Pre-Operative Tumor Localization and Evaluation of Extra-Capsular Extension of Prostate Cancer: How Misleading Can It Be?

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Purpose: To verify the accuracy of transrectal ultrasound-guided prostatic biopsy (TRUS Bx), magnetic resonance imaging (MRI) and their combination in evaluating the laterality of prostate cancer and to determine the accuracy of MRI in assessing extra-capsular extension of prostate cancer.

Materials and Methods: We retrospectively reviewed our past 100 consecutive series of radical prostatectomy performed between February 2010 and April 2012 at our institution. Their TRUS Bx and MRI results were compared with the pathology of the radical prostatectomy specimens. For tumor localization, we calculated the accuracies in unilateral diseases, bilateral diseases, overall accuracies and Cohen Kappa concordance coefficient of TRUS Bx, MRI and their combination. For the assessment of extra-capsular extension, we calculated the sensitivity, specificity, positive predictive value, negative predictive value, overall accuracy, likelihood ratio positive and likelihood ratio negative of MRI.

Results: Eighty-two percent of our radical prostatectomy specimens had bilateral tumor involvement and 32% had extra-capsular extension. The accuracies of TRUS Bx in unilateral disease, bilateral disease and overall accuracy were 15.2%, 91.4% and 43.6%, respectively. The accuracies of MRI in unilateral disease, bilateral disease and overall accuracy were 11.1%, 66.7% and 38.9%, respectively. When combining the assessment of TRUS Bx and MRI, the accuracies in unilateral disease, bilateral disease and overall accuracy were 16.7%, 75% and 55.6%, respectively. The Cohen Kappa concordance co-efficient of TRUS Bx, MRI, and combination of them were 0.1165, -0.2047 and -0.1084, respectively. The positive predictive value, negative predictive value, sensitivity, specificity, overall accuracy, likelihood ratio positive and likelihood ratio negative of MRI in assessing extra-capsular extension were 33.3%, 69.8%, 5.9%, 94.9%, 67.9%, 1.16 and 0.99, respectively.

Conclusion: TRUS Bx, MRI, and their combination had poor concordance and limited accuracies in assessment of the laterality of tumor involvement. The combination of TRUS Bx and MRI offered a better of accuracy when compared to either modality alone. MRI was a specific, but not sensitive tool in assessing the presence of extra-capsular extension.

Keywords: neoplasm invasiveness; prostatic neoplasms; image interpretation; neoplasm staging; predictive value of tests; sensitivity and specificity; magnetic resonance imaging.

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INTRODUCTION

Since the adoption of prostate-specific antigen (PSA) testing, the incidence of prostate cancer had been gradually climbing up in the ranking of most prevalent cancers. In the United States, prostate cancer had become the most common solid-organ cancer diagnosed in 2012.[1] In Hong Kong, prostate cancer ranked fifth with 1,492 new cases registered in 2010.[2] In addition, a larger proportion of prostate cancer was diagnosed in their early and low-risk stage.[3] Thus, the demand for definitive treatment, such as radical prostatectomy, was unprecedented.

Continence and erectile function are two major concerns affecting the post-operative quality of life. Nerve-sparing technique was shown to offer early return of continence[4] and preservation of erectile function,[5] hence nerve-sparing prostatectomy had become the standard of care for organ-confined prostate cancer.[6] Pre-operative risk assessment and tumor localization are important for operative decisions. Tools for pre-operative tumor localization, however, had arguable accuracy despite technological advancement. Transrectal ultrasound-guided 12-core prostatic biopsy (TRUS Bx) was used to diagnose and to determine the laterality of prostate cancer. Magnetic resonance imaging (MRI) of the prostate, besides the laterality of tumor, also provides information regarding extra-capsular extension of the tumor.[7]

Based on our experience, we conducted this review with the primary objective to determine the accuracy of TRUS Bx, MRI and their combination in evaluating the laterality of prostate cancer. Our second objective was to determine the reliability of MRI in assessing extra-capsular extension of prostate cancer.

MATERIALS AND METHODS

We retrospectively reviewed our past 100 consecutive series of radical prostatectomy performed between February 2010 and April 2012 at our institution. Their TRUS Bx and MRI results were compared with the final pathology of the radical prostatectomy specimens. All radical prostatectomy specimens were submitted for standardized slicing and processing,[8] and were reported by experienced pathologists.

