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Staging Urinary Bladder Cancer after Transurethral Biopsy: Value of Fast Dynamic Contrast-enhanced MR Imaging¹

PURPOSE: To evaluate contrast enhancement patterns of urinary bladder cancer and surrounding structures and to evaluate a fast dynamic first-pass magnetic resonance (MR) imaging technique in tumor and node staging and in differentiation of urinary bladder cancer from postbiopsy effects.

MATERIALS AND METHODS:

Sixty-one consecutive patients with histologically proved urinary bladder cancer were referred to undergo unenhanced and dynamic MR imaging 1–4 weeks after transurethral resection or biopsy. Subtraction and time (to beginning of enhancement) images were acquired.

RESULTS: Results with unenhanced T1- and T2-weighted images were compared with those obtained with the unenhanced images plus dynamic contrast material-enhanced single-section turbo fast low-angle shot (FLASH) images. Urinary bladder cancer started to enhance 6.5 seconds \pm 3.5 (standard deviation) after the beginning of arterial enhancement, which was 4 seconds earlier than most other structures (postbiopsy tissue, 13.6 seconds \pm 4.2). In differentiation of postbiopsy tissue from malignancy on the basis of the beginning of enhancement depicted on time and subtracted images, accuracy improved from 79% to 90% ($P < .02$) and specificity improved from 33% to 92% (not significant). Overall, tumor staging accuracy improved significantly from 67% to 84% ($P < .01$) by adding the turbo FLASH images.

CONCLUSION: Fast dynamic first-pass MR imaging, with at least one image acquired every 2 seconds, improved delineation of urinary bladder cancer, tumor staging, and detection of metastases.

CARCINOMA of the urinary bladder is one of the most common malignant tumors of the urinary tract in male and female patients. Its treatment and prognosis are largely determined by the depth of tumor infiltration and the extent of metastases (1). Therefore, exact staging is mandatory. As clinical staging is not reliable for deeply infiltrative tumors, more accurate methods are needed. Computed tomography (CT) is a valuable tool, but many reports have shown the superiority of magnetic resonance (MR) imaging for the evaluation of urinary bladder cancer (2–10). Although MR imaging is better than CT for staging urinary bladder cancer, CT is more commonly used in most centers because of its greater availability and of the greater familiarity with this technique. Recently, several authors have described the use of gadolinium-enhanced MR imaging for staging urinary bladder cancer (10,11–14). With intravenously administered gadopentetate dimeglumine, visualization of small tumors improved (10,12–14) and increased accuracy of local staging was reported (11,14). The best staging results with contrast material-enhanced MR were obtained with fast T1-weighted imaging (9).

Most patients are referred for MR staging following transurethral resection (TUR), with histologically proved invasion of the muscle layers of the

bladder wall. Even when gadolinium enhancement is used, however, differentiation between residual tumor and edema, scar, or granulation tissue remains problematic in patients after TUR (12,14–17).

Fast MR imaging, with at least two images acquired every second, depicts the first pass of the bolus of contrast material, which has resulted in improved differentiation between benign and malignant lesions of the breast and musculoskeletal system (18,19). The purpose of this study was to evaluate the enhancement patterns of urinary bladder cancer and its surrounding structures. We also assessed the value of fast MR imaging during the first pass of the bolus of contrast material to help differentiate residual tumor from postbiopsy effects, stage tumors, and detect node metastases.

MATERIALS AND METHODS

In this prospective study, 61 consecutive patients (47 men and 14 women, aged 38–82 years [mean, 61 years]) with histologically proved urinary bladder cancer were referred to undergo MR imaging within 1–4 weeks after TUR or biopsy. Two of these patients had undergone neoadjuvant chemotherapy, and they had also undergone MR imaging examination before chemotherapy. Fifty-seven of the 61 patients were scheduled subsequently to undergo curative ($n = 42$) or palliative salvage ($n = 15$) cystectomy, because they

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Abbreviations: FLASH = fast low-angle shot, MP-RAGE = magnetization-prepared rapid gradient echo, SI = signal intensity, TUR = transurethral resection.

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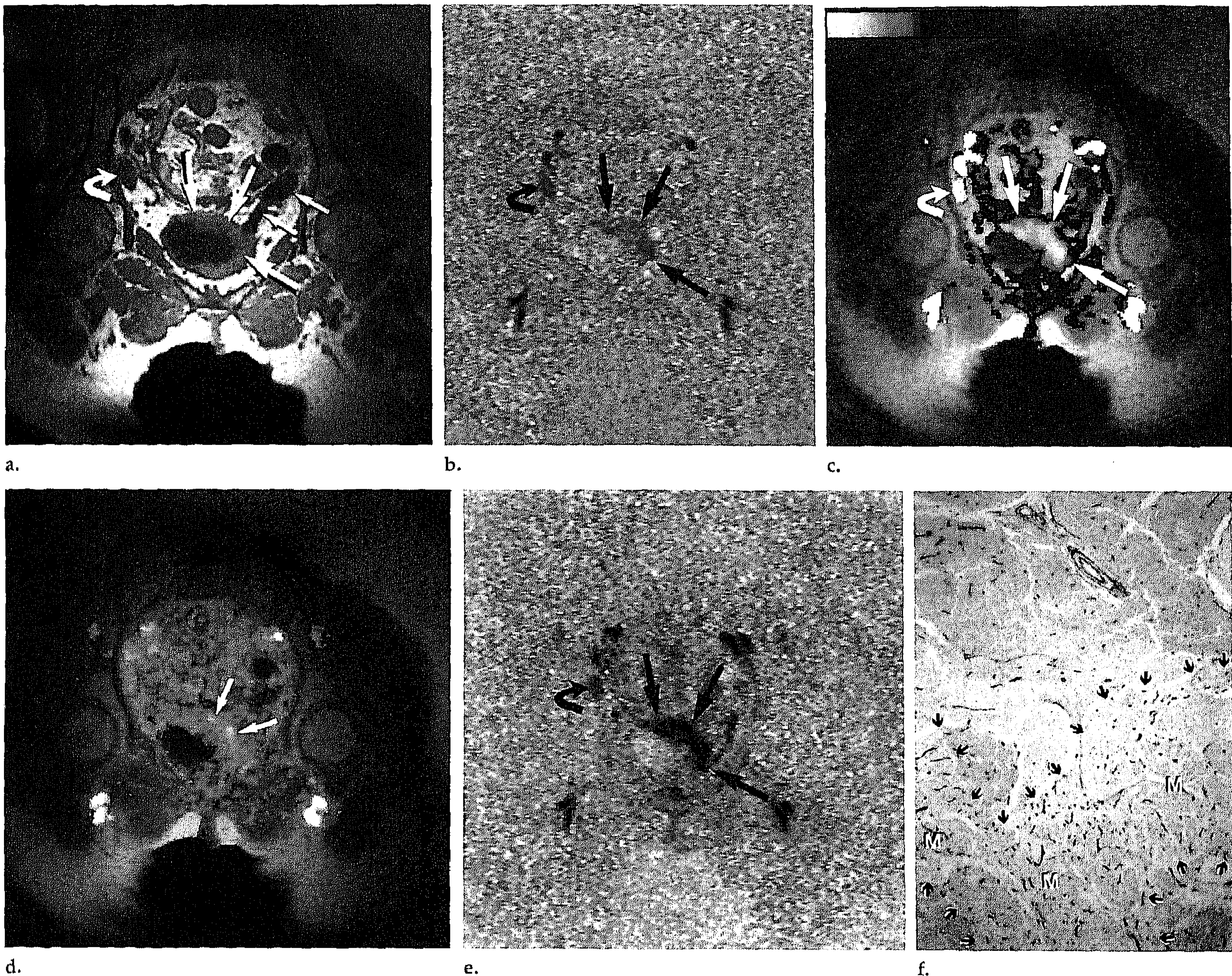


