Eur. Radiol. 9, 1722–1736 (1999)

European
Radiology

Review article

MR imaging of the male pelvis

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Abstract. Prostate and urinary bladder cancer are the most frequently encountered malignancies of the urinary tract. Appropriate use of the different imaging techniques is crucial for accurate assessment of prognosis and for the development of appropriate treatment planning. Especially determination of local tumor extension and detection of nodal or bone metastases is extremely important. In this regard MR imaging is the most promising imaging technique. Therefore, in this review its role in staging these malignancies is evaluated and compared with clinical staging, and other imaging techniques. Finally, future developments, such as new sequences, new contrast agents, the role of surface coils and MR-guided biopsy, are considered. Also, the preferred radiological approach is discussed.

Key words: Prostate cancer – Urinary bladder cancer – MR imaging – Neoplasms

Introduction

In the Western world, the most frequently encountered pelvic diseases are neoplasms. Urinary bladder and prostate cancer are the most commonly seen diseases of the male pelvis by radiologists. Therefore, this paper focuses on these diseases. Magnetic resonance imaging is the most promising technique in visualizing these tumors; therefore, the emphasis is on this imaging modality.

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Urinary bladder carcinoma

Benign tumors of the urinary bladder are rare. More than 95 % of all bladder neoplasms are malignant [1]. These lesions are rarely encountered even in large radiological practices.

Approximately 90–95 % of urinary bladder malignancies are transitional cell carcinomas, and 5–10 % consist of squamous cell and adenocarcinoma. The remaining include sarcomas, metastasis from other primary tumors, and urachal adenocarcinomas. In children embryonal rhabdomyosarcomas are the most common bladder neoplasm. Approximately two thirds of the malignant tumors are superficial and are usually papillary. One third of the tumors show infiltration in or beyond the muscular layer of the bladder wall [2, 3].

Bladder cancer is responsible for 4.5 % of all new malignant neoplasms and 1.9 % of cancer deaths in the United States. In 1993 approximately 52,000 new cases were registered in the United States. The mortality was approximately 10,000. Malignant tumors of the bladder are predominantly seen in the sixth and seventh decade of life; however, increasing numbers of patients less than 30 years of age present malignant bladder disease. These malignancies occur more commonly in males than in females, with a ratio of approximately 4:1.

Because the bladder is the most common location of urinary tract, radiologists are frequently called on to participate in the diagnostic work-up and staging of patients with bladder cancer. Appropriate use of the different available imaging techniques is crucial for an accurate assessment of prognosis and for the development of appropriate treatment planning. In this paper clinical aspects including staging, treatment, and prognosis of patients with urinary bladder cancer are described.

As MR imaging is the most accurate imaging technique, its role is reviewed and illustrated. The appearance on MR images of the normal urinary bladder and carcinoma is shown. Patient handling, the choice of

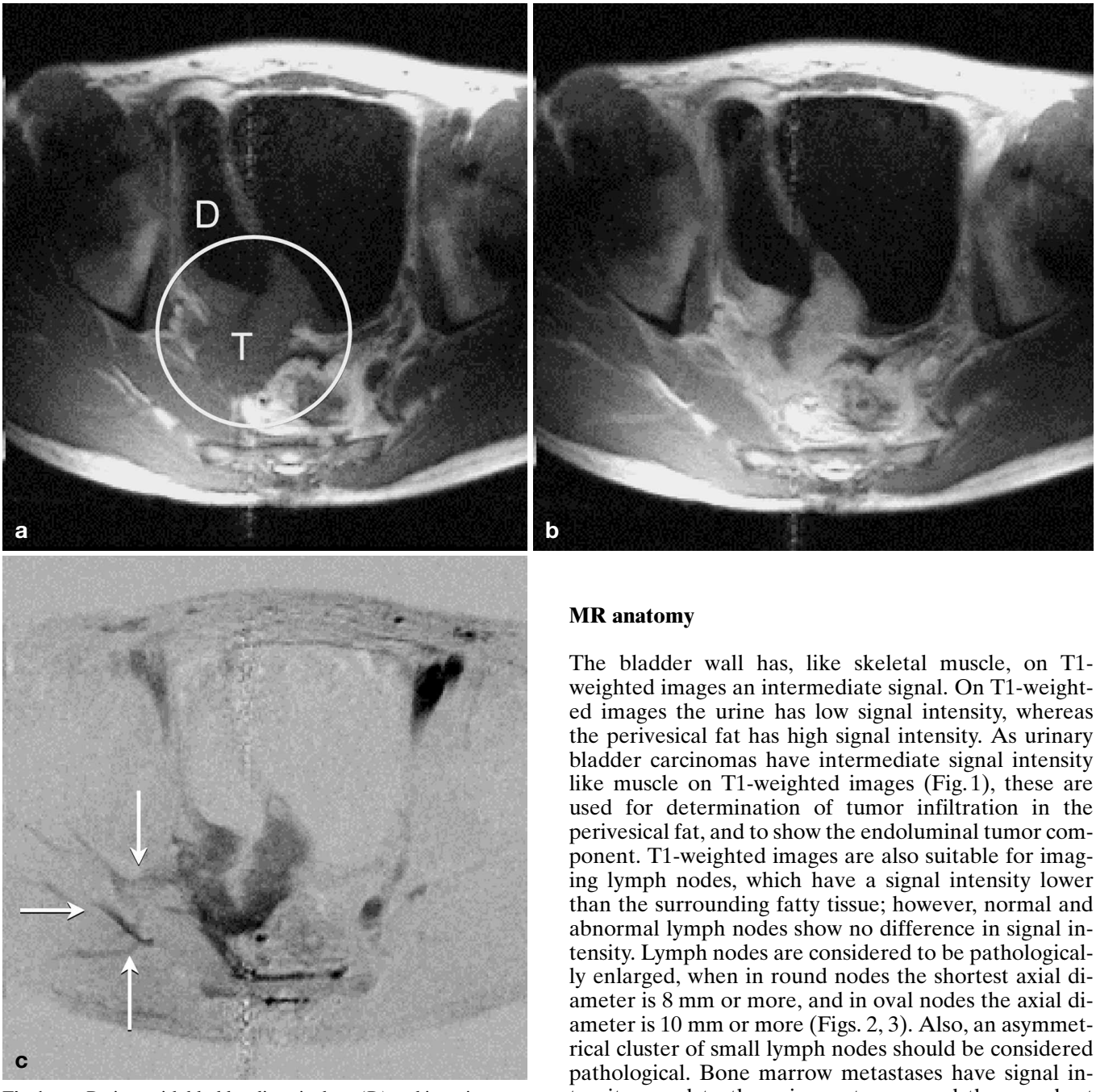

Fig. 1 a–c. Patient with bladder diverticulum *(D)* and invasive cancer (stage T4B). **a** Axial T1-weighted GRE image shows tumor *(T)* extending into the perivesical fat *(circle)*. **b** Same image 2 min post contrast injection shows more enhancement of tumor compared with wall. **c** Subtraction of **a** and **b** shows tumor enhancement in between pelvic muscles *(arrows)*. This infiltration is not visible on T2-weighted images (see Fig. 4)

pulse sequences, and contrast agents is discussed. The role of MR imaging in staging urinary bladder carcinoma is evaluated and compared with clinical staging and CT scanning. Finally, future developments, such as new sequences, the role of surface coils, and MR-guided biopsy, is considered. Also, the preferred radiological approach is discussed.

MR anatomy

The bladder wall has, like skeletal muscle, on T1-weighted images an intermediate signal. On T1-weighted images the urine has low signal intensity, whereas the perivesical fat has high signal intensity. As urinary bladder carcinomas have intermediate signal intensity like muscle on T1-weighted images (Fig. 1), these are used for determination of tumor infiltration in the perivesical fat, and to show the endoluminal tumor component. T1-weighted images are also suitable for imaging lymph nodes, which have a signal intensity lower than the surrounding fatty tissue; however, normal and abnormal lymph nodes show no difference in signal intensity. Lymph nodes are considered to be pathologically enlarged, when in round nodes the shortest axial diameter is 8 mm or more, and in oval nodes the axial diameter is 10 mm or more (Figs. 2, 3). Also, an asymmetrical cluster of small lymph nodes should be considered pathological. Bone marrow metastases have signal intensity equal to the primary tumor, and thus are best recognized on T1-weighted images, on which there is a good contrast between these metastases and the surrounding fatty bone marrow.

On T2-weighted images the bladder wall has low signal intensity. Perivesical fat has low or high signal intensity depending on the type of T2-weighted sequence used. Urine has high signal intensity (Fig. 4). Bladder cancer has intermediate signal intensity, which is higher than bladder wall or late fibrosis and lower than the urine. T2-weighted images are used for determination of depth of tumor infiltration in the bladder wall, to differentiate tumor from late fibrosis, to assess invasion into the prostate, uterus, or vagina, and to confirm bone marrow metastases seen on T1-weighted images.

