Imaging of Lymph Nodes – MRI and CT

15

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CONTENTS

15.1 Background

In patients with cancer, the demonstration or exclusion of lymph node metastases is an important component of tumor staging besides evaluation of local tumor extent and has crucial implications for the patient's prognosis and therapeutic strategy, especially when deciding on curative versus palliative treatment. CT, with its limited contrast resolution, cannot differentiate metastasis from normal lymph node tissue. Unfortunately, MRI is also not able to distinguish between benign and malignant lymph node enlargement despite its proverbial high soft tissue contrast. This limitation of MRI is due to the fact that lymphatic tissue and tumor have similar T1 and T2 relaxation times, as well as proton densities [3]. For these reasons, both CT and MRI rely on size as the only criterion for identifying metastatic lymph nodes. In general, a transverse diameter of 10 mm or greater is considered to indicate nodal metastasis. With currently available CT and MRI technology, it is not possible to identify metastases in lymph nodes of normal size. Although these limitations apply to both CT and MRI, MRI has some advantages over CT. These are not primarily due to the higher soft tissue contrast or the free selection of imaging planes but result from the superiority in local staging of pelvic tumors. It has been shown, for example, that in case of an early stage tumor the probability that lymph node metastases are present is very low, while a tumor invading beyond the organ is typically associated with lymph node metastases. For this reason, lymph node staging by MRI should always take into account the local tumor stage. Noninvasive lymph node imaging may be improved in the future by the use of a specific intravenous contrast agent on the basis of iron oxide nanoparticles [2, 6]. These agents have completed the clinical trial phase and are expected to be approved for clinical use in the near future.

15.2 Indications

There is no absolute indication for abdominal MRI or CT for lymph node imaging alone. Lymph node evaluation is always done in conjunction with imaging performed for the evaluation of the local tumor stage and metastatic spread in general.

What is discussed here, therefore, applies to those lymph node stations seen on MR or CT images

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acquired for diagnostic evaluation of a primary pelvic tumor. Of particular interest are gynecologic tumors of the true pelvis. Here, MRI is superior to CT for local tumor evaluation.

In the future, however, a lymphotrophic IV contrast agent might lead to new indications for MRI of the lymph nodes. As mentioned above, applications for clinical approval of such agents have been filed.

15.3 Technique

15.3.1 MRI

The body phased-array coils available today allow imaging of the entire abdomen with high resolution and should be used whenever available to assess retroperitoneal lymph nodes in addition to evaluating the regional pelvic lymph nodes in all MRI examinations of a primary pelvic tumor. In patients with cervical or endometrial cancer, the demonstration of suspicious retroperitoneal lymph nodes is important for therapeutic planning in patients scheduled for postoperative radiotherapy.

Transverse images enable good initial evaluation of abdominal and pelvic lymph nodes. These images may be supplemented by coronal images for evaluation of the retroperitoneal lymph nodes or angulated coronal slices for lymph nodes along the external iliac vessels to assess their topographic relationship to the great vessels, but also to estimate the short-to-long axis ratio of the lymph nodes. Coronal slices are also highly suitable for assessing mesenteric and omental lymph nodes. Alternatively, slices in different orientations for lymph node assessment can be reconstructed from a 3D volume slab. In very rare cases it may become necessary to obtain double-angulated images for improved evaluation of a suspicious lymph node. What is important for lymph node imaging is to administer a spasmolytic agent to eliminate motion artifacts due to peristalsis (e.g. Buscopan or glucagon in patients with contraindications to Buscopan).

15.3.2 Pulse Sequences

Table 15.1 gives an overview of the sequences most suitable for lymph node assessment in different body regions (see also Chap. 1). As a rule, it is not necessary to obtain both T1- and T2-weighted images for identifying enlarged lymph nodes. Instead, choosing the sequence that provides the best anatomic detail resolution is recommended. Breath-hold imaging should be performed without fat suppression in order to achieve a high signal-to-noise ratio. When T2-weighted sequences with multiple signal averag-

Table 15.1. Pulse sequences recommended for MRI of abdominal lymph nodes. (Modified from [16])

