# Experience improves staging accuracy of endorectal magnetic resonance imaging in prostate cancer: what is the learning curve?

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**Introduction:** Accurate clinical staging is critical in guiding treatment for patients with prostate adenocarcinoma. Endorectal magnetic resonance imaging (MRI) has been advocated to improve staging accuracy. In order to assess the learning curve for endorectal MRI interpretation, we compared two cohorts of patients with high-risk prostate who underwent endorectal MRI at a center with limited prior exposure to this imaging modality.

Materials and methods: Data for all patients who received a preoperative endorectal MRI followed by radical prostatectomy were prospectively collected. MRI was performed in patients with a high level of suspicion for extracapsular disease based on biopsy Gleason score, prostate specific antigen level, and digital rectal examination or if the Memorial Sloan-Kettering

## Introduction

Prostate cancer is the most common non-cutaneous malignancy found in male patients. In 2005, it was

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Address correspondence to Dr. John M. Corman, Department of Urology, Virginia Mason Medical Center, C7-URO, 1100 9th Avenue, Seattle, WA 98101 USA nomogram predicted a greater than 30% likelihood of extracapsular disease. The MRI results of our first 40 patients (group 1) and our second 40 patients (group 2) were compared to assess for improvement.

**Results:** Between October 2003 and September 2005, 80 patients underwent an endorectal MRI followed by radical prostatectomy. Mean age and median PSA were 58.4 (range 43 - 74) and 6.4 (range 0.048 -115.0), respectively. MRI findings were compared to the pathological findings from the radical prostatectomy specimen. Sensitivity, specificity, positive predictive value, and negative predictive value for detection of extracapsular disease were 31.3% versus 64.7%, 70.8% versus 78.3%, 41.7% versus 68.8%, and 60.7% versus 75.0%, respectively in group 1 versus group 2. The accuracy of MRI for detecting extracapsular extension was 52.5% in group 1 compared to 72.5% in group 2.

**Conclusions:** In our series, endorectal MRI initially did not accurately predict tumor stage in patients with prostatic adenocarcinoma. With further experience, the accuracy of MRI substantially improved and approached the results from centers with significant experience in the interpretation of endorectal prostate MRI.

Key Words: prostate cancer, endorectal, MRI, staging

estimated that approximately 230,090 new cases of prostate cancer would be diagnosed in the United States. It is further estimated that approximately 30,350 patients would succumb to this disease in 2005.<sup>1</sup> While many treatment options do exist, clinical staging is an important aspect that helps to guide the treatment algorithm. Prostate specific antigen (PSA), digital rectal examination (DRE), physical examination, laboratory values, nuclear bone scan, and computed tomography are just a few of the clinical parameters we currently use to obtain accurate staging. Preoperative Gleason score, percent of positive biopsy cores, and serum PSA have been shown to be independent predictors of extracapsular disease on multivariate analysis.<sup>2,3</sup> However, clinical assessment may understage prostate cancer patients in up to 40% of cases.<sup>4</sup>

Extracapsular extension (ECE) in radical prostatectomy specimens is an adverse prognostic feature and patients with ECE are significantly more likely to have disease recurrence than patients with organ confined adenocarcinoma. Patients are at a higher risk of having positive surgical margins if ECE is found on histologic evaluation, thus increasing the risk of biochemical recurrence following treatment.<sup>3,5,6</sup> Improvement in clinical staging may facilitate patient counseling regarding the likelihood of requiring multi-modality therapy.

To enhance the accuracy of clinical staging, endorectal MRI has been introduced as a pretreatment tool. Recent studies have shown that endorectal MRI findings may help identify ECE prior to definitive treatment. Similarly, endorectal MRI findings have been shown to be independent predictors for ECE on multivariate analysis.<sup>7</sup> Endorectal MRI has a reported accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 61%-91%, 13%-100%, 47%-100%, 38%-82%, and 57%-90%, respectively, for detecting extracapsular extension in various studies with diverse patient populations.<sup>7-23</sup>

We reviewed our experience with endorectal MRI in those patients who subsequently underwent radical prostatectomy. Our purpose was to assess the learning curve required in order for endorectal MRI to become a clinically useful test for the local staging of prostate cancer at an institution with limited prior experience.

