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Prostate Cancer Localization with Dynamic Contrast-enhanced MR Imaging and Proton MR Spectroscopic Imaging

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Purpose: To prospectively determine the accuracies of T2-weighted magnetic resonance (MR) imaging, dynamic contrast material–enhanced MR imaging, and quantitative three-dimensional (3D) proton MR spectroscopic imaging of the entire prostate for prostate cancer localization, with whole-mount histopathologic section findings as the reference standard.

Materials and Methods: This study was approved by the institutional review board, and informed consent was obtained from all patients. Thirty-four consecutive men with a mean age of 60 years and a mean prostate-specific antigen level of 8 ng/ml were examined. The median biopsy Gleason score was 6. T2-weighted MR imaging, dynamic contrast-enhanced MR imaging, and 3D MR spectroscopic imaging were performed, and on the basis of the image data, two readers with different levels of experience recorded the location of the suspicious peripheral zone and central gland tumor nodules on each of 14 standardized regions of interest (ROIs) in the prostate. The degree of diagnostic confidence for each ROI was recorded on a five-point scale. Localization accuracy and ROI-based receiver operating characteristic (ROC) curves were calculated.

Results: For both readers, areas under the ROC curve for T2-weighted MR, dynamic contrast-enhanced MR, and 3D MR spectroscopic imaging were 0.68, 0.91, and 0.80, respectively. Reader accuracy in tumor localization with dynamic contrast-enhanced imaging was significantly better than that with quantitative spectroscopic imaging (P < .01). Reader accuracy in tumor localization with both dynamic contrast-enhanced imaging and spectroscopic imaging was significantly better than that with T2-weighted imaging (P < .01).

Conclusion: Compared with use of T2-weighted MR imaging, use of dynamic contrast-enhanced MR imaging and 3D MR spectroscopic imaging facilitated significantly improved accuracy in prostate cancer localization.

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The sensitivity of systematic sextant ultrasonography (US)-guided biopsy for prostate cancer detection is low (39%–52%) because more than 40% of prostate cancer lesions are iso-echoic (1–4) and central gland tumors are difficult to detect. Use of magnetic resonance (MR) imaging may result in higher localization rates. At T2-weighted MR imaging, prostate cancer often appears as an area of low signal intensity in a bright normal peripheral zone. Detecting prostate cancer in the central gland is difficult because this area often contains benign prostatic hyperplasia, which has signal intensity similar to that of cancer. Previous studies involving the use of T2-weighted imaging revealed accuracies of 67%–72% in tumor localization (5,6).

Proton MR spectroscopic imaging can be used to detect and localize prostate cancer (7,8). Proton MR spectra of prostate cancer tissue reveal a reduced or depleted citrate level and an increased choline level compared with the levels of these substances in healthy or benign tissue. The addition of MR spectroscopic imaging has resulted in a 90% positive predictive value for the sextant localization of tumors in the peripheral zone of the prostate gland (6). Because cancer tissue can exist anywhere in the prostate, the use of a three-dimensional (3D) method to image the entire prostate is essential (9). The usefulness of MR spectroscopic imaging in detecting and localizing cancer in the transition zone of the prostate has been addressed only during the past 5 years (10).

Dynamic contrast material–enhanced MR imaging (hereafter dynamic imaging) is reported to be an effective tool in visualizing the pharmacokinetics of gadolinium uptake in the prostate (11–13). Dynamic imaging has facilitated accuracies in prostate cancer localization of up to 80% (17,18).

To our knowledge, there have been no reported studies in which investigators evaluated prostate cancer localization by using T2-weighted, dynamic, and MR spectroscopic imaging in the same patient for assessment of the peripheral, transitional, and central zones of the prostate. Thus, the purpose of our study was to prospectively determine the accuracies of T2-weighted imaging, dynamic imaging, and quantitative 3D proton MR spectroscopic imaging of the entire prostate for prostate cancer localization, with whole-mount histopathologic sections as the reference standard.