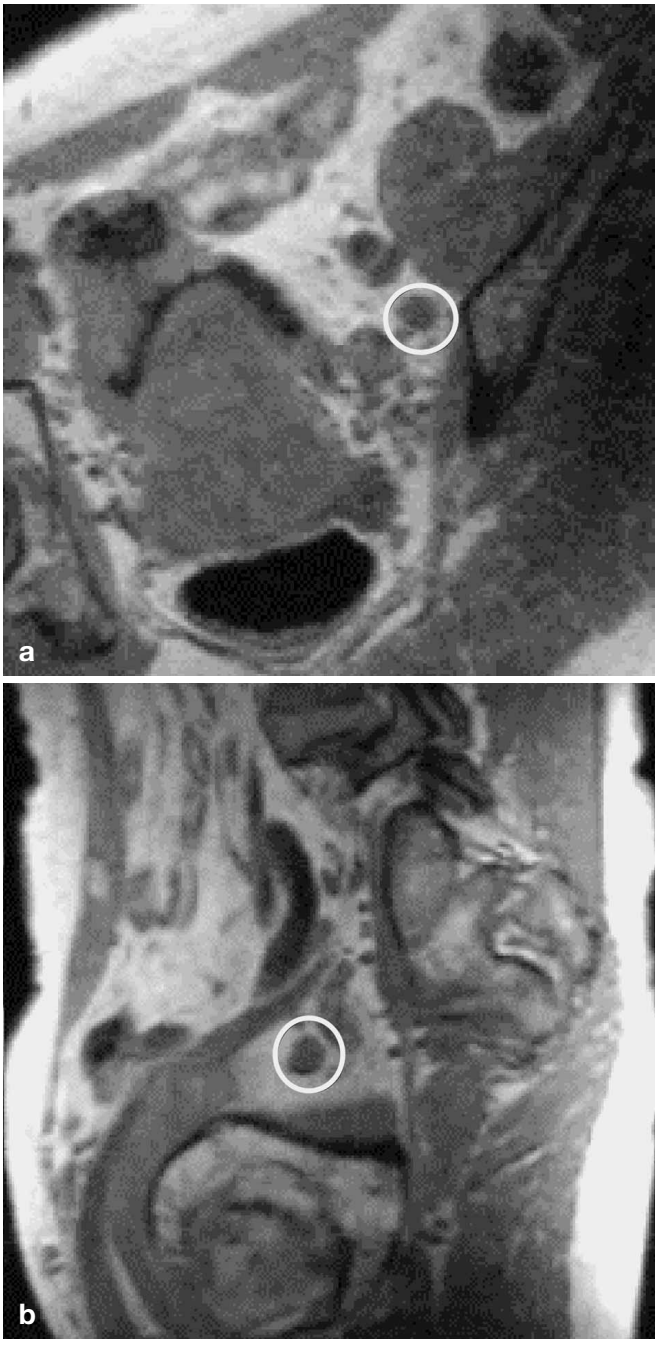

Fig. 2 a, b. Three-dimensional MP-RAGE in round enlarged lymph node metastases. Three-dimensional MP-RAGE reconstructed images in **a** angulated sagittal plane, and **b** angulated axial plane perpendicular to long axis of node show nodal size to be $1.1 \times 0.9 \times 0.9$ mm *(circle)* which is pathological. Surgery confirmed metastasis. A node is considered pathologically enlarged if an oval node has minimal axial diameter of 10 mm or more, and/or if a round node has a minimal axial diameter of 8 mm or more. A node is round when the longitudinal axis/short axis ratio is more than 0.8

Optimizing MR images

Several factors must be considered when trying to optimize MR images of the urinary bladder, urinary bladder carcinoma, and its metastases. These factors are related both to patients and to technique. Numerous patient-related factors are important for optimal MR imaging of the urinary bladder. The most important are motion-artifact reduction and the degree of bladder distension.

Making the patient feel at ease can reduce voluntary motion artifacts. Sedatives may be effective in claustrophobic patients [4]. Respiration, intestinal peristalsis, and bladder motion cause involuntary motion artifacts. To reduce bowel motion, patients can be given 0.5 ml of glucagon IV before the examination and 1.5 ml of glucagon IV by a drip infusion during the examination. To reduce respiration movements, an adjustable belt can be wrapped around the abdomen to cause a slight compression.

Optimal bladder distension is very important. In a bladder that is not sufficiently distended, the bladder wall is thickened, which makes it difficult to recognize small tumors. If the bladder becomes too full, the patient becomes restless. Flat tumors can be missed because of too much extension of the wall. Optimal bladder filling can be achieved by asking the patient to void 2 h before the examination and then not again until the end of the MR examination.

Magnetic field strength, selection of appropriate pulse sequences, use of surface coils, and administration of contrast agents must be considered when trying to optimize MR images of the urinary bladder. Field strengths varying from 0.02 to 1.5 T are used. Imaging at high field strengths has certain advantages, such as higher signal-to-noise ratios and allowing the use of thin slices and ultra-fast scanning techniques. Disadvantages are higher costs, stronger chemical-shift artifacts, and a lower T1-contrast. In general, the reported staging results using different field strengths are comparable [2].

Sequences

For staging of urinary bladder cancer, both T1- and T2-weighted images have to be used. For T1-weighted images, conventional two-dimensional spin-echo (SE), two- or three-dimensional gradient-echo (GRE), or three-dimensional magnetization prepared gradient echo (MP-RAGE) sequences can be chosen [5, 6]. For T2-weighted imaging fast-SE sequences are considered state of the art in the pelvis.

Surface coils

By using surface coils, image quality in the pelvis can be improved considerably [7]. Phased-array body coils are especially well suited for pelvic MR imaging. The high signal-to-noise ratio obtained with these coils facilitates excellent image quality with superior spatial resolution. Recently, endorectal coils have been developed. These coils produce excellent images of the prostate and seminal vesicles, and show promise for staging of urinary bladder tumors. With these coils exact delineation of

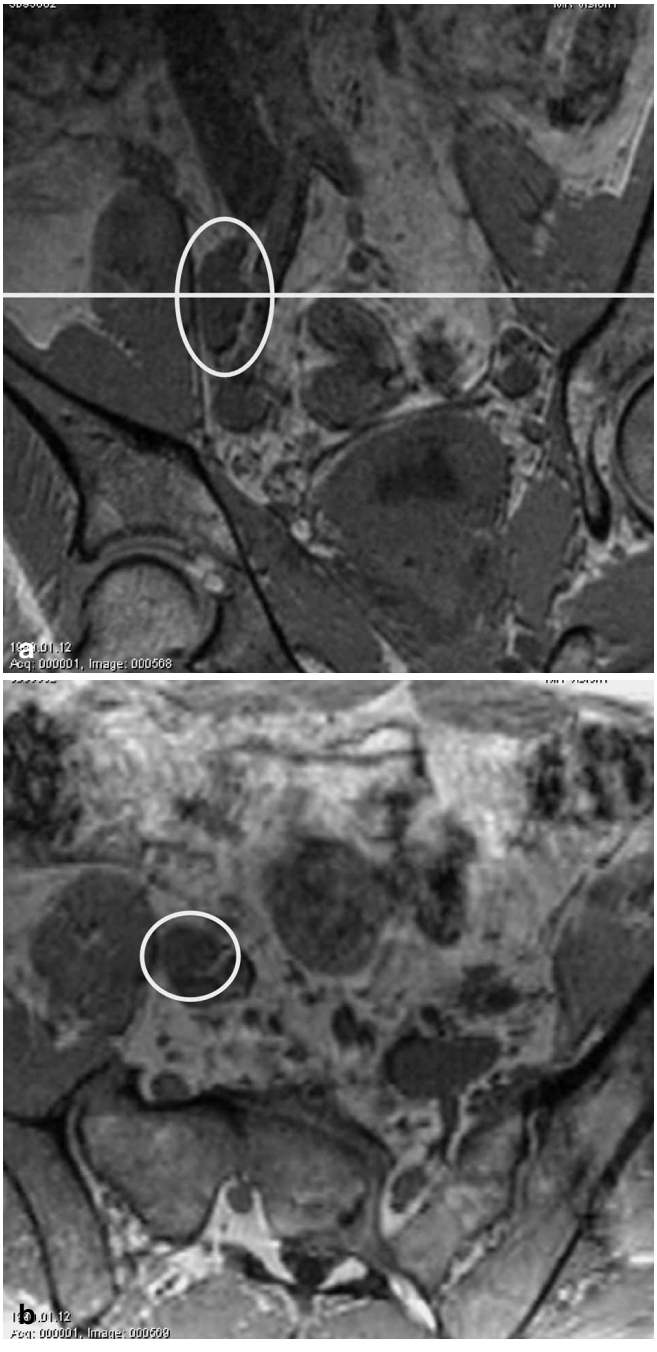

Fig. 3 a, b. Three-dimensional T1-weighted MR images in oval enlarged lymph node metastases. Three-dimensional MP-RAGE reconstructed images in **a** angulated coronal, and **b** angulated axial plane, perpendicular to long axis of node (presented by *line* in **a**), allows nodal size evaluation in three dimensions (size = 3.2 × 1.3 × 1.2 mm; *circle*). Shape of node can also be determined. Surgery confirmed metastasis

urinary bladder carcinoma and the muscle layer of the dorsal bladder wall is possible, which may result in a more accurate recognition of muscular invasion. However, a simple endorectal coil cannot clearly visualize the entire bladder wall; therefore, the use of these coils is limited to tumors on the dorsal wall and the bladder base.

