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Efficacy of Using Three-Tesla Magnetic Resonance Imaging Diagnosis of Capsule Invasion for Decision-Making About Neurovascular Bundle Preservation in Robotic-Assisted Radical Prostatectomy

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Purpose: To evaluate the efficacy of using 3-tesla (T) magnetic resonance imaging (MRI) diagnosis of extracapsular extension (ECE) for decision-making about neurovascular bundle (NVB) preservation in robot-assisted radical prostatectomy (RARP) for prostate cancer (PC).
Materials and Methods: We prospectively collected data on PC patients (n=67) who underwent preoperative 3-T MRI before RARP. The choice between nerve sparing or resection was based on 3-T MRI findings of ECE. We compared the MRI findings with the pathological data on surgical margins. Our clinical staging in this study was defined only by MRI.
Results: When the data were divided by prostate lobe (right lobe or left lobe, n=134), 3-T MRI showed 28 positive cases of ECE in 134 prostate lobes, allowing NVB preservation in 42 cases (31.3%). Nerve-sparing surgery was achieved in 38.7% of cases in which clinical T2 staging by MRI was reported. The pathological data revealed that 10 of 134 prostate lobes had positive ECE. The overall sensitivity, specificity, positive predictive value, and negative predictive value for predicting stage T3 (positive ECE) by side were 60.0% (12 of 20 sides), 86.0% (98 of 114 sides), 42.9% (12 of 28 sides), and 92.5% (98 of 106 sides), respectively.
Conclusions: Three-T MRI prior to RARP enables the use of ECE diagnosis to guide decision-making about NVB preservation, with comparatively high specificity and negative predictive value. Further prospective studies are underway to reach more definitive conclusions.

Keywords: *Diagnoses; Magnetic resonance imaging; Prostatectomy; Robotics*

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INTRODUCTION

Prostate cancer (PC) increasingly presents as early-stage disease clinically owing to increased screening, including prostate-specific antigen (PSA) screening. The standard of care for organ-confined cancers has been retropubic radical prostatectomy, which carries a substantial risk of morbidity, including incontinence and impotence [1]. Robot-assisted radical prostatectomy (RARP) provides improved visualization of the surgical field and improved instrument control compared with open and laparoscopic prostatectomy [2]. However, surgeons performing RARP lack the tactile feedback upon which they have traditionally relied to determine the extent of resection [3].

In this situation, preoperative detection of extracapsular extension (ECE) may be necessary to guide the surgical strategy in radical prostatectomy, to achieve PC-negative margins, and to spare the neurovascular bundles (NVBs) as much as possible to preserve erectile function and good postoperative continence [4-6].

In most cases, current PC staging is based on clinical assessment, notably, digital rectal examination (DRE), to sense a nodule or an extraprostatic rigid mass during prostate palpation. This clinical approach seems outdated, however, because DRE has low specificity [7]. Prostatic magnetic resonance imaging (MRI) appears to be a promising method for detecting PC and even for evaluating ECE during the pretreatment workup [8-10]. However, data about the specific role of prostatic MRI in PC staging are still lacking [11]. Moreover, racial differences have been reported in PC tumor aggressiveness and invasion characteristics [12]. Specific racial guidelines for decision making about nerve sparing may need to be established.

In this study, we evaluated the utility of 3-T MRI for assessing ECE and indicating the appropriateness of NVB sparing during RARP in a Japanese patient population.

MATERIALS AND METHODS

1. Patients

In this single-institution study, 67 patients with clinical T2 or T3 disease diagnosed by MRI and who did not undergo neoadjuvant hormonal therapy were included between October 2010 and September 2012. All patients had biopsy-proven PC. Preoperative 3-T MRI was performed to determine the feasibility and extent of a nerve-sparing RP. The following data were collected: age at diagnosis, preoperative PSA level, clinical staging, pathological staging, and Gleason score from biopsy and surgical specimens. The Kobe University Institutional Review Board approved this protocol. Written informed consent was obtained from all participants before inclusion in the study.

