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Local staging of prostate cancer: comparative accuracy of T2-weighted endorectal MR imaging and transrectal ultrasound

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Abstract

Objective—The objective of this study was to compare the accuracy of T2-weighted magnetic resonance (MR) imaging and transrectal ultrasound (TRUS) for staging of prostate cancer.

Material and methods—A total of 101 men with biopsy-proven prostate cancer undergoing both T2-weighted endorectal MR imaging and B-mode TRUS for local tumor staging prior to radical prostatectomy were retrospectively identified. Three MR readers rated the likelihood of locally advanced disease using a 5-point scale. An ultrasound reader performed the same rating. Staging accuracy was compared using receiver operating characteristic curves.

Results—Staging accuracy was not significantly different between MR imaging (A_z = 0.69–0.70) and TRUS (A_z = 0.81, P>.05).

Conclusions—T2-weighted MR imaging demonstrates comparable accuracy to B-mode TRUS for depicting locally invasive prostate cancer.

Keywords

MRI; Ultrasound; Staging; Prostate cancer; Genitourinary

1. Introduction

Based on estimates for 2010, prostate cancer remains the most common noncutaneous cancer in men [1]. Local staging of prostate cancer plays an important role in planning treatment and predicting prognosis. For example, patients with locally advanced prostate cancer, defined as the presence of extracapsular extension or seminal vesicle invasion, are over six times more likely to have biochemical recurrence after radical prostatectomy when compared to patients with organ-confined disease [2]. Similarly, 92% of patients with cancer confined to the gland remain free of disease progression after 10 years postradical prostatectomy, whereas only 71.4% and 37.4% of patients remain disease free with extracapsular extension or seminal vesicle invasion, respectively, [3]. Accordingly, patients with locally advanced prostate cancer are often offered other treatments, such as definitive radiotherapy and/or androgen deprivation therapy [4]. B-mode transrectal ultrasound and T2-weighted endorectal magnetic resonance (MR) imaging are the predominant imaging

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modalities for local staging of prostate cancer. An early multi-institutional trial published in 1990 demonstrated no significant difference in accuracy between body-coil-only MR imaging and transrectal ultrasound for local staging of prostate cancer [5], but this result is of questionable relevance to current practice, given the advances in imaging technologies over the last 20 years. Current prostate MR imaging is typically performed with high-resolution endorectal coils and more advanced pulse sequences. Our institution has performed several thousands of such high-resolution 1.5 Tesla (T) endorectal coil MR imaging for over 15 years using similar protocols and have maintained a comprehensive imaging and clinical database.

Transrectal ultrasound imaging has qualitatively improved with the development of higher frequency and more penetrating beams and better image-processing algorithms. Despite these advances and the importance of local staging to the management of this common malignancy, no recent large studies have reported a “head-to-head” comparison of these two modalities to our knowledge. Therefore, we undertook this study to revisit and compare the accuracy of endorectal MR imaging and transrectal ultrasound for the local staging of prostate cancer.

2. Materials and methods

2.1. Patients

This single-institution study was approved by our institutional Committee on Human Research with a waiver of informed consent and was compliant with the Health Insurance Portability and Accountability Act. Data from 2714 consecutives surgical prostate cancer patients were accrued prospectively in a urologic oncology database at our institution. Of these patients, we retrospectively identified 101 consecutive men with biopsy-proven prostate cancer who underwent endorectal MR imaging and transrectal ultrasound (within 180 days) at our institution over 12 years between May 1997 and April 2009 prior to radical prostatectomy (performed no more than 180 days after the last imaging study). All patients underwent endorectal MR imaging at least 6 weeks postbiopsy to prevent artifacts from postbiopsy hemorrhage. Patients who received potentially confounding neoadjuvant therapy prior to surgery were considered ineligible for inclusion. The mean patient age was 59 years (range, 42–75 years). The median serum prostatic specific antigen level was 6.9 ng/ml (range, 1.1–38.0 ng/ml). The median interval between endorectal MR imaging and transrectal ultrasound was 29 days, with 90% of patients having the studies done within 70 days (range, 0–115 days). Thirty-two patients had ultrasound done prior to MR imaging, 1 patient had both studies done on the same day, and 68 patients had MR imaging performed prior to ultrasound. The median interval between the last imaging study (endorectal MR imaging or transrectal ultrasound) and radical prostatectomy was 69 days, with 75% of patients having the procedure done within 100 days (range, 0–178 days).