TRUS Bx with at least 12 cores, performed at our institution and elsewhere with retrievable pathology reports were included for analysis. Our institution adopted the use of Aloka Prosound 6 ultrasound machine (Prosound Alpha 7, Aloka, Tokyo, Japan) and Pajunk Delta Cut Biopsy System.

Table 1. Tumor characteristics (n = 100).

Variables		%
PSA level ng/mL		
	< 10	64
	10-20	29
	> 20	7
Gleason score		
	3 + 3	79
	3 + 4 / 4 + 3	19
	4 + 4 or above	2
Laterality on final pathology		
	Bilateral	82
	Left only	11
	Right only	7
Extra-capsular extension		
	Absent	68
	Present	32

Key: PSA, prostate-specific antigen.

In order to minimize the confounding factor of using different MRI scanners and sequences, only those scans performed at our institution were included. We used the Siemens Magnetom Avanto 1.5-Tesla MRI system (Siemens Magnetom Avanto, Erlangen, Germany). With a pelvis-phased body array coil system, our scanner produced T1 and T2 images with contrast phase, as well as diffusion weight images. Our MRI scans were reported by at least one experienced radiologist. The above specifications were in accordance with the minimal requirement established by the European Consensus Meeting in 2009.[7] The key information we retrieved from the MRI reports were laterality of the tumor, and whether there was extra-capsular extension. Regarding the evaluation of tumor laterality, we calculated the accuracy in unilateral disease, accuracy in bilateral disease, and overall accuracy for TRUS Bx, MRI and their combination. Bilateral disease in combination was defined as bilateral disease in either TRUS Bx or MRI, or when TRUS Bx and MRI indicated unilateral disease of opposite sides. We calculated the Cohen Kappa to indicate the concordance of TRUS Bx, MRI and their combination with the final pathology.

Statistical Analysis

Statistical analysis was performed using the Statistical Pack-

Table 2. Accuracy in prediction of tumor laterality.

Variables		Final Pathology				Cohen Kappa (κ)	Data Analysis (%)
		Right only	Left only	Bilateral	Total		
TRUS Bx (n = 94)	Right only	4	4	19	27	0.1165 95% CI = 0.0066 – 0.2265	Accuracy of unilateral disease = 15.2 Accuracy of bilateral disease = 91.4 Overall accuracy = 43.6
	Left only	1	5	26	32		
	Bilateral	2	1	32	35		
	Total	7	10	77	94		
MRI (n = 56) Visible (n = 36) Not seen (n = 20)	Right only	0	0	8	8	-0.2047 95% CI = -0.4397 – 0.0302	Accuracy of unilateral disease = 11.1 Accuracy of bilateral disease = 66.7 Overall accuracy = 38.9
	Left only	0	2	8	10		
	Bilateral	4	2	12	18		
	Total	4	4	28	36		
Combination (n = 36)	Right only	0	0	5	5	-0.1084 95% CI = -0.3767 – 0.1600	Accuracy of unilateral disease = 16.7 Accuracy of bilateral disease = 75 Overall accuracy = 55.6
	Left only	0	2	5	7		
	Bilateral	4	2	18	24		
	Total	4	4	28	36		

Keys: CI, confidence interval; TRUS Bx, transrectal ultrasound-guided prostatic biopsy; MRI, magnetic resonance imaging.

age for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 10.0. Regarding extra-capsular extension, we computed the sensitivity, specificity, positive predicted value, negative predictive value, overall accuracy, likelihood ratio positive and likelihood ratio negative of MRI in assessing the presence of extra-capsular extension in the final pathology.

RESULTS

Table 1 showed the tumor characteristics of our cohort of 100 patients who underwent radical prostatectomy. Sixty-four patients had a pre-operative PSA level of less than 10 ng/mL, 29 patients had a level between 10 and 20 ng/mL, while 7 patients had a level greater than 20 ng/mL. Regarding Gleason score, 79 patients had a score of 3 + 3 in the final pathology, 19 patients had a score of 7, while 2 patients had a score of 8 or above. Regarding laterality of tumor in the prostatectomy specimen, 82 patients had bilateral tumor involvement, while 18 had unilateral disease. Among these 100 radical prostatectomy specimens, 32 had extra-capsular extension.