Figure 1. Well-differentiated transition cell carcinoma of the bladder, stage T4a, with poorly differentiated metastasis in the right iliac lymph node. (a) Unenhanced T1-weighted three-dimensional MP-RAGE image shows urinary bladder cancer (long arrows), with dilatation of the left ureter (short arrows) and enlarged lymph node (curved arrow). (b) Subtracted image obtained 6.25 seconds after the start of arterial enhancement shows beginning node (curved arrow) and tumor (straight arrows) enhancement. (c) In time image, each color represents 1.25 second. Node enhancement starts at 2.5 seconds, and tumor enhancement starts at 6.25 seconds. Straight arrows indicate urinary bladder cancer; curved arrow indicates enlarged lymph node. (d) In the slope image, maximal slope of enhancement is color coded. Although the center of the tumor shows higher slope value (arrows), tumor cannot be delineated on the basis of this image. (e) Maximal SI image (at 45 seconds) shows more enhancement of tumor (straight arrows) and node metastasis (curved arrow). (f) Histologic section with vascular stain of enlarged lymph node shows more pathologic vessels (brown structures [arrows]) in the metastatic part of the node than in normal lymphatic tissue. Metastatic area (M) is surrounded by pathologic vessels. Node metastases were poorly differentiated transition cell carcinoma, whereas primary bladder tumor consisted of well-differentiated transition cell carcinoma with less neovascularization. (Q-bend stain; original magnification, $\times 30$.)

had either a highly malignant (grade 3) superficial tumor or an invasive tumor found at TUR or biopsy. The remaining four patients were undergoing 1-year follow-up TUR.

MR imaging was performed at 1.5 T (Magnetom 63/84 SP 4000; Siemens Medical Systems, Erlangen, Germany), with use of a Helmholtz double-surface coil. To reduce bowel motion, 0.5 mL glucagon was administered intravenously before the examination, and 1.5 mL glucagon was administered intravenously during the examination, by means of a drip infusion. To reduce respiratory movements, an adjustable belt was wrapped around the patient's abdomen, to cause slight compression.

Initially, three-dimensional T1-weighted magnetization-prepared rapid gradient

echo (MP-RAGE) imaging was performed (repetition time msec/echo time msec/inversion time msec = 10/4/500, 10° flip angle, 1.2-mm effective section thickness, 192×256 matrix, 300-mm field of view, two signals acquired, 9-minute acquisition time). The ordering of the phase-encoding steps in k space was sequential.

Multipolar reconstruction was performed with the MP-RAGE data, to obtain the plane in which the tumor and, eventually, the pelvic lymph nodes were optimally visible. In this plane and in the axial or sagittal planes in the first 10 patients, a T2-weighted spin-echo image was acquired (2,000/100, 192×256 matrix, 300-mm field of view, 8-mm section thickness, 2-mm intersection gap, two signals acquired). In the remaining 51 patients a fast spin-echo image was

acquired (3,000/90 [effective], 12 echo trains, 320×512 matrix, 300-mm field of view, 8-mm section thickness, 2-mm intersection gap, three signals acquired). During intravenous bolus injection of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) (0.1 mmol per kilogram of body weight) in the section in which the tumor and, if present, enlarged lymph nodes were optimally visualized, 60 images were acquired with a magnetization-prepared single-section turbo fast low-angle-shot (turbo FLASH) sequence (7/3/15, 10° flip angle, 128×256 matrix, 350-mm field of view, 8-mm section thickness), with one image obtained every 2.5 seconds in 25 cases (two signals acquired) and one image obtained every 1.25 second in the remaining 36 cases (one signal acquired).

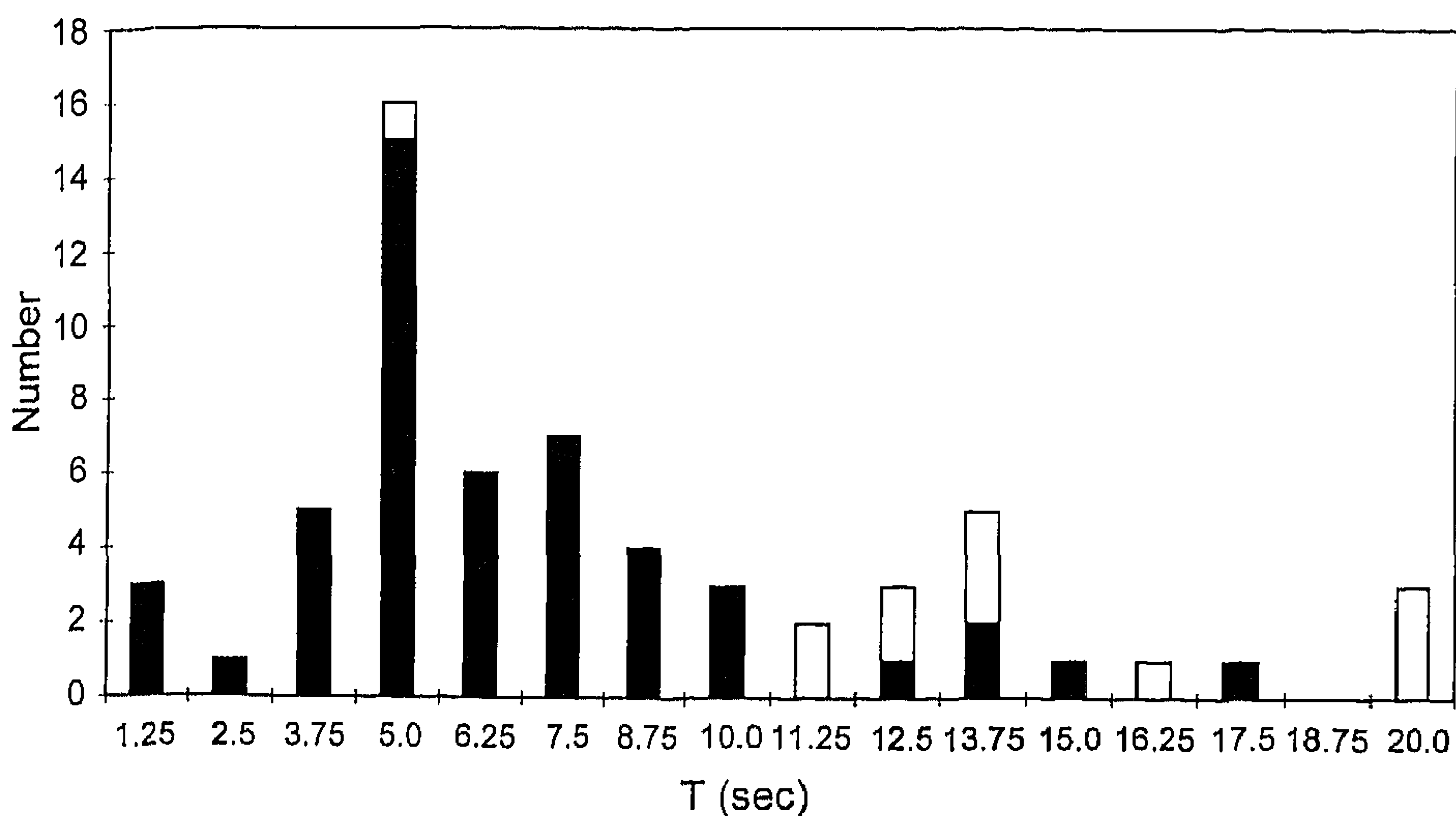


Figure 2. Time (T) of lesion enhancement after the start of arterial enhancement. Solid box = cancer, open box = postbiopsy tissue.

