Staging Urinary Bladder Cancer: Value of T1-Weighted Three-Dimensional Magnetization Prepared–Rapid Gradient-Echo and Two-Dimensional Spin-Echo Sequences

OBJECTIVE. The purpose of this study was to evaluate a magnetization prepared–rapid gradient-echo (MP-RAGE) sequence as a three-dimensional T1-weighted MR imaging technique for staging urinary bladder cancer and to compare this technique with a commonly used two-dimensional T1-weighted spin-echo sequence technique.

SUBJECTS AND METHODS. For 28 consecutive patients with urinary bladder cancer, MR findings and staging results were compared with histopathologic findings after surgery or autopsy. MR imaging was performed at 1.5 T with a Helmholtz double-surface coil. Conventional T1-weighted spin-echo, three-dimensional MP-RAGE, T2-weighted spin-echo or turbo-spin-echo, and dynamic T1-weighted fast gradient-echo sequences were used. Signal difference-to-noise ratios and T1 contrast were calculated by use of operator-defined regions of interest.

RESULTS. The signal difference-to-noise ratios for fluid-tumor and fat-tumor were, respectively, factors of 1.6 and 2.7 better with T1-weighted spin-echo sequences. T1 contrast of fluid-tumor was a factor of 2.6 better with three-dimensional MP-RAGE sequences, resulting in better recognition of small tumors, ascites, and dilated ureters. T1 contrast for fat-tumor was a factor of 2.0 better with T1-weighted spin-echo sequences. With the MP-RAGE sequence, motion artifacts were fewer in number than those noted with the T1-weighted spin-echo sequence, and susceptibility artifacts were equal in number to those noted with the T1-weighted spin-echo sequence. Using the three-dimensional technique, we performed off-line reconstruction of 1- to 2-mm high-resolution images in every desired plane. Because of higher spatial resolution, the availability of multiplanar reconstructions, and better fluid-tumor contrast and despite lower signal difference-to-noise ratios, three-dimensional MP-RAGE images resulted in better recognition of local tumor extension (n = 11), adhesions and bowel wall invasion (n = 5), lymph node metastases (n = 2), and bone marrow metastases (n = 2). The staging accuracy for the combination of three-dimensional MP-RAGE, T2-weighted, and dynamic sequences was 93%; that for the combination of two-dimensional T1-weighted spin-echo, T2-weighted, and dynamic sequences was 78%. Nodal staging was also more accurate with MP-RAGE sequences (accuracy of 93% vs 86% for T1-weighted spin-echo sequences).

CONCLUSION. Compared with two-dimensional T1-weighted spin-echo imaging, three-dimensional MP-RAGE imaging resulted in a 15% improvement in staging. Our findings suggest that optimal staging of urinary bladder carcinoma requires three-dimensional imaging techniques.

Because the urinary bladder is situated close to other organs, proper staging of urinary bladder carcinoma requires multiplanar imaging [1]. However, because of the imaging time required for the currently available two-dimensional (2D) techniques, only a limited number of imaging planes (about three) can be obtained during examination of one patient. We hypothesize that optimal delineation and staging of urinary bladder carcinoma requires three-dimensional (3D) techniques with off-line multiplanar reconstruction of high-resolution images in every desired plane. The introduction of short-TR (<10 msec) gradient-echo sequences that use a contrast preparation pulse, such as snapshot fast low-angle shot (FLASH), turbo-FLASH, and magnetization prepared–rapid gradient-echo (MP-RAGE), significantly

Received January 11, 1994; accepted after revision August 11, 1994.

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AJR 1995;164:109–115
reduced imaging time while maintaining sufficient signal-to-noise and signal difference-to-noise (SDN) ratios for clinical applications [2-4]. For T1-weighted 3D imaging, the use of a 3D MP-RAGE sequence has been described [3-6]. Reported advantages of this sequence compared with other 3D gradient-echo methods include fewer motion artifacts, fewer susceptibility artifacts, and fewer vascular artifacts [3].