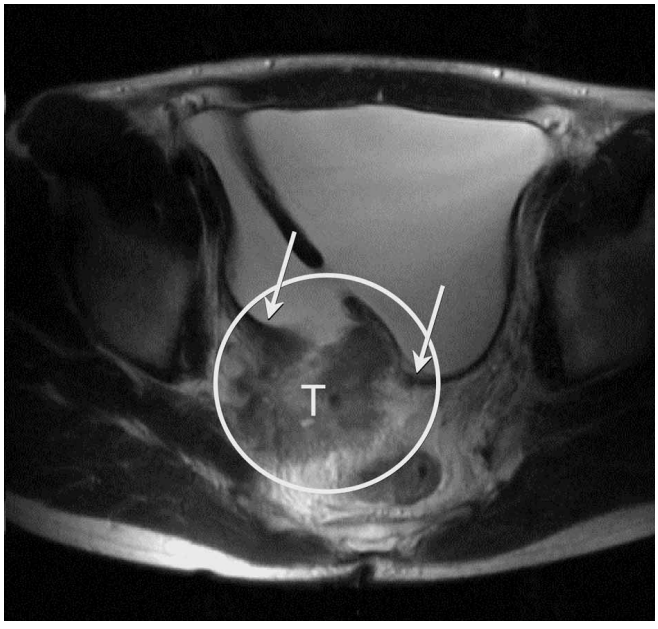

Fig. 4. Same patient as Fig. 1. On axial high-resolution T2-weighted MR images, disruption of the normal low signal intensity bladder wall is present *(arrows)*, which argues for at least deep muscular invasion of the wall. Also there is invasion in the perivesical fat

Contrast agents

Urinary bladder carcinomas develop neovascularization [8]; therefore, this malignant tumor shows on contrast-enhanced MR images early and more enhancement compared with normal wall. As urinary bladder cancer enhances to a greater extent the bladder wall and most surrounding structures, contrast-enhanced T1-weighted images facilitate determination of muscular invasion and perivesical tumor extension; however, differentiation between post-biopsy tissue and malignancy remains difficult when using slower techniques, i. e., one image every 30 s.

Fast dynamic MR imaging, using at least one image every 2 s provides the best separation between post-biopsy effects and urinary bladder cancer [9]. With this technique, early enhancement of urinary bladder cancer can be displayed. The enhancement of urinary bladder starts approximately 6 s after arterial enhancement, which is approximately 4 s earlier compared with other, benign tissues such as post-biopsy tissue. When the beginning of enhancement is used as a criterion, the accuracy in differentiating post-biopsy effects from tumor improved from 80 to 90 %, and staging accuracy from 67 to 84 % [9]. Also, this fast technique facilitates visualization of early enhancement of metastatic lymph nodes and bone marrow metastases (Fig. 5).

Staging

Local tumor extension, the degree of lymph node and distant metastases, and the histological tumor type largely determine treatment and prognosis; therefore, exact

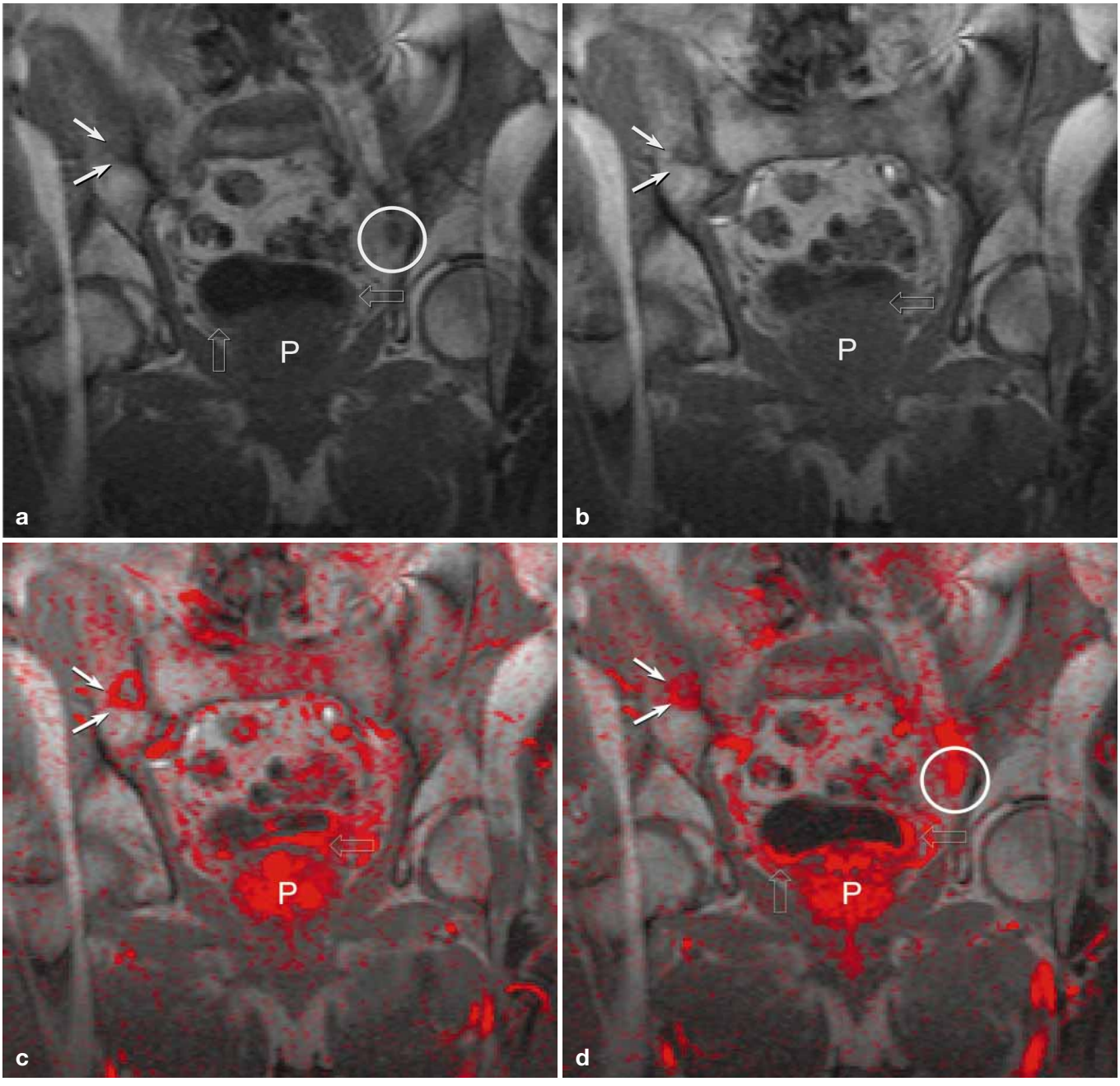

Fig. 5 a–d. Patient with invasive bladder cancer (stage T3B), with nodal and bone marrow metastases. **a,b** Coronal T1-weighted fast-low-angle-shot (FLASH) images show enlarged prostate *(P)*, enlarged node *(circle)* and bone marrow lesion *(arrows)*. Also thickening of bladder wall *(open arrows)*. **c,d** Dynamic images (identical to **a** and **b**) acquired 8 s after beginning of arterial enhancement is projected in *red*. Bladder tumor *(open arrows)*, enlarged node *(circle)*, and bone marrow lesion *(arrows)* show early enhancement, which suggests malignancy. Especially ring-like enhancement of bone marrow lesion is highly suggestive for metastasis, and can be recognized on both slices. Histology and follow-up confirmed nodal and bone marrow metastases

staging is imperative. To determine local tumor extension (T), presence of lymph node (N), and distant metastases (M) the "Union Internationale Contre le Cancer" (UICC) proposed a uniform clinical staging method (Fig. 6; Table 1). In addition to this classification, also the American, Jewett-Strong classification is used [2].

In superficial tumors, i. e., tumors without muscle invasion (stages Ta and T1), patients are treated with local endoscopic resection followed by adjuvant intravesical installations. In patients with a tumor invading the muscle layer of the bladder wall or with only minimal perivesical extension (stages T2a–T3 a) an attempt at cure is made by radical cystectomy and lymphadenectomy. However, if the tumor is in an advanced stage (stages T3b–T4 b) or if there are nodal or distant metastases, the patient will receive palliative chemo- or radiation therapy.

