

## ARTICLE

# Imaging of testicular germ cell tumours

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### Abstract

In testicular germ cell tumour (GCT), imaging plays a central role in assessment of tumour bulk, sites of metastases, monitoring response to therapy, surgical planning and accurate assessment of disease at relapse. The primary modality used for imaging patients with GCT is computed tomography (CT) but plain film radiography, ultrasound, magnetic resonance imaging (MRI) and positron emission tomography (PET) may all have roles to play. This article reviews the role of imaging of testicular germ cell tumours.

**Keywords:** Testicular tumours; germ cell neoplasia; imaging; CT; MRI; PET.

## Introduction

Testicular germ cell tumours (GCT) are an increasingly common group of tumours, particularly in young males. The success of current management strategies is such that the majority of patients can expect to be cured. This success hinges on accurate disease assessment and application of chemotherapy and radiotherapy. Serum markers can be useful surrogate markers of disease activity, but they cannot accurately assess disease bulk or locate sites of tumour spread. For these purposes imaging is invaluable and now plays an integral role not only in assessment of tumour bulk and sites of metastases but also in monitoring response to therapy, surgical planning and accurate assessment of disease at relapse. The primary modality used for imaging patients with these tumours is computed tomography (CT) but plain film radiography, ultrasound and magnetic resonance imaging (MRI) also have roles to play. Positron emission tomography (PET) scanning is now being more widely used but its optimal role has yet to be agreed. This article reviews the literature relating to imaging in testicular germ cell tumours. It covers the role of imaging from diagnosis through staging to post-treatment monitoring and surveillance and evidence for the use of imaging.

## Diagnosis

The diagnosis of germ cell tumours (GCT) is made by a biopsy or at orchidectomy. Testicular GCT most commonly presents as a painless palpable mass (up to 95% of cases)<sup>[1]</sup>. In up to 10% of cases, it may present with dull scrotal ache, pain or acute fever<sup>[2]</sup>. In patients with retroperitoneal metastases or disseminated disease, backache, malaise, lethargy and other systemic features may be the presenting findings<sup>[3]</sup>. Imaging is largely used to confirm the presence of disease and assess its extent.

Testicular ultrasound (which should be performed using a 7.5 MHz probe) is used in primary assessment of the testes to confirm diagnosis, to distinguish from other scrotal abnormalities and to screen for abnormalities such as microlithiasis in the contralateral testis<sup>[2,4–6]</sup>. Sonographically, testicular tumours are usually well defined and hypoechoic relative to the normal testicle, although some may display a heterogeneous echotexture, calcification or cystic change (Fig. 1). Tumours may display increased vascularity on colour and power Doppler with respect to surrounding normal testicular tissue but this is not specific and may not be demonstrated in small tumours<sup>[7]</sup>. Ultrasound cannot be used to reliably differentiate between tumour types. For this purpose, MRI may be useful<sup>[8,9]</sup>.

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**Table 1** TNM staging classification of testicular tumours<sup>[10]</sup>**Primary tumour**

The extent of the primary tumour is classified after radical orchidectomy (pT)

pTX	Primary tumour cannot be assessed (if no radical orchidectomy has been performed, TX is used)
pT0	No evidence of primary tumour (e.g. histological scar in testis)
pTis	Intratubular germ cell neoplasia
pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade into the tunica albuginea but not the tunica vaginalis
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis
pT3	Tumour invades spermatic cord with or without vascular/lymphatic invasion
pT4	Tumour invades scrotum with or without vascular/lymphatic invasion

**Regional lymph nodes***Clinical involvement*

NX	Regional nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node mass $\leq 2$ cm in greatest dimension or multiple lymph nodes none $> 2$ cm in greatest dimension
N2	Metastasis with a lymph node mass $> 2$ cm but $< 5$ cm in greatest dimension, or multiple lymph nodes, any one mass $> 2$ cm but $\leq 5$ cm in greatest dimension
N3	Metastasis with a lymph node mass $> 5$ cm in greatest dimension

*Pathological involvement*

pN0	No regional lymph node metastases
pN1	Metastasis with a lymph node mass $\leq 2$ cm in greatest dimension and 5 or fewer positive nodes, none $> 2$ cm in greatest dimension
pN2	Metastasis with a lymph node mass $> 2$ cm but $\leq 5$ cm in greatest dimensions; or more than five nodes positive, none $> 5$ cm; or evidence of extranodal extension of tumour
pN3	Metastasis with a lymph node mass $> 5$ cm in greatest dimension