The purpose of this prospective study was to evaluate the usefulness of a T1-weighted 3D MP-RAGE sequence for patients with urinary bladder carcinoma and to compare this technique with the accepted standard pulse sequence for T1-weighted imaging. Hence, a comparison was made with 2D T1-weighted spin-echo (SE) sequences, and staging results for the combination of 3D MP-RAGE, T2-weighted, and dynamic sequences were compared with the results for the combination of 2D T1-weighted SE, T2-weighted, and dynamic sequences.

**Subjects and Methods**

Twenty-eight consecutive patients with biopsy-proven urinary bladder carcinoma were referred after transurethral resection or biopsy for local and regional preoperative staging by MR imaging. MR imaging was performed at 1.5 T (Magnetom 63/84 SP/4000; Siemens Medical, Erlangen, Germany) with a Helmholtz double-surface coil. For reduction of bowel motion, patients were given 0.5 ml of glucagon IV before the examination and 1.5 ml of glucagon IV by a drip infusion during the examination. For reduction of respiration movements, an adjustable belt was wrapped around the abdomen to cause slight compression.

In the 3D MP-RAGE implementation that we used, T1 weighting was obtained by means of a 180° inversion pulse for magnitude preparation. For each of the phase-encoding steps in the second dimension, the inversion preparation was applied and then rapid gradient-echo data acquisition was done; the latter step extended into the phase-encoding for the third dimension. The sequence parameters were as follows: 10/4/500 (TR/TE/inversion time), flip angle = 10°, matrix = 192 x 256, field of view (FOV) = 250 mm, two acquisitions, and in-plane spatial resolution = 1.3 x 1.0 mm. A total of 128 contiguous images were obtained in 9 min; the section thickness was 1.5-1.9 mm. From this image set, off-line multiplanar reconstructions of images in specific planes were performed. The slice thickness for the reconstructions was 1-2 mm. T1-weighted SE images were acquired in axial, sagittal, and coronal planes for each patient. Parameters were representative of those in routine clinical use (TR/TE = 600/15, matrix = 256 x 256, FOV = 300 mm, slice thickness = 6 or 8 mm, slice gap = 1 mm, two acquisitions, in-plane spatial resolution = 1.2 x 1.2 mm, and imaging time = 5 min). The MP-RAGE sequence technique was performed at the beginning of the MR examination, before the T1-weighted SE images were acquired. In addition to the T1-weighted sequences, 18 T2-weighted SE sequences were applied in two planes with the following parameters: TR/TE = 2000/100, matrix = 192 x 256, FOV = 300 mm, slice thickness = 8 mm, slice gap = 2 mm, and two acquisitions; alternatively, 10 turbo-SE sequences were applied with the following parameters: TR/TE = 3000/90, echo train length = 12, matrix = 312 x 512, FOV = 300 mm, slice thickness = 8 mm, slice gap = 2 mm, and three acquisitions. Also, in the slice position that depicted the largest amount of the tumor, a single-slice dynamic T1-weighted turbo-FLASH sequence (TR/TE/inversion time = 7/3/10, flip angle = 8°, matrix = 128 x 256, FOV = 250 mm, slice thickness = 10 mm, one image per second, and two acquisitions) was applied during injection of a bolus of gadopentetate dimeglumine (0.1 mmol/kg of body weight).

SDN ratio and T1 contrast calculations were done with measurements of the mean signal intensities from operator-defined regions of interest (Fig. 1). The SE and reconstructed 3D MP-RAGE images were oriented identically and depicted identical anatomic regions. However, with T1-weighted SE sequences, the slice thickness was 8 mm, and with reconstructed 3D MP-RAGE sequences, the slice thickness was 1 to 2 mm. SDN ratios and T1 contrast were calculated for fluid (=urine)-tumor and fat-tumor with the following equations:

\[
\text{SDN}_{M} = \frac{(S_{T} - S_{0})}{N}
\]
\[
\text{SDN}_{F} = \frac{(S_{F} - S_{T})}{N}
\]
\[
\text{T1 contrast}_{t-u} = \frac{(S_{T} - S_{u})}{S_{T}}
\]
\[
\text{T1 contrast}_{f-t} = \frac{(S_{F} - S_{T})}{S_{F}}
\]

where \(S_{T}\), \(S_{U}\), and \(S_{F}\) are the mean signal intensities for tumor (t), urine (u), and fat (f), respectively, and N is the mean signal intensity for the background noise. The region of interest for noise was placed anterior or posterior to the patient in the phase-encoding direction; motion artifacts were avoided as much as possible.

