Magnetic resonance imaging predictors of extracapsular extension of prostate cancer: Do they accurately reflect pT3 staging?

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Purpose

The purpose of study was to retrospectively investigate whether the MR imaging features could help predict ECE, volume and stage of prostate cancer (pT3 stage) with histopathologic findings as reference.

Methods and Materials

This article relies on images generated at The Radiology Department in Taunton and Somerset Hospital, NHS Trust, based in Taunton, United Kingdom. It is a modern 764 bedded general hospital. It provides acute and community services to a population of approximately 330,000, living in the west side of the country.

This is a retrospective study. Between December 2004 and September 2006, medical records of 22 patients were enrolled in this study if they met the following criteria: (a) specimens obtained with transrectal ultrasonography (US)-guided sextant biopsy were available for review and suspicious of ECE. (b) no radiation, chemo-, or hormone therapy prior to surgery and (c) complete transverse T1-weighted and T2-weighted MR images were retrievable for review.

MR imaging was performed with a 1.5 Tesla MRI scanner. Fast spin-echo Axial, transverse and coronal T2-Weighted images were obtained with the following parameters: TR 4000-4500 ms; TE 85-90ms, 3-mm section thickness and no intersection gap, 14-cm field of view, 256 x 192 matrix from below the prostatic apex to above the seminal vesicles. Spin-echo T1-Weighted images were obtained with the following parameters: TR/TE 600-700/10-20ms; 4-mm slice thickness; 1-mm intersection gap; 256 x192 matrix; and FOV 14cm from below the prostatic apex to the level of the aortic bifurcation.

MRI criteria

A focal hypointense mass in the peripheral zone on T2-weighted MR images without corresponding hyperintense signal on T1-weighted MR images was considered to represent tumor.

The diagnosis of ECE based on MR imaging features described in previous literature [11], findings included at least one of the following:

- Low signal intensity in the base of the prostate.
- Extension into the periprostatic fat contiguous with low-signal-intensity tumor in the gland.

- Broad contact with the capsule (>12 mm)

- Irregular capsular bulge.

- Obliteration of the rectoprostatic angle.

- Asymmetry or involvement of the neurovascular bundle.

- Focal low signal intensity in one or both sides of seminal vesicle.

On the basis of these findings, the likelihood of ECE of prostate cancer for the right and left prostatic lobes was estimated. These criteria were studied in the retrieved scans and correlated with the results from the final pathologic report following surgery. Correlation was done according to TNM staging; (one lobe (stage T3a), two lobes (T3b) or seminal vesicle invasion (T3c)). (Table 1)

**Table 1. Tumor Staging Categories based on data on TNM stage in the 1997 publication of the American Joint Committee on Cancer [12].**

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor is clinically unapparent, not palpable, or not visible with imaging.</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor is confined within prostate.</td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor involves one lobe.</td>
</tr>
<tr>
<td>T2b</td>
<td>Tumor involves both lobes.</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor extends through prostatic capsule or seminal vesicles.</td>
</tr>
<tr>
<td>T3a</td>
<td>Tumor has unilateral ECE.</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor has bilateral ECE.</td>
</tr>
<tr>
<td>T3c</td>
<td>Tumor invades seminal vesicles.</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades other structures, as urinary bladder, internal sphincter, and rectal wall.</td>
</tr>
</tbody>
</table>

**Seminal vesicle invasion**

MR images were evaluated for seminal vesicle invasion (SVI). The features included lack of preservation of normal grapelike architecture of the seminal vesicle on T2-weighted
images, focal or diffuse low signal intensity within the seminal vesicle or obliteration of the angle between the prostate and seminal vesicle on sagittal MR images.

**Tumor volume**

The area that was suspected of being tumor was outlined on T2-weighted images by using a picture archiving communication system workstation free-form region-of-interest tool. The area was multiplied by the section thickness to calculate the volume for that section. The volumes for all sections were added to calculate the entire tumor volume.

Correlation between measurements of tumor volume based on MR images and pathologic specimens for each of the 22 lesions was depicted.

**Statistical Analysis**

For statistical analysis, patient-by-patient evaluation was performed. A true-positive finding was considered in case of correlation of an imaging finding and estimated volume with histopathologic results with respect to the extraprostatic extension location (extracapsular extension, and seminal vesicle invasion). A false negative result was considered when MRI failed to depict pathologically proven ECE. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated. \( P < 0.05 \) was considered significant.

**Results**

The mean age of the 22 patients was 61 years (range, 33 to 81).