2. Three-tesla MRI

MRI was performed by using a 3-T MR scanner (Intera Achieva, Philips Healthcare, Amsterdam, The Netherland) with a phased-array pelvic coil for signal reception. No endorectal coil was used in this study. All patients underwent sagittal, coronal, and axial oblique turbo spin-echo T2-weighted imaging, and all MRI findings were evaluated by a single radiologist (S.T.). Additionally, patients underwent echo-planar diffusion-weighted imaging (DWI) with calculation of apparent diffusion coefficients and dynamic contrast-enhanced imaging. The criteria for a positive cancer finding were as follows: 1) low-intensity imaging in both T2-weighted imaging and apparent diffusion coefficient or 2) enhancing in the early phase but washed out in dynamic imaging. An antiperistaltic agent, 0.5 mg glucagon, was administrated intravenously just before the MRI examinations, and an additional 0.5 mg was administered immediately preceding the acquisition of dynamic contrast enhanced MR. A minimum of 8 weeks was required between the date of the MRI and the previous biopsy to reduce the influence of postbiopsy change in diagnostic accuracy on the basis of Hricak's study [5], in which the median interval between MRI and biopsy was 8 weeks. Prostate biopsy was performed transrectally with 12 cores (6 sextant, 2 from the far peripheral zone [PZ], and 4 cores from the transitional zone [TZ]).

Common criteria was used to determine ECE and local staging grade. Low-intensity lesions on T2-weighted MR images within the PZ of the prostate were considered suspicious for tumor [13]. In the TZ, areas with homogeneous low signal intensity, ill-defined margins, or lack of capsule were interpreted as tumor foci. Asymmetric bulging, an irregular margin, or direct extension of the lesion in the periprostatic fat or NVB was graded as capsular penetration (stage T3a). Signs of seminal vesicle invasion included low intensity in one or both seminal vesicles (stage T3b). The radiological findings were compared with the final operative histological reports.

3. RARP procedure

RARP with lymph node resection was performed with a da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) using the standard procedure [14]. Briefly, 4 robotic arms and 2 additional trocars as assistants were used in a 30-degree Trendelenburg position by a transperitoneal approach. Nerve-sparing procedures used an athermal, antegrade interfascial method with minimization of traction. The decision for nerve-sparing was based on MRI findings and preoperative International Index of Erectile Function Questionnaire-25 scores.

4. Histological evaluation

The prostate was serially sectioned from base to apex into different levels (depending on the size of the prostate) for histological analysis and labeled as right or left and anterior or posterior apex, midgland, and base. Seminal vesicles were also analyzed separately. All reports were reviewed to determine the presence of ECE and seminal vesicle invasion and to compare staging at the pathologic examination and MRI in each prostate lobe (2 lobes in one patient).

5. Statistical analyses

Diagnostic accuracy was measured as sensitivity, specificity, positive predictive value, and negative predictive value. Univariate analysis was calculated for ECE and achievement of nerve-sparing. A p-value of 0.05 or less was considered as statistically significant. A Mann-Whitney U test and a chi-square test were used to determine significant differences. Statistical analysis was conducted with XLSTAT (Addinsoft, New York, NY, USA).

RESULTS

1. Extracapsular invasion

The characteristics of all patients are shown in Table 1. All patients underwent 3-T MRI before RALP (Table 1). The preoperative 3-T MRI results showed that when the samples were divided by prostate side or lobe (right side or left side), 106 of 134 sides were ECE negative and 28 of 134 were ECE positive (Table 2). The representative MRI findings of the positive ECE and negative ECE sides are shown in Fig. 1. Pathologic examination of the surgical specimens in all 67 patients revealed that 50 patients (74.6%) had disease confined to the prostate (pT2) and 17 patients (25.4%) had locally advanced disease (pT3). The pathological stages were pT2a (n=11), pT2b (n=6), pT2c (n=33), pT3a (n=15), and pT3b (n=2) (Table 1).