Weighting	Plane	Sequence	TR (ms)	TE (ms)	Flip angle (°)	ETL (e.g.)	FS	Matrix ($N_{phase} \times N_{frequ}$)	FOV (mm)	N_{SL}	N_{AC}	SD (mm)	T_{AC} (min)	Breath-hold
PD/T1[a]	tra	TSE	~1500	10–15	–	3	No	228×512	320 (6/8)	23	3	8	about 5	no
T1 (fast)	tra (sag/cor)	GRE	165	4–5	90	–	Yes/ no	128×256	320 (6/8)	19–23	1	8	0.3	yes
T2[b]	tra	TSE respiratory triggering	2500	80	–	7–15	Yes	168×320	300 (6/8)	48	2	4	5-7	no
T2 (fast)	tra (sag/cor)	single-shot TSE (e.g. HASTE), preset parameters						128×256	320 (6/8)	21	1	8	0.3	yes

Interslice gap always 20% of slice thickness (distance factor, 0.2).
Note: A body phased-array coil is recommended for acquisition of high-resolution TSE/FSE sequences and breath-hold sequences.
[a]Recommended for high-resolution imaging of pelvic lymph nodes (with administration of spasmolytic agent)
[b]Recommended for high-resolution imaging of retroperitoneal lymph nodes (with administration of spasmolytic agent)

ing are used, fat suppression (either spectral saturation or inversion prepulse) improves the demarcation of lymph nodes by depicting them with high signal intensity. For imaging of the female pelvis, a high-resolution T1- or proton density-weighted sequence should be acquired extending from the region of the aortic bifurcation to the pelvic floor, which will allow excellent evaluation of the pelvic lymph nodes when the sequence is obtained with administration of a spasmolytic agent. If available, the sequence should be acquired as a fast or turbo SE sequence with a rather short effective echo time (about 10–15 ms). Additional T1- or T2-weighted transverse images, preferably acquired during breath-hold, typically allow good evaluation of enlarged retroperitoneal lymph nodes (T1w GRE, T2w single-shot TSE, both during breath-hold). Alternatively, T2-weighted sequences with respiratory triggering (e.g. respiratory belt or cushion, navigator imaging [9]) in combination with spasmolysis provide images of the upper and middle abdomen with excellent image quality and good detail resolution. Additional imaging in coronal or sagittal planes should ideally be performed using sequences that can be acquired during breath-hold, which are not only faster but also provide an adequate image quality in coronal orientation, which is highly susceptible to degradation by motion artifacts when acquisition times are long (e.g. T1w GRE, T2w single-shot TSE).

15.3.3 Intravenous Unspecific Contrast Agents

There is no indication for administration of an unspecific Gd-based MR contrast agent with distribution in the extracellular space (e.g. Magnevist or Omniscan) for lymph node imaging. However, on T1w images, an unspecific contrast agent can improve the differentiation of lymph nodes from vessels. If an IV contrast agent is administered for evaluation of the primary tumor, necrosis in metastatic lymph nodes may be seen better.

15.3.4 Intravenous Tissue-Specific Contrast Agents

Tissue-specific contrast agents with accumulation in healthy lymph node tissue have been extensively investigated in clinical trials but still await approval for clinical use (Sinerem, Guerbet, Paris). This is why only an outlook can be given here. Tissue-specific contrast agents are based on very small superparamagnetic iron oxide nanoparticles with a diameter of about 20 nm (ultrasmall superparamagnetic iron oxide particles – USPIO). Following peripheral venous administration, they extravasate from the capillary vascular bed into the interstitial spaces in all body regions and reach the draining nodes with the lymphatic fluid [12, 14, 15]. In intact lymph nodes, USPIO are taken up by macrophages and their strong T2-relaxation-time-shortening effect produces a signal loss that is best appreciated on T2*w GRE sequences. Metastatic lymph nodes do not accumulate the particles and hence show unchanged signal intensity. Once USPIO-based preparations have been approved and ongoing analysis of clinical trials confirm available results, these agents will be indicated for MRI of abdominal and pelvic lymph nodes, and there will be an indication for MRI in the diagnostic evaluation of lymph nodes.

15.3.5 CT

There are no specific technical requirements for CT of the lymph nodes. The reader is referred to the protocols presented in Chapter 1.

15.4 Imaging of Normal Lymph Nodes – MRI/CT

With conventional MR imaging techniques, lymph nodes are visualized when they have a size of at least 1.0–1.5 cm [10]. Optimized imaging techniques (body phased-array coil, 512 matrix, 3D acquisition) or state-of-the-art spiral or multislice CT scanners depict lymph nodes as small at about 3–5 mm [7, 8]. These techniques usually allow good evaluation of the lymph nodes adjacent to the straight great vessels (Fig. 15.1).