Among the medical records of 22 patients enrolled in this study, and according to the histological data, 12 had ECE (8 unilateral (stage T3a), one had bilateral ECE (stage T3b), and three had seminal vesicle invasion (stage T3c)). Ten patients had organ confined malignancy. (Table 2)

According to MR imaging features, 13 patients were reported as having extracapsular extension (10 with stage T3a, No cases with stage T3b and 3 with stage T3c), 9 patients had organ confined malignancy. MRI reported three False-positive cases. One false positive case displayed low signal intensity in the base of the prostate which extends to the periprostatic fat on T2 weighted images yet it was staged as stage T2b after surgery. Another false positive case occurred due to poor image quality because of motion artifact caused by bowel motion. The third case was interpreted as irregular capsular bulge with focal hypointensity yet the tumor was locally confined pathologically (Fig 4).
Table 2. Comparison of Pathologic and MR Imaging Findings

<table>
<thead>
<tr>
<th>Total</th>
<th>Pathologic Findings</th>
<th>MR findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Organ-confined</td>
<td>Extracapsular extension</td>
</tr>
<tr>
<td>13</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>22</td>
<td>10</td>
<td>12</td>
</tr>
</tbody>
</table>

Sensitivity for ECE = 10/12 (83%)
Specificity for ECE = 7/10 (70%)
Positive predictive value for ECE = 10/13 (76%)
Negative predictive value for ECE = 7/9 (77%)

Table 3. Percentage of Correct Staging, Understaging, and Overstaging in 22 Patients:

<table>
<thead>
<tr>
<th>MRI</th>
<th>Staging</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/22 (77%)</td>
<td>Correct</td>
</tr>
<tr>
<td>2/22 (9%)</td>
<td>Understaging</td>
</tr>
<tr>
<td>3/22 (13%)</td>
<td>Overstaging</td>
</tr>
</tbody>
</table>

Overall Accuracy = 17/22 (77%)

MRI correctly reported 10 cases of 12 cases of pathologically confirmed ECE and 7 cases of 10 organ confined disease with accuracy of 77%. Thus MRI down staged two cases, and over staged three cases. (Table 3)
In the evaluation of ECE MR achieved a sensitivity of 83%, specificity of 70%, positive predictive value of 76% and negative predictive value of 77% (Table 1).

**Table 4. Diagnostic criteria in Detecting Extraprostatic Extension with T2-weighted MR Images and pathologic correlation.**

<table>
<thead>
<tr>
<th>Pathological ECE</th>
<th>Number</th>
<th>MR findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(88%)8</td>
<td>9</td>
<td>Irregular capsular bulge.</td>
</tr>
<tr>
<td>5 (71%)</td>
<td>7</td>
<td>Broad contact with the capsule &gt;</td>
</tr>
<tr>
<td>1(33%)</td>
<td>3</td>
<td>Extension into the periprostatic fat</td>
</tr>
<tr>
<td>1 (33%)</td>
<td>3</td>
<td>Obliteration of the rectoprostatic angle.</td>
</tr>
<tr>
<td>(66%)2</td>
<td>3</td>
<td>Low signal intensity in the base of the prostate.</td>
</tr>
<tr>
<td>(50%)1</td>
<td>2</td>
<td>Asymmetry or involvement of the neurovascular bundle.</td>
</tr>
<tr>
<td>(100%) 3</td>
<td>3</td>
<td>Focal low signal intensity in one or both sides of seminal vesicle.</td>
</tr>
</tbody>
</table>

(Number in parenthesis is the diagnostic accuracy).

On the basis of MR imaging features of ECE, the most accurate diagnostic feature to detect ECE was the presence of focal low signal intensity in one or both sides of seminal vesicle (Fig 3). Irregular capsular bulge (Fig 4B), and Broad contact with the capsule (Fig 2 and Fig 6) also were significant predictors of ECE. \( P < 0.05 \) (Table 4)
Asymmetry or involvement of the neurovascular bundle displayed less diagnostic accuracy.

(Fig 2A)

Seminal vesicle invasion

MRI features that predicted SVI were low signal intensity within the seminal vesicle (Fig 3A, B), lack of preservation of the architecture of the seminal vesicle and obliteration of the angle between the prostate and seminal vesicle on sagittal MR images (Fig 3 C, D). MRI detected the three cases of pathologically proven seminal vesicle invasion.

Tumor Volume

MRI predicted tumor volumes were correlated with pathological volumes. The mean volume of 22 tumor lesions captured on MR imaging was 2.3 cc (range, 0.25-11.6 cc). The mean volume detected histopathologically was 1.5 cc (range, 0.4-7.2 cc). Of the 22 matched lesions, 10 were predominantly or entirely within the peripheral zone and twelve had an ECE on pathological examination. Measurements based on MR findings underestimated tumor volume in five of the twelve ECE cases (Fig 2), and overestimated volume in four of them (Fig 5) (Table 5). There was significant overlap in MR values between tumors larger than 3cm3 on pathologic examination and those smaller than 3cm3. (Fig 1).
Fig.: Figure 1. Scatter plot diagram shows correlation between volume determined by MR imaging and actual tumor volume but this correlation was not statistically significant (P = 0.07).