TABLE 1. Patients' characteristics

Characteristic	Value
No. of patients	67
Age (y), median (range)	67 (51–74)
PSA (ng/mL), median (range)	6.99 (2.87–27.6)
Clinical stage	
T2a	28
T2b	3
T2c	20
T3a	16
Pathological stage	
T2a	11
T2b	6
T2c	33
T3a	15
T3b	2
Gleason score of biopsy	
6	13
7	30
8	24
Gleason score of prostatectomy	
6	2
7	54
8	11

PSA, prostate-specific antigen.

2. Comparison between MRI and pathological data

In the MRI and pathological findings, the overall sensitivity, specificity, and positive predictive value for predicting ECE according to the findings by every prostate side and the negative predictive value were 60.0% (12 of 20 sides), 86.0% (98 of 114 sides), 42.9% (12 of 28 sides), and 92.5% (98 of 106 sides), respectively (Table 2).

3. Correlation of MRI with nerve-sparing and pathological data

On the basis of the 3-T MRI findings, nerve-sparing surgery was performed on 42 of 134 sides (31.3%). Nerve-sparing surgery was achieved in 38.7% of sides with no ECE reported by 3-T MRI. All 41 sides with negative ECE on MRI underwent nerve-sparing surgery with no positive surgical margins (100%). Table 3 shows the nerve-sparing procedure, pathological stage, and positive surgical margin rate in the MRI groups with and without ECE. All values were significantly different (Table 3).

DISCUSSION

Approximately 40% of patients with localized PC choose some form of surgical resection for treatment [15]. In any

TABLE 2. Comparison between MRI and pathological findings

Parameter	Pathological stage	
	T3	T2
Magnetic resonance imaging stage		
Positive ECE	12	16
Negative ECE	8	98
Sensitivity	60.0%	
Specificity	86.0%	
Positive predictive value	42.9%	
Negative predictive value	92.5%	

ECE, extracapsular extension.

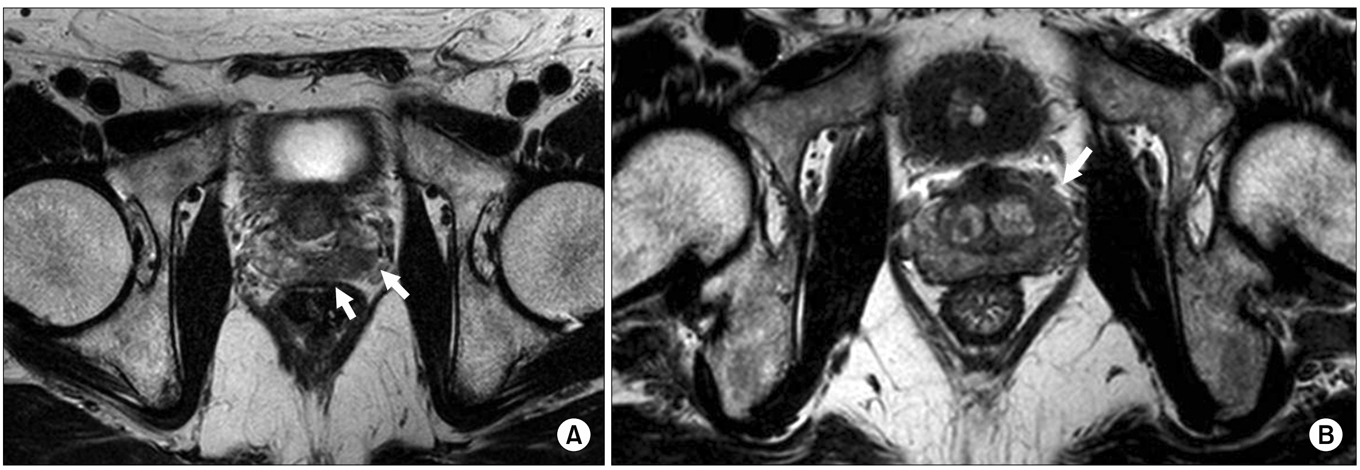

FIG. 1. Representative cases with positive (prostate cancer-positive part is shown by an arrow) (A) and negative (B) extracapsular extension magnetic resonance imaging findings are shown.