2.2. MR imaging technique

MR imaging was performed with a 1.5-T scanner (Signa; GE Healthcare, Milwaukee, WI, USA). Images were acquired using a body coil for excitation and an inflatable balloon-covered endorectal coil (Medrad, Pittsburgh, PA, USA) combined with a pelvic phase-array coil for signal reception. After acquisition of sagittal scout images, axial fast spin-echo T2-weighted images were obtained from the seminal vesicles to the prostatic apex (repetition time (ms)/echo time (ms), 5,000/102; section thickness, 3 mm with no intersection gap; three signals acquired; field of view, 14 cm; acquisition matrix, 256 × 192; no phase wrap). Coronal and sagittal fast spin-echo T2-weighted images were then acquired with the same acquisition parameters, except for an echo time of 96 ms and a field of view of 16 cm. Images were analytically corrected for coil reception profiles with software (Prostate

Analytical Coil Correction; GE Healthcare). This protocol has been used at our institution for over 15 years.

2.3. Transrectal ultrasound technique

Transrectal ultrasound was performed with the B&K Medical Diagnostic Hawk System and variable frequency biplane transducer model 8808/8818 (B&K Medical, Herlev, Denmark), or Hitachi Medical Systems Hi Vision 5500 (Hitachi Medical Systems, Tokyo, Japan) and variable frequency end-fire transducer EUP-V53W or biplane transducer EUP-U533 by a single operator (K.S.). Grayscale scanning was performed at 7.5–9 and 5–6.0 MHz for larger glands to gain better penetration and to visualize the anterior gland. Any findings suspicious for extracapsular extension or seminal vesicle invasion by B-mode transrectal ultrasound were documented along with their location on a standardized form.

2.4. Image interpretation

Three independent radiologists with 3, 6, and 13 years of experience in the interpretation of prostate MR images, respectively, reviewed the MR studies on a picture archiving and communication system workstation (Impax; Agfa, Mortsel, Belgium). Each reader rated the likelihood of locally advanced disease (i.e., extracapsular extension and/or seminal vesicle invasion) on each side of the prostate on a 5-point scale (1 = *definitely absent*, 2 = *probably absent*, 3 = *indeterminate*, 4 = *probably present*, and 5 = *definitely present*). The MR imaging determination of extracapsular extension and seminal vesicle invasion was based on T2-weighted imaging and previously described criteria and subjective reader expertise. Previously reported signs of locally advanced disease include any one of the following: capsular bulging, asymmetry or involvement of the neurovascular bundle, obliteration of the rectoprostatic angle, and tumor extension into the seminal vesicle [6]. A single independent urologist with 26 years of experience in the interpretation of transrectal ultrasound images of the prostate performed the same 5-point scale rating for B-mode transrectal ultrasound images using still frame images and video clips he scanned. The likelihood of extracapsular extension by transrectal ultrasound was ranked and documented on a standardized form and report based on bulging, distortion, and irregularity of the prostatic capsule as previously described [7]. MR imaging readers knew that the patients had biopsy-proven prostate cancer but were unaware of histopathologic results or demographic information. The ultrasound reader was also aware of demographic information.

2.5. Histopathologic review

Specimens removed at radical prostatectomy were marked with ink and fixed overnight in 10% buffered formalin. Transverse step sections were obtained at 3- to 4-mm intervals in a plane perpendicular to the posterior prostatic wall. Paraffin sections were cut at 3 microns and stained with hematoxylin and eosin for preparation of slides. Histopathologic reports were generated that noted tumor location, grade, size, and local stage. In particular, the presence and laterality of extracapsular extension and/or seminal vesicle invasion were recorded.

2.6. Statistical analysis

The hemiprostate, rather than the prostate sextant, was used as the unit of analysis in this study because of the known limitations and anatomic registration errors inherent in sextant-based approaches [8,9]. MR imaging and transrectal ultrasound findings of locally advanced disease on each side of the prostate were compared to the reference standard of histopathologic findings on that side of the prostate. To account for the clustering effect related to the artificial division of the prostate (right and left side), we used generalized estimating equations. The performance of each technique and reader was described using

receiver operating characteristic curves. We used cluster resampled bias-corrected bootstrap confidence intervals to compare the areas under the receiver operating characteristic curves (A_z) [10]. Because we used three readers for MR imaging evaluation, we examined interreader agreement using the κ statistic derived using bootstrapping. The degree of observer agreement as indicated by the κ statistic was interpreted as follows: 0 to 0.2 = *slight agreement*, 0.21 to 0.4 = *fair agreement*, 0.41 to 0.6 = *moderate agreement*, 0.61 to 0.8 = *substantial agreement*, and 0.81 to 1 = *almost perfect agreement* [11]. All statistical calculations were performed using Stata 11 (College Station, TX, USA). For all statistical analyses, a probability value of less than .05 was considered significant.

3. Results

3.1. Histopathologic results

In the 101 men forming the study group, Gleason scores ranged from 5 to 10, with 76% (45/101) considered low-risk category (Gleason ≤ 6), 33.7% (34/101) intermediate-risk (Gleason = 7), and 21.8% (22/101) high-risk (Gleason ≥ 8). Twenty-three (22.7%) of 101 patients had locally advanced disease, consisting of 16 patients with unilateral extracapsular extension alone, 4 with seminal vesicle invasion alone, 1 with bilateral disease, and 3 with both extracapsular extension and seminal vesicle invasion. Of these three men, one had unilateral extracapsular extension and unilateral seminal vesicle invasion, one had unilateral extracapsular extension and bilateral seminal vesicle invasion, and one had bilateral extracapsular extension and seminal vesicle invasion.

3.2. Imaging results

Imaging interpretation results are detailed in Table 1. A_z values (and 95% confidence intervals) for the local staging accuracy by T2-weighted MR imaging for the three readers in the study were 0.69 (0.58–0.79), 0.70 (0.60–0.80), and 0.70 (0.59–0.72), respectively. The A_z value (and 95% confidence interval) for the local staging accuracy by B-mode transrectal ultrasound was 0.81 (0.72–0.90). The A_z value for transrectal ultrasound was not statistically different (P>.05) from any of the three values for T2-weighted MR imaging (Fig. 1). The three MR readers demonstrated moderate interobserver agreement with a combined reader κ value of 0.56 (95% confidence interval of 0.39–0.73, $p < .001$). Representative images depicting extracapsular extension interpreted as “definitely present” and “probably present” obtained from T2-weighted endorectal MR imaging and grayscale transrectal ultrasound are shown in Figs. 2 and 3, respectively. Fig. 4A and B illustrates the same cancer focus depicted on both transrectal ultrasound and MR imaging.

4. Discussion

Transrectal ultrasound remains the most common modality used for prostate cancer imaging. However, transrectal ultrasound is often used as a way to identify the prostate and guide systematic biopsies rather than as an imaging modality for local staging [12,13]. Arguably, this reflects the fact that transrectal ultrasound is usually performed by urologists rather than radiologists, and their experience and comfort level in evaluating images for extracapsular extension may be lower. Conversely, T2-weighted endorectal MR imaging is generally performed by a radiologist and has demonstrated repeated utility in tumor localization and prostate cancer staging [14–17]. Concerns regarding cost and variability related to reader experience may account for the low utilization of endorectal MR imaging in patients with prostate cancer. Although costs remain similar to other pelvic MR imaging examinations, our results demonstrate similar accuracy between readers with varying experience levels with moderate interobserver agreement ($\kappa = 0.56$). The relative similar accuracy may, at least partly, be explained by the progressive maturation in knowledge of radiologists when interpreting MR imaging studies of the prostate. Our results suggest that both T2-weighted

endorectal MR imaging and B-mode transrectal ultrasound are equivalently accurate in the local staging of patients with prostate cancer, with the caveat that the urologist interpreting the ultrasound is well versed in prostate image interpretation. From a practical perspective, this suggests that urologists should gain more experience and place greater effort into staging prostate cancer during transrectal ultrasound-guided diagnostic biopsy or refer such patients for staging by endorectal MR imaging after a positive biopsy. The rationale to refer such patients to MR imaging is not only because it offers at least equivalent staging accuracy, but also because MR imaging provides a multiparametric evaluation with depiction of metabolic, vascular, and molecular changes in prostate cancer provided by spectroscopic, perfusion, and diffusion-weighted sequences, respectively. Endorectal MR imaging also provides an opportunity for assessment of locoregional adenopathy or bone metastases that cannot be assessed by transrectal ultrasound. It should be noted that such added benefits were not assessed as part of our study as many of these sequences were not obtained in the older scans. However, the anatomic T2-weighted endorectal scan parameters were similar for all patients.

The findings in our study are consistent with three relatively older reports demonstrating that T2-weighted endorectal MR imaging and transrectal ultrasound have similar accuracy in local staging of prostate cancer [5,18,19]. However, our findings conflict with three other studies demonstrating higher accuracy for T2-weighted MR imaging [20–22]. Given that ultrasound is highly operator dependent, this discrepancy may, at least partly, be explained by the extensive 26-year experience of our transrectal ultrasound reader who likely increased the overall transrectal ultrasound accuracy in our study. Additionally, demographic data were often available for the ultrasound reader, whereas MR imaging readers were blinded to such information. Hence, our results likely represent a “best-case” scenario for transrectal ultrasound. Conversely, the similar accuracy and moderate interobserver agreement seen for the three MR readers, despite variable experience levels, suggest that T2-weighted MR imaging may be a more robust and reproducible modality for local staging of prostate cancer. Timing of imaging may have also contributed to discrepancy between results. In our study, the ultrasound images were obtained prior to biopsy, whereas the majority of MR images were conducted postbiopsy; hence, postbiopsy hemorrhage and/or scarring may have conceivably further complicated MR image interpretation. There are other potential explanations for the differences in reported results, including variability in magnet strength, MR pulse sequences, types of MR coils used, quality of ultrasound equipment, and statistical techniques. With respect to the latter, it should be noted that many older studies failed to address the interdependence between prostate segments by using generalized estimating equations to account for the clustering effect of dividing the same prostate into right and left sides or into sextants. In a broader context, there are few recent data on the relative utility of endorectal MR imaging versus transrectal ultrasound for prostate cancer evaluation outside of staging. We are aware that serial MR imaging changes are correlated with disease progression in patients choosing active surveillance for management, but no such correlation can be shown for serial transrectal ultrasound [12,23].

Our study has multiple limitations. It was a single-institution retrospective study, with the associated potential for bias. For example, referral of patients to MR imaging was not based on any fixed criteria, and it is conceivable that patients with grossly obvious locally advanced disease on transrectal ultrasound never underwent MR imaging or radical prostatectomy. However, even if our population was skewed by such selection factors to lower-risk disease, it would presumably have been equally confounding for both modalities since we only included patients who underwent both studies. Second, we had an insufficient number of cases of seminal vesicle invasion to conduct a separate analysis of endorectal MR imaging and transrectal ultrasound in predicting seminal vesicle invasion independent from

extracapsular extension. A larger sample size would have yielded a more detailed analysis of extracapsular extension versus seminal vesicle invasion and may have shown a statistically significant difference between endorectal MR imaging and transrectal ultrasound. Third, only a single ultrasound reader was available for transrectal ultrasound interpretation; hence, it was not possible to analyze transrectal ultrasound interreader variability. Fourth, as this was a retrospective study, we were unable to investigate multiparametric endorectal MR imaging, a more comprehensive study that would also include gadolinium-enhanced dynamic sequences, diffusion-weighted images, and MR spectroscopic imaging. However, we contend that although multiparametric MR imaging may help increase detection of lesions, T2-weighted anatomic imaging is the most important parameter used for evaluating extracapsular extension secondary to the limited spatial resolution of the other parameters. Similarly, newer ultrasound techniques such as microbubble contrast agent imaging and elastography were not investigated with transrectal ultrasound; albeit, their usefulness in prostate cancer has not yet been convincingly demonstrated in the literature. Finally, this study was conducted in a single institution, a highly specialized tertiary care center, and the results may not be generalizable to community practices, especially those with less experienced ultrasound interpreters.