Nonactivated lymph nodes or lymph nodes not enlarged by metastasis have a mean diameter of only a few millimeters (abdominal lymph nodes 3–5 mm, pelvic lymph nodes about 3 mm, determined by CT [4, 13]) and are usually not visualized on MR images. If they are seen, normal lymph nodes are markedly hypointense relative to surrounding fat on T1-weighted images, moderately

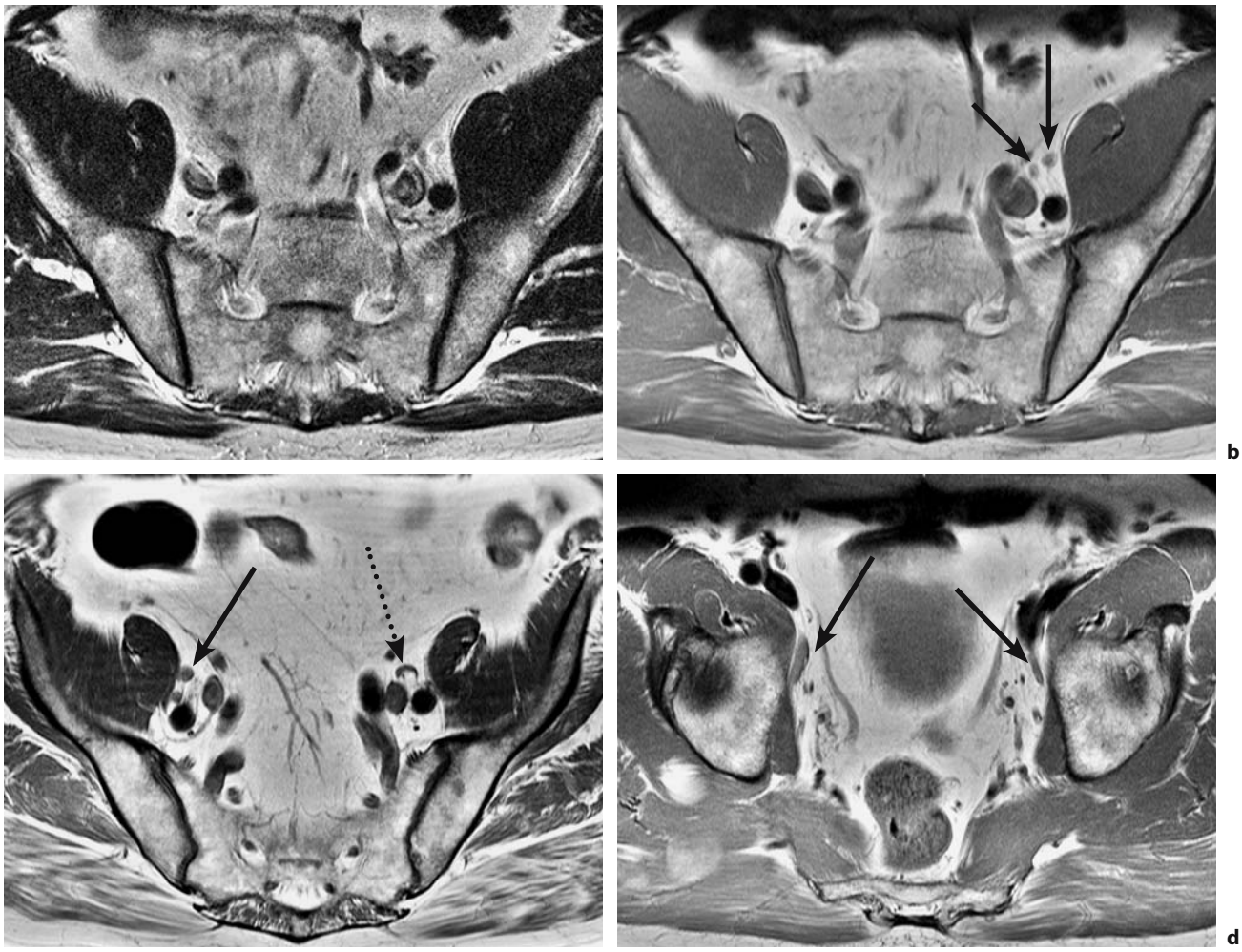

Fig. 15.1a–d. Normal pelvic lymph nodes. Axial MR images acquired with (**a**) T2w TSE sequence and (**b-c**) T1w TSE sequence at different levels (**a** and **b** are from the same level) (1.5 T). Small lymph nodes with a rounded appearance (**a–c**, *straight arrows* in **b** and **c**) are seen. They have low signal intensity on T1 and are nearly isointense to surrounding fat on T2. In addition, a lymph node on the left (*curved arrow*) is depicted with good visualization of the fatty hilus (fibrolipomatous degeneration, *dotted arrow* in **c**). Elongated lymph nodes on both sides at the pelvic wall (*arrows*, **d**)