To determine enhancement patterns of iliac or femoral arteries, bladder wall, and tumor, time-signal intensity (SI) curves were made in operator-defined regions of interest. To quantify maximal tumor enhancement, a tumor-to-bladder wall enhancement ratio was determined with the following formula: $(\Delta SI_{\text{lesion}} - \Delta SI_{\text{bladder wall}}) \div \Delta SI_{\text{bladder wall}}$, with $\Delta SI_{\text{lesion}}$ and $\Delta SI_{\text{bladder wall}}$ being the difference in SI at maximal enhancement, which occurs 45 seconds after the onset of arterial enhancement in the lesion and normal bladder wall, respectively.

The dynamic single-section images were transferred to a workstation (Hewlett-Packard, Palo Alto, Calif). With software written by one of the authors (N.K.), subtraction turbo FLASH images, color-coded time and slope images, and maximal SI images were calculated (Fig 1) (the software is available on request). In time images, the beginning of enhancement of tumor and other tissues in relation to the beginning of arterial enhancement is color coded and projected over the unenhanced image. The beginning of enhancement is defined as an increase of 10 arbitrary units above baseline noise. In the slope image, the slope of maximal SI increase is color coded. The maximal SI images display maximal enhancement 45 seconds after the beginning of arterial enhancement. The subtraction technique is commercially available on most MR imaging systems.

The images were interpreted prospectively by two investigators (J.O.B., G.J.J.), who were not acquainted with the clinical and surgical results, except that prior biopsy had revealed carcinoma. The location of the tumor and biopsy site were unknown to them. On subtraction and time images, the onset of enhancement after arterial enhancement was registered. On slope images and maximal SI images, the slope of the maximal enhancement rate and maximal final enhancement were evaluated for the tumor and other structures such as postbiopsy lesion, normal bladder wall, bowel loops, prostate or uterus, bone marrow, and muscle. On the slope images, a lesion was considered ma-

lignant if the slope value was higher in the tumor than in surrounding structures.

On the basis of earlier experience (20) with time images, a lesion was considered malignant if enhancement started within 10 seconds after the beginning of arterial enhancement. A lesion was considered benign (eg, postbiopsy tissue) if enhancement started later. With these criteria, differentiation between tumor and postbiopsy tissue with unenhanced imaging was compared with differentiation with unenhanced plus turbo FLASH imaging. Also, staging results were evaluated with both sets of images. Staging was performed according to the TNM system (21). Local tumor staging was performed on the basis of the criteria of Fisher et al (2). Node staging was performed as described by Barentsz et al (22): To determine node size, the maximal long-axis and axial size were measured. 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 as the shortest axial size divided by the long axis. Lymph nodes were considered to be pathologically enlarged when the index was more than 0.8 (a round node), with a shortest axial size of 8 mm or more, or when the index was less than 0.8, with a shortest axial size of 10 mm or more. An asymmetric cluster of small lymph nodes was also considered pathologic.

Findings in all patients were confirmed at histologic examination. Imaging results were correlated with histopathologic findings after cystectomy ($n = 57$) or with the findings at repeated TUR ($n = 4$). On the basis of findings on the MR images, specimen sectioning for pathologic examination was performed by the pathologist (H.P.) with one of the radiologists (J.O.B.). Specimen sectioning was performed in the plane in which the turbo FLASH image was obtained.

RESULTS

There were no differences between the two observers in determining the

beginning of lesion enhancement. Figure 2 depicts the beginning of lesion enhancement in relation to the start of enhancement of the iliac or femoral artery. In 12 patients, no residual malignancy was present after TUR performed before MR imaging. In these cases, a lesion was visible on the unenhanced images. In 11 of the cases, enhancement began more than 10 seconds after arterial enhancement (Fig 3). In 47 of the remaining 49 cases, the bladder cancer could be visualized on the single-section dynamic image. In two cases, no tumor was visible on the three-dimensional MP-RAGE images, which resulted in incorrect section acquisition in the FLASH image. Findings in these cases were recorded as false negative. In 44 of the remaining 47 cases, the urinary bladder cancer started to enhance within 10 seconds after the artery (mean, 6.5 seconds \pm 3.5 [standard deviation]). Postbiopsy tissue started to enhance 13.6 seconds \pm 4.2 after arterial enhancement. These differences between urinary bladder cancer and postbiopsy tissue are significant ($P < .0001$, two-tailed P value).

Results of differentiating postbiopsy effects from malignancy with and without the dynamic FLASH images, with a threshold of 10 seconds, are presented in Table 1. The only false-positive result occurred in the case of a patient with early lesion enhancement after 5.0 seconds. Findings at histologic examination revealed granulation tissue with hyperemia. The five false-negative cases included two patients in whom the wrong section was imaged, two with superficial bladder cancer, and one in whom the lesion consisted predominantly of postbiopsy tissue with one microscopic area of residual tumor (Fig 4).

In all cases, maximal SI of all structures was reached within 45 seconds after the start of arterial enhancement. Maximal lesion enhancement values in relation to wall enhancement ($(\Delta SI_{\text{lesion}} - \Delta SI_{\text{bladder wall}}) \div \Delta SI_{\text{bladder wall}}$) showed considerable overlap between cancer and postbiopsy effects. With the slope images, differentiation between benign and malignant lesions was impossible. In only 16 of 61 patients could the malignant nature of the lesion be recognized on the basis of the higher slope value on these images.

Enhancement of the following structures was seen before the 10-second threshold: bowel loops in 12 of 61 cases (Fig 5d), bone marrow in six, muscle in three, uterus and parametrial tissue in two, and benign prostatic hypertrophy in three. In all of

Table 1
Differentiation between Tumor and Postbiopsy Tissue

Finding	Histologic Stage after Cystectomy		Total
	No Tumor	Tumor	
Unenhanced T1- and T2-weighted Imaging*			
No tumor	4	5	9
Tumor	8	44	52
Total	12	49	61
Unenhanced T1- and T2-weighted and Dynamic Imaging†			
No tumor	11	5	16
Tumor	1	44	45
Total	12	49	61

* Accuracy, 79%; sensitivity, 90%; specificity, 33%; positive predictive value, 87%; negative predictive value, 44%.

† Accuracy, 90%; sensitivity, 90%; specificity, 92%; positive predictive value, 98%; negative predictive value, 69%.