Table 2 showed our results in pre-operative evaluation of tumor laterality. There were 94 patients whose TRUS Bx reports were available for analysis. Fifty six patients had their MRI scans performed at our institution, among which 20 scans did not visualize the biopsy-proven prostate cancer. Therefore we performed our analysis based on the remaining 36 MRI scans. The accuracies of TRUS Bx in unilateral disease, bilateral disease and overall accuracy were 15.2%, 91.4% and 43.6%, respectively. The accuracies of MRI in unilateral disease, bilateral disease and overall accuracy were 11.1%, 66.7% and 38.9% respectively. When combining the assessment of TRUS Bx and MRI, the accuracies in unilateral disease, bilateral disease and overall accuracy were 16.7%, 75% and 55.6%, respectively. The concordance of TRUS Bx, MRI and their combination, as indicated by their Cohen Kappa co-efficient, were 0.1165, -0.2047 and -0.1084, respectively.

Table 3 demonstrated our analysis regarding the assessment of extra-capsular extension. Among these 56 patients, 17 (30.4%) had extra-capsular extension on the prostatectomy specimens. The positive predictive value, negative predictive value, sensitivity, specificity, overall accuracy, likelihood ratio positive and likelihood ratio negative of MRI in assessing extra-capsular extension were 33.3%, 69.8%, 5.9%, 94.9%, 67.9%, 1.16 and 0.99, respectively.

DISCUSSION

TRUS Bx is one of the most important pre-operative investigations to determine the tumor laterality, however, our results fell short of satisfying. Due to the multifocal nature of prostate cancer, 82% of all radical prostatectomy specimens in our series were bilaterally involved. As these foci were microscopically present, they easily succumbed to sampling

Table 3. Accuracy in prediction of extra-capsular extension.

Variables		Pathology			
		ECE	No ECE	Total	
MRI (n = 56)	ECE	1	2	3	PPV = 1/3 (33.3%) NPV = 37/53 (69.8%) Sensitivity = 1/17 (5.9%) Specificity = 37/39 (94.9%) Overall accuracy = 38/56 (67.9%) LR (+) = 1.16 LR (-) = 0.99
	No ECE	16	37	53	
	Total	17	39	56	

Keys: PPV, positive predictive value; NPV, negative predictive value; LR (+), likelihood ratio positive; LR (-), likelihood ratio negative; MRI, magnetic resonance imaging; ECE, extra-capsular extension.

error in TRUS Bx. As a result, most of the apparently unilateral disease in TRUS Bx turned out to be bilaterally involved in the prostatectomy specimens. This resulted in a very disappointing accuracy in unilateral disease of 15.2%. Notwithstanding, the accuracy in bilateral disease was a reassuring 91.4%. The Cohen Kappa coefficient of TRUS Bx was 0.1165, indicating only slight agreement between TRUS Bx and final pathology. It was evident that TRUS Bx had limited reliability in evaluating unilateral disease.

A handful of cases where TRUS Bx indicated unilateral disease turned out to be unilaterally involved on the opposite side in the prostatectomy specimens. This situation was also present in other similar studies.[9,10] This "unilateral vanishing cancer syndrome" was another proof of the multifocal nature of prostate cancer.

Advances in MRI had allowed a combination of modern MRI sequences into a more informative multi-parametric MRI scanning. To address the diversity in techniques and image interpretation, the European Consensus Meeting had established a set of guidelines regarding the multi-parametric MRI scanning.[7] The evidence regarding multi-parametric MRI scanning was conflicting. Although in general the performance of multi-parametric MRI was reckoned promising,[11,12] there existed conflicting opinion regarding its accuracy and usefulness.[13]

We routinely recommended MRI scanning for all patients diagnosed with prostate cancer who opted to undergo radical prostatectomy. The scan was scheduled 8-12 weeks after TRUS Bx. Among the 56 MRI scans performed at our institution, 20 scans could not visualize a biopsy-proven prostate cancer. For the remaining 36 scans, the accuracy in unilateral disease was 11.1% and the accuracy in bilateral disease was 66.7%, both of which were worse than those of TRUS Bx. This resulted in an overall accuracy of 38.9%. The Cohen Kappa coefficient of MRI was negative, which indicated no agreement between MRI evaluation and final pathology. Our results clearly showed that the use of our MRI scanning sequences, which met the minimal requirement as suggested by the European Consensus Meeting[7] was suboptimal. The adoption of higher magnetic field power and endorectal coil, as well as the addition of dynamic contrast enhancement and spectroscopy could arguably increase the sensitivity and accuracy in tumor localization.[11]

The complementary combination of TRUS Bx and MRI was able to improve the accuracy in evaluating unilateral disease, as well as the overall accuracy, when compared to either modality alone. The overall accuracy of their combination reached 55.6%.