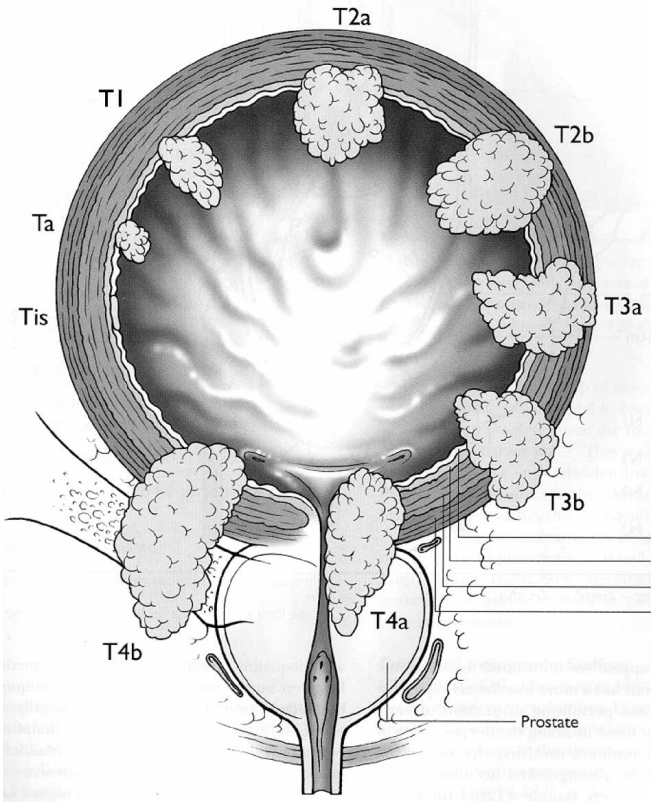

Fig. 6. TNM staging system. (From [25])

Table 1. TNM classification and Jewett-Strong staging system for urinary bladder cancer

Jewett-Strong		TNM Histopathological findings
O	T0	No tumor
O	Tis	Carcinoma in situ
O	Ta	Papillary tumor, confined to epithelium (= mucosa)
A	T1	Tumor invades subepithelial connective tissue (= lamina propria)
B1	T2a	Tumor invades superficial muscle (inner half)
B2	T2b	Tumor invades deep muscle (outer half)
B2	T3a	Tumor with microscopic invasion of perivesical fat
C	T3b	Tumor with macroscopic invasion of perivesical fat
D1	T4a	Tumor invades surrounding organs
D1	T4b	Tumor invades pelvic or abdominal wall
D1	N1–3	Pelvic lymph node metastases
D2	M1	Distant metastases
D2	N4	Lymph node metastases above the bifurcation

As clinical staging is not reliable to determine tumor extension beyond the bladder wall, other methods are needed. Computed tomography is a valuable addition, but since the introduction of pelvic MR imaging in 1983, several reports have attested to the superiority of this technique for staging urinary bladder carcinoma [1, 2, 3].

Magnetic resonance imaging appears to be superior to CT for staging carcinoma of the urinary bladder. Multi-planar imaging allows better visualization of the bladder dome, trigone, and adjacent structures such as the prostate and seminal vesicles. The accuracy of MR imaging in staging bladder cancer varies from 73 to 96%. These values are 10–33% higher than those obtained with CT [10]. Recently, several reports have been published on the staging of urinary bladder carcinoma with the use of IV gadolinium contrast. A 9–14% percent increase in local staging accuracy has been reported using these contrast agents. Furthermore, when using contrast agents, visualization of small tumors (> 7 mm) is improved. Best staging results using IV gadolinium contrast material are obtained with very fast T1-weighted sequences [8, 9]. This can be explained by previous enhancement of tumors compared with surrounding tissues. Although contrast-enhanced MR imaging has advantages over the use of unenhanced T2-weighted sequences, such as higher signal-to-noise ratio and shorter acquisition time, it is advised not to skip the T2-weighted images. Large prospective studies in this regard are necessary.

The role of MR imaging in nodal and bone marrow staging is discussed below together with prostate cancer.

In summary, based on published reports and our own experience [2, 3, 10, 11], Table 2 offers an overview of the value of the several staging techniques for urinary bladder. Magnetic resonance imaging and clinical staging complement each other. Magnetic resonance imaging is the most accurate technique for differentiating the various stages of deeper infiltrating tumors (stages T2 and higher), whereas clinical staging is the best technique for differentiating between acute edema, early granulation tissue, and the various stages of superficial tumors (stages Ta and T1). When MR imaging is available, CT is no longer needed.

Future developments

Technological improvements are being introduced rapidly. With the new-generation MR scanners faster sequences with a higher resolution can be applied. With new MR units it is possible to perform a high-resolution T1-weighted 3D MP-RAGE sequence with isometric voxels ($1.4 \times 1.4 \times 1.4$ mm) in 5 min. Also, ultra-fast multi-slice dynamic imaging becomes possible. At this moment, seven slices can be made with a time resolution of 2 s, allowing evaluation of urinary bladder cancer and its metastases with high specificity at multi-slice. The high signal-to-noise ratio, obtained with new phased-array coils, facilitates the use of a fast T2-weighted sequence with a 1024×1024 matrix. For the evaluation of the extent of muscle invasion,

Table 2. Accuracy of different staging techniques. *M +* bone marrow infiltration; *T0* no malignancy, e. g., scar, fibrosis, granulation tissue, hypertrophy; *T +* malignancy, + + highly accurate; + accurate; *0* not accurate; – not possible

Stage	Clinical staging including transurethral resection	CT	MR imaging
T0-T +	+ +	–	+
Tis-Ta	+ +	–	–
Ta-T1	+ +	–	–
T1-T2a	+ +	–	0
T2a-T2b	0	–	+ +
T2b-T3a	–	–	–
T3a-T3b	–	+ +	+ +
T3b-T4a	–	+	+ +
T4a-T4b	–	+	+ +
N0-N +	–	+	+
M0-M +	–	0/ +	+ +

the combination of an external with an endorectal phased-array coil and these sequences seems promising.

Fast dynamic imaging

The behavior of urinary bladder cancer after IV injection of a Gd-containing contrast agent as documented with fast dynamic MR imaging and time-images are 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 in selecting those who would benefit from adjuvant therapy [9]. Fast dynamic MR imaging is more accurate compared with conventional unenhanced MR imaging in the follow-up of chemotherapy [12].

MR-guided biopsy

Magnetic resonance imaging has advantages over other imaging modalities for biopsy guidance. Magnetic resonance imaging, being a three-dimensional imaging technique, facilitates multiple angulated biopsy which can be best performed under MR guidance. A nice example in bladder cancer is the three-dimensional visualization of (enlarged) lymph nodes and the subsequent MR-guided biopsy (Fig. 7). In a preliminary study we performed MR-guided biopsies in 13 patients with slightly enlarged nodes; in 10 of them biopsy was true positive [13]. Another advantage of (contrast-enhanced) MR imaging is the higher specificity and sensitivity in showing urinary bladder cancer and possible metastases compared with ultrasonography or CT scanning. Based on the enhancement pattern of the tumor, with MR imaging, the part of the tumor that contains the most pathological vessels, and thus the most viable part of the tumor, can be localized and biopsied. At this moment, specially designed MR units are being developed in order to simplify localization under MR guidance and to reduce biopsy time. With regular MR scanners biopsies must be performed in the way it is done with CT. Special non-magnetic needles are available; however, efforts must be made to further reduce susceptibility artifacts of these needles.

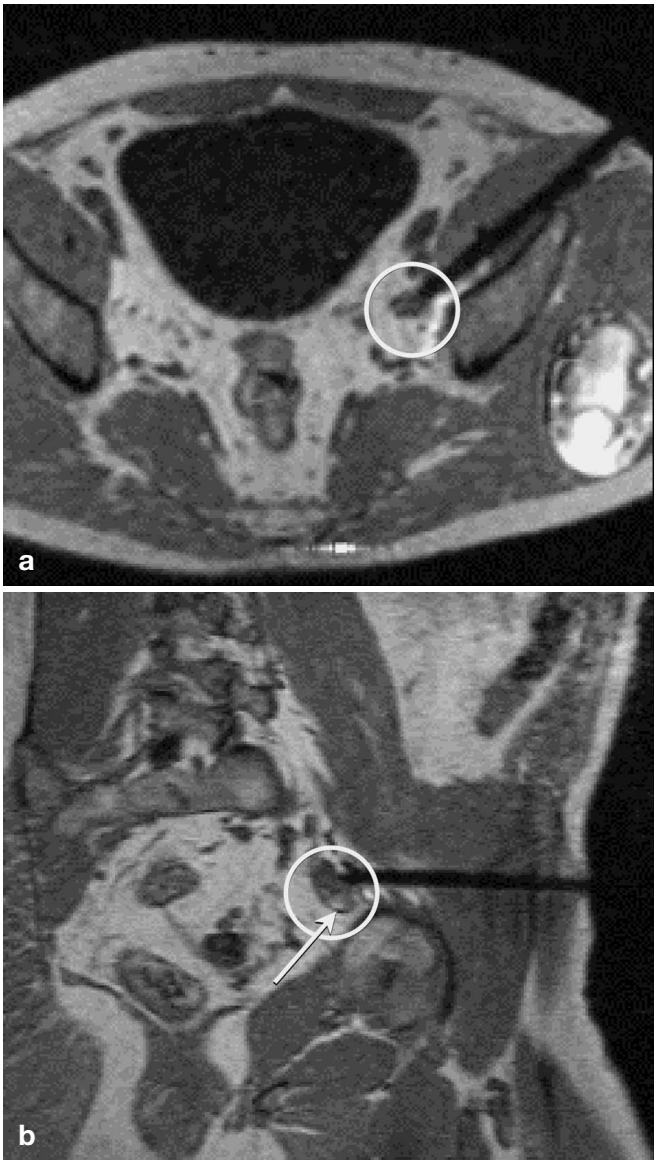

Fig. 7 a, b. Magnetic-resonance-guided nodal biopsy. Patient with lymph node metastasis. **a** Axial and **b** semi-sagittal T1-weighted 3D MP-RAGE images during MR-guided biopsy. Needle is visible as *black line*. Tip of needle is situated at edge of enlarged node. In **b** internal structure of node can be recognized. A caudal small area of high signal intensity *(arrow)* represents fat in node. Biopsy at this site would have resulted in false-negative finding. Now needle was directed more cranial and biopsy was positive