hypointense on PD images, and isointense to fat or slightly hyperintense on T2-weighted images. At times, the fatty hilus can be differentiated from the stroma in a normal lymph node (Fig. 15.1c). Typical retroperitoneal lymph nodes are oval, while lymph nodes along the pelvic walls (internal iliac nodes, obturator nodes) may appear as elongated structures several centimeters in length (Fig. 15.1d). A schematic representation for referring to the different abdominal and pelvic lymph node stations is presented in Figure 15.2.

In the pelvic region, lymph nodes may be difficult to distinguish from elongated iliac vessels on nonangulated axial images. This applies especially to T1w images, which depict both lymph nodes and vessels with low signal intensity. Differentiation is improved after intravenous contrast administration. On TSE images, vessels have low signal intensity. The differentiation between vessels and lymph nodes is optimal on PDw sequences which depict vessels as signal voids and lymph nodes with intermediate signal (compare Fig 15.1).

In patients without a known primary tumor, lymph nodes with a transverse diameter of 5–10 mm should be mentioned in the report without comment as their size is above the mean value for “normal”

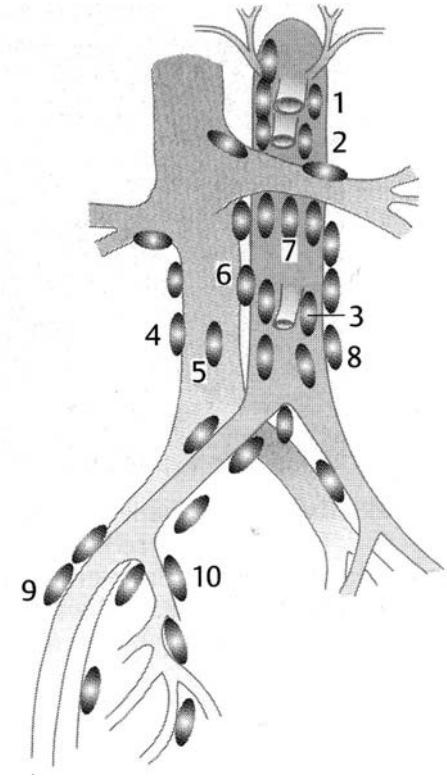

Fig. 15.2. Retroperitoneal lymph nodes. *1,* coelical lymph nodes; *2* and *3,* mesenterial lymph nodes; *4,* paracaval lymph nodes; *5,* precaval lymph nodes; *6,* interaortocaval lymph nodes; *7,* preaortic lymph nodes; *8,* paraaortic lymph nodes; *9,* external iliac lymph nodes; *10,* internal iliac lymph nodes

lymph nodes [1, 4, 13]. In general, lymph nodes with a transverse diameter of 10 mm or greater are considered suspicious for metastasis.

15.5 Imaging of Abnormal Lymph Nodes – MRI/CT

For lymph node staging, the reader should consult one of a standard reference (e.g. [11]). In general, the lymph node stage determined from MRI or CT findings plays only a small role in therapeutic decision making. If imaging demonstrates enlarged lymph nodes at sites that do not correspond to the first site of lymphatic spread of the patient's primary tumor, this is an important finding because these lymph nodes should then be removed, not least for histologic examination.

Most abdominal tumors initially metastasize along the draining lymphatic pathways, first invading the regional nodes and later also the distal lymph node stations. Rarely, metastatic occlusion of lymphatic drainage can give rise to an atypical pattern of metastatic spread with primary distal or contralateral lymph node metastases. Pelvic tumors (uterus, cervix, upper third of vagina, urinary bladder) typically first spread to the lymph nodes of the pelvic wall (obturator nodes, external and internal iliac nodes). In patients with a primary tumor in one of these locations which is confined to the organ or appears as an early-stage tumor on MR imaging, visible but not pathologically enlarged lymph nodes (5–10 mm) are typically not considered suspicious. If, however, the primary tumor invades adjacent structures, such slight lymph node sizes can be considered suspicious for metastasis (Figs. 15.3–15.7).