Regarding the assessment of extra-capsular extension, our results showed that MRI was a highly specific, but not sensitive tool. The specificity was as high as 94.9%, but the sensitivity was unacceptably low at 5.9%. This might be partly explained by the difference between macroscopic and microscopic extra-capsular extension. The other explanation might be the inter-observer variability in deciphering the MRI images.

The inter-observer variability, and the differences in imaging criteria used for a positive MRI finding contributed to the wide range of accuracy in MRI performance.[11] In an attempt to standardize the interpretation and reporting of MRI scanning, the European Society of Urogenital Radiology had proposed the Prostate Imaging Reporting and Data System (PI-RADS) scoring system.[14] The adoption of this objective and structured reporting system, together with designating an experienced group of urogenital radiologists for the interpretation, might aid to reduce the inter-observer variability and to enable comparison among different patients.

As new technologies regarding MRI scanning was devel-

oping inexorably, we believed the role of MRI in prostate cancer could be potentially pivotal when making important clinical decisions in the future.

CONCLUSION

TRUS Bx, MRI and their combination had poor concordance and limited accuracies in evaluating the laterality of tumor involvement. The combination of TRUS Bx and MRI offered a better overall accuracy when compared to either modality alone. MRI was a specific, but not sensitive tool in assessing the presence of extra-capsular extension. When planning for nerve-sparing radical prostatectomy, urologists should recognize the limitations of each pre-operative investigation in terms of tumor localization and assessment of extra-capsular extension.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. 2012;62:10-29.
2. Hong Kong Cancer Registry, Hospital Authority, Hong Kong. Accessed on: www.ha.org.hk/cancereg.
3. Cooperberg MR, Broering JM, Kantoff PW, Carroll PR. Contemporary trends in low risk prostate cancer: risk assessment and treatment. J Urol. 2007;178:S14-9.
4. Srivastava A, Chopra S, Pham A, et al. Effect of a risk-stratified grade of nerve-sparing technique on early return of continence after robot-assisted laparoscopic radical prostatectomy. Eur Urol. 2013;63:438-44.
5. Meuleman EJ, Mulders PF. Erectile function after radical prostatectomy: a review. Eur Urol. 2003;43:95-101.
6. Montorsi F, Wilson TG, Rosen RC, et al. Best practice in robot-assisted radical prostatectomy: recommendations of the Pasadena Consensus Panel. Eur Urol. 2012;62:368-381.
7. Dickinson L, Ahmed HU, Allen C, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European Consensus Meeting. Eur Urol. 2011;59:477-94.
8. Samaratunga H, Montironi R, True L, et al. International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. Working group 1: specimen handling. Mod Pathol. 2011;24:6-15.
9. Frota R, Stein RJ, Turna B, et al. Are prostate needle biopsies predictive of the laterality of significant cancer and positive surgical margins? BJU Int. 2009;104:1599-603.
10. Jeong CW, Ku JH, Moon KC, et al. Can conventional magnetic resonance imaging, prostate needle biopsy, or their combination predict the laterality of clinically localized prostate cancer? Urology. 2012;79:1322-7.
11. Kirkham AP, Emberton M, Allen C. How good is MRI at detecting and characterizing cancer within the prostate? Eur Urol. 2006;50:1163-74.
12. Puech P, Huglo D, Petyt G, Lemaitre L, Villers A. Imaging of organ-confirmed prostate cancer: functional ultrasound, MRI and PET/computed tomography. Curr Opin Urol. 2009;19:168-76.
13. Kelloff GJ, Choyke P, Coffey DS, Prostate Cancer Imaging Working Group. Challenges in clinical prostate cancer: role of imaging. Am J Roentgenol. 2009;192:1455-70.
14. Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. Eur Radiol. 2012;22:746-57.