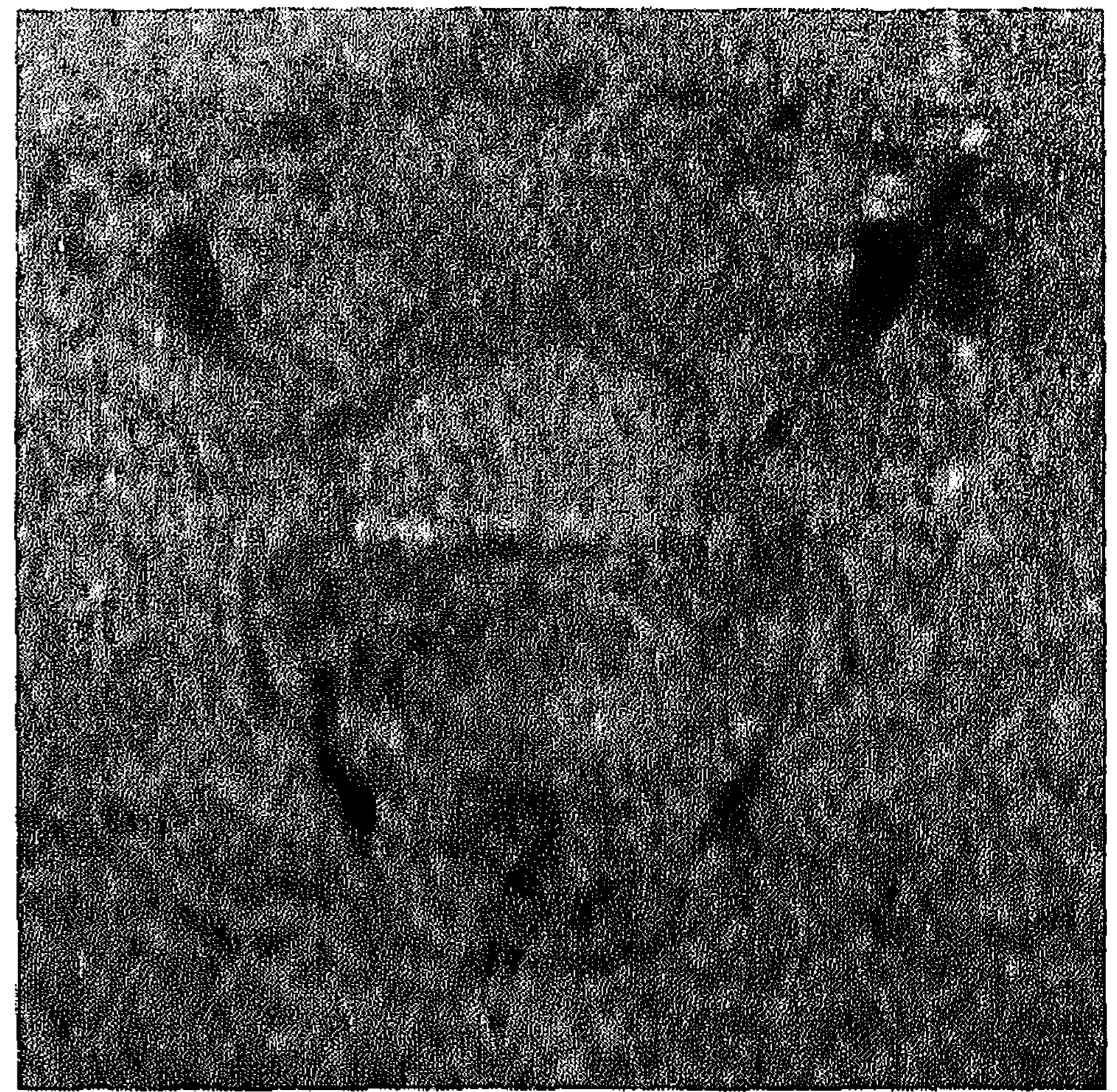
these cases, however, urinary bladder cancer showed earlier enhancement. These structures could be separated from bladder cancer on the unenhanced images on the basis of their location and morphology.

There was disagreement in tumor staging between the two observers in three cases. One observer judged disease of a lower stage in one case; the other observer judged disease of a higher and lower stage in one case each. The interobserver variation was therefore 5%. The results presented in Tables 1–3 represent the data for both observers. In cases of disagreement, the diagnosis was decided by consensus. Results of tumor staging are presented in Table 2. The additional use of the dynamic FLASH images improved overall staging results significantly, from 67% to 84% ($P < .01$, McNemar test). Better accuracy was mainly due to better differentiation between postbiopsy tissue and malignancy ($n = 7$) and to better recognition of extravesical tumor extension ($n = 4$) (Fig 5). There was no difference in staging accuracy in patients who underwent imaging 1 week versus 4 weeks after TUR. In five patients, postbiopsy hemorrhage was present that could be differentiated from tumor by its lack of contrast enhancement.

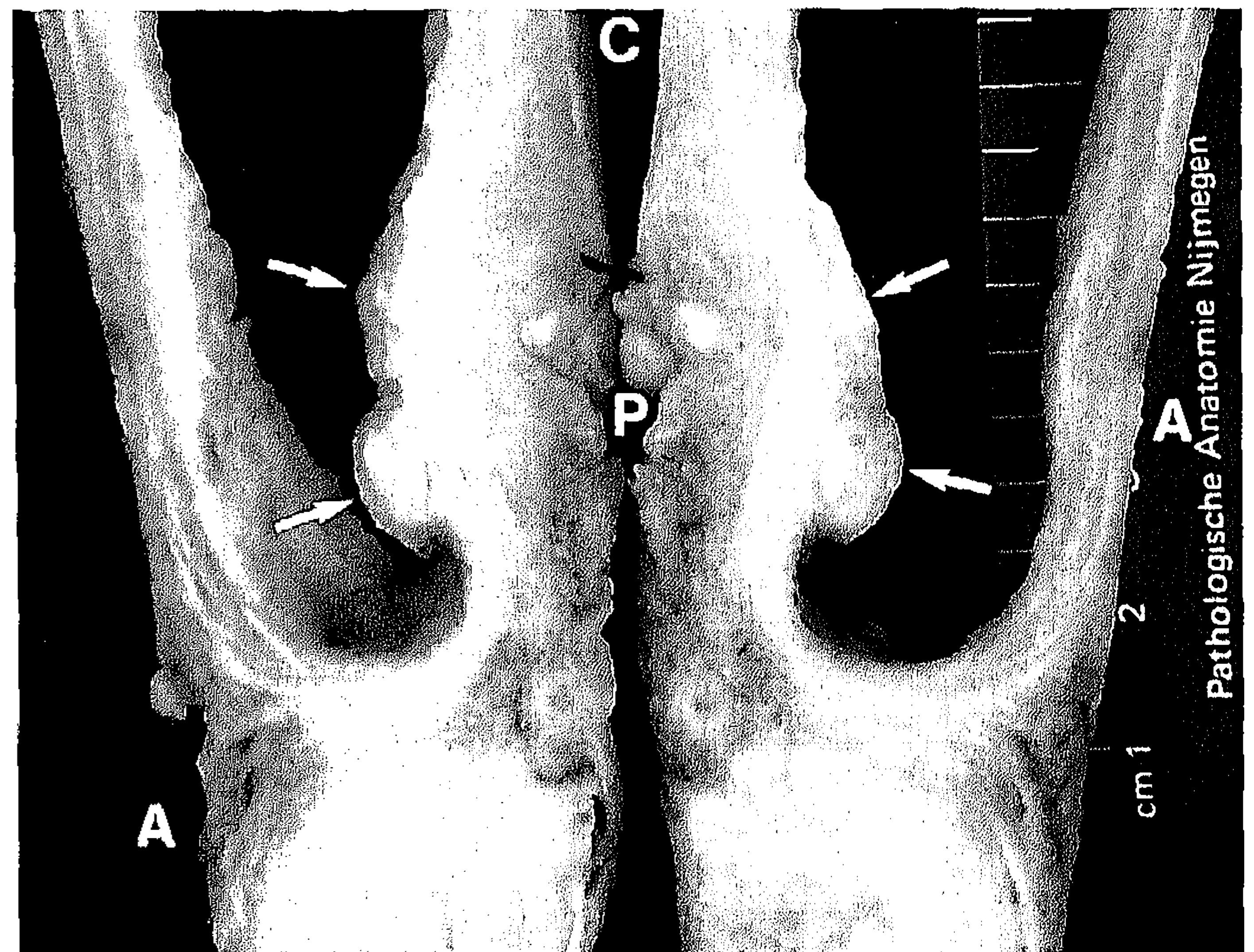
There was disagreement between the observers in node staging in one case. One of the observers considered a marginally enlarged node to be negative. Table 3 presents the results of node staging. In 11 cases, the T1-



a.



b.



c.

Figure 3. Granulation tissue after TUR. (a) T1-weighted image shows mass (arrows). (b) On subtraction image obtained 15 seconds after the start of arterial enhancement, no mass enhancement is present, which is evidence of postbiopsy tissue. (c) Findings at pathologic examination confirmed granulation tissue (arrows). A = anterior, P = posterior, C = cranial. Ruler indicates centimeters.

weighted MP-RAGE images correctly showed enlarged lymph nodes. In one case this enlargement was caused by reactive enlargement with atypical cells; in the other 10 cases node enlargement was caused by metastases. In the remaining 46 cases, the three-dimensional MP-RAGE image correctly showed normal-size lymph nodes, but microscopic metastases were missed in four cases.