When images in axial and coronal or sagittal planes are available, the radiologist can assess the configuration of enlarged lymph nodes. Nodal metastasis is more likely when an enlarged lymph node has a spherical shape. In X-ray lymphography this phenomenon is referred to as spherical transformation. In contrast, reactive hyperplasia is more likely when an enlarged lymph node has an elongated oval shape. The use of high-resolution 3D pulse sequences improves the evaluation of individual lymph nodes compared to conventional 2D sequences and makes it easier to measure the short and long axes and determine the short-to-long axis ratio (S/L ratio). Using a 3D MP RAGE sequence with a voxel size of 1.0×1.3×1.6 mm, Jager and coworkers [8] were able to identify pelvic lymph nodes as small as 3 mm. In this study, the authors used a short axis diameter greater than 8 mm and an S/L ratio of over 0.8 (rounded lymph node) as criteria for malignancy. However, despite optimal morphologic resolution, the sensitivity for detecting metastatic nodes was only 60% (prostate cancer) and 83% (bladder cancer), while specificity was high at 98% for both tumors. In a study of pelvic lymph nodes in patients with cervical cancer, MRI had a sensitivity of 75% and specificity of 88% using a threshold of 1.5 cm for pelvic lymph nodes. Even lateral differences in the size of pelvic lymph nodes are not a reliable criterion as long as the lymph nodes are less than 10 mm in diameter [10]. The poor sensitivities are due to the fact that

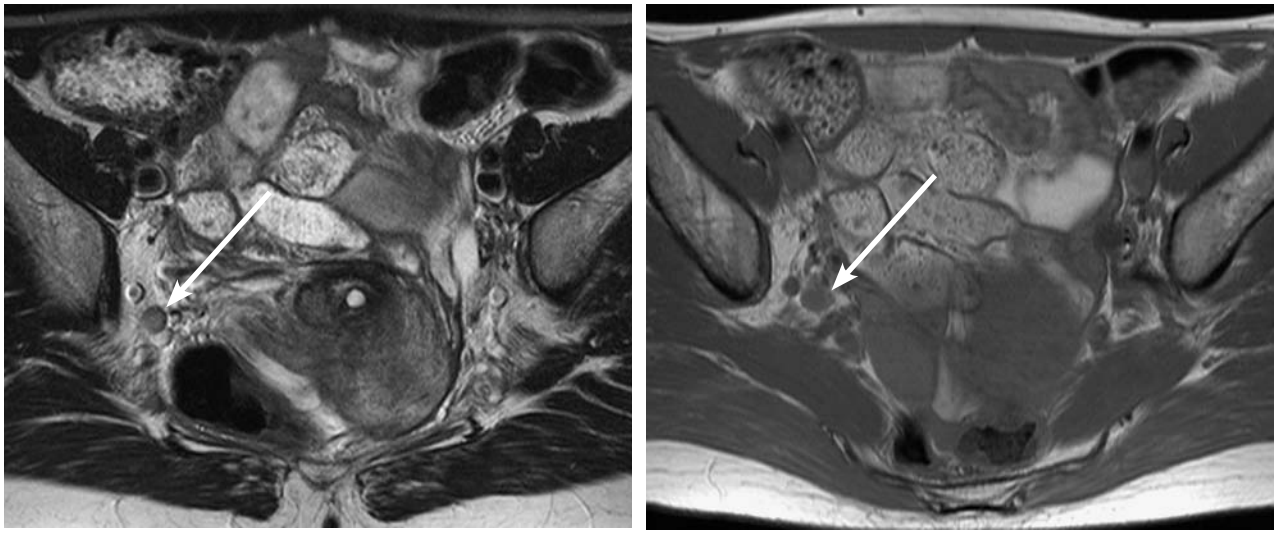

Fig. 15.3a,b. Slightly enlarged metastatic lymph node in the area of the internal iliac artery (*arrow*). Axial images obtained with (**a**) T2w TSE sequence and (**b**) T1w TSE sequence in a patient with advanced cervical cancer