References: H. M. Hanafy; Radiodiagnosisi, Ain shams university, Cairo, EGYPT

Table 5. MRI estimated tumor volume for ECE with pathological correlation

<table>
<thead>
<tr>
<th>Histopathological Volume</th>
<th>MRI Estimated Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>Negative for ECE</td>
</tr>
<tr>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>22</td>
<td>10</td>
</tr>
</tbody>
</table>
Sensitivity = 58%; specificity = 54%; positive predictive value = 63%; negative predictive value = 66%

If 3 cm³ had been used as the volume threshold on pathologic specimens for diagnosing ECE in matched lesions, measurements based on MRI findings showed a 58% sensitivity; 54% specificity; 63% positive predictive value and 66% negative predictive value.

**Fig.**: Figure 2. Histologically confirmed stage T3b prostate carcinoma in a 66-year-old patient. (A & B) Transverse T1 MR images show a suspicious low-signal-intensity lesion (star) in the central and right peripheral zone in broad contact with capsule. Asymmetry of the neurovascular bundles (arrow) with hypointense tumor tissue at...
the right side. Staging was T3a. (C) Volume of lesion in peripheral region of prostate was underestimated by 43% on MR images. (D) Sagittal transrectal US scans show possible tumor in right posterior prostatic peripheral zone as fairly well-defined hypoechoic region (star) abutting the capsule.

References: H. M. Hanafy; Radiodiagnosisi, Ain shams university, Cairo, EGYPT
**Fig.** Figure 3. Biopsy-proved adenocarcinoma in a 61-year-old man. (A, B) T2-weighted axial and (E) sagittal MR images obtained at the level of the base of the prostate show a low-signal-intensity tumor (*) in the base of the left lobe. Seminal vesicles demonstrate low signal intensity, mass effect, and loss of normal architecture.
suggesting its invasion centrally (arrows). (C -F) T2-weighted sagittal images, angle and fat plane between the prostate and seminal vesicle is obliterated (curved arrow). Extreacapsular extension to seminal vesicles (stage T3c) was pathologically proven. **References:** H. M. Hanafy; Radiodiagnosis, Ain shams university, Cairo, EGYPT

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**Fig.** Figure 4. (A,B) Axial T1-weighted image obtained through the prostate demonstrates hypointensities in the prostate gland with left sided bulging (black arrows) towards the rectoprostatic angle. C. T1WI depicts a hyperintense pelvic lymph node (white arrows). D. Sagittal T2 WI displays the normal appearance of seminal vesicles (curved arrow). MRI suggested ECE of cancer prostate, but histopathological results was a locally confined stage T2a prostate cancer. **References:** H. M. Hanafy; Radiodiagnosisi, Ain shams university, Cairo, EGYPT
Fig.: Figure 5. Histopathologic stage pT3a prostate cancer in a 57-year old man. Fast spin-echo T2-weighted axial MR image through the middle of the prostate was obtained. (A, B, C) A large tumor focus is seen as an area of decreased signal intensity in the left peripheral zone and in the base of prostate (*). There is slight irregular bulging of the adjacent prostatic margin and interruption of the regular hypointense prostatic capsule with slightly hyperintense tumor causing disruption of periprostatic fat planes (arrows). Histopathologic report confirms left ECE, with tumor extending into the periprostatic fat. (D) Volume of lesion in peripheral region of prostate was overestimated by 63% on MR images.

References: H. M. Hanafy; Radiodiagnosisi, Ain shams university, Cairo, EGYPT
Fig.: Figure 6. Biopsy-proved adenocarcinoma in a 74-year-old man. T2-weighted axial MR image shows anterior and left sided low-signal-intensity lesion in the peripheral zone with focal bulging and interruption of low-signal-intensity fibromuscular stroma of the capsule (white arrows). The fat plane between the prostate and the posterior urinary bladder is obliterated (black arrows). Picture was highly suggestive of ECE and was proved histopathologically.

References: H. M. Hanafy; Radiodiagnostics, Ain shams university, Cairo, EGYPT
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centrally (arrows). (C-F) T2-weighted sagittal images, angle and fat plane between the prostate and seminal vesicle is obliterated (curved arrow). Extracapsular extension to seminal vesicles (stage T3c) was pathologically proven.