Enlarged lymph nodes in 11 patients and normal-size lymph nodes in nine patients could be included in the dynamic FLASH single section together with the bladder tumor. Enlarged nodes in 11 patients and normal-size nodes in three patients showed contrast enhancement that was as early as ($n = 9$) or earlier than ($n = 5$) enhancement in the tumor in the urinary bladder (Fig 1). In one pa-

tient with an enlarged node without metastases and in one patient with a normal-size lymph node, early enhancement was false positive. Early enhancement in two patients permitted metastases in normal-size lymph nodes to be recognized (Fig 6). Histologic examination of specimens obtained in the remaining six patients with late or unenhancing normal-size nodes did not reveal metastases.

DISCUSSION

Superficial bladder cancer (eg, without muscular invasion) is found in two-thirds of all patients with bladder tumors. Superficial bladder cancer can be treated with local endoscopic resection with or without adjuvant intravesical installations of chemotherapeutic agents. Further staging is not

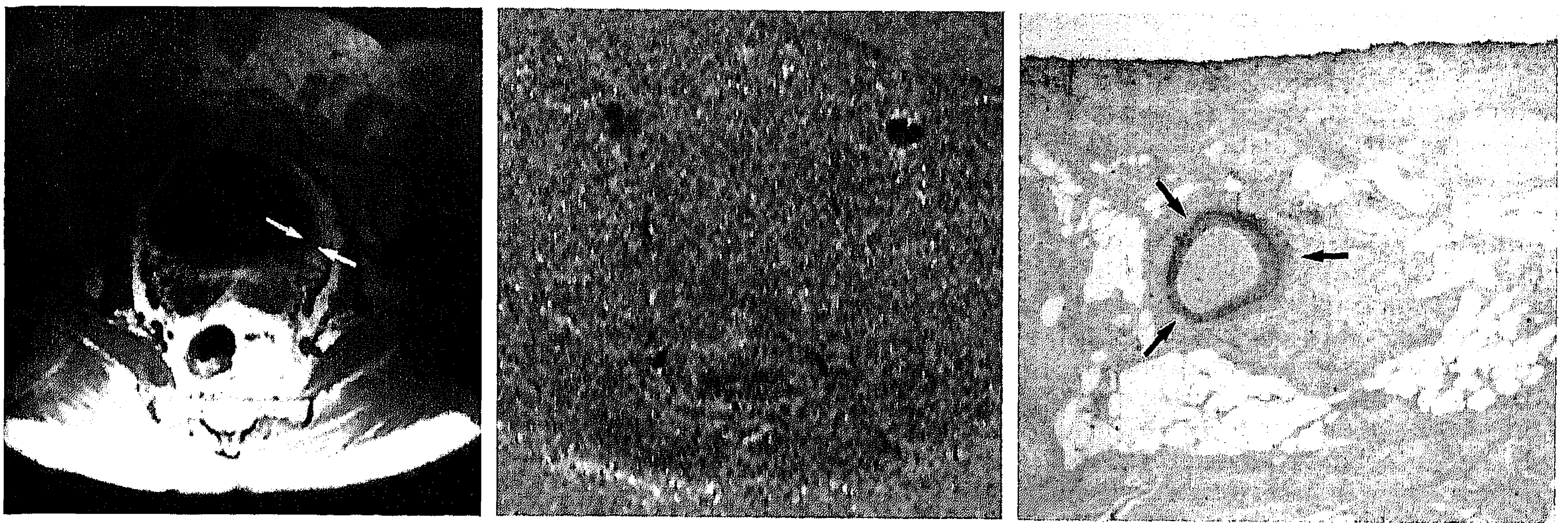


Figure 4. Granulation tissue after TUR in a patient with one microscopic area of residual transition cell carcinoma in the muscle layer (stage T2). (a) T1-weighted image shows slight thickening of the bladder wall near the left ostium (arrows). (b) Subtraction image obtained 15 seconds after the start of arterial enhancement shows no tumor enhancement. (c) Findings at histologic examination revealed predominantly granulation tissue and fibrosis, with one microscopic area of residual tumor (arrows). (Hematoxylin-eosin stain; original magnification, $\times 20$.)

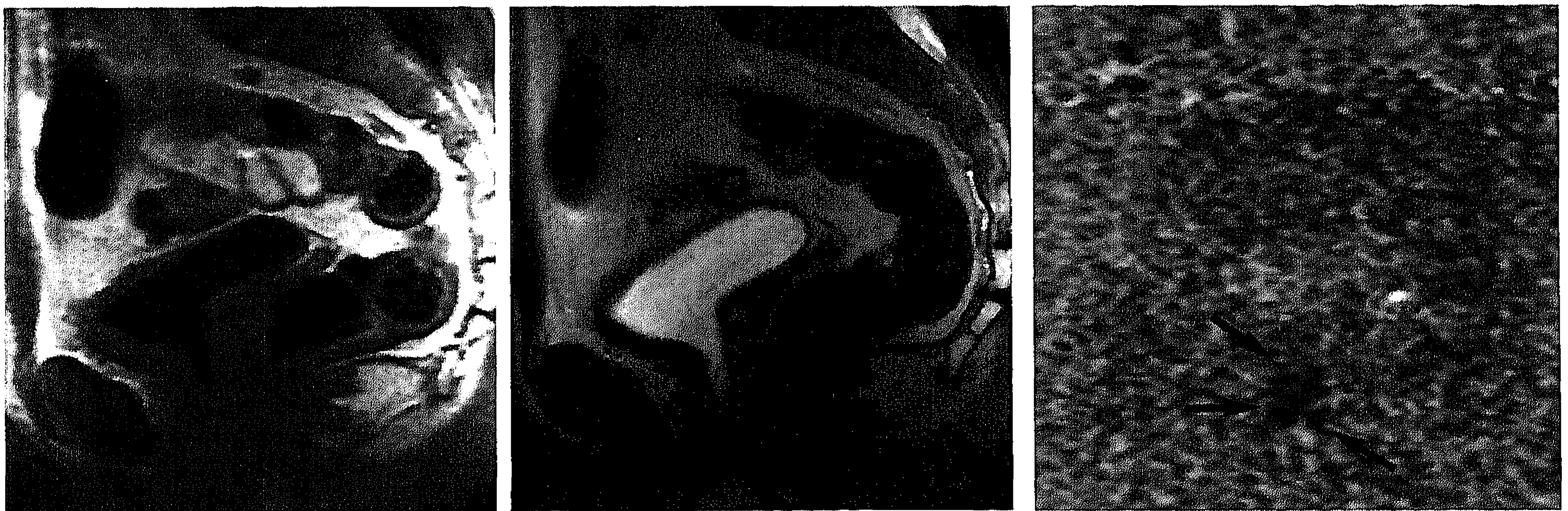


Figure 5. Transition cell carcinoma with prostatic invasion (stage T4a). (a) T1-weighted MP-RAGE image and (b) T2-weighted fast spin-echo image show no tumor. On (c) subtraction image obtained 5.0 seconds after the start of arterial enhancement and (d) time image, early enhancement at 5.0 seconds in prostate (arrows) is visible, which is evidence of stage T4a urinary bladder cancer. In d, each color represents 1.25 second. Note early enhancement of rectum and sigmoid colon. Bowel enhancement starts at 6.25 seconds and can be differentiated from respiration motion of the cranioventral part of the abdominal wall. Motion artifacts show random distribution of multiple colors, including green-white. (e) Findings at histologic examination confirmed urinary bladder cancer with invasion in prostatic tubules (arrows). (Hematoxylin-eosin stain; original magnification, $\times 20$.)

necessary in this group, because the distinction of superficial from invasive tumors can be made at TUR or biopsy. This is an integral part of clinical staging. In patients with invasive tumors, staging is necessary to select treatment with curative cystectomy versus palliative chemotherapy or radiation therapy. The best staging technique in this group of patients is MR imaging (10).