The images were interpreted independently by two investigators, who were unaware of the clinical and surgical findings and of other MR imaging findings. The quality of the T1-weighted SE and 3D MP-RAGE images was scored as good or poor. An image was considered to be of poor quality when the delineation of the structures was degraded by motion artifacts and to be of good quality when these artifacts did not degrade image quality. Motion artifacts were defined as ghosting or unsaturation (e.g., of bowel loops). The investigators performed multiplanar reconstructions of the MP-RAGE data in what they thought to be the optimal plane. Local tumor infiltration, the existence of pathologically enlarged lymph nodes, and pelvic bone marrow metastases were evaluated by the two investigators in accordance with existing TNM criteria [7]. For determination of the sizes of lymph nodes, the maximal long axis and the minimal axial size were measured. The minimal axial size was defined in a plane perpendicular to the long axis through the thickest part of the node. From these measurements an index was calculated: the shortest axial size was divided by the long axis. Lymph nodes were considered pathologically enlarged when the index was greater than 0.8 and the minimal axial size was 8 mm or more (a round node) or when the index was less than 0.8 and the minimal axial size was 10 mm or more. An asymmetric cluster of small lymph nodes was also considered pathologic. Also, additional abnormalities and the time necessary for carrying out the multiplanar reconstructions were recorded. Finally, the findings of both investigators—based on the combination of 2D T1-weighted SE, T2-weighted, and dynamic contrast-enhanced images and the combination of 3D MP-RAGE, T2-weighted, and dynamic contrast-enhanced images—were compared with histopathologic findings from surgery or autopsy. Twenty-seven patients underwent cystectomy and lymph node dissection. In six patients with advanced urinary bladder carcinoma (stage T4a or T4b), cystectomy was performed for palliation. Autopsy was performed on one patient who died 2 weeks after the MR examination.

To evaluate the sensitivity of MP-RAGE to susceptibility artifacts, both investigators evaluated the effect of an oral ferrite contrast agent (oral magnetic particles; Nycemed, Oslo, Norway) on both the 3D MP-RAGE and the T1-weighted SE sequences for 10 patients. The images were evaluated for blurring artifacts, such as unsharpness of the oral magnetic particle-filled bowel loops, and metallic artifacts, visible as areas of high and low signal intensities in the oral magnetic particle-filled bowel loops.

**Results**

The SDN ratios and T1 contrast are presented in Table 1. The T1-weighted SE images had higher SDN ratios than the
3D MP-RAGE images. T1 contrast between fluid and tumor was better with 3D MP-RAGE images. The signal intensity of urine was lower, which helped in the visualization of urinary bladder carcinoma in 11 patients, the peripheral zone of the prostate in 11 patients, ascites in two patients (Fig. 2), and mild ureter dilatation in three patients. T1 contrast between fat and tumor was better with T1-weighted SE images. All 3D MP-RAGE images were of good quality, whereas motion artifacts caused the quality of the 2D T1-weighted SE images to be poor for five patients. These motion artifacts were caused by respiration and movement of the patients in poor health (Figs. 2 and 3). Although calculation of a specific slice took only a fraction of a second, the entire multiplanar reconstruction evaluation took 5-15 min, depending on the difficulty encountered in delineating structures and the experience of the investigator. In staging, both investigators had prospectively similar findings for 26 of the 28 patients. In the evaluation of susceptibility artifacts caused by the oral contrast agent, equal results were obtained for eight of the 10 patients.