## Materials and methods

We evaluated all patients in our institutional board review approved database who underwent radical retropubic prostatectomy after receiving an endorectal MRI to assess for the presence of ECE. All patients were diagnosed with adenocarcinoma of the prostate via transrectal ultrasound-guided biopsy of the prostate. All patients in this study presented with intermediate to high risk clinically localized prostate cancer or locally advanced prostate carcinoma. The specific indications for obtaining an endorectal MRI include a clinical stage T2b-3, serum PSA > 20 ng/ml, Gleason sum > 7 on biopsy, the presence of high volume disease, or a predicted likelihood of greater than 30% of ECE on pre-operative nomogram.

All exams were performed on Siemens 1.5 T Symphony MRI unit, using a combination of phasedarray pelvic surface coil and endorectal coil (Medrad, MRInnervu coil). The endorectal coil was inserted by a radiologist, and several scout images were obtained to verify adequate coil position. The endorectal coil was repositioned as needed. Imaging sequences were then performed, consisting of axial T2-weighted (TR 3360, TE 102) FSE, matching axial T1-weighted (TR 500, TE 14) FSE, sagittal and coronal T2-weighted FSE. Field of view 16 cm, slice thickness 4 mm with 10% gap, matrix 448 x 256, 2 averages. A large field of view (38 cm) coronal T1-weighted sequence was also performed to assess adenopathy and osseous structures in pelvis.

The images were interpreted prospectively by a consensus of at least two radiologists out of a group of four radiologists. Radiologists had access to clinical data including PSA levels and pathologic reports at time of interpretation. All radiologists had at least 5 years of experience in interpretation of general MRI. None of the radiologists had specialized training in genitourinary radiology with only one having had a limited experience reading endorectal MRI. All cases were evaluated for signs of extracapsular extension of tumor, including gross tumor protrusion through the prostatic capsule, deformity of contour of the capsule, irregular capsular thickening, asymmetry of neurovascular bundles, and loss of rectoprostatic angle. Tumor extension into seminal vesicles was also evaluated based on asymmetry of signal and/or size of seminal vesicles. Finally, cases were evaluated for enlarged (> 10 mm short axis diameter) lymph nodes and suspicious osseous lesions.

After radical prostatectomy, the specimen was fixed in formalin. The posterior margin and the rest of the specimen were marked in two different colors. The bladder neck, apex, and base were removed and sectioned separately. The remaining prostate was sectioned in 3 mm-5 mm slices from the apex to the base. Every other slice of the right side followed by every other slice on the left side was submitted. Transverse sections of the insertion of the SVs into the prostate were also performed. The presence of adenocarcinoma at the level or beyond the level of the prostatic capsule (including microscopic disease) was used as the definition of ECE. Accuracy was defined as a positive correlation between MRI findings and pathological findings for ECE, SV, or both.

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## Results

Endorectal MRI was performed in eighty consecutive patients at our institution who subsequently underwent radical retropubic prostatectomy between October 2003 and September 2005. Mean age and median PSA prior to surgery were 58.4 years (range 43 - 74) and 6.4 ng/ml (mean 10.13 ng/ml, range 0.48 - 115.0), respectively, Table 1. This PSA range extends to values higher than most radical prostatectomy series due to a subset of patients who were concurrently enrolled in a high-risk prostate cancer clinical trial. Preoperative clinical stage was T1c, T2, and T3 in 34 (42.5%), 37 (46.3%), and 9 (11.3%) patients, respectively. MRI was obtained in those patients who met the inclusion criteria as explained previously. Eighteen patients (22.5%) received neoadjuvant therapy with either chemotherapy (sixteen patients), hormones (one patient), or radiation therapy (one patient). Thirteen patients received two MRI studies prior to surgical resection in conjunction with their participation in a neoadjuvant chemotherapy trial. In patients who received two MRI studies, the study performed closest to the time of surgery was used for analysis.

Postoperative pathologic stage was T2, T3a, T3b, and T4 in 46 (57.5%), 20 (25.0%), 13 (16.3%), and 1 (1.3%) patients, respectively. Positive margins were noted in 27 (33.8%) patients. Pathologic stage for patients with positive margins was T2, T3, and T4 in 11/46 (23.9%), 15/33 (45.5%), and 1/1 (100%) patients, respectively. Four (5.0%) patients had positive lymph nodes on final pathological examination. Two of the patients with positive nodes had MRIs that were suspicious for ECE.