**Distant metastases**

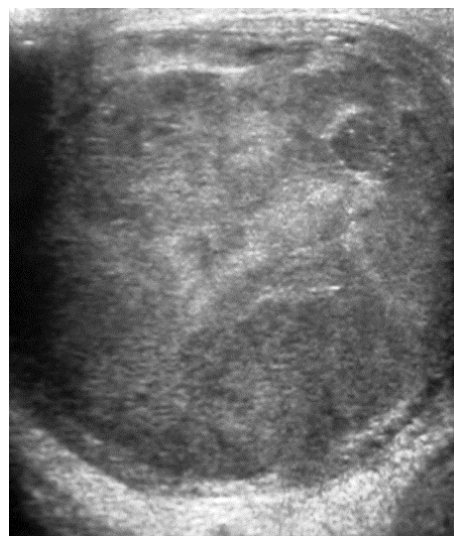
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node or pulmonary metastasis
M1b	Distant metastasis other than to non-regional lymph nodes and lungs

## Staging

Once a diagnosis of testicular germ cell tumour has been made, assessment of disease extent must be performed prior to initiating therapy. The European Germ Cell Cancer Consensus Group (EGCCCG) recommend that TNM staging be used<sup>[10]</sup> (Table 1) and that patients be categorised using the International Germ Cell Cancer Collaborative Group (IGCCCG) classification which stratifies patients into good, intermediate and poor prognostic groups. This latter classification is based on histology, location of primary tumour and metastases and levels of serum markers (Table 2)<sup>[11]</sup>. A further staging classification, devised at The Royal Marsden Hospital (UK) and widely used in the UK and Europe, is shown in Table 3.

When staging tumours, knowledge of the patterns of spread enables prediction of sites of disease and may improve the accuracy of assessment. Testicular tumours spread via vascular or lymphatic invasion (Figs. 2–5). Vascular spread is most commonly to the lungs. Lung metastases may vary in appearance with respect to the histology of the primary tumour; those from NSGCT appear as multiple small peripheral nodules whereas seminoma metastases tend to be larger masses (Fig. 2). Other sites of metastatic spread include the brain (most common in trophoblastic teratomas), bones and liver

(Figs. 3 and 4). Other sites of metastases, though rarely seen and usually only in the setting of advanced disease, include the adrenals, kidneys, spleen, pleura, pericardium and peritoneum.



**Figure 1** Testicular carcinoma. Ultrasound demonstrating heterogeneous echotexture throughout the testicle.

**Table 2** International Germ Cell Consensus classification<sup>[11]</sup>**Non-seminoma***Good prognosis: all of the following*

- AFP <1000 ng/ml and HCG <5000 iu/l (1000 ng/ml) and LDH <1.5 × upper limit of normal (N) and
- Non-mediastinal primary
- No non-pulmonary visceral metastases (NPVM)

*Intermediate prognosis: all of the following*

- AFP 1000–10 000 ng/ml, or HCG 5000–50 000 iu/l, or LDH 1.5–10 × N and
- Non-mediastinal primary site and
- No NPVM

*Poor prognosis: any of the following*

- AFP >10 000 ng/ml or HCG >50 000 iu/l or LDH >10 × N or
- Mediastinal primary site or
- NPVM

**Seminoma***Good prognosis*

- No NPVM
- Any primary site
- Normal AFP, any HCG, any LDH

*Intermediate prognosis*

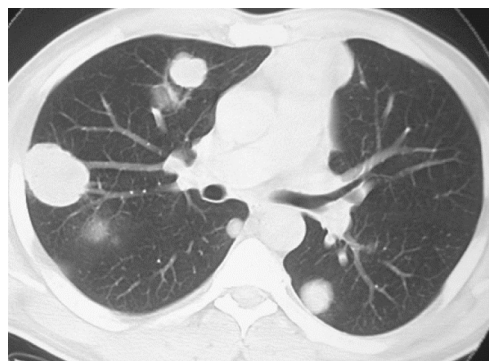
- NPVM present

**Note:** AFP = alphafetoprotein; B-HCG = B-human chorionic gonadotrophin; LDH = lactate dehydrogenase; CNS = central nervous system.