**Fig. 4:** Figure 4. (A,B) Axial T1-weighted image obtained through the prostate demonstrates hypointensities in the prostate gland with left sided bulging (black arrows) towards the rectoprostatic angle. C. T1WI depicts a hyperintense pelvic lymph node (white arrows). D. Sagittal T2 WI displays the normal appearance of seminal vesicles (curved arrow). MRI suggested ECE of cancer prostate, but histopathological results was a locally confined stage T2a prostate cancer.
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Conclusion

MR imaging currently is not in widespread use in staging prostate cancer. [3]. Controversy over its role, differences in reader experience and lack of accepted diagnostic criteria have resulted in a wide range of results reported for MR imaging in the detection of ECE of prostate cancer which reflects a lack of consensus about the still-evolving role of this modality. [13].

Pretreatment knowledge of ECE is important for both treatment selection and treatment planning. In treatment planning for radiation therapy or surgery (particularly if nerve-sparing surgical techniques are used), knowledge of ECE location is helpful for tumor localization to target prostate biopsy and selection of the appropriate treatment approach. [14].

The present study was performed to investigate the MR imaging features that can help predict ECE of prostate cancer.

In this study group, MRI proved a sensitivity of 83% and a specificity of 70% in detecting an extracapsular extension in patients with a pathologically proven ECE. MR imaging identified 13 cases of ECE with three False-positive cases. One false positive case displayed low signal intensity in the base of the prostate which extends to the periprostatic fat on T2 weighted images yet it was staged as stage T2b after surgery. Another false positive case occurred due to poor image quality because of motion artifact caused by bowel motion. The third case was interpreted as irregular capsular bulge with focal hypointensity yet the tumor was locally confined pathologically (Fig 4).

A wide range of specificities and sensitivities of MR in the assessment of ECE have been reported in the literature, varying from 68% to 95.4% and 17% to 84% respectively. [14]. This was due to a combination of factors including differences in radiologists' experience and subspecialty training as well as a lack of standardised diagnostic criteria [13].

The relatively small number of patients in the current study may have affected the statistical relevance. However, results are compared with previous studies [15 and 16] who gave a lower sensitivity; 64% and 62% respectively. To the contrary, a higher specificity of 95.4% was obtained in a study of Wang et al, 2004 [14].

Among the diagnostic criteria studied to detect ECE with T2-weighted MR in this study group, irregular capsular bulge, broad contact with the capsule and Low signal intensity in the base of the prostate were of the most significant predictors of ECE. These criteria correctly diagnosed 88%, 71% and 66% respectively when correlated with pathological results.

To the contrary, a study of Fütterer et al, 2005 [9].mentioned that however the capsular bulge sign did not change the overall accuracy; it was not used because it may
lead to false-positive findings. Prostatitis and post-biopsy hemorrhage may give same appearance. This sign was not also of significant value in another study of Cornud et al, 2002 [16].

Only one of three cases with histologically proven extension into the periprostatic adipose tissue was detected with MRI with an accuracy of 33%. (Fig.5). Engelbrecht et al, 2002 [8] stated that that penetration into periprostatic fat should be more than 3 mm to confidently diagnose ECE by MRI.

Current results suggest that MR imaging is accurate in demonstrating Seminal vesicle invasion (SVI) prior to radical prostatectomy in all cases of histologically proven SVI. Low signal intensity within a seminal vesicle that has lost its normal architecture was highly predictive of SVI. This criterion was the most significant predictor of ECE in our study. Sagittal sections were helpful in demonstrating the obliterated fat plane and angle between the prostate and seminal vesicles. (Fig.3C, D)

Sala et al, 2006 [17] studied the presence or absence of SVI in their study group and documented an accuracy of MR imaging in diagnosis of SVI in more than 90% of their patients.

Similarly, Hricak et al, 2007 [2] stated that MRI is highly predictive of SVI with 80% sensitivity and 99% specificity. They also mentioned that a combination of transverse, coronal, and sagittal sections facilitate evaluation of seminal vesicle and bladder neck invasion.

This study found a poor correlation between tumor volumes calculated from MR images and those found at pathologic examination. Measurements based on MR findings underestimated tumor volume in five of the twelve ECE cases, and overestimated volume in four of them with no clear reasons identified.

To the contrary, Jager et al, 1996 [18] reported a significant correlation between tumor volume calculated with MR images and that of the pathological specimen (p < 0.001), but accuracy was not enough to be helpful in making clinical decisions.

A similar study of Coakley et al, 2002 [10] mentioned that MR estimation of tumor volume is probably more accurate with higher tumor volumes.

Following the current results, we come to conclusion that the application of specific criteria in the interpretation of MR images achieved high diagnostic accuracy in the prediction of extracapsular extension of prostate cancer. Yet the accuracy was not satisfactory for predicting actual tumor volume.

Further studies are recommended using special endorectal coils to provide high-resolution images of the prostate by increasing the signal-to-noise ratio and the spatial resolution.
The addition of other types of MR imaging sequences should help further increase the level of confidence and promote acceptance by clinicians in detection and characterization of prostate cancer by providing functional and molecular information.

References