TABLE 3. Nerve-sparing procedures and surgical margin status related to ECE predicted by MRI and pathological stage

	Negative ECE in MRI	Positive ECE in MRI	p-value
Procedure			<0.05
NS	41	1	
No NS	65	27	
Pathological stage			<0.05
pT2	98	15	
pT3	8	13	
Positive surgical margin rate	8/106 (7.5%)	13/28 (46.4%)	<0.05

ECE, extracapsular extension; MRI, magnetic resonance imaging; NS, nerve sparing.

surgical approach, surgeons must balance the desire to achieve a cancer-free resected margin with the need to minimize postoperative morbidity, which may involve incontinence and erectile dysfunction [16]. The NVB, which mediates erectile function, lies posterolateral or lateral on the prostatic capsule and adjacent to the PZ of the prostate, where 70% of PCs arise [17]. In RP, surgeons typically identify and spare the NVB if possible; however, cases with suspicious ECE need to be widely resected to include the NVB and surrounding tissues to achieve negative surgical margins. This procedure may not be easy in traditional open RP owing to individual patient anatomy or severe blood loss [18].

The goal in nerve-sparing RP is to preserve the greatest amount of nerve tissue possible without compromising surgical margins. Robotic-assisted surgery has been spreading in Japan, and RARP was included under government medical insurance in 2012. Robotic technology is a step forward, as it provides increased magnification, high-definition imaging, and wristed instrumentation and is associated with significantly less blood loss than open surgery [19]. For optimal nerve-sparing outcome, the preoperative search for ECE in the prostate and the accurate staging of PC appear to be key points in the pretherapeutic workup for indicating whether the nerve-sparing approach is feasible. There are currently no guidelines for this in Japan.

Unlike clinical variables (PSA values and findings from DRE), results from MRI are spatially localized and allow surgeons to individually sculpt the extent of surgical resection as mentioned above [3]. In recent years, MRI with field intensities of 3 T, a significant increase in the signal compared with 1.5-T MRI, has become commonplace [20]. Three-T MRI maintains imaging quality while significantly reducing imaging time and increasing the signal-to-noise ratio up to twofold. Because of the increased signal-to-noise ratio and the improved spatial resolution at 3 T, improvements in the localization and detection of PC can be expected [21]. Regarding the efficacy of 3-T MRI for ECE determination, a previous study showed that sensitivity was 66.7% and specificity 100% for the detection of ECE in 27 PC cases [22]. In another study, the accuracy of 3-T endorectal MRI prediction of ECE was 75% [23]. Our data showed an overall sensitivity and specificity for predicting ECE of 60.0% and 86.0%, respectively, which is comparable with previous studies.

According to the literature, 1.5-T MRI performed with an endorectal coil is currently the standard imaging method for staging PC [9]. However, this method has several problems related to examination tolerance, movement, near-field effect, capsular profile deformation artifacts connected to coil use, and cost [24]. Staging by 1.5-T MRI with an endorectal coil shows extremely variable results (a detection range of 13% to 95% for ECE and 25% to 72% for extension to seminal vesicles) [9,11]. Our study used 3-T MRI with a phased-array pelvic coil that allows fewer artifacts and thus provides comparatively acceptable quality images for decision-making about nerve-sparing surgery.