Patients referred for MR imaging have often undergone TUR or biopsy. Staging with MR imaging after TUR has been shown to be problematic, as differentiation between tumor and edema and granulation or scar tissue on T2-weighted images is limited. Differentiation remains impossible even with gadolinium-enhanced imaging (12,14-17).

During the first pass of the bolus of contrast material, the difference in concentration between the intra- and extravascular component is maximal. In this phase, transportation of contrast material from the vessels into the tissues occurs rapidly, and more rapidly in lesions with neovasculariza-

tion (23) such as urinary bladder and breast carcinoma (18,24,25). Therefore, these lesions show earlier enhancement compared with tissues without neovascularization. After about 30–45 seconds, an equilibrium phase, or maximal-enhancement phase, is reached in which the difference in contrast material concentration in the intra- and extravascular space decreases. Images obtained 45 seconds after the beginning of arterial enhancement display the maximal SI, because at this time in all patients both urinary bladder and mass have reached their maximal SI, which persists for at least several minutes (Fig 7 [plateau phase]).

Conventional gadolinium-enhanced MR images depict enhancement in this plateau phase, when the difference in enhancement between urinary bladder cancer and other tissues has already decreased (Fig 7). Thus according to the findings in this study, use of a fast imaging technique—at least one image acquired every 2 seconds—at the beginning of enhancement provides the best information to help differentiate malignant from benign lesions. Findings on images that depict maximal SI information are less reliable. Kim et al (15) also demonstrated that staging based on images obtained after 20 seconds was more often correct than staging based on images obtained later. The images obtained at 20 seconds are obtained before the plateau phase; at 20 seconds the differences in SI between urinary bladder cancer and nonmalignant structures are still greater than is depicted on images obtained in the plateau phase (Fig 7).

Determination of the slope value did not allow reliable recognition of malignant lesions. This finding conflicts with that of Verstraete et al, who found slope images to be of value in distinguishing benign from malignant lesions (19). The difference between their results and ours may be explained by the heterogeneous distribution of the slope values for bladder cancer, which made differentiation difficult. Moreover, Verstraete et al used parametric images with a fat suppression factor instead of color-coded images (19).

The beginning of enhancement can be quantitatively determined on the basis of time images just by looking at the color. Therefore, there was no interobserver variability in assessment of the start of lesion enhancement. At fast dynamic MR imaging, urinary bladder cancers showed early enhancement 6.5 seconds after the beginning of arterial enhancement, which in most patients occurred 4

Table 2
Staging Results in 61 Tumors

MR Imaging Stage	Histopathologic Stage					
	T0	Ta–T2	T3a	T3b	T4a	T4b
Unenhanced T1- and T2-weighted Imaging						
T0	4	0	2	1	2	0
Ta–T2	6	8	0	0	0	0
T3a	2	2	7	2	1	0
T3b	0	0	0	11	1	0
T4a	0	0	1	0	7	0
T4b	0	0	0	0	0	4
Total	12	10	10	14	11	4
Unenhanced T1- and T2-weighted and Dynamic Imaging						
T0	11	3	1	1	0	0
Ta–T2	0	5	0	0	0	0
T3a	1	2	9	1	0	0
T3b	0	0	0	12	1	0
T4a	0	0	0	0	10	0
T4b	0	0	0	0	0	4
Total	12	10	10	14	11	4

seconds earlier than in surrounding normal organs or postbiopsy tissue. With use of a turbo FLASH technique that applied a threshold of 10 seconds after the beginning of arterial enhancement, the accuracy for differentiation of postbiopsy effects from tumor improved from 79% to 90%, and the specificity increased from 33% to 92%. These results are in agreement with other reported data (18,19) that show imaging in the first-pass phase, with at least one image acquired every 2 seconds, has a higher specificity in the distinction of a benign from a malignant lesion. Caution should be exercised, however, because early enhancement may occasionally occur in benign lesions that contain abundant hypervascular granulation tissue or in prostatitis, and it may occur in other malignant tissue such as prostate cancer. False-negative findings may be seen in small tumors without considerable neovascularization, as was the case in two of our patients in whom a thin layer of superficial tumor did not show early enhancement.

Tanimoto et al (26) also found that fast dynamic imaging improved staging accuracy. They found an 85% accuracy with fast SE imaging with one image acquired every 7 seconds, a 74% accuracy with delayed enhancement imaging, and a 58% accuracy with unenhanced imaging. In their study, however, only patients without previous TUR were included, so no information was obtained about staging after TUR. Our technique differs from theirs in several ways: The sequence we used is six times faster than the sequence they used, our perception of minimal differences in en-

Table 3
Lymph Node Staging

MR Imaging Stage	Pathologic Stage after Cystectomy		
	N0	N+	Total
Unenhanced T1- and T2-weighted Imaging*			
N0	42	4	46
N+	1	10	11
Total	43	14	57
Unenhanced T1- and T2-weighted and Dynamic Imaging†			
N0	41	2	43
N+	2	12	14
Total	43	14	57

* Accuracy, 91%; sensitivity, 71%; specificity, 98%; positive predictive value, 91%; negative predictive value, 91%.

† Accuracy, 93%; sensitivity, 86%; specificity, 95%; positive predictive value, 86%; negative predictive value, 95%.

hancement was increased by our use of subtraction and time images, and finally the turbo FLASH sequence we used is highly sensitive for minimal contrast enhancement (27). As enhancement differences are minimal between tumor and tissue after TUR, imaging with a sequence with a 7-second time resolution is expected to be less effective than imaging with the turbo FLASH technique we used.

Our overall accuracy in tumor staging improved significantly, from 67% to 84% ($P < .01$, McNemar test), owing to improved differentiation between postbiopsy effect and urinary bladder cancer and to better depiction of extravesical tumor extension. Further-