**Table 3** The Royal Marsden Hospital staging classification for testicular germ cell tumours<sup>[30]</sup>

Stage	Definitions
I	No evidence of metastases
IM	Rising serum markers with no other evidence of metastases
II	Abdominal node metastases
A	<2 cm in diameter
B	2–5 cm in diameter
C	>5 cm in diameter
III	Supradiaphragmatic node metastases
M	Mediastinal
N	Supraclavicular cervical axillary
O	No abdominal node metastases
ABC	Node size defined as in Stage II
IV	Extralympathic metastases
	Lung
L1	≤3 metastases
L2	>3 metastases all <2 cm in diameter
L3	>3 metastases, one or more >2 cm in diameter
H+	Liver metastases
Br+	Brain metastases
Bo+	Bone metastases

Lymphatic spread reflects the retroperitoneal embryological origin of the testis. Spread occurs via lymphatic channels which pass through the inguinal ring (accompanying the spermatic cord and testicular vessels) to enter retroperitoneal nodes (Fig. 5). Right-sided tumours normally spread to right-sided nodes around the IVC (most commonly lower retroperitoneal, aortocaval or paracaval). Left-sided tumours normally spread to lymph nodes on the left, adjacent to the aorta (most commonly just below the left renal hilum). In the absence of bulky ipsilateral adenopathy, contralateral spread is unusual, and if seen as the only site of metastasis, histological proof of tumour involvement should be sought prior to instigation of therapy<sup>[12]</sup>. Pelvic adenopathy is also

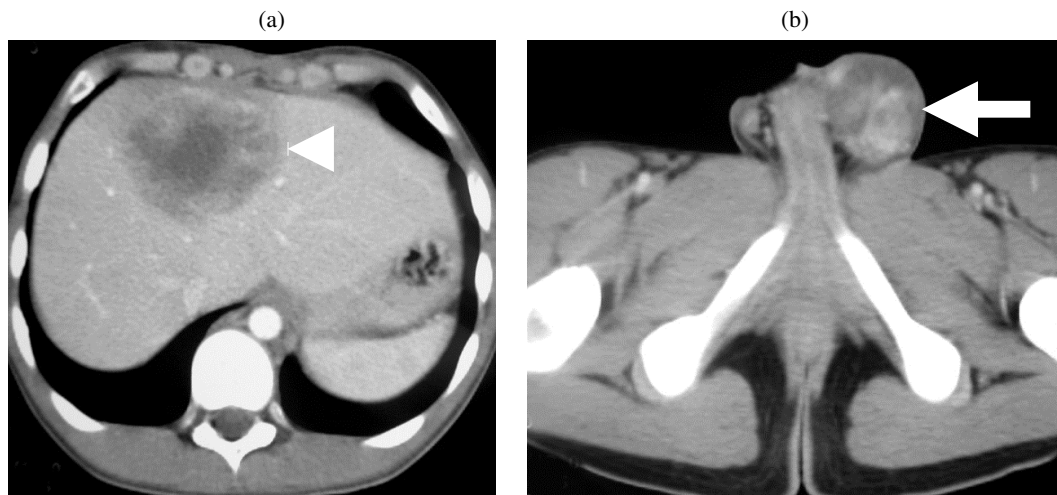


**Figure 2** Lung metastases. CT image showing multiple lung masses in a patient with metastatic testicular seminoma.

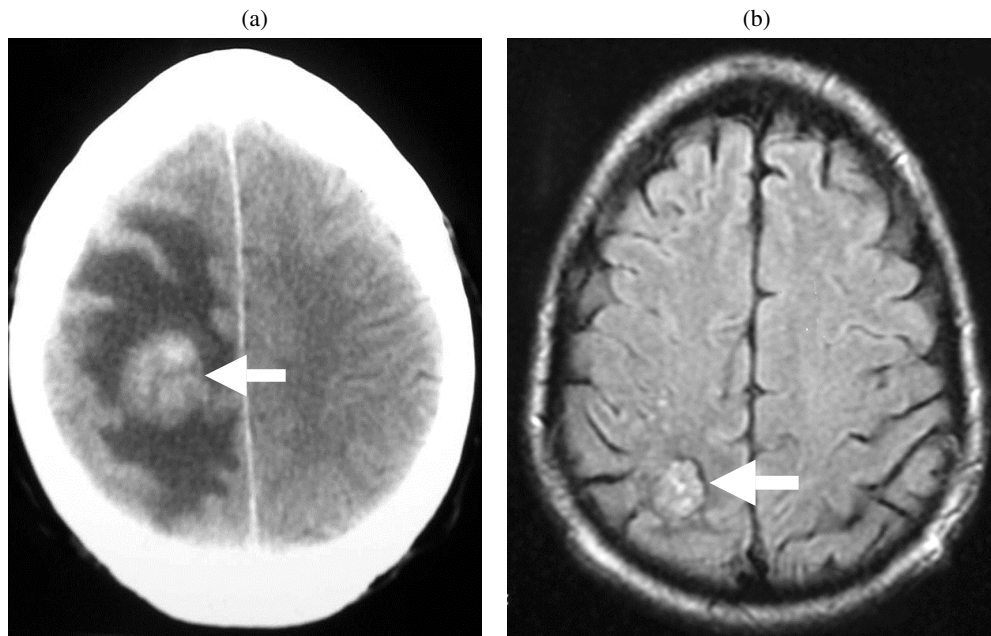
uncommon in the absence of bulky disease elsewhere or history of maldescent or previous scrotal surgery<sup>[13]</sup>. Echelon nodes, which are sites of nodal disease, identified more frequently at relapse than during primary disease, have been described<sup>[14]</sup>. On the right the echelon node is sited laterally between the L1 and L3 vertebrae<sup>[15]</sup>. On the left a similar node has been described as lying on iliopsoas<sup>[16]</sup>.