DWI is a complementary functional technique that may have utility in the detection, quantification, and grading of PC [25]. DWI data can be postprocessed to give apparent diffusion coefficient maps, which assist in detection and localization. Dynamic contrasted-enhanced (DCE) MRI is another complementary functional MR technique that assesses the relative tissue perfusion within the prostate. Detection and characterization are improved by the addition of DCE-MRI to T2-weighted images [26]. For overall PC detection, multiparametric MRI showed better quality than any individual MRI sequence [27]. In this study, we used T2-weighted imaging, DWI, and DCE-MRI for PC staging, which may have contributed to our results showing a statistically significant trend for the surgeon to perform fewer NVB-sparing procedures if the MRI reported ECE than if no ECE was reported. The same trend was also mentioned by Roethke et al as significant ($p < 0.01$) in their study [28]. An important question is the influence of preoperative MRI on the positive surgical margin rate. In our study, patients with ECE on MRI had a higher positive surgical margin rate than did patients who were not suspicious for ECE. Additionally, there were no positive surgical margins with nerve-sparing procedures in the group shown to be ECE negative on MRI.

This study have some limitations. First, the number of cases may not have been enough for definitive conclusions. Second, we did not use an endorectal coil. Even though an endorectal coil could have provided better spatial resolution, this approach has several limitations, including increased cost and examination time, a nonuniform signal across the prostate, and an increase in motion artifacts owing to rectal peristalsis. Third, this was a single-arm study and did not include a comparative group, for instance, a 1.5-T MRI group. These limitations will be overcome in our future studies.

CONCLUSIONS

We found that 3-T MRI showed comparatively acceptable results for staging PC and accurately detecting ECE to guide decision-making for nerve-sparing surgery in RARP. Our data offer evidence that 3-T MRI might improve decision-making about nerve-sparing surgery, although a prospective study with a comparison group and larger number of cases is still needed.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