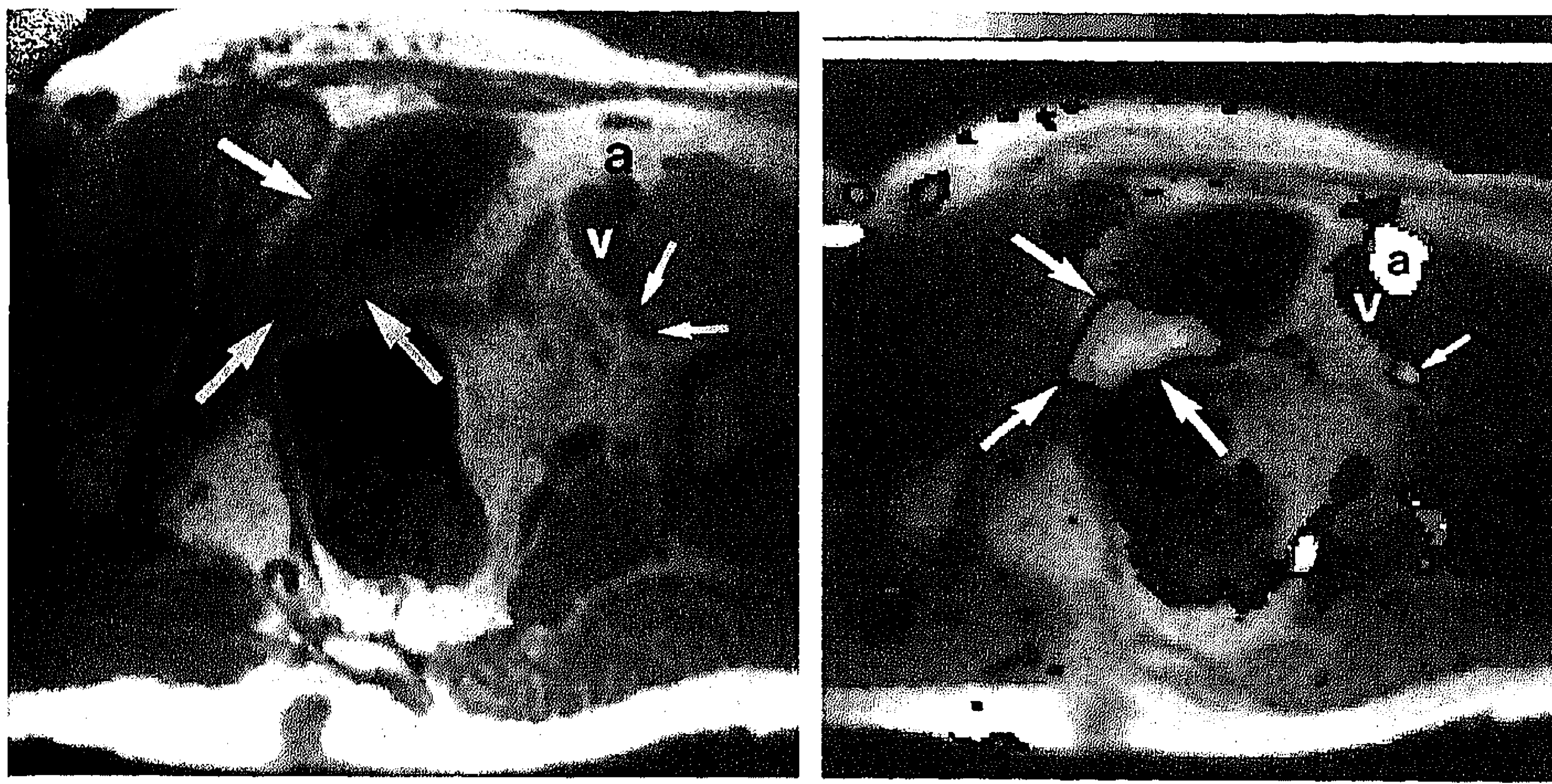


Figure 6. Transition cell carcinoma, stage T4a, on right side, with normal-size lymph node containing metastasis on left side. (a) T1-weighted MP-RAGE image shows tumor (long arrows) and normal-size ($11 \times 6 \times 6$ mm) lymph node (short arrows). (b) Time image shows equal early enhancement of bladder tumor (long arrows) and node (short arrow) at 6.25 seconds after the start of arterial enhancement. Findings at histologic examination confirmed normal-size metastatic lymph node. *a* = artery, *v* = vein.

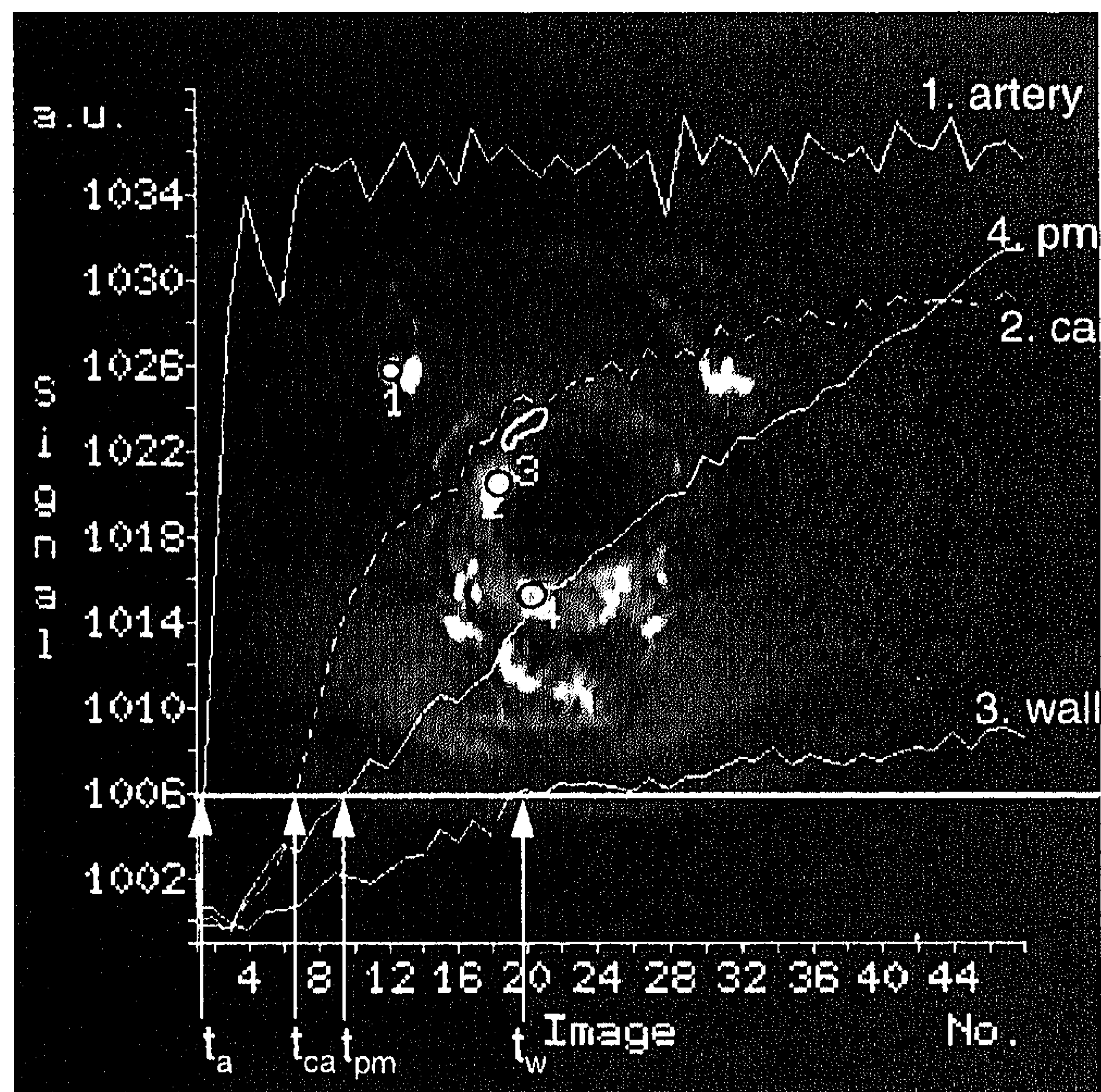


Figure 7. Time (*t*)-to-SI (*Signal*) curve shows different enhancement patterns of regions of interest of various tissues and the importance of fast imaging in the early first-pass phase. Every image represents 1.25 second. At time t_a , the arterial enhancement above the noise threshold starts to become visible, followed shortly by urinary bladder carcinoma (*ca*) at time t_{ca} , parametrium (*pm*) at time t_{pm} , and bladder wall (*wall*) at time t_w . The difference in SI between urinary bladder carcinoma and parametrium is highest in the first-pass phase. At 45 seconds, in the equilibrium phase, most structures have reached their maximal SI. The difference between urinary bladder carcinoma and parametrium is less prominent at this time. *a.u.* = arbitrary units.

more, interobserver variation was only 5%. The overall accuracy for tumor staging on the basis of unenhanced images in this study (67%) is low compared with accuracies reported by other authors (69%–93%) (2–16,22). This may be explained by the fact that

all of our patients were examined 1–4 weeks after TUR or biopsy. In all other studies, MR imaging was not performed within 4 weeks after TUR or biopsy. We found no differences in staging early (1 week) versus later (4 weeks) after TUR; therefore, our technique

can be used 1 week after TUR. We obtained high-resolution T2-weighted images, but results with unenhanced MR images might have been better if we had used thinner, 4–5-mm-thick sections without an intersection gap.