MRI findings were compared to the pathological

### TABLE 1. Patient demographics

Mean age (years)	<b>Group 1</b> 57.9 (46-72)	<b>Group 2</b> 59.0 (43-75)
Median PSA (ng/ml)	5.6 (1.15-26.1)	6.9 (0.48-115.0)
Neoadjuvant chemotherapy	6 (15%)	10 (25%)
Clinical stage: T1c T2 T3	21 (52.5%) 15 (37.5%) 4 (10.0%)	13 (32.5%) 22 (55.0%) 5 (12.5%)
Pathological stage: T2 T3a T3b T4	24 (60.0%) 7 (17.5%) 8 (20.0%) 1 (0.03%)	22 (55.0%) 13 (32.5%) 5 (12.5%) 0 (0.0%)

	E	CE	
	Group 1	Group 2	
Sensitivity	31.3%	64.7%	
Specificity	70.8%	78.3%	
PPV	41.7%	68.8%	
NPV	60.7%	75.0%	
Accuracy	52.5%	72.5%	
	SVI		
	Group 1	Group 2	
Sensitivity	22.2%	20.0%	
Specificity	100%	94.3%	
PPV	100%	33.3%	
NPV	81.6%	89.2%	
Accuracy	80.0%	85.0%	
ECE = extracaps	ular extension; SV	I = seminal vesicle	
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involvement; PPV = positive predictive value; NPV = negative predictive value

findings after prostatectomy, Table 2. Preoperative clinical stage by MRI was T2, T3a, and T3b in 52 (65.0%), 24 (30.0%), and 4 (5.0%) patients, respectively. In regards to local tumor extent, MRI understaged 17 (21.3%) and overstaged 12 (15.0%) of patients. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detection of ECE were 31.3%, 70.8%, 41.7%, and 60.7%, respectively in group 1. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detection of ECE were 64.7%, 78.3%, 68.8%, and 75.0%, respectively in group 2. The accuracy of MRI in the detection of ECE was 52.5% in group 1 compared to 72.5% in group 2 (p=0.104). Overall accuracy of MRI in detecting both ECE and SV involvement improved from 45% in group 1 to 62.5% in group 2 (p = 0.116).

## Discussion

In the early 1990s, endorectal MRI was introduced as a clinical staging tool for patients with prostate adenocarcinoma. The preoperative assessment of ECE of prostate adenocarcinoma is a useful factor in guiding treatment selection for patients with high-risk prostate cancer. Patients with ECE are at increased risk for biochemical recurrence after prostatectomy and may require multi-modality therapy.<sup>24</sup> Differentiating between clinical stage T2 and T3 disease is of great importance before proceeding with treatment.

Endorectal MRI appears to be a useful preoperative staging tool at centers that have experience with this imaging modality and radiologists specialized in genitourinary imaging. Previous studies, however, have not delineated a time frame for gaining proficiency in interpretation of endorectal MRI. A recent study by Wang et al reviewed 344 patients who underwent endorectal MRI imaging and concluded that endorectal MRI result is an independent predictor of ECE on multivariate analysis.<sup>7</sup> Of the ten radiologists interpreting the studies, four had specialty training in genitourinary radiology with the remaining six having at least 6 years of experience of clinical MRI interpretation since fellowship. With respect to evaluating ECE in their study, endorectal MRI had a sensitivity, specificity, PPV, and NPV of 42.2%, 95.4%, 74.5%, and 83.8%, respectively. Nakashima et al reviewed the effectiveness of endorectal MRI in determining ECE in 95 patients. Each radiologist in this study had over 20 years of experience.<sup>14</sup> They reported a sensitivity, specificity, PPV, and NPV of 57.1%, 82.1%, 57.1%, and 82.1%, respectively. They also reported an accuracy rate of 74.7% in detecting ECE. Bernstein retrospectively reviewed 124 patients with clinical stage T1c prostate cancer who underwent endorectal MR prior to radical prostatectomy.<sup>12</sup> They found a PPV of 38.7%, NPV of 75.3% and an accuracy of 79%. Only 41.2% of these patients had a Gleason score of 7 or greater indicating many may have had lower risk disease than our cohort which could make comparisons unreliable. These same authors had previously reported on 445 patients with high-risk prostate cancer and reported an accuracy of 70% and 94% for endorectal MRI detection of ECE and SV invasion, respectively.<sup>11</sup> While our initial cohort evaluated with endorectal MRI was far inferior to these series, our subsequent forty patients revealed comparable results with an accuracy of 72.5% in detection of ECE.

The interpreting radiologists reviewed the first cohort of cases after surgical and pathological data had been obtained for final comparison. After this review the radiologists learned to rely more upon the coronal and sagital imaging planes for evaluation, particularly in assessing tumor extension from the base of the gland and into the seminal vesicles. In the initial cohort, in keeping with previously reported literature, we relied greatly upon images acquired in the axial plane. As part of the learning curve, in the second cohort, coronal and sagital plane images were utilized with greater emphasis.