REFERENCES

1. Hugosson J, Stranne J, Carlsson SV. Radical retropubic prostatectomy: a review of outcomes and side-effects. Acta Oncol 2011;50 Suppl 1:92-7.
2. Frota R, Turna B, Barros R, Gill IS. Comparison of radical prostatectomy techniques: open, laparoscopic and robotic assisted. Int Braz J Urol 2008;34:259-68.
3. McClure TD, Margolis DJ, Reiter RE, Sayre JW, Thomas MA, Nagarajan R, et al. Use of MR imaging to determine preservation of the neurovascular bundles at robotic-assisted laparoscopic prostatectomy. Radiology 2012;262:874-83.
4. Brown JA, Rodin DM, Harisinghani M, Dahl DM. Impact of preoperative endorectal MRI stage classification on neurovascular bundle sparing aggressiveness and the radical prostatectomy positive margin rate. Urol Oncol 2009;27:174-9.
5. Hricak H, Wang L, Wei DC, Coakley FV, Akin O, Reuter VE, et al. The role of preoperative endorectal magnetic resonance imaging in the decision regarding whether to preserve or resect neurovascular bundles during radical retropubic prostatectomy. Cancer 2004;100:2655-63.
6. Labanaris AP, Zugor V, Takriti S, Smiszek R, Engelhard K, Nutzel R, et al. The role of conventional and functional endorectal magnetic resonance imaging in the decision of whether to preserve or resect the neurovascular bundles during radical retropubic prostatectomy. Scand J Urol Nephrol 2009;43:25-31.
7. Hsu CY, Joniau S, Oyen R, Roskams T, Van Poppel H. Detection of clinical unilateral T3a prostate cancer - by digital rectal examination or transrectal ultrasonography? BJU Int 2006;98:982-5.
8. Cornud F, Flam T, Chauveinc L, Hamida K, Chretien Y, Vieillefond A, et al. Extraprostatic spread of clinically localized prostate cancer: factors predictive of pT3 tumor and of positive endorectal MR imaging examination results. Radiology 2002;224:203-10.
9. Girouin N, Mege-Lechevallier F, Tonina Senes A, Bissery A, Rabilloud M, Marechal JM, et al. Prostate dynamic contrast-enhanced MRI with simple visual diagnostic criteria: is it reasonable? Eur Radiol 2007;17:1498-509.
10. Villers A, Puech P, Mouton D, Leroy X, Ballereau C, Lemaitre L. Dynamic contrast enhanced, pelvic phased array magnetic resonance imaging of localized prostate cancer for predicting tumor volume: correlation with radical prostatectomy findings. J Urol 2006;176(6 Pt 1):2432-7.
11. Jager GJ, Ruijter ET, van de Kaa CA, de la Rosette JJ, Oosterhof GO, Thornbury JR, et al. Local staging of prostate cancer with endorectal MR imaging: correlation with histopathology. AJR Am J Roentgenol 1996;166:845-52.
12. Xu Z, Bensen JT, Smith GJ, Mohler JL, Taylor JA. GWAS SNP Replication among African American and European American men in the North Carolina-Louisiana prostate cancer project (PCaP). Prostate 2011;71:881-91.
13. Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22:746-57.
14. Orvieto MA, Patel VR. Evolution of robot-assisted radical prostatectomy. Scand J Surg 2009;98:76-88.
15. Bhatnagar V, Kaplan RM. Treatment options for prostate cancer: evaluating the evidence. Am Fam Physician 2005;71:1915-22.
16. Kundu SD, Roehl KA, Eggener SE, Antenor JA, Han M, Catalona WJ. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. J Urol 2004;172(6 Pt 1):2227-31.
17. Costello AJ, Brooks M, Cole OJ. Anatomical studies of the neurovascular bundle and cavernosal nerves. BJU Int 2004;94:1071-6.
18. Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, et al. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. Eur Urol 2009;55:1037-63.
19. Lowrance WT, Tarin TV, Shariat SF. Evidence-based comparison of robotic and open radical prostatectomy. ScientificWorldJournal 2010;10:2228-37.
20. Bloch BN, Rofsky NM, Baroni RH, Marquis RP, Pedrosa I, Lenkinski RE. 3 Tesla magnetic resonance imaging of the prostate with combined pelvic phased-array and endorectal coils; Initial experience(1). Acad Radiol 2004;11:863-7.
21. Kim CK, Park BK, Han JJ, Kang TW, Lee HM. Diffusion-weighted imaging of the prostate at 3 T for differentiation of malignant and benign tissue in transition and peripheral zones: preliminary results. J Comput Assist Tomogr 2007;31:449-54.
22. Augustin H, Fritz GA, Ehammer T, Auprich M, Pummer K. Accuracy of 3-Tesla magnetic resonance imaging for the staging of prostate cancer in comparison to the Partin tables. Acta Radiol 2009;50:562-9.
23. Hegde JV, Chen MH, Mulkern RV, Fennessy FM, D'Amico AV, Tempany CM. Preoperative 3-Tesla multiparametric endorectal magnetic resonance imaging findings and the odds of upgrading and upstaging at radical prostatectomy in men with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 2013;85:e101-7.
24. Chandra RV, Heinze S, Dowling R, Shadbolt C, Costello A, Pedersen J. Endorectal magnetic resonance imaging staging of prostate cancer. ANZ J Surg 2007;77:860-5.
25. Tan CH, Wei W, Johnson V, Kundra V. Diffusion-weighted MRI in the detection of prostate cancer: meta-analysis. AJR Am J Roentgenol 2012;199:822-9.
26. Mazaheri Y, Shukla-Dave A, Hricak H, Fine SW, Zhang J, Inurrigarro G, et al. Prostate cancer: identification with combined diffusion-weighted MR imaging and 3D 1H MR spectroscopic imaging--correlation with pathologic findings. Radiology 2008;246:480-8.
27. Turkbey B, Mani H, Shah V, Rastinehad AR, Bernardo M, Pohida T, et al. Multiparametric 3T prostate magnetic resonance imaging to detect cancer: histopathological correlation using prostatectomy specimens processed in customized magnetic resonance imaging based molds. J Urol 2011;186:1818-24.
28. Roethke MC, Lichy MP, Kniess M, Werner MK, Claussen CD, Stenzl A, et al. Accuracy of preoperative endorectal MRI in predicting extracapsular extension and influence on neurovascular bundle sparing in radical prostatectomy. World J Urol 2012 Jan 17 [Epub]. http://dx.doi.org/10.1007/s00345-012-0826-0.