Materials and Methods

Patient Characteristics

From April 2002 up to June 2004, 34 consecutive men (mean age, 60 years; range, 50–69 years) who had biopsies proved and clinically localized prostate cancer and met our study criteria underwent endorectal coil MR examinations before undergoing radical prostatectomy. MR imaging was performed at least 3 weeks after the last transrectal US-guided sextant biopsy. Patients who were scheduled for radical prostatectomy within 6 weeks (range, 1–41 days; median, 10 days) after MR imaging were included in the study. Patient exclusion criteria were previous hormonal therapy, positive lymphadenectomy results, contraindications to MR imaging (eg, cardiac pacemakers, intracranial clips), and contraindications to endorectal coil insertion (eg, anorectal surgery, inflammatory bowel disease). Our study was approved by the institutional review board, and informed consent was obtained from all patients.

MR Image Acquisition Protocol

The MR images were obtained with a 1.5-T system (Sonata; Siemens Medical Systems, Erlangen, Germany) by using a combination of an endorectal coil (Medrad, Pittsburgh, Pa) and a pelvic phased-array coil. The endorectal coil was inserted and inflated with approximately 80 mL of air. In all patients, peristalsis was suppressed with an intramuscular injection of 1 mg of glucagon (Glucagen; Nordisk, Gentofte, Denmark) before the examination. The imaging protocol—after quick validation of the patient’s position and coil positioning with fast gradient-echo imaging—was as follows: First, multislice T2-weighted multiple-spin-echo images (in-plane spatial resolution of 0.55 × 0.55 mm, 3500–4400/132 [repetition time msec/echo time msec], 180° flip angle, 11–15 sections, 4-mm section thickness, echo train length of 15, 280-mm field of view, 240 × 312 matrix) were obtained in three orthogonal planes covering the prostate and the seminal vesicles.

Second, a spectroscopist with 4 years experience (T.W.J.S.) performed 3D MR spectroscopic imaging of the entire prostate by using a section-selected box drawn closely around the prostate and a point-resolved spectroscopic sequence (19). The nominal voxel size before apodization was 6 × 6 × 6 mm, the repetition time was 650 msec, and the

Advance in Knowledge

The accuracy of prostate cancer localization with dynamic contrast-enhanced MR imaging and MR spectroscopic imaging was significantly greater (P < .01) than that with T2-weighted MR imaging.

Abbreviations:

$A_p$ = area under ROC curve
$k_{ep}$ = rate constant between extracellular extravascular space and plasma space
$K_{trans}$ = volume transfer constant
$MPGS$ = mean pharmacokinetic score
$ROC$ = receiver operating characteristic
$ROI$ = region of interest
$3D$ = three-dimensional
$\psi_e$ = estimate of the extracellular volume

Author contributions:

Guarantor of integrity of entire study, J.J.F.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, J.J.F.; clinical studies, J.J.F., S.W.T-P.J.H., T.W.J.S., J.V., P.V., C.A.H., J.A.W., A.H., J.O.B.; statistical analysis, J.J.F., H.J.H., P.F.M.K.; and manuscript editing, all authors

Authors stated no financial relationship to disclose.
echo time was 120 msec. Hamming filter–weighted signal averaging was performed with five acquisitions in the center of k-space and resulted in a total measurement time of 12 minutes (9).

Third, 3D T1-weighted spoiled gradient-echo images (34/1.6, 14° flip angle, 10 transverse partitions on a 3D slab, 4-mm section thickness, 280-mm field of view, 77 × 256 matrix) were acquired during an intravenous bolus injection of a paramagnetic gadolinium chelate—0.1 mmol of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) per kilogram of body weight—which was administered with a power injector (Spectris; Medrad) at 2.5 mL/sec and followed by a 15-mL saline flush. With this sequence, the 3D volume with 10 partitions was acquired every 2 seconds for 120 seconds, with the same positioning and center as the transverse T2-weighted sequence covering the entire prostate. Before contrast material injection, the same transverse 3D T1-weighted gradient-echo sequence (with the exception of 800/1.6 and an 8° flip angle) was used to obtain proton-density images, with identical positioning to allow calculation of the relative gadolinium chelate concentration curves.