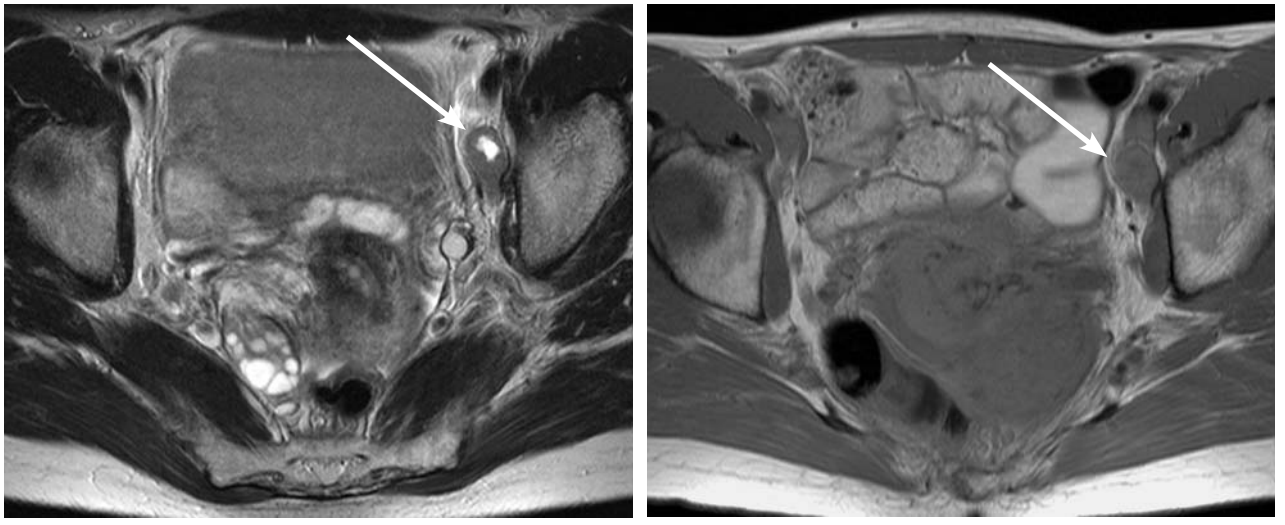

Fig. 15.4a,b. Abnormally enlarged metastatic lymph node on the left immediately posterior to the external iliac vein (*arrow*). Axial images obtained with (**a**) T2w TSE sequence and (**b**) T1w TSE sequence in a patient with advanced cervical cancer. The T2w image depicts the central necrosis with fluid signal intensity

the size criterion is rather unspecific because small metastases in normal-sized lymph nodes are quite common and nonmetastatic lymph nodes may show reactive enlargement. A histopathologic study of 310 pelvic lymphadenectomies identified lymph node metastases in 40 patients (12.9%) [5]. The nodal metastases were apparent on gross inspection in only six cases, while only histology identified the metastases in the other 34 cases.

Another major factor contributing to the poor performance of MRI in lymph node assessment is the fact that the signal intensities of lymph nodes on either T1- or T2-weighted images do not allow differentiation of normal and metastatic lymph nodes [3]. Both reactively enlarged nodes and metastatic nodes have low signal intensity on T1 and high signal intensity on T2 relative to surrounding fatty tissue. More reliable criteria are only avail-