### TABLE 1: SDN Ratios and T1-Contrast for 3D MP-RAGE and 2D T1-Weighted SE Sequences

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (mean ± SD) for:</th>
<th>Improvement with (Factor):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3D MP-RAGE SE SE 3D MP-RAGE</td>
<td></td>
</tr>
<tr>
<td>SDN ratio for tumor-urine</td>
<td>6.23 ± 2.48 10.15 ± 7.27 1.6</td>
<td></td>
</tr>
<tr>
<td>SDN ratio for fat-tumor</td>
<td>9.75 ± 5.70 25.92 ± 14.80 2.7</td>
<td></td>
</tr>
<tr>
<td>T1 contrast for tumor-urine</td>
<td>2.1 ± 1.5 0.8 ± 0.4 2.6</td>
<td></td>
</tr>
<tr>
<td>T1 contrast for fat-tumor</td>
<td>1.1 ± 0.5 2.3 ± 2.4 2.0</td>
<td></td>
</tr>
</tbody>
</table>

The T1-weighted SE images and the 3D MP-RAGE images equally showed nondisturbing blurring artifacts in five patients and nondisturbing metallic artifacts in four patients (Fig. 2). For all patients examined with 3D MP-RAGE, flow void occurred in the arteries, and the signals from veins were of a slightly higher intensity than those on the T1-weighted SE images. However, with multiplanar evaluation of the 3D MP-RAGE results, the round or oval lymph nodes could always be differentiated from the tubular veins.

Three-dimensional evaluation and higher spatial resolution led to clearer distinction of tumor invasion or of adhesions attached to bowel loops (Fig. 4) or to the pelvic wall in five patients, and to recognition of a vesicovaginal fistula in one patient (Fig. 5), a tumor invasion in the trigone of the bladder in one patient, and a small tumor at the ureter ostium in one patient (Fig. 3). The overall accuracies of MR imaging for local tumor staging, including T2-weighted and dynamic sequences, were 78% with the T1-weighted SE sequence and 93% with the 3D MP-RAGE sequence (Table 2). Because of previous transurethral resection, which is included in clinical staging, no residual tumor was present in seven patients. For two patients, granulation tissue was misinterpreted as tumor with both T1-weighted SE and 3D MP-RAGE sequences. With the T1-weighted SE sequence, infiltrative tumors were overstaged and understaged in both of these two patients. For each of these patients, the 3D MP-RAGE images allowed correct staging.

With 3D MP-RAGE, lymph nodes could be evaluated in three dimensions. Multiplanar reconstruction made it possible to measure the long axis and the minimal axial size of the node. Twenty-two patients had no lymph node metastases. Of the remaining six patients, two had microscopic lymph node metastases in normally sized nodes. Both the SE and the 3D MP-RAGE techniques failed to show these micrometastases. Four patients had enlarged lymph nodes, which were all correctly identified by the 3D MP-RAGE technique. Their sizes
patients, 3D MP-RAGE revealed more (smaller) metastases of a diameter of 4 mm, not visible on the T1-weighted SE images. The better capability of the 3D MP-RAGE technique to visualize lymph nodes also was illustrated by the recognition of normally sized, oval, flat nodes with a minimal axial diameter on MR images correlated exactly with histopathologic findings. For one of these patients, SE images showed a normally sized lymph node; however, on MP-RAGE images, an enlarged lymph node was found (Fig. 6). Surgery revealed a pathologically enlarged node with metastases. For another patient, a node appeared enlarged on T1-weighted SE images. However, 3D MP-RAGE images correctly revealed that this node was of a normal size (Fig. 7). The overall accuracies for lymph node staging were 93% with the 3D MP-RAGE sequence and 86% with the T1-weighted SE sequence. The reported accuracy of local staging improved with this sequence from 78% to 93%, and that for nodal staging improved from 86% to 93%. Compared with results reported in the literature [8-20], the accuracy of local staging was high, particularly when one takes into account the fact that staging was performed after transurethral resection or biopsy. A possible explanation is the use of a dynamic fast sequence. Further prospective studies with this sequence are being performed. The reported accuracy of local staging ranges from 73% to 92%, and that of nodal staging ranges from 73% to 96% [8-20]. Improvement in lymph node staging ranges from 73% to 96% [8-20]. Improvement in local staging is attributable to better recognition of a small tumor and better delineation of a perivesical tumor from bowel loops or the pelvic side wall. Improvement in lymph node staging is attributable to the ability to evaluate the long axis and the minimal axial diameter of lymph nodes and the use of thin slices. Pelvic lymph nodes are usually orientated parallel to the iliac vessels. Therefore, especially in patients with elongated vessels and with the use of conventional imaging techniques, high spatial resolution, and decreased vascular and motion artifacts. There are no reports of its application to urinary bladder carcinoma. Nevertheless, because the bladder is closely situated to other organs and usually is surrounded by fat, a 3D T1-weighted sequence shows promise in determining the optimal plane for evaluating the extent of urinary bladder carcinoma. Imaging in an optimal plane may improve staging [1].