In the near future fast, high-resolution, dynamic contrast-enhanced MR imaging of the urinary bladder further improves the diagnosis, staging, and follow-up of patients with urinary bladder cancer; therefore, this technique is utilized more and more frequently in these patients. Magnetic-resonance-guided biopsy contributes to a less invasive diagnosis, resulting in better treatment planning.

Preferred radiological approach

At present, MR imaging is the first modality of choice in imaging the urinary bladder and its cancer. However, due to limited resources in the Health Care System this technique should only be used to obtain information which directly influences therapeutic management and outcome. To achieve this, both knowledge of urologists of MR imaging and knowledge of radiologist of clinical handling is needed; therefore, continuous education and communication between these two specialties is a necessity.

Detection of bladder cancer should be performed by cystoscopy and histology. Once bladder cancer is diagnosed, the next step should be staging. For superficial tumors, clinical staging, which includes transurethral resection, is the best technique. In addition, an IVU can be performed to rule out multifocal carcinoma in pyelum or ureter. Superficial tumors, without muscle invasion (stages < T2) are treated with local endoscopic resection with or without adjuvant intravesical installations. Follow-up is performed by means of repeated cystoscopy every 3–6 months. No further radiological imaging is needed in these patients.

If, however, there is muscle invasion, further staging should be performed with MR imaging. Patients with muscle invasion (stages T2a and T2b), with perivesical infiltration (stages T3a and T3b), or with invasion into prostate, vagina, or uterus (stage T4a) are treated by radical cystectomy and lymphadenectomy. In cases of pelvic sidewall or abdominal wall infiltration (stage T4b) or metastases in pelvic lymph nodes or bone marrow, palliative chemo- or radiation therapy is given. Follow-up of these therapies can be best monitored with fast dynamic MR imaging.

Prostate cancer

The prostate continues to be the leading cancer site among American men with 184,500 new cases in the U.S. accounting for 29% of new cancer cases in men [14]. It has been estimated that 39,200 men in the U.S. died of prostate cancer in 1998. This makes prostate cancer the second most common cause of cancer-related death in men [15, 16]. Furthermore, the probability of developing prostate cancer from birth to death is 20% [16]. Treatment selection is dependent on patient age and health, cancer stage and grade, morbidity and mortality of treatment, as well as patient and physician preference. The mainstay for organ-confined disease is either radical surgery or curative radiotherapy [17, 18]. This is only considered an option in the absence of seminal vesicle infiltration (SVI), extension through the prostatic capsule (extra-capsular extension, ECE) or metastatic disease. Therefore, the purpose of staging is the possible detection of extraprostatic disease. Clinical staging by digital rectal examination (DRE) and prostate specific antigen (PSA) remains as yet inaccurate. Imaging modalities, such as transrectal ultrasound (TRUS) and MR imaging, can be used to increase staging accuracy. This review deals with the current possibilities and limitations of MR imaging in the staging of prostate cancer.

Clinical staging methods

Accurate staging of prostate cancer is important, because treatment decisions are based mainly on the local extent of prostate cancer (ECE, SVI) and the presence of metastatic disease (lymphatic or hematogeneous). Digital rectal examination is not an accurate staging method, as there are no gross characteristics that are reliable for distinguishing benign from malignant nodules [19]. Furthermore, the interobserver agreement among urologists for detection of prostate cancer by DRE is only fair [20]. Data accumulated from carefully examined prostatectomy specimens revealed that DRE underestimates the local extent of cancer in 40–60% of the cases [21, 22]. Prostate specific antigen is the most accurate marker to screen for prostate cancer but has limited accuracy in staging because there is a substantial overlap in PSA concentrations and pathological stages. Nevertheless, the combination of serum PSA concentration and other variables, such as tumor grade, volume, and clinical stage, significantly enhance the predictive value of serum PSA for the pathological stage [23, 24]. The probability of ECE, SVI, and nodal involvement can be predicted by using the normograms of Partin et al. [23] that use clinical stage, Gleason score, and serum PSA.

MR imaging

Magnetic resonance imaging of the prostate is still in an exploratory phase and this technique is not yet advocated as a routine staging procedure. Prostate MR imaging should be performed in centers where at least 25–50 patients per year are examined and the results can be compared with histology, preferably whole mount specimen [25]. Currently, the major clinical indication for MR imaging is detection of ECE, SVI, as well as nodal and bone marrow metastasis, which are contraindications for radical prostatectomy [26]. Prostate cancer is usually visible as a low signal intensity lesion in a bright peripheral zone on a T2-weighted image (Fig. 8). The differential diagnosis of low signal intensity areas includes cancer, hemorrhage, prostatitis, effects of hormonal or radiation treatment, benign prostate hyperplasia (BPH), scar, calcifications, smooth muscle hyperplasia, and fibromuscular hyperplasia [27]. Hemorrhage, mostly a result from biopsy, can be differentiated from cancer by evaluation of T1-weighted images. Hemorrhage is hyperintense on these images, whereas cancer has the same intensity compared with adjacent normal tissue. Benign prostate hyperplasia, smooth muscle hyperplasia and fibromuscular hyperplasia is located mostly in the central zone (CZ) and transitional zone (TZ), whereas cancer is located primarily in the peripheral zone (PZ). Calcifications are common in all locations

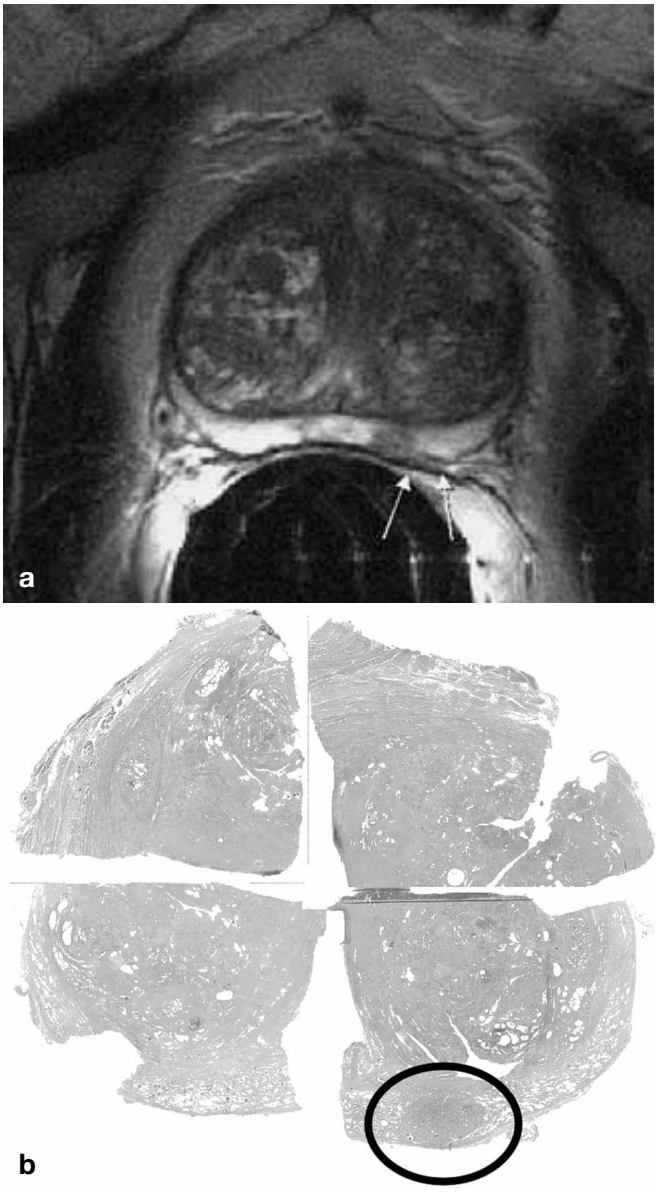

Fig. 8 a, b. Patient with prostate cancer with minimal extracapsular invasion. **a** T2-weighted axial TSE image obtained with endorectal coil (Medrad, Pittsburg, Pa.). Large benign prostatic hypertrophy of central zone shows mixed signal intensity. Tumor *(circle)* is clearly visible as low-signal lesion in high-signal peripheral zone. There is minimal bulging of capsule *(arrows)*. **b** Whole mount section revealed minimal capsular invasion at this site