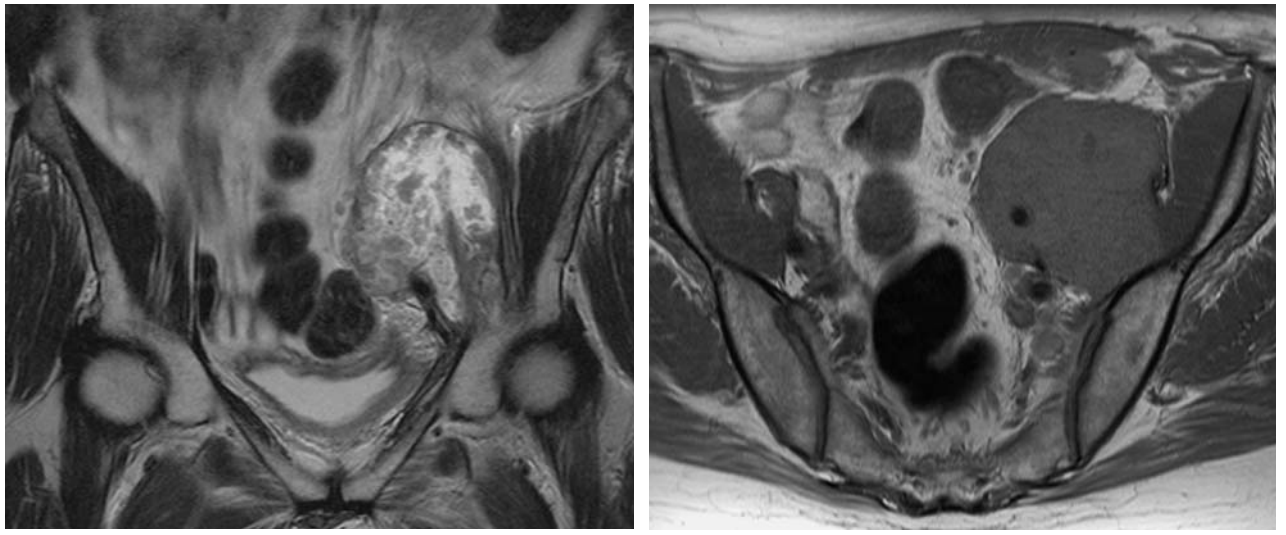

Fig. 15.5a,b. Large lymph node metastasis at the left pelvic wall with encasement of the external iliac vessels. (**a**) Coronal T2w TSE image and (**b**) axial T1w TSE image in a patient with advanced cervical cancer

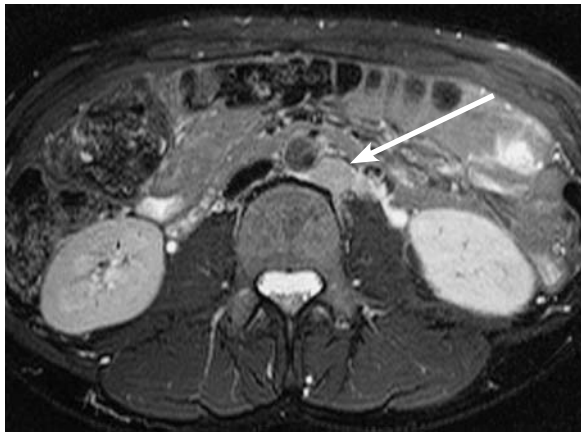

Fig. 15.6. Retroperitoneal (para-aortic) lymph node metastasis in a patient with endometrial cancer (*arrow*). Axial T2w TSE image obtained with respiratory triggering using the navigator technique

able for advanced nodal metastasis, for example, central necrosis, which is clearly identified as a hyperintensity within a metastatic node on T2-weighted images. Moreover, lymph node conglomeration and multiple enlarged lymph nodes are highly indicative of nodal metastasis, especially in patients with a primary known to metastasize to the affected nodes.

15.5.1 Contrast Administration

The standard unspecific contrast agents used in MRI and CT lead to an increase in signal intensity or density of both reactively enlarged and metastatic lymph nodes following IV administration and do not improve the differentiation of reactive and metastatic nodes [7]. The visualization of central necrosis in a metastatic node is improved after contrast administration.

Superparamagnetic iron oxide particles, on the other hand, are a promising new approach for improving MR imaging of lymph nodes (Fig 14.8). One USPIO preparation (Sinerem – Guerbet, Paris) has been investigated for lymph node imaging in different body regions (pelvis, abdomen, mediastinum, head and neck, axilla). Final analysis of these studies is under way, and approval for clinical application is expected in the near future. In a study of 58 patients with urinary bladder cancer, Deserno and coworkers showed that USPIO improved sensitivity to 96% compared with 76% for the size criterion, while specificity decreased only slightly from 99% to 95% [2]. It is noteworthy that MRI in this study demonstrated metastases in 10 of 12 lymph nodes that were not enlarged (< 10 mm). In a study of patients with prostate cancer, Harisinghani and coworkers showed that USPIO-enhanced MRI had a sensitivity of 90% compared to 35% for the size criterion when analyzing individual lymph nodes [6].