Despite the lower SDN ratios and T1 contrast between tumor and fat with the 3D MP-RAGE sequence, the accuracy for local staging improved with this sequence from 78% to 93%, and that for nodal staging improved from 86% to 93%. Compared with results reported in the literature [8-20], the accuracy of local staging was high, particularly when one takes into account the fact that staging was performed after transurethral resection or biopsy. A possible explanation is the use of a dynamic fast sequence. Further prospective studies with this sequence are being performed. The reported accuracy of local staging ranges from 73% to 92%, and that of nodal staging ranges from 73% to 96% [8-20]. Improvement in local staging is attributable to better recognition of a small tumor and better delineation of a perivesical tumor from bowel loops or the pelvic side wall. Improvement in lymph node staging is attributable to the ability to evaluate the long axis and the minimal axial diameter of lymph nodes and the use of thin slices. Pelvic lymph nodes are usually orientated parallel to the iliac vessels. Therefore, especially in patients with elongated vessels and with the use of conventional imaging techniques, high spatial resolution, and decreased vascular and motion artifacts. There are no reports of its application to urinary bladder carcinoma. Nevertheless, because the bladder is closely situated to other organs and usually is surrounded by fat, a 3D T1-weighted sequence shows promise in determining the optimal plane for evaluating the extent of urinary bladder carcinoma. Imaging in an optimal plane may improve staging [1].

TABLE 2: Comparison of Staging Results for 2D T1-weighted and 3D MP-RAGE Sequences

<table>
<thead>
<tr>
<th>Sequences</th>
<th>Stage Determined by MR Imaging</th>
<th>Total No. of Patients</th>
<th>No. of Patients with the Following Histologic Stage (After Cystectomy):</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D T1-weighted SE, T2-weighted, and dynamic</td>
<td>T0 5 Ta-2 1 T3a 2 T3b 5 T4a 3 T4b 1</td>
<td>28</td>
<td>7 2 8 5 4 2 28</td>
</tr>
<tr>
<td>3D MP-RAGE, T2-weighted, and dynamic</td>
<td>T0 5 Ta-2 1 T3a 8 T3b 5 T4a 4 T4b 2</td>
<td>28</td>
<td>7 2 8 5 4 2 28</td>
</tr>
</tbody>
</table>

Note.—TO = no tumor; Ta-2 = stage Ta, T1, or T2.
(A) 62-year-old female with invasive urinary bladder carcinoma after hysterectomy. (A and B, Sagittal spin-echo (600/15) image (A) shows fat plane between urinary bladder carcinoma and sigmoid colon. However, in sagittal three-dimensional magnetization prepared-rapid gradient-echo (10/4/500, 8° flip angle) image (B), this layer is disrupted (large arrow), arguing for adhesions or infiltration into sigmoid colon. Fatty layer of higher signal intensity is visible (small arrows) between bladder tumor (T) and vagina, indicating that adhesion is more likely than invasion.

C, Photograph of cystectomy specimen. Histopathologic examination confirmed fibrous adhesion (arrow).

Fig. 5.—35-year-old female patient with recurrence of urinary bladder carcinoma. (A and B, Axial spin-echo (600/15) image (A) shows tumor (curved arrows) infiltrating vagina but no fistula. Angulated sagittal three-dimensional magnetization prepared-rapid gradient-echo (10/4/500, 10° flip angle) image (B) shows vesicovaginal fistula (straight arrows). This finding was confirmed at surgery.

Axial, coronal, or sagittal planes, it is difficult to determine the long axis and the minimal axial diameter correctly. The use of 1–2-mm-thick slices also reduces partial volume effects and improves the delineation of lymph nodes. The degrees of differentiation between deep and superficial muscle invasion and between scar or granulation and tumor were equal with both sequence combinations. This result can be explained by the fact that for this task, T2-weighted and dynamic fast sequences are needed [17, 21, 22]. The same T2-weighted and dynamic sequences were used for the 3D MP-RAGE and 2D T1-weighted SE techniques.