SV involvement is a poor prognostic feature and places patients at a higher risk of biochemical

recurrence after radical prostatectomy. These patients have an increased risk of lymph node metastases and have a worse prognosis even in the presence of negative lymph nodes.<sup>25,26</sup> Actuarial 10-year PSA failure free survival rate was only 43% for patients with seminal vesicle involvement in a series of 955 patients from Johns Hopkins Hospital.<sup>27</sup> The preoperative clinical staging of SV involvement would likely alter treatment selection in high risk patients. In order to predict SV involvement, several authors have advocated the use of endorectal MRI for this purpose. Groups have reported accuracy rates of 81% to 95%.<sup>28</sup> In this study, endorectal MRI had an accuracy of 85.0% when assessing SV involvement during our more recent experience.

Timing is one of many factors influencing the reliability of endorectal MRI interpretation. Postbiopsy hemorrhage may interfere with the interpretation of MRI thereby decreasing accuracy. White et al found that performing MRI at least 21 days after prostate biopsy significantly improved staging accuracy.<sup>29</sup> When biopsies were performed within 21 days, there was a tendency to overstage the local extent of the tumor. Other authors have also investigated the optimal timing of MR imaging and recommended a time interval of 3 weeks after prostate biopsy.<sup>30</sup> In our series, only two patients had their MRI study within 3 weeks of their biopsy. MRI accurately predicted the local extent of the tumor in both these patients and so did not negatively impact our results.

The most difficult factor to control when comparing the results of prostate endorectal MRI is interobserver variability. Radiologists' level of experience is an important factor that may affect the accuracy of prostate MRI.<sup>31-33</sup> Allen et al reported the sensitivity of magnetic resonance imaging detection of ECE was 50% for general radiologists compared to 72% for a radiologist with specialized interest in prostate MRI.<sup>31</sup> Another study by Mullerad et al demonstrated superior results for endorectal MRI when comparing genitourinary specialized radiologists versus radiologists with experience in general body MR imaging but not genitourinary MRI.<sup>32</sup> For this reason, the applicability of results from large, tertiary referral centers to community medical centers is likely unreliable. Thus, the usefulness of endorectal MRI in the community setting is questionable.

For radiologists without specialized training in MR imaging of the prostate, the learning curve required to obtain results comparable to centers of excellence is unknown.

Experience improves staging accuracy of endorectal magnetic resonance imaging in prostate cancer: what is the learning curve?

None of our radiologists had specialty training in genitourinary radiology and none had an extensive experience reading endorectal MRIs prior to beginning our study. Our results, therefore, are more representative of a community hospital without radiologists specialized in genitourinary imaging. Initially, we found endorectal MRI to be poorly reliable compared to other reported series with an accuracy of only 52.5% for detection of ECE and 45.0% in accurately detecting both ECE and SV invasion together. We believed that the accuracy of endorectal MRI would improve with experience. After the initial forty patients, our results markedly improved and approached those of reported series from centers of excellence, which have determined endorectal MRI to be a useful preoperative staging tool.

We did not use MR spectroscopy in this study. Published series report improved results with MR spectroscopy as compared to endorectal MRI alone. In the study by Wang et al, MR spectroscopic imaging was performed in 62.8% of their patients, while 37.2% underwent endorectal MRI alone.<sup>7</sup> Although the authors concluded that MR spectroscopy did not result in a statistically significant difference in interpretation in image interpretation (p < 0.206), there appeared to be a trend toward improvement. Furthermore, studies have shown that MR spectroscopy particularly improves performance with less experienced radiologists which would make this technique particularly useful in the community setting.<sup>34</sup>

We recognize the limitations of this study which include a small sample size and the fact that although the radiologist team was blinded as to the ultimate histologic outcome, they did have access to preoperative clinical variables, a factor possibly contributing to bias.

## Conclusions

We evaluated endorectal MRI as a preoperative staging tool for patients with newly diagnosed prostate cancer at a center with limited experience with this imaging modality. Initially, we were unable to reproduce the same level of accuracy as other published studies. The reliability of endorectal MRI subsequently improved and was eventually comparable to other reported series following our initial forty studies. Endorectal MRI may be useful at medical centers without specialized radiologists experienced in genitourinary MRI after overcoming an initial learning curve.

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