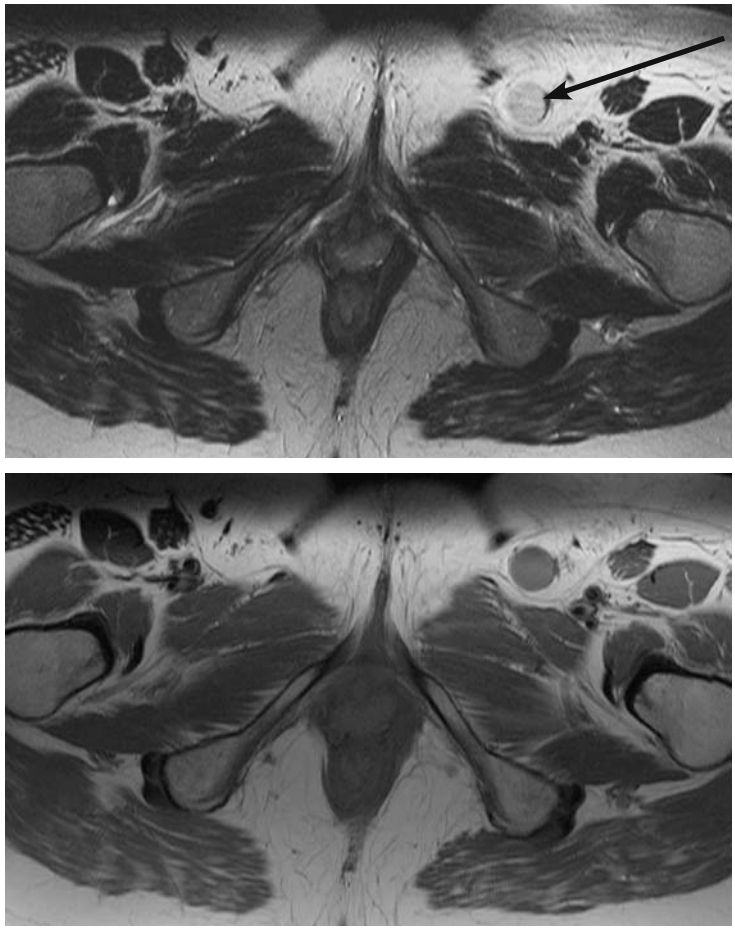

Fig. 15.7a,b. Abnormally enlarged metastatic inguinal lymph node on the left (*arrow*). Axial images obtained with (**a**) T2w TSE sequence and (**b**) T1w TSE sequence in a patient with vulvar cancer

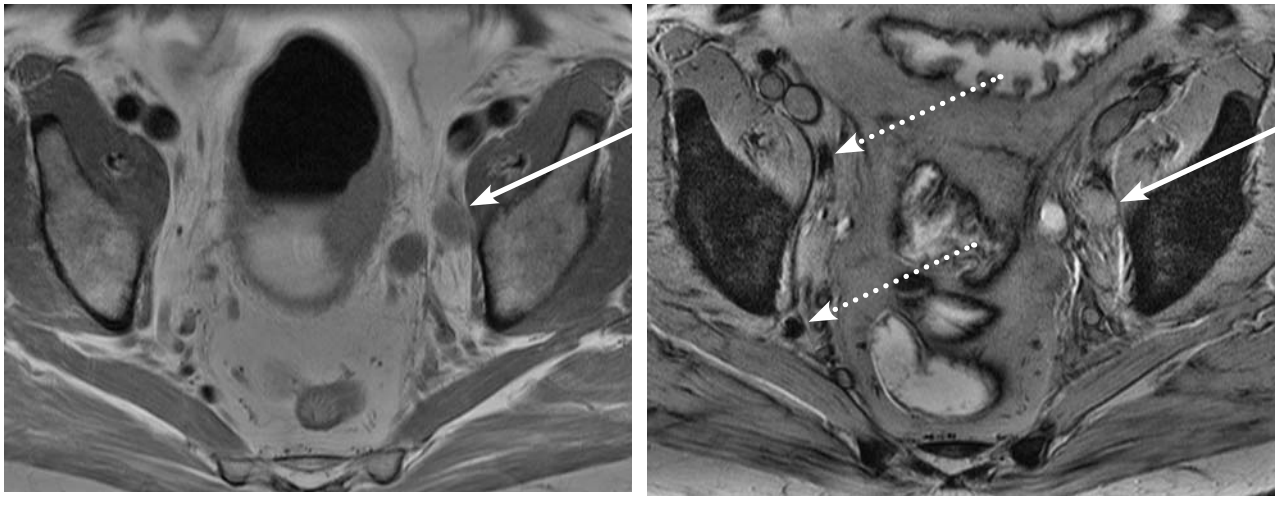

Fig. 15.8a,b. MR lymphography following intravenous administration of ultrasmall iron oxide particles (USPIO) in a patient with metastatic lymph nodes. Axial images obtained with (**a**) T1w SE sequence and (**b**) T2*w GRE sequence 24 h after intravenous injection of USPIO. Slightly enlarged lymph node at the left pelvic wall (*arrow*) with muscle signal intensity on T1 and unchanged signal on USPIO-enhanced image indicating nodal metastasis, which prevents uptake of the particles. Widening of the distal ureter due to infiltration of the left ureteral orifice. In nonmetastatic pelvic lymph nodes homogeneous signal due to contrast agent uptake of on the right (*dotted arrows*). (USPIO for MR lymphography are at the clinical trial stage)

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