**Data Postprocessing**

An operator-independent standard postprocessing protocol was applied to the MR spectroscopic imaging data. These data were filtered with a Hamming filter in the three spatial dimensions and zero filled to a 16 × 16 × 16 matrix before Fourier transformation in the spatial dimensions. The residual water was removed from the spectral data (by fitting a low-frequency, exponentially decaying sine-cosine function to the time point moving average signal in the time domain), a Hamming filter was applied in the time domain, and Fourier transformation and phase correction were performed by using the Syngo software (Siemens Medical Systems) on the MR unit. Resonance areas were determined by using an automatic Gaussian curve fitting routine. The dynamic MR postprocessing procedure, which took 10 minutes per patient, was performed by an MR technologist with 4 years experience.

Functional dynamic imaging parameters were estimated as follows: Each MR signal enhancement–time curve was first fitted to a general exponential signal intensity model, as described previously (12). Consequently, the curve was reduced to a model with five parameters: baseline signal enhancement; start of signal enhancement, which defined the onset of the exponential curve; time to peak (TTP), which was the exponential constant; peak enhancement, which was the signal amplitude at which the exponential curve leveled off; and washout, defined as the slope of the late part of the exponential curve. The reduced signal enhancement–time curve was converted to a reduced tracer concentration–time curve (12,20) (with the tracer concentration in millimoles per milliliter) such that peak enhancement was effectively converted to gadolinium concentration. The reduced plasma concentration–time curve was estimated by using the reference tissue method (21). Deconvolution of the plasma profile and estimation of the pharmacokinetic parameters conformed to the theoretical derivations (22) but were implemented in the reduced signal space as $v_o = P_{tissue}/P_{plasma}$, $k_{ep} = 1/(TTP_{tissue} - TTP_{plasma})$, and $K_{trans} = v_o \cdot k_{ep}$, where $v_o$ is an estimate of the extracellular volume (expressed as a percentage), $K_{trans}$ is the volume transfer constant (1 per minute), $k_{ep}$ is the rate constant (1 per minute) between the extracellular extravascular space and the plasma space, and $P$ is the plateau of the gadolinium concentration. The subscript “tissue” refers to a measurement in the tissue being investigated, and the subscript “plasma” refers to the reference tissue plasma estimates. The reference tissue was automatically determined by selecting the set of voxels in the entire pelvic volume that had moderate signal enhancement.

Software developed in house was used to fit contrast curves robustly and convert the fitted curves in a physiologic compartment model by using a personal computer (Intel Pentium III [650-MHz]; Dell, Round Rock, Tex). The dynamic MR parameters were color coded and rendered semitransparently over T2-weighted images.

**Scoring and Evaluation of Data**

All T2-weighted, spectroscopic, and dynamic MR data sets were prospectively evaluated and scored without prior knowledge of the prostate-specific antigen level or biopsy results. Radiologists A (J.J.F.) and B (S.W.T.P.J.H.) independently interpreted and scored all three data sets. The two radiologists had different levels of experience in evaluating prostate MR images. Radiologist A had more experience (4 years) in prostate cancer MR imaging at the beginning of this study, having evaluated approximately 350 prostate imaging studies. Radiologist B had 2 years experience and had evaluated approximately 130 studies.

For tumor localization, the prostate was divided into the apex, middle, and base of the gland. The apex and the base were divided into quadrants, and the middle was divided into sextants. Thus, in each case, the prostate was divided into 14 regions of interest (ROIs). The readers graded their confidence that cancer was present in each of these ROIs on a five-point scale: Grade 1 indicated definitely no tumor present; 2, probably no tumor; 3, tumor possible; 4, tumor probable; and 5, tumor definitely present.

