cancer: a prospective, population-based study in Sweden. JAMA 1997; 277(6): 467-71.

[5] Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. JAMA 1999; 281(17): 1591-7.

[6] Coakley FV, Qayyum A, Kurhanewicz J. Magnetic resonance imaging and spectroscopic imaging of prostate cancer. J Urol 2003; 170(6 Pt 2): S69-75; discussion S75-6.

[7] Punglia RS, D'Amico AV, Catalona WJ, *et al*. Effect of verification bias on screening for prostate cancer by measurement of prostate-specific antigen. N Engl J Med 2003; 349(4): 335-42.

[8] Wefer AE, Hricak H, Vigneron DB, *et al*. Sextant localization of prostate cancer: comparison of sextant biopsy, magnetic resonance imaging and magnetic resonance spectroscopic imaging with step section histology. J Urol 2000; 164(2): 400-4.

[9] Rabbani F, Stroumbakis N, Kava BR, Cookson MS, Fair WR. Incidence and clinical significance of false-negative sextant prostate biopsies. J Urol 1998; 159(4): 1247-50.

[10] Engelbrecht MR, Jager GJ, Laheij RJ, Verbeek AL, van Lier HJ, Barentsz JO. Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis. Eur Radiol 2002; 12(9): 2294-302.

[11] Sandblom G, Dufmats M, Olsson M, Varenhorst E. Positron emission tomography with C11-acetate for tumor detection and localization in patients with prostate-specific antigen relapse after radical prostatectomy. Urology 2006; 67(5): 996-1000.

[12] Soloviev D, Fini A, Chierichetti F, Al-Nahhas A, Rubello D. PET imaging with 11C-acetate in prostate cancer: a biochemical, radiochemical and clinical perspective. Eur J Nucl Med Mol Imaging 2008; 35(5): 942-9.

[13] Huang Y, Isharwal S, Haese A, *et al*. Prediction of patient-specific risk and percentile cohort risk of pathological stage outcome using continuous prostate-specific antigen measurement, clinical stage and biopsy Gleason score. BJU Int 2011; 107(10): 1562-9.

[14] Tamada T, Sone T, Jo Y, *et al*. Apparent diffusion coefficient values in peripheral and transition zones of the prostate: comparison between normal and malignant prostatic tissues and correlation with histologic grade. J Magn Reson Imaging 2008; 28(3): 720-6.

[15] Padhani AR, Liu G, Koh DM, *et al*. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. Neoplasia 2009; 11(2): 102-25.

[16] Turkbey B, Shah VP, Pang Y, *et al.* Is apparent diffusion coefficient associated with clinical risk scores for prostate cancers that are visible on 3-T MR images? Radiology 2011; 258(2): 488-95.

[17] Hambrock T, Somford DM, Huisman HJ, *et al*. Relationship between apparent diffusion coefficients at 3.0-T MR imaging and Gleason grade in peripheral zone prostate cancer. Radiology 2011; 259(2): 453-61.

[18] Weis J, Jorulf H, Bergman A, *et al*. MR spectroscopy of the human prostate using surface coil at 3 T: metabolite ratios, age-dependent effects, and diagnostic possibilities. J Magn Reson Imaging 2011; 34(6): 1277-84.

[19] Franiel T, Stephan C, Erbersdobler A, *et al*. Areas suspicious for prostate cancer: MR-guided biopsy in patients with at least one transrectal US-guided biopsy with a negative finding--multiparametric MR imaging for detection and biopsy planning. Radiology 2011; 259(1): 162-72.

[20] Heijmink SW, Futterer JJ, Hambrock T, *et al*. Prostate cancer: body-array versus endorectal coil MR imaging at 3 T--comparison of image quality, localization, and staging performance. Radiology 2007; 244(1): 184-95.

[21] Dickinson L, Ahmed HU, Allen C, *et al.* Scoring systems used for the interpretation and reporting of multiparametric MRI for prostate cancer detection, localization, and characterization: could standardization lead to improved utilization of imaging within the diagnostic pathway? J Magn Reson Imaging 2013; 37(1): 48-58.

[22] Singh AK, Kruecker J, Xu S, *et al*. Initial clinical experience with real-time transrectal ultrasonography-magnetic resonance imaging fusion-guided prostate biopsy. BJU Int 2008; 101(7): 841-5.

[23] Xu S, Kruecker J, Turkbey B, *et al*. Real-time MRI-TRUS fusion for guidance of targeted prostate biopsies. Comput Aided Surg 2008; 13(5): 255-64.

[24] Lecornet E, Ahmed HU, Hu Y, *et al*. The accuracy of different biopsy strategies for the detection of clinically important prostate cancer: a computer simulation. J Urol 2012; 188(3): 974-80.

[25] Kasivisvanathan V, Dufour R, Moore CM, *et al*. Transperineal magnetic resonance image targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. J Urol 2013; 189(3): 860-6.

[26] Moore CM, Robertson NL, Arsanious N, *et al*. Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. Eur Urol 2013; 63(1): 125-40.

Received: October 08, 2013 Revised: November 22, 2013 Accepted: December 02, 2013