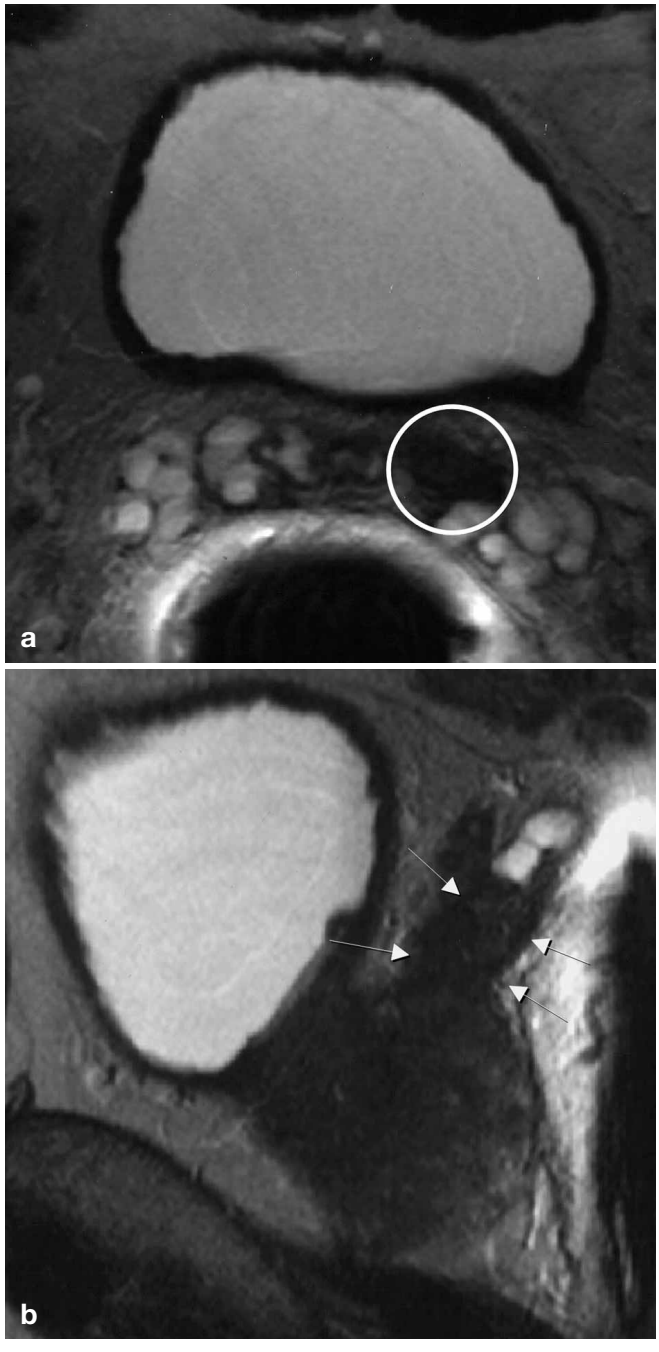

Fig. 9 a, b. Patient with prostate cancer and invasion of left seminal vesicle. **a** T2-weighted axial and **b** sagittal TSE images show abnormal low signal intensity in left seminal vesicle *(arrows)*. Confirmed by histology

of the prostate; however, these may be differentiated from cancer based on their distinct oval form. Scars are rare. Detection of cancer in the CZ and TZ is generally not possible, as this area is commonly replaced by BPH, which has an identical signal.

Staging

Several MR imaging criteria for ECE have been used. Table 3 presents commonly used criteria for ECE with its specificity and sensitivity. Most frequent used criteria are asymmetry of the neurovascular bundle, obliteration of the rectoprostatic angle, and bulging of the prostate capsule (Fig. 8). Seminal vesicle infiltration is detected by an abnormal asymmetric low signal intensity within the lumen on T2-weighted images (Fig. 9) [28]. It should be noted that amyloid deposits, stones, or blood could also cause low signal intensity of the seminal vesicles on T2-weighted images [27, 28, 29, 30].

In staging MR imaging should have a high specificity for periprostatic extension, to ensure that only few pa-

Table 3. Criteria to predict extracapsular extension of prostate cancer. – not determined

Criteria for capsular penetration	Reference	Accuracy (%)	Specificity (%)	Sensitivity (%)	Positive predictive value (%)
Asymmetry of neurovascular bundle	[61]	70	95	38	–
Obliteration of rectoprostatic angle	[61]	71	88	50	–
Bulge	[40]	72	79	46	28
Overall impression	[40]	71	72	68	32
Extracapsular tumor	[40]	73	90	15	34

tients will be deprived of a potentially curative therapy [31]. Sensitivity for periprostatic extension is of minor importance, because even a low sensitivity is an improvement in clinical staging [31]. Magnetic resonance imaging is considered cost-effective if performed in a subgroup of patients with a prior-probability of ECE of at least 30%, i.e., a PSA > 10 or a Gleason grade > 7 [32].

The initial accuracy in 1990 for the staging of prostate cancer with MR imaging was 69% [33]. Since then the most prominent change has been the development of an endorectal coil (ERC), which resulted in faster imaging and improved spatial resolution. Accuracy for ECE with the ERC has shown a wide range between 58 and 90% [34, 35, 36, 37]. Several reasons for this wide range can be given. Firstly, due to the rapidly developing MR imaging technique, different studies have used different imaging protocols. Secondly, due to inexperience with this new method, considerable interobserver variation may be present. A third important reason is that different studies use different criteria for ECE (Table 3) resulting in different accuracies. Although this variation remains, the use of an ERC is considered to be an improvement in the conventional MR examination [36, 37, 38]. Although major developments have changed the MR imaging technique, it still remains impossible to detect microscopic ECE [33, 35, 39, 40]. The detection of SVI is generally not a problem using the ERC: accuracies range between 81 and 96% (Fig. 9) [34, 36, 37, 39]. T1- and T2-weighted images should be acquired at least 2 weeks after the prostate biopsy as hemorrhage decreases staging accuracy [41].

In addition to its role in staging, MR imaging is useful in reducing the number of false-negative prostate biopsies in patients with elevated PSA and repeated negative (TRUS-guided) biopsies. With MR imaging prostate cancer can be detected and then an MR-directed biopsy can be performed. Using MR imaging as a method of detecting cancer lesions in a group of 36 patients with negative biopsies and elevated PSA values, an accuracy of 78%, a positive predictive value of 74%, and a negative predictive value of 84% was achieved [42].

In summary, the role of MR imaging in local staging is not yet clearly defined; however, it is considered to be cost-effective in a select group of patients. Seminal vesicle infiltration can be detected with high accuracy, which is an advantage in comparison with TRUS alone.

Metastatic disease

Computed tomography and MR imaging are reported to be the most accurate non-invasive methods of detecting pelvic lymph node metastases. Scheidler et al. [43] concluded that CT and two-dimensional MR imaging perform similarly in the detection of lymph node metastasis, with a trend toward an improved accuracy of MR imaging; therefore, both MR imaging and CT are recommended, because unlike LAG they are non-invasive. A recent study using MR imaging with a three-dimensional technique has revealed an accuracy of 90%, a positive predictive value of 94%, and a negative predictive value of 89% in the detection of nodal metastasis in bladder and prostate cancer [6]. This is clinically relevant, because a high detection accuracy of nodal metastasis can facilitate the indication for (MR-guided) biopsy [13], which in case of a positive biopsy can avoid an invasive pelvic lymph node dissection. The multi-planar reconstructions obtained with this technique allow the evaluation of not only nodal size but also nodal shape. This is important because the cut-off point between normal and metastatic nodes differ for round and oval nodes (Figs. 2, 3). The smallest lymph node diameter that can be detected by this method is 2 mm. Different sensitivities and specificities are acquired depending on the selection of cut-off size [6, 44, 45]. In our department, we use a minimal axial diameter of 8 mm for round nodes and 10 mm for oval nodes as the upper limit of normal.

Because of high cost, CT and MR imaging in detection of nodal metastasis should be performed only in a select group of patients with high risk for nodal metastases, which can be predicted by DRE, PSA, and biopsy Gleason score [6, 23, 46].