Nodal disease superior to the level of the renal hila occurs via direct spread. In cases of seminoma spread of disease above the diaphragm may occur via the thoracic duct into the posterior mediastinum. In NSGCT, however, spread is more random involving the anterior mediastinum, aortopulmonary window, hilar, supraclavicular and neck lymph nodes but excluding the posterior mediastinum and subcarinal regions<sup>[17]</sup>.

The primary imaging modality currently used for staging disease is computed tomography (CT). Its



**Figure 3** Metastatic non-seminomatous germ cell tumour. Contrast-enhanced CT shows (a) liver metastasis and (b) the left testicular tumour (arrow).



**Figure 4** Brain metastasis. (a) Contrast-enhanced CT showing an enhancing mass (arrow) in the right parietal lobe with surrounding oedema. (b) FLAIR MR image following treatment shows the lesion to be smaller and the surrounding oedema to have resolved.

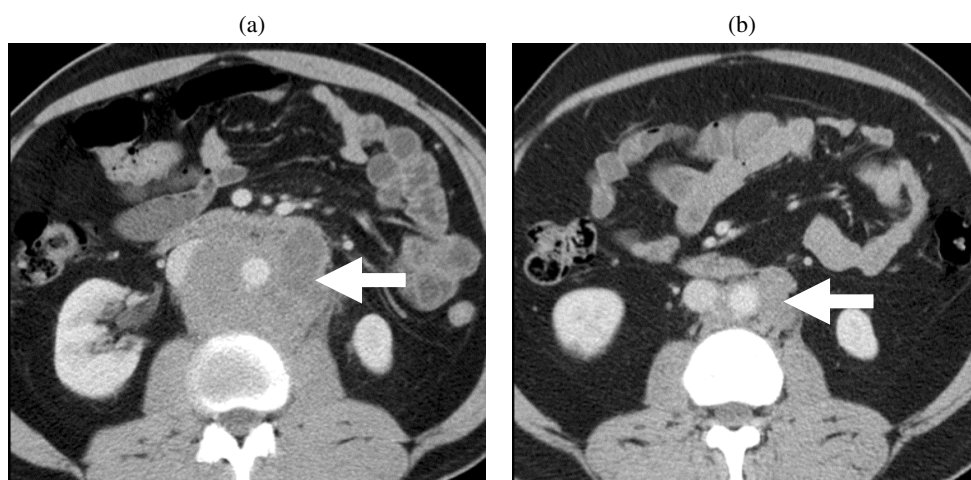
overall accuracy approaches 80%<sup>[18]</sup>. Current EGCCCG guidelines state that patients should receive contrast-enhanced CT of thorax, abdomen and pelvis<sup>[19]</sup>. The exception to this is in patients with seminoma and no retroperitoneal disease, where chest radiography (in place of thoracic CT) is thought sufficient to assess the thorax for metastases<sup>[20]</sup>.

#### *Computed tomography (CT)*

Overall, CT has been shown to be the most sensitive method of assessing metastatic disease in the thorax, abdomen and pelvis, though it is recognised that it may

understage disease in up to 25% of cases<sup>[21]</sup>. It has also been found to be the most sensitive method of assessing supraclavicular, mediastinal and pleural disease<sup>[22–28]</sup>. With respect to thoracic imaging, use of multidetector CT has not been shown to increase nodule detection when compared to that using single-slice CT for slice thicknesses of 5 mm<sup>[29]</sup>. However, the ability to produce submillimetre sections will undoubtedly increase the sensitivity of multislice CT for nodule detection.