The image interpretation session consisted of three parts: First, by using the five-point scale, the two readers independently interpreted and scored the T2-weighted images in random patient case order in terms of a low-signal-intensity area. In the central gland, the criterion for cancer presence was an area of homogeneously low signal intensity with ill-defined margins. Benign prostatic hyperplasia was defined as round well-defined inhomogeneous lesions. In addition, nonenhanced T1-weighted images were evaluated to rule out false-positive findings caused by postbiopsy hemorrhage (23).

Second, during a different reading session with a different case order, held at least 3 weeks after the reading of the first data sets, all MR spectra in all in...
cluded patients were independently inter-
terpreted. The spectra in each ROI were interpreted and judged to be benign or malignant by using a five-point scale, essentially as described by Jung et al (24). To define the five categories of this scale (Table 1), we used the mean values (and standard deviations) of metabolite ratios from the initial results of a multicenter study (25) and the same acquisition method. In that study, the mean (± standard deviation) choline-creatine–to-citrate ratio for benign tissue in the patients was 0.36 ± 0.15. The benign prostate tissue could be separated into different tissues with the following reported mean choline-creatine–to-citrate ratios: 0.30 ± 0.14 for the benign peripheral zone, 0.38 ± 0.14 for the benign central gland (central and transitional zones combined), and 0.41 ± 0.17 for the benign periurethral zone. This five-point scale was adapted for scoring tissue in the peripheral zone and the central gland. Choline-to-creatine ratios also were assessed. The readers were allowed to judge MR spectra that showed substantial lipid contamination, poor spectral signal-to-noise ratio, or baseline misalignment to be unusable.

Third, during another reading session with a different case order, held at least 3 weeks after the reading of the previous data sets, maps of the following dynamic MR parameters were assessed: contrast material washout, \( v_c \), \( k_{ep} \), and \( K^*_{trans} \), as derived from the reduced tracer concentration–time curve. The parametric scale was subjectively evaluated. Each reader separately scored these parameters by using a five-point scale. On the basis of the presence, asymmetry, and degree of enhancement (ie, described as no to maximal enhancement), these four dynamic MR parameters were evaluated in random order. The presence of washout is highly indicative of prostate cancer (15). In cases of no enhancement, this parameter was assigned a score of 1 (no tumor present). Thus, the readers assigned four ratings for the dynamic MR images—one for each parameter. These ratings could not be regarded as independent; however, the different characteristics of the parameter images were reflected in these ratings. In addition, a mean pharmacokinetic score (MPKS) was derived by computing the mean of the pharmacokinetic parameter scores assigned during the observations. The readers were allowed to deem dynamic MR parameter images as unusable if the patient moved during MR imaging and thus caused severe motion artifacts or if the parameter score was not calculated correctly owing to technical problems. The MR spectroscopic and dynamic images were assessed in conjunction with the T2-weighted images.

**Histopathologic Analysis**

All radical prostatectomies were performed by one of three oncologic urologists, including one author (J.A.W., with 18 years experience) and two other urologists with 11 and 5 years experience, all of whom had knowledge of the MR imaging results. The prostatectomy specimens were fixed overnight in 10% neutral buffered formaldehyde and coated with India ink. The seminal vesicles were separated from the prostate and examined separately. Axial whole-mount step specimens were cut into 4-mm sections in a plane parallel to the transverse T2-weighted imaging plane. All sections were routinely embedded in paraffin. Tissue sections of 5 μm were prepared and stained with hematoxylin-eosin. The presence and extent of cancer were outlined on the glass slide cover by an experienced genitourinary pathologist (C.A.H.) who had 13 years experience and was blinded to the MR imaging results. The prostatectomy specimens were staged according to the 1997 TNM classification system (26). The volumes of all independent cancers were calculated (by C.A.H.) as the sum of the surface areas of a given cancer multiplied by the section thickness. Volumes were expressed in cubic centimeters.