Hematogeneous metastases are most common in the axial skeleton. Currently, the mainstay for the detection of bone metastases is a radionuclide bone scan. However, it is well known that bone scans can yield false-negative findings, especially in cases of very aggressive metastases. Furthermore, the technique has a high false-positive rate due mainly to degenerative disease, healing fractures, and various metabolic disorders and their complications (e.g., osteoporosis and osteomalacia). It has been demonstrated that bone scintigraphy seems to be unnecessary in the evaluation of newly diagnosed, untreated prostate cancer with no clinical signs of bone pathology and serum PSA levels of < 10 ng/ml [47]. In patients with an elevated PSA (> 10 ng/ml) or with locally advanced tumors, bone scans are considered to be

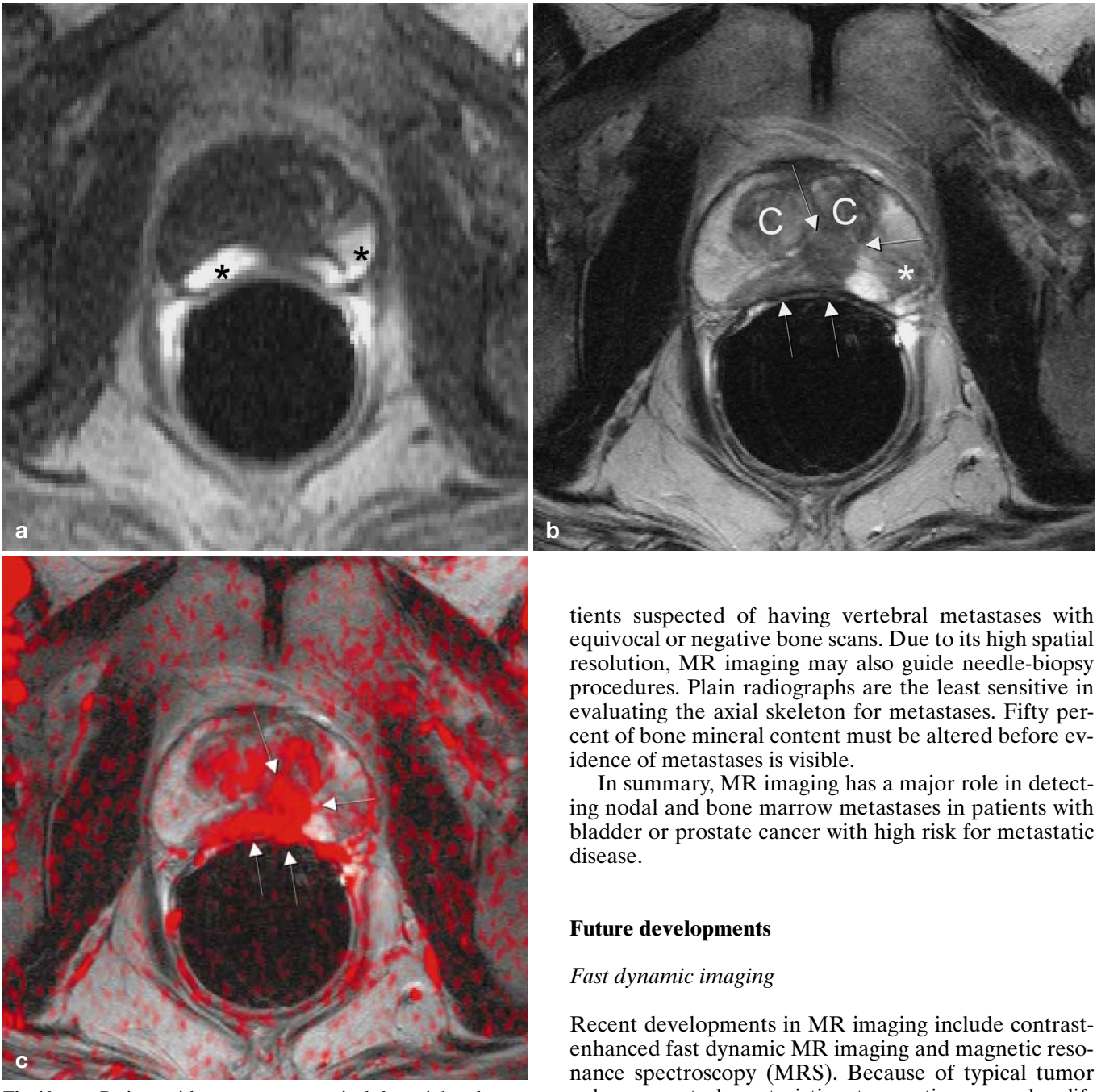

Fig. 10 a–c. Patient with prostate cancer in left peripheral zone with post-biopsy hematoma. **a** Axial T1-weighted FLASH MR image shows high signal intensity *(asterisk)* representing hematoma. On **b** axial T2-weighted TSE image hematoma *(asterisk)*, central zone *(C)*, and lesion *(arrows)* show low signal intensity and cannot be separated. In **c** dynamic information 8 s after beginning of arterial enhancement is displayed in *red* over **b**. In this image prostate cancer can be correctly recognized based on early enhancement *(arrows)*, and separated from central zone benign prostate hyperplasia and hematoma. Confirmed by histology

worthwhile for detecting both asymptomatic and symptomatic metastasis. Magnetic resonance imaging is more sensitive in detecting bone marrow metastases compared with radionuclide bone scanning [48]. Therefore, MR imaging can be useful in the evaluation of patients suspected of having vertebral metastases with equivocal or negative bone scans. Due to its high spatial resolution, MR imaging may also guide needle-biopsy procedures. Plain radiographs are the least sensitive in evaluating the axial skeleton for metastases. Fifty percent of bone mineral content must be altered before evidence of metastases is visible.

In summary, MR imaging has a major role in detecting nodal and bone marrow metastases in patients with bladder or prostate cancer with high risk for metastatic disease.

Future developments

Fast dynamic imaging

Recent developments in MR imaging include contrast-enhanced fast dynamic MR imaging and magnetic resonance spectroscopy (MRS). Because of typical tumor enhancement characteristics, tumor tissue can be differentiated from normal tissue by fast dynamic contrast-enhanced MR imaging. On contrast-enhanced MR imaging prostate cancer shows a typical early and rapidly accelerating enhancement compared with normal tissues [49, 50, 51] which can be used to detect the tumor and to evaluate ECE or SVI (Figs. 10, 11). Other fields where dynamic MR imaging may have a potential role are therapy monitoring and the prediction of therapy success of systemic therapy of prostate cancer [51]. Current problems with the detection with dynamic MR imaging of prostate carcinoma involve the large variation in enhancement patterns among patients with prostate carcinoma and the overlapping enhancement pattern of BPH [52]. As the differences in enhancement between carcinoma and normal prostate

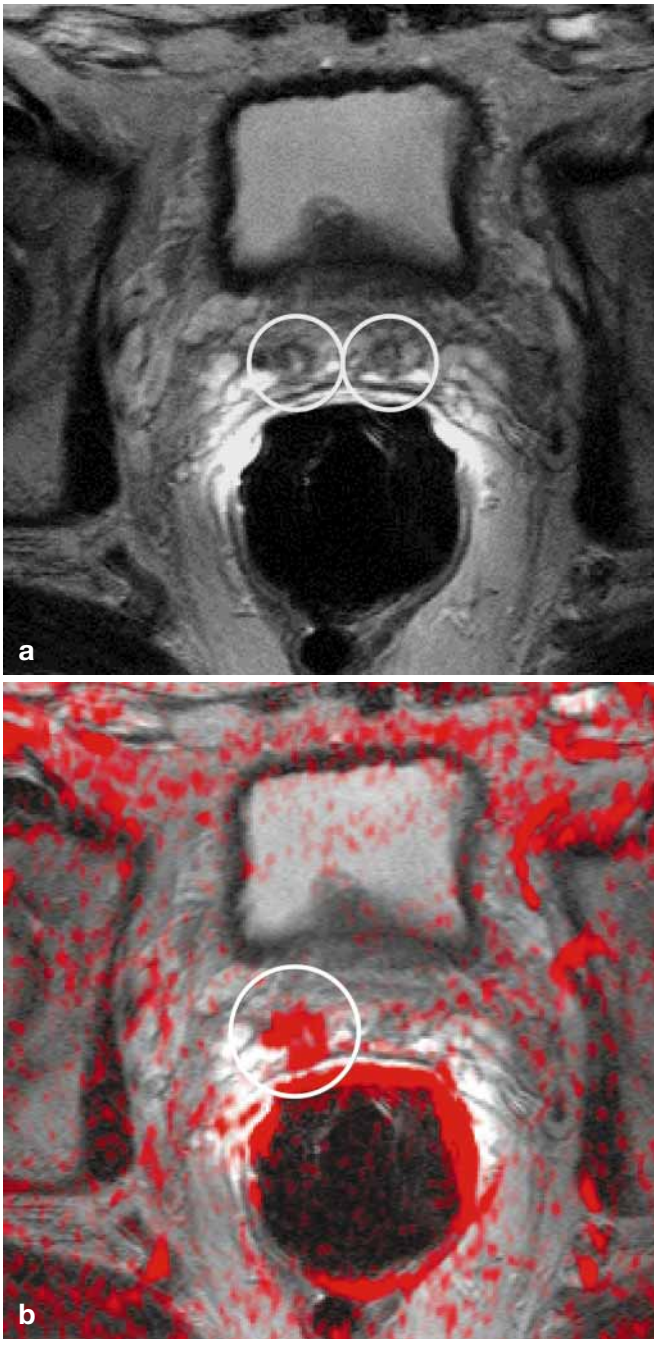

Fig. 11 a, b. Patient with prostate cancer and seminal vesicle infiltration on right side. **a** Axial T2-weighted TSE image shows low signal intensity in both seminal vesicles *(circles)*. In **b** dynamic information 8 s after beginning of arterial enhancement is displayed in *red* over **a**. Right seminal vesicle shows early enhancement *(circle)*. Histology confirmed seminal vesicle infiltration on right side

or BPH may be minimal, fast sequences should be applied. In our institution we use a time resolution of 2 s. With this resolution information of seven slices can be obtained.