Lymph node metastases are usually of soft tissue density. Large volume seminomatous disease may, however, have a central low density secondary to necrosis, whereas in large volume NSGCT complex cysts allied



**Figure 5** Retroperitoneal lymphadenopathy. Contrast-enhanced CT (a) before and (b) after chemotherapy shows retroperitoneal lymphadenopathy (arrow) encasing the aorta. The post-chemotherapy scan shows significant reduction in the burden of retroperitoneal lymphadenopathy.

with foci of soft tissue may be seen<sup>[30]</sup>. In large volume disease the diagnosis is rarely in doubt. Assessment of small volume lymphadenopathy, which has significant implications for patient staging and management, is unfortunately the Achilles' heel of CT. The detection of microscopic deposits of tumour in normal-sized nodes and the distinction between tumoral and inflammatory adenopathy are beyond the scope of CT. In light of these handicaps it comes as no surprise that false negative CT examinations occur, thus limiting its diagnostic accuracy. CT is unable to identify small volume disease in normal-sized nodes in up to 30% of patients with GCT<sup>[31–35]</sup>.

Studies performed to assess the effect of different thresholds of significance for lymph node size have been performed<sup>[36,37]</sup>. Essentially, they confirm the logical notion that, by reducing the lymph node size accepted as normal, the likelihood of detecting positive nodes increases, but the specificity of the test decreases. It has been shown that by using 10–15 mm as the upper limit of normal, up to 44% of scans were false negative<sup>[38–40]</sup>. A further complication of trying to standardise upper limits of normal is that normal nodes in the superior retroperitoneum are smaller than those in the inferior retroperitoneum on CT<sup>[41–43]</sup>. Standardization of normality as such has not been agreed; thus institutions vary in their practice. An assessment schema is given (Table 4)<sup>[30]</sup>. For practical purposes a cut-off of 10 mm is used to differentiate between normal and abnormal lymph nodes. Those measuring between 8 and 10 mm are treated as suspicious. These measurements must, however, be taken in the overall context of the patient's situation such as risk of disease, marker levels, etc. Laterality of the tumour is an additional consideration. Sites suspicious of disease warrant further investigation; this could include tissue sampling, biochemical markers, additional imaging such as PET scanning (see below) and further follow-up imaging.

**Table 4** Lymph node size at various anatomic sites: short axis diameter, upper limits of normal

Site	Group	Short axis size (mm)
Head and neck	Cervical	10 (<10 mm with central necrosis)
Axilla		10
Mediastinum	Subcarinal	12
	Paracardiac	8
	Retrocaval	6
	All other sites	10
Abdomen	Gastrohepatic ligament	8
	Porta hepatis	8
	Portacaval	10
	Coeliac axis to renal artery	10
	Renal artery to aortic bifurcation	12
Pelvis	Common iliac	9
	External iliac	10
	Internal iliac	7
	Obturator	8

For the detection of disease beyond the chest, abdomen and pelvis, CT of the brain is not undertaken as part of routine staging in all patients but is indicated in those with high-risk factors (e.g. multiple lung metastases, HCG > 10 000) and in patients with suspected metastatic disease on clinical grounds<sup>[44,45]</sup>. Brain metastases are often haemorrhagic and usually demonstrate enhancement after intravenous contrast administration (Fig. 4)<sup>[30]</sup>.

### Ultrasound

Ultrasound is not routinely used in staging of disease. Assessment of retroperitoneal and pelvic nodes has been shown to be not as reliable when compared to CT or MRI<sup>[19]</sup>. Indeed, it has been reported that up to

17% of small volume disease may be missed. However, ultrasound is useful in the assessment of solid intra-abdominal organs, e.g. the liver, and as a guide for needle placement during biopsy.

### *Magnetic resonance imaging (MRI)*

Use of MRI to date has been limited in part due to its long examination times, high cost and low availability. However, with the advent of new, shorter sequences and techniques and increasing MRI availability, it is likely that there will be an increase in its use. The use of MRI in staging testicular GCT is emerging. When compared to CT, MRI is known to have better soft tissue contrast resolution and be at least as accurate in detection of retroperitoneal lymph nodes<sup>[46]</sup> though it is not as accurate in detecting lung metastases<sup>[47,48]</sup>. MRI is of use in detection and characterisation of central nervous system, musculoskeletal and hepatic metastases. Furthermore it has also been found to be useful in demonstration of IVC tumour invasion, enteric fistulae<sup>[8,9]</sup> and demonstration of vascular anatomy in patients prior to retroperitoneal lymph node surgery. MRI may also be used in those patients where intravenous contrast cannot be given and as a problem