### Table 1

<table>
<thead>
<tr>
<th>Malignancy Score and Score Definition</th>
<th>Peripheral Zone</th>
<th>Central Gland</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Definitely benign tissue</td>
<td>≤0.44</td>
<td>≤0.52</td>
</tr>
<tr>
<td>2: Probably benign tissue*</td>
<td>&gt;0.44–0.58</td>
<td>&gt;0.52–0.66</td>
</tr>
<tr>
<td>3: Possibly malignant tissue*</td>
<td>&gt;0.58–0.72</td>
<td>&gt;0.66–0.80</td>
</tr>
<tr>
<td>4: Probably malignant tissue*</td>
<td>&gt;0.72–0.86</td>
<td>&gt;0.80–0.94</td>
</tr>
<tr>
<td>5: Definitely malignant tissue</td>
<td>&gt;0.86</td>
<td>&gt;0.94</td>
</tr>
</tbody>
</table>

Source.—Reference 25.

* Data are choline-creatine-to-citrate ratio ranges.

**Data Analyses**

The two radiologists in consensus compared the ROIs with the histopathologic specimens 1 month after evaluating the image data. The T2-weighted MR images were aligned with the whole-mount sections. The morphologies of the central gland and peripheral zone, apex, and base of the prostate; cysts; calcifications; and urethra were used as landmarks. Aligning MR images and whole-mount sections is considered difficult (17). Although to our knowledge no literature on this process is available, we were confident of being within an accuracy of 8 mm (two image sections). An ROI detected with MR imaging was considered to be true-positive when the imaging results correlated with the conclusive histopathologic findings, as mentioned earlier. An ROI was considered to be positive if cancer was present. To allow for reasonable differences in registration and morphology between the evaluated imaging and histopathologic findings, the histopathologically and imaging-detected tumors were considered to be of comparable sizes if the maximum transverse diameter measured at...
MR imaging was within 50%–150% of the maximum transverse diameter measured at histopathology (27). All other nodules detected at MR imaging were considered to be false-positive.

Statistical Analyses
For statistical analysis, the sensitivity, specificity, positive and negative predictive values, and overall accuracy in the localization of prostate cancer were calculated by dichotomizing the readings. Scores of 3–5 were considered to indicate the presence of prostate cancer. The T2-weighted, spectroscopic, and dynamic MR results were compared by using the McNemar test. The analysis was repeated for nodules with a histopathologic volume of 0.5 cm³ or greater, because tumors with volumes of less than 0.5 cm³ are considered to be less relevant clinically (28,29).

Receiver operating characteristic (ROC) curves comprehensively summarize the performance of multiple modalities at different operating levels. A summary measure of the ROC curve is the area under the curve (AUC), for which statistical tests have been developed for ROC analyses. In ROI-ROC analysis, ROI sampling is accounted for and multiple modalities and readers can be compared by using bootstrapping (30,31). ROI-ROC analysis has been used in the process for premarket approval of a lung computed tomography computer-aided diagnosis study conducted by the Food and Drug Administration (premarket approval P030012, July 8, 2004) and recently in the sextant localization of local prostate cancer recurrence (32).

All P values reported were derived at two-sided tests; P < .05 was considered to indicate statistical significance. Statistical analyses were performed by using R language, version 2.1.0 (33), and SPSS, version 12, software (SPSS, Chicago, Ill).

Results
No patients were excluded (Fig 1) (34). Table 2 provides a summary of patient characteristics and histopathologic findings. A total of 476 ROIs (34 patients times 14 ROIs) were evaluated with each imaging technique. A total of 71 prostate cancer nodules were observed. Forty-nine (69%) of these tumors were observed in the peripheral zone, and 22 (31%) were observed in the central gland.