MRS

Image-guided proton MRS (1H MRS) is a technique which provides metabolic information about the prostate gland, which may be used for in situ characterization, diagnosis, and therapy evaluation of prostate cancer. Although the examination is comparable with MR imaging, the spatial resolution is lower (down to 0.24 cm^3 has been reported for the prostate) [55] and the information obtained is related to metabolites rather than anatomy. It has been shown that prostate cancer is characterized by a decreased level of citrate and an increased level of (phospho) choline [54]. Especially in the PZ, tumor tissue can be identified by an increased choline/citrate (or choline + creatine/citrate) signal ratio [54, 55]. Correlations have been reported between metabolite ratios and the histological grade in human prostate cancers [56]. The addition of 1H MRS to (dynamic) MR imaging can improve tumor visualization and spatial extent [53, 57]. Potential areas of prostate cancer management that may benefit from the 1H MRS information include targeted TRUS-guided biopsies for patients with PSA levels indicative of cancer but negative previous biopsies, therapy monitoring (watchful waiting), and guiding focal prostate cancer therapies [57].

Nodal staging

An important limitation of CT and MR imaging in the evaluation of nodal metastasis is that both imaging methods depend on enlargement of lymph nodes as a criterion for metastasis. The problem is that metastasis may also be present in normal-sized nodes, thus causing low sensitivities (75–78 %) [6, 45] by not recognizing metastasis in normal-sized nodes. A solution to this problem may be the use of lymph-node-specific MR contrast agents. New MR contrast agents with ultrasmall superparamagnetic iron oxide particles are currently under investigation. In normal lymph nodes with functioning macrophages the iron oxide particles are phagocytosed and thereby decrease the signal intensity on MR imaging (Fig. 12). Metastatic nodes, lacking macrophages, do not take up the contrast agent and hence show no change in signal on post-contrast images [58]. These agents may increase sensitivity for nodal metastasis, by detection of metastasis in normal-sized nodes. Preliminary results suggest an improved accuracy in the detection of metastasis in normal-sized nodes using a lymph-node-specific MR contrast agent [59].

Conclusion

Accurate staging of prostate carcinoma is essential for making treatment decisions; however, pre-operative clinical staging is inaccurate. Digital rectal examination and PSA can only provide an inexact indication of local extent. Addition of other parameters, such as number of positive biopsies and biopsy grade, improves clinical

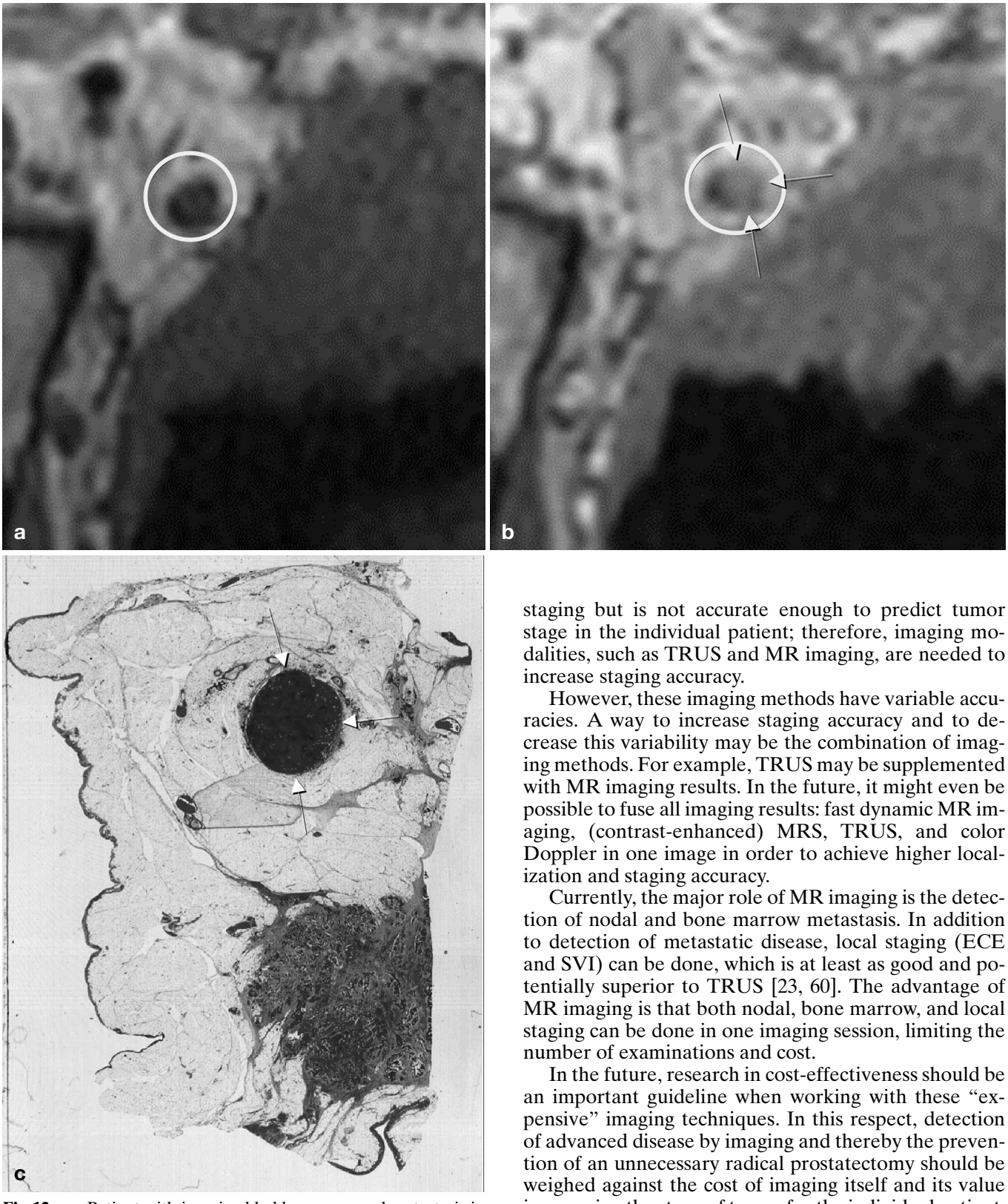

Fig. 12a–c. Patient with invasive bladder cancer and metastasis in normal-sized lymph node. **a** Pre-contrast T1-weighted 3D MP-RAGE image in axial plane shows node with 7-mm diameter. **b** Image (same sequence) 24 h post-IV injection of USIOP (Sinerem, Guerbet, Paris, France) shows node with decreased signal intensity on right rim, and slight increase of signal intensity in central–left part *(arrows)*. **c** Histology confirmed 5-mm size metastasis in this central–left part

staging but is not accurate enough to predict tumor stage in the individual patient; therefore, imaging modalities, such as TRUS and MR imaging, are needed to increase staging accuracy.

However, these imaging methods have variable accuracies. A way to increase staging accuracy and to decrease this variability may be the combination of imaging methods. For example, TRUS may be supplemented with MR imaging results. In the future, it might even be possible to fuse all imaging results: fast dynamic MR imaging, (contrast-enhanced) MRS, TRUS, and color Doppler in one image in order to achieve higher localization and staging accuracy.

Currently, the major role of MR imaging is the detection of nodal and bone marrow metastasis. In addition to detection of metastatic disease, local staging (ECE and SVI) can be done, which is at least as good and potentially superior to TRUS [23, 60]. The advantage of MR imaging is that both nodal, bone marrow, and local staging can be done in one imaging session, limiting the number of examinations and cost.

In the future, research in cost-effectiveness should be an important guideline when working with these "expensive" imaging techniques. In this respect, detection of advanced disease by imaging and thereby the prevention of an unnecessary radical prostatectomy should be weighed against the cost of imaging itself and its value in assessing the stage of tumor for the individual patient. In this view it remains very important to select appropriate patients for staging with the imaging techniques mentioned herein. Finally, it must be mentioned that the role of imaging, especially MR imaging and MRS, is rapidly changing and improving and more research needs to be done to establish its definite role.

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