Possible reasons for the better performance of the 3D MP-RAGE sequence are the multiplanar reconstruction capability, the high spatial resolution, and the decreased partial volume effects. With the MP-RAGE data set, multiplanar reconstruction of high-resolution 1–2-mm-thick slices in every desired plane is possible within a short time. Multiplanar reconstruction resulted in an improved perception of the spatial relationship and contiguity of urinary bladder carcinoma to surrounding structures. Other authors also have found that image planes perpendicular to the bladder wall at the tumor site result in better staging [1]. With 2D sequences, the optimal plane cannot be determined in advance; therefore, 3D sequences should perform better. Furthermore, the ability to reconstruct an image in an arbitrary plane, without the need to use repeated acquisitions, helps shorten the time that the patient must be within the magnet. With 3D MP-RAGE sequences, the entire pelvis can be imaged within 9 min, resulting in 128 1.5-mm-thick contiguous...
Bon marrow lesion (arrow).

Fig. 6—69-year-old male patient with 

confirmed lymph node metastases. Angiography of GI is presented in A by block line.

Bone marrow lesion (arrow). This image shows the typical features of bone marrow lesions and is helpful in the diagnosis of bone marrow involvement.

Fig. 7—55-year-old male patient with metastases.
slices. In the same amount of time, only two T1-weighted SE image sets can be acquired. With three orthogonal T1-weighted SE sequences, as were used in this study, certain areas of the pelvis are not visualized, a fact that may cause unexpected tumor locations to be overlooked.

T1 contrast between fluid and tumor appeared better on the 3D MP-RAGE images than on the T1-weighted SE images. Small amounts of ascites, intraluminal tumor extension of small bladder cancers, and small bladder wall diverticula are usually difficult to depict on T1-weighted SE images, especially when higher field strengths are used, as T1 relaxation times increase with field strength [23]. Because of the increased T1 contrast between fluid and tumor, these structures can be differentiated better with 3D MP-RAGE sequences. With the use of the Helmholtz double-surface coil, shortening of TR and TE and thus improvement of T1 contrast with T1-weighted SE sequences are limited by the specific absorption rate. Compared with that on 2D T1-weighted SE images, the signal in veins on 3D MP-RAGE images was higher, resulting in slightly less clear differentiation between veins and lymph nodes. However, because of the multiplanar reconstruction capability with the 3D MP-RAGE technique, it was easy to delineate nodes from veins correctly in all cases. For five patients who were in poor health, the quality of the T1-weighted SE images was degraded because of respiration and movement artifacts. For reduction of these artifacts, respiratory compensation techniques can be used; however, these techniques are not readily available on all scanners. Although the MP-RAGE sequence was performed at the beginning of the MR examination, before the T1-weighted SE sequence, the MP-RAGE images showed fewer motion artifacts, obviating the need for respiratory compensation techniques.

Susceptibility artifacts, for example, those caused by ferrite bowel contrast material, have been reported to be serious with gradient-echo sequences (e.g., FLASH). However, with 3D MP-RAGE sequences, these artifacts were not considered disturbing and were comparable to those occurring with 2D T1-weighted SE sequences. This result may be explained by the very short TE (4 msec) used in the former sequences [24].

With our current 3D MP-RAGE technique, no T2-weighted information can be obtained. Furthermore, it has been predicted that this sequence type will have a relatively decreased sensitivity for gadolinium-based contrast agents [25], which also are essential for staging urinary bladder carcinoma. However, the multiplanar reconstruction is fast enough to enable a determination of the optimal planes for additional T2-weighted and dynamic sequences in the same examination session.

With the 3D MP-RAGE sequence, 3D T1-weighted information for the entire pelvis can be obtained in 9 min, permitting reconstruction of high-resolution ultrathin images of any orientation within a short time and providing good visualization of the extent of urinary bladder cancer, nodal size, and bone marrow metastases. Compared with conventional T1-weighted SE sequences, MP-RAGE sequences allowed better tumor staging, better nodal staging, and better depiction of small pelvic bone marrow metastases. In this study, staging of urinary bladder carcinoma was improved from 78% to 93%.

REFERENCES