T2-weighted, MR Spectroscopic, and Dynamic Imaging
A total of 112 histopathologic sections contained cancer. The overall accuracies of T2-weighted imaging in localizing prostate cancer (Fig 2) were 69% (328 of 476 ROIs) and 67% (317 of 476 ROIs) for readers A and B, respectively, with no significant differences between the readers. When small (< 0.5 cm³) tumors were excluded, localization accuracy increased from 69% and 67% to 71% and 69% for the readers (Table 3); however, the difference was not significant.

At MR spectroscopic imaging, the two readers deemed 86 and 116 of the 476 ROIs to be unusable and excluded from further analyses. Ninety-eight corresponding histopathologic sections contained cancer. The localization accuracies of MR spectroscopic imaging (Fig 2) of the peripheral zone and central gland were 76% (150 of 196 ROIs) and 82% (155 of 188 ROIs), respectively, for reader A and 75% (144 of 192 ROIs) and 83% (145 of 174 ROIs), respectively, for reader B. For both readers, the localization accuracy of MR spectroscopic imaging was significantly increased (P < .05) compared with that of T2-weighted imaging. The localization accuracy increased from an average of 79% to 85% (reader A) and 82% (reader B) for localization of tumors with volumes of 0.5 cm³ or greater (Table 3); however, the difference was not significant.

At dynamic imaging, the two readers deemed 14 and 76 of the 476 ROIs to be unusable and excluded from further analyses. For readers A and B, respectively, 111 and 106 histopathologic sections were positive for tumor. Reading the dynamic images in conjunction with the T2-weighted images resulted in accuracies of 81%–91% (Table 3) for the localization of tumors with volumes of 0.5 cm³ or greater (34).
of 0.5 cm³ or greater. For both readers, diagnostic performance in the localization of tumors with volumes of 0.5 cm³ or greater was significantly increased ($P < .05$) compared with that of T2-weighted imaging. For both readers, $v_e$ had the highest accuracy for tumor localization (Fig 2) and washout had the highest specificity.

**Comparison of MR Imaging Approaches**

The two readers’ data were pooled because their results were consistent. The presented ROI-ROC curves are based on these pooled data. Differences in performance of the individual dynamic imaging parameters and the MPKS are presented in Figure 3. The MPKS performed significantly better ($P < .01$) than the best ranking dynamic MR parameter, $v_e$, and thus better than all of

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**Figure 2**

(a) Transverse T2-weighted multiple-spin-echo image (4200/132) of prostate. (b–d) Pharmacokinetic maps of calculated $K_{trans}$ (b), $k_p$ (c), and washout (d), overlaid on T2-weighted image. (e) Overlay of volume of interest, MR spectroscopic matrix, and spectra on T2-weighted image, with spectra of eight voxels outlined in detail (right). Voxels in inset (right) show markedly reduced citrate (Ci) signal and increased choline-creatine (Cho/Cr)-to-citrate ratio in central gland of prostate (red box). Cho = choline. (f) Whole-mount histopathologic section at corresponding level shows tumor (T, outlined in blue) occupying almost entire left prostate lobe, including central gland. The tumor can be identified on both pharmacokinetic (b–d, circled in red) and spectroscopic (e, voxels with deviating metabolite ratios, in red box) maps.
the dynamic MR parameters individually. $K_{\text{trans}}$ and $v_e$ performed significantly better than washout ($P < .01$). Comparisons of these parameters at per-ROI analysis versus those at per-patient analysis revealed only minor nonsignificant differences.

Differences in performance among T2-weighted imaging, MR spectroscopic imaging, the MPKS, and the MPK$S$ (ie, dynamic imaging) and MR spectroscopic imaging combined for prostate cancer localization in the peripheral zone and the central gland are presented in Figure 4. The MPKS performed significantly better than quantitative MR spectroscopic imaging ($P < .01$). Both the MPKS and spectroscopic imaging performed significantly better than T2-weighted imaging ($P < .01$). Again, comparisons of per-ROI and per-patient analysis results revealed only minor differences.

**Discussion**

Our study results demonstrate that using dynamic MR imaging or MR spectroscopic imaging to localize prostate cancer, as compared with using T2-weighted MR imaging, facilitates significantly improved accuracy.