The FLASH sequence may be of value in the assessment of lymph node metastases. At CT, lymph node metastases were reported to enhance (28). Likewise, in our study, enhancement of metastatic nodes was also seen at MR imaging. All metastatic nodes that were depicted at turbo FLASH imaging showed enhancement as early or even slightly earlier than the bladder tumor. Earlier enhancement was explained by a higher grade of malignancy in one patient (Fig 1). In two patients, this technique was sensitive enough to depict metastases in normal-size ($11 \times 6 \times 5$ -mm) nodes. To our knowledge, this has not been reported to have occurred with any noninvasive imaging modality before. Because the turbo FLASH sequence is a single-section technique, its ability to depict normal-size lymph nodes is not truly assessed. A majority of normal-size lymph nodes are not imaged in this single-section examination. Nevertheless, in six patients the turbo FLASH single-section technique correctly depicted late or no node enhancement in normal-size nodes without metastases. In one patient with an enlarged node and in one patient with a normal-size node without metastases, however, early enhancement was found. The value of this technique for depicting node metastases in normal-size nodes, therefore, necessitates further investigation. The combination of the three-dimensional MP-RAGE and dynamic technique has a high accuracy (93%) in the staging of lymph nodes in this study. Therefore, this technique can help select patients for lymph node biopsy prior to planned cystectomy. Note, however, that the difference in accuracy for node staging between unenhanced and enhanced images was not statistically significant.

A major limitation of the present technique is that it can be performed in only a single section, with moderate resolution (128×256 matrix) and signal-to-noise ratio. In two patients, the section level was incorrect. Because bladder cancer can “crawl” superficially along the bladder wall and invade at different sites, it is possible to pick the wrong level on the basis of the three-dimensional data set. In another patient, microscopic residual tumor was not depicted. In most patients, tumor and normal-size nodes

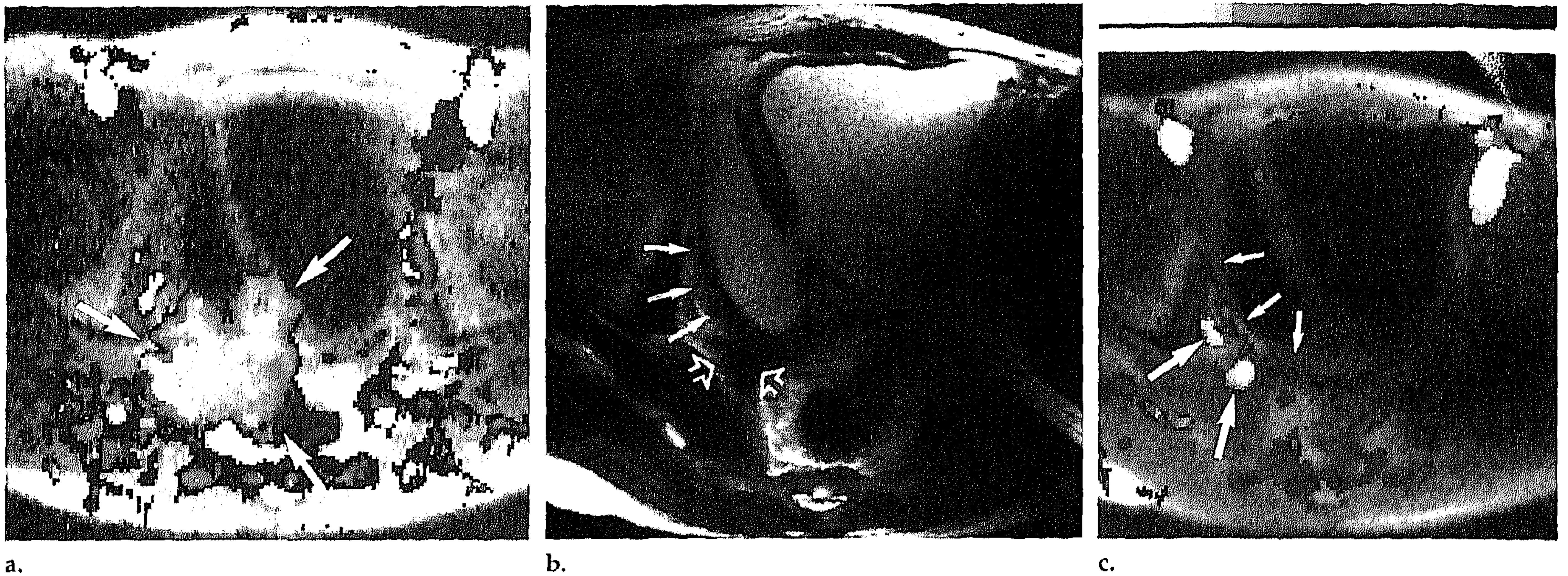


Figure 8. Stage T4b transition cell carcinoma before and after chemotherapy. (a) On time image obtained before chemotherapy, tumor (arrows) in bladder diverticulum starts to enhance 2.5 seconds after the start of arterial enhancement. (b) Fast spin-echo T2-weighted image obtained after chemotherapy shows residual wall thickening (solid arrows) and residual low-SI area in perivesical fat (open arrows), which are evidence of stage T3a or T3b malignancy. (c) On time image obtained after chemotherapy, bladder wall thickening starts to enhance 12.5 seconds after the start of arterial enhancement (short arrows). Low-SI area shows two foci of early enhancement (long arrows). The unenhanced images (not shown) revealed that these foci represent vessels and not tumor. On time images, arteries are always depicted as much larger, owing to pulsation artifacts (visible in Figs 1c and 6b). Findings at histologic examination (not shown) confirmed absence of malignancy.

could not both be included in the FLASH section. The results of our study, however, show that use of fast techniques, even in a single section, results in better differentiation between postbiopsy tissue and tumor and in improved staging. New ultrafast multisection dynamic techniques with a higher resolution will have to be developed to enable multisection fast dynamic MR imaging during the first-pass phase of contrast enhancement. With these techniques, the entire tumor volume could be delineated with a high specificity.

Although the differentiation between postbiopsy tissue and urinary bladder cancer at turbo FLASH time imaging is better than at imaging with existing techniques, the present limitations of this sequence do not justify obviating cystectomy in patients without early lesion enhancement. On the other hand, on the basis of better recognition of extravesical tumor extension and lymph node metastases with this technique, a more appropriate treatment decision can be made between curative cystectomy and palliative or neoadjuvant chemotherapy.

The behavior of urinary bladder cancer after intravenous injection of a gadolinium-containing contrast agent, as documented on fast dynamic MR images and time images, is a reflection of its neovascularity. Microvessel quantification is reported to be an independent predictor of survival in patients with invasive bladder cancer and might be useful to help select patients who would benefit from adju-

vant therapy (24,25). Perhaps fast dynamic contrast-enhanced MR imaging could be used to help select and follow-up patients who undergo neoadjuvant chemotherapy. Initial results with this technique in the follow-up of patients after chemotherapy are promising (Fig 8), but further prospective studies are needed.

We conclude that fast dynamic contrast-enhanced turbo FLASH imaging with at least one image acquired every 2 seconds results in improved detection and staging of urinary bladder cancer. Time images that display the beginning of enhancement in relation to arterial enhancement permit more accurate differentiation between postbiopsy effects and tumor, which results in improved tumor staging in patients within 4 weeks after TUR or biopsy. Additionally, this technique may help detect metastases in normalized nodes. Currently, however, this technique cannot be performed in multiple sections. Therefore, new ultrafast multisection dynamic techniques need to be developed to enable imaging of the entire tumor volume and all regional lymph node areas. ■

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