Our findings suggest that B-mode ultrasound demonstrates similar accuracy for depicting locally invasive disease as compared to T2-weighted MR imaging and should be performed more rigorously when evaluating for extracapsular extension. However, it must be reiterated that the findings suggest a best-case scenario for transrectal ultrasound as a result of a highly experienced sonographic interpreter. Additional MR parameters, access to demographic information, and evaluation of un-biopsied “clean” prostates may have potentially yielded results favoring MR imaging. Additionally, critical information about local lymph node and osseous metastases is not evaluated by transrectal ultrasound. However, we feel that the above MR imaging limitations are common and often representative of standard clinical practice because of the typical sequence in which transrectal ultrasound imaging and MR imaging are performed. More emphasis on the initially obtained transrectal ultrasound images for locoregional cancer spread may obviate the need for more expensive MR imaging at experienced centers.

5. Conclusions

In conclusion, T2-weighted endorectal MR imaging is of comparable accuracy to B-mode transrectal ultrasound for depicting extracapsular and seminal vesicle extension of prostate cancer for experienced readers. Accordingly, at highly experienced centers, either test may be acceptable for demonstrating locally invasive disease in patients with prostate cancer.

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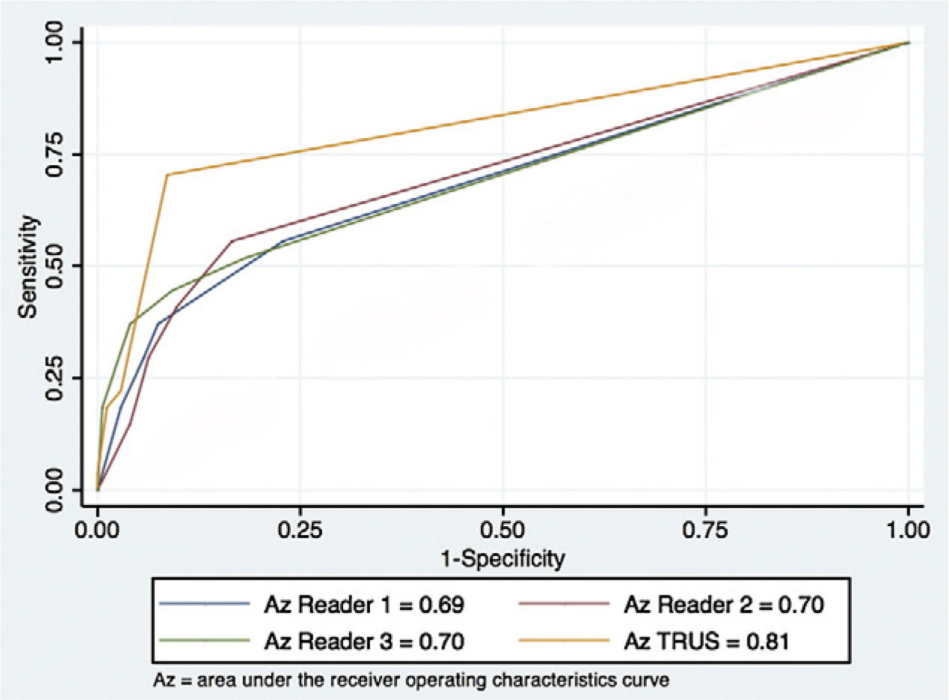

Fig. 1.

Receiver operating characteristic curves for MR imaging (Readers 1–3) and transrectal ultrasound for predicting extracapsular extension or seminal vesicle invasion (Reader 1: A_z = 0.69, Reader 2: A_z = 0.70, Reader 3: A_z = 0.70, transrectal ultrasound: A_z = 0.80; Readers 1–3: κ = 0.56).

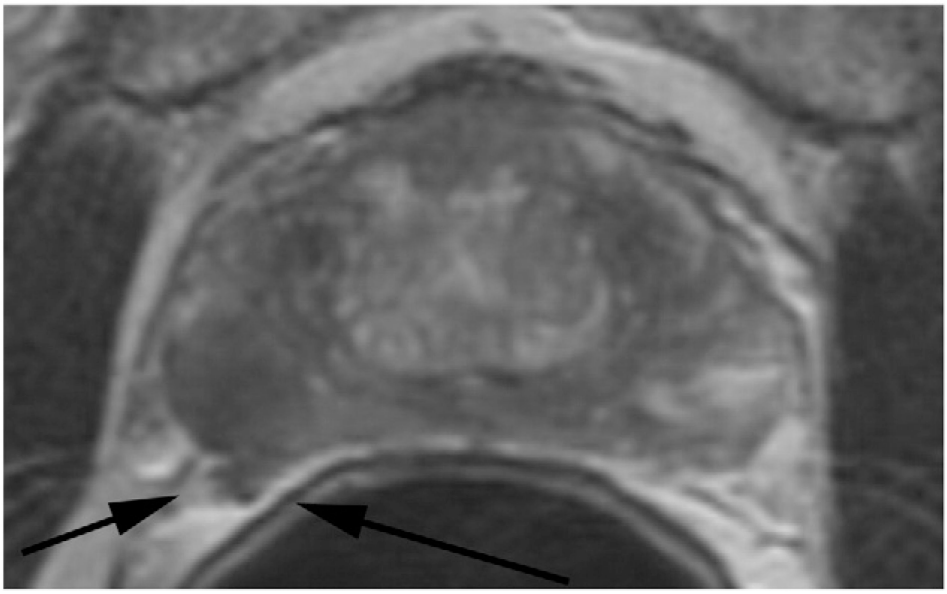

Fig. 2.
Fifty-six-year-old man with prostate cancer. Axial plane T2-weighted endorectal MR image depicting right peripheral zone hypointense lesion with involvement of the neurovascular bundle and obliteration of the rectoprostatic angle, interpreted as 5 (*definitely present*).

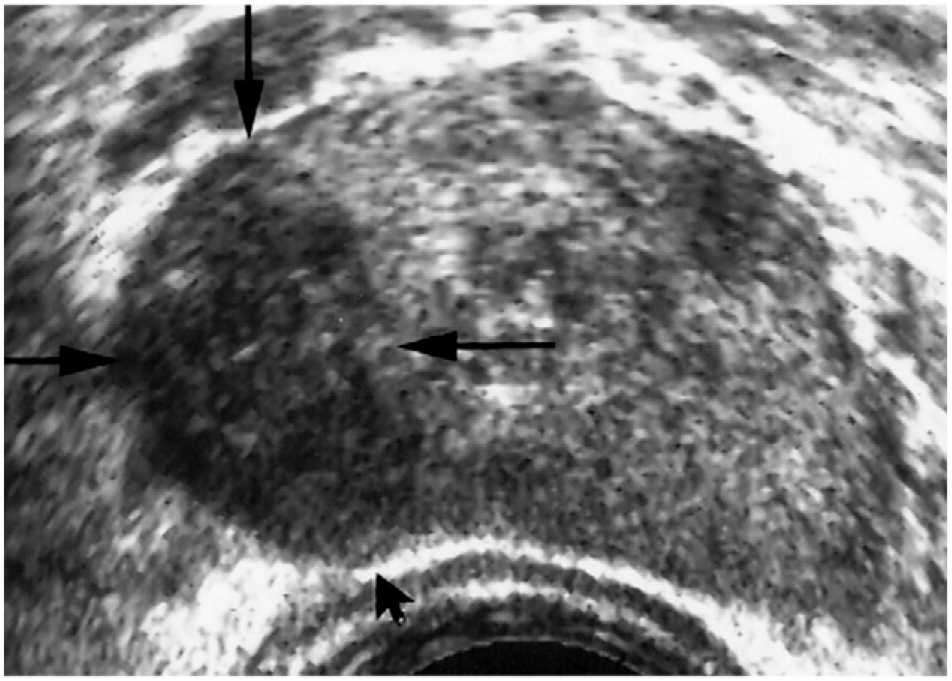

Fig. 3.
Sixty-two-year-old man with prostate cancer. Axial plane grayscale transrectal ultrasound image depicting right peripheral zone hypoechoic lesion demonstrating capsular bulge and irregularity, interpreted as 4 (*probably present*).

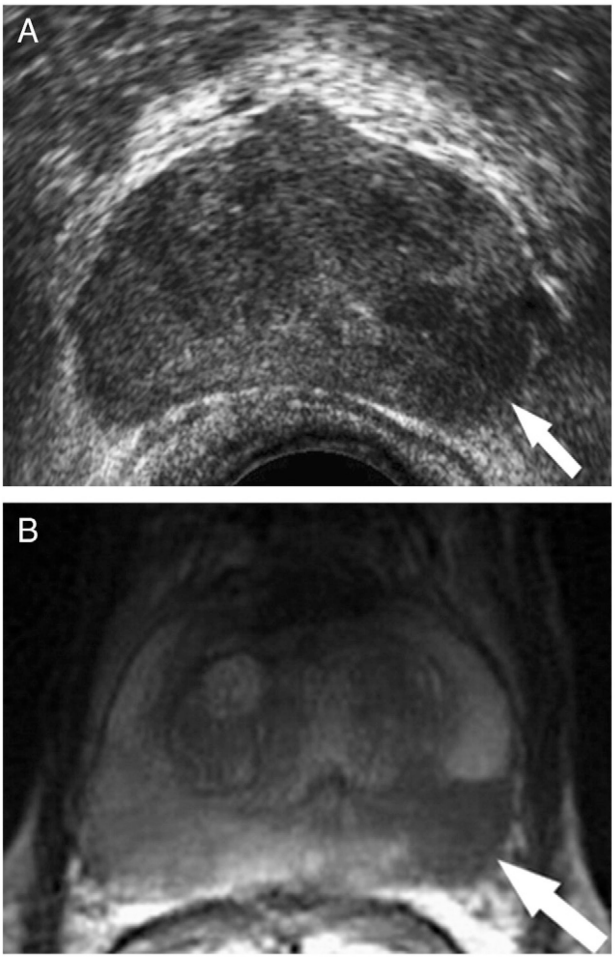

Fig. 4.
Fifty-nine-year-old man with prostate cancer. Left peripheral zone lesion demonstrating pericapsular bulge seen on both axial transrectal ultrasound (A) and axial T2-weighted MR imaging (B).

Table 1

Extracapsular extension and seminal vesicle invasion: results of imaging interpretation per reader

			Likelihood of disease based on imaging																			
			Absent				Probably absent				Indeterminate				Probably present				Present			
			R1	R2	R3	US	R1	R2	R3	US	R1	R2	R3	US	R1	R2	R3	US	R1	R2	R3	US
SVI	Right	Positive	3	4	3	5	0	0	0	1	0	2	1	0	2	0	2	0	1	0	0	0
		Negative	95	95	94	95	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	Left	Positive	1	2	1	3	1	0	1	1	0	0	0	0	0	0	0	0	2	2	2	0
		Negative	95	95	96	97	0	1	1	0	1	0	0	0	1	0	0	0	0	1	0	0
ECE	Right	Positive	5	6	4	3	2	0	0	4	1	0	1	0	0	3	3	1	1	0	1	1
		Negative	71	78	75	84	16	3	9	5	0	4	3	2	2	3	4	1	3	4	1	0
	Left	Positive	5	2	5	3	1	4	1	5	2	1	1	1	2	1	1	2	1	3	3	0
		Negative	68	74	74	80	12	8	8	7	3	4	6	1	4	1	2	2	3	3	0	0

SVI, seminal vesicle invasion; ECE, extracapsular extension; R1, MR imaging, reader 1; R2, MR imaging, reader 2; R3, MR imaging, reader 3; US, ultrasound images reader.