Scheidler et al (6) observed the potential usefulness of combined morphologic and metabolic information for localizing prostate cancer at MR imaging in clinical practice. An accuracy of 88% was achieved for tumor lateralization (right or left prostatic lobe). In their study, assessment was focused on the peripheral zone. However, in our study, a 3D MR spectroscopic technique was used (9) to image the entire prostate. Besides the peripheral zone, the transition and central zones were included in our analysis. Receipt of MR signals from the central and transition zones is limited when an endorectal coil with a limited diameter is used. The signal intensity decreases in the ventral part of the prostate (ie, central and transitional zones) as a result of the distance from the coil conductors. In our study, 69% of the prostate tumor nodules were located in the peripheral zone. This is in concordance with the 65%–74% of nodules in the peripheral zone reported in the literature (35,36). Thus, 31% of the prostate cancer nodules would have been missed if we had focused on the peripheral zone only.

In our study, the localization accuracies of MR spectroscopic imaging, 82% and 85%, were within the range of previously reported accuracies: 67%–88% (6,24,37,38). Our results were obtained by using a quantitative 14-ROI approach. However, in the other studies, only the peripheral zone was evaluated and a sextant approach was used. Jung

**Table 3**

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PPV</th>
<th>NPV</th>
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<tr>
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<td>67 (75/112)</td>
<td>73 (264/364)</td>
<td>71 (339/476)</td>
<td>43 (75/175)</td>
<td>88 (264/301)</td>
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<td>Reader B</td>
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<td>90 (401/448)</td>
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<td>91 (401/440)</td>
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<td>$v_e$</td>
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<td>98 (310/315)</td>
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<td>96 (297/308)</td>
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<td>87 (403/462)</td>
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<td>85 (94/111)</td>
<td>80 (282/351)</td>
<td>81 (376/462)</td>
<td>58 (94/163)</td>
<td>80 (282/351)</td>
</tr>
</tbody>
</table>

Note.—Data are results for localization of tumors with volume of 0.5 cm$^3$ or greater, expressed as percentages, with the numbers of ROIs used to calculate the percentages in parentheses. NPV = negative predictive value, PPV = positive predictive value.
et al (24) used a cutoff score of 4 or higher on a five-point scale to evaluate a standardized prostate MR spectroscopic imaging system with additional criteria. We focused on the accuracy of each technique separately for localization in the entire prostate. Although we used a cutoff score of 3 or higher on the same five-point scale, specificities of 84% and 87% were achieved. These findings and those of Jung et al (24) suggest that reading 3D MR spectroscopic images of the entire prostate in particular is valuable for achieving high specificity.

The dynamic MR parameter data show that individual pharmacokinetic parameters do not differ significantly in localization performance. The MPKS performs significantly better than individual dynamic MR parameters, MR spectroscopic imaging, and T2-weighted imaging. The fact that the MPKS outperforms individual dynamic MR parameters means that each dynamic MR parameter yields independent diagnostic information. The MPKS is a simple diagnostic parameter that can be readily applied. The P values derived at patient-based analysis hardly differed from those derived at ROI-based analysis. This can be explained by a low intrapatient correlation between the ROIs. For both readers, washout had a specificity of 96% for the localization of tumors with volumes of 0.5 cm$^3$ or greater. This result is concurrent with the findings of Engelbrecht et al (15).

We studied the location and extent of the cancers, which are important for treatment and diagnostic reasons. When the location is assessed, standard ROC analysis techniques cannot be used. Several alternative free-response ROC analysis techniques are being developed to test for differences in modalities and/or readers (39). In response to criticisms that alternative free-response ROC analysis involves unrealistic assumptions, the jackknife alternative free-response ROC technique emerged (40,41). In ROI-ROC analysis, each ROI is evaluated by each reader with each modality (31). ROI-ROC analyses that enable multiple modalities and readers to be compared can be performed by using bootstrapping (30). The search for the most statistically powerful ROC analysis that includes assessment of the location and local extent of cancer is the subject of investigation (42).

Postbiopsy hemorrhage is known to degrade T2-weighted images and the accuracy of prostate cancer evaluation (23). T1-weighted images can be used to detect areas of such biopsy artifacts. In our study, MR imaging was performed at least 3 weeks after the last US-guided biopsy. Because the hemorrhage may not be completely absorbed after this period, it is difficult to differentiate biopsy-related low signal intensity from tumor on T2-weighted images, and false-positive findings may be introduced. In our study, at least one of six biopsies was positive. Patients with postbiopsy artifacts were not excluded because this group is seen in daily practice.

As expected, excluding small (<0.5 cm$^3$) tumors from the analysis resulted in increased localization accuracy. The resulting accuracies, however, were not significantly different from those achieved at all the tumors. Because estimation of larger tumor volumes is more accurate (37), it is assumed that the localization of large tumors will be improved. In our study, the mean tumor volume at histopathology was 0.98 cm$^3$ per patient. This is low compared with the volumes reported in previous studies (1.24–2.90 cm$^3$) (37,43).

In our study, two functional MR imaging techniques were evaluated. Our evaluation revealed several differences between the two techniques. The MR spectroscopic imaging spectra were analyzed by using a quantitative approach, which was basically independent of prior knowledge regarding the presence of cancer in the prostate, and T2-weighted image findings, which were used as background to the metabolic information. The dynamic imaging data, with T2-weighted image findings as background, were read subjectively. This method was chosen because in the literature, different approaches have been used to analyze dynamic imaging data and absolute values of dynamic MR parameters may vary among patients (15,44). The precise clinical value of quantitative analysis of dynamic MR parameters will have to be evaluated further in the future. For these reasons, MR spectroscopic imaging can be used to detect and localize prostate cancer, whereas dynamic imaging can be used to localize tumors in patients with proved prostate cancer. The larger sizes of MR spectra voxels compared with the
sizes of parametric dynamic image voxels may have resulted in MR spectroscopic imaging having a lower localization accuracy than dynamic imaging of small tumors in our study.

Our study had several limitations, including a small number of patients. Nevertheless, significant results were obtained at dynamic and MR spectroscopic imaging localization of prostate cancer. Two radiologists compared the tumor locations with the histopathologic data after reading the images, and this may have introduced information bias. However, the comparisons were performed 1 month after all readings. Another limitation was the relatively large number of MR spectra that were deemed unusable by the readers—especially the less experienced one. Use of a more automated approach based on objective criteria for spectral quality may improve such situations. Furthermore, our experience with MR spectroscopic imaging increased during the study and thereby resulted in improved quality of the spectra and reduced examination time; however, these factors were not evaluated in detail. MR imaging was performed after prostate biopsy, with at least 3 weeks between the two procedures. This factor may have introduced spectral degradation (45). As yet, we have not evaluated the possible relationships between the aggressiveness of the prostate cancer observed in the histopathologic specimens and the MR spectroscopic and dynamic imaging parameters.

We believe the clinical implications of improved prostate cancer localization with dynamic and MR spectroscopic imaging apply (a) for patients with increasing prostate-specific antigen levels and negative image-guided biopsy (for suspicious lesions) results; (b) for evaluation of tumor location and of the distance to the neurovascular bundle and the prostate capsule to determine if nerve-sparing surgery is possible—especially in laparoscopic procedures where there is no tactile information; and (c) for planning of intensity-modulated radiation therapy (46), which requires exact localization of the prostate cancer to administer an extra boost of radiation in addition to the normal dose.

In conclusion, our study data indicate that dynamic MR imaging and MR spectroscopic imaging of the entire prostate are significantly more accurate than T2-weighted MR imaging for prostate cancer localization. Our results suggest that if these advanced techniques are included in the MR imaging protocol, the localization of prostate cancer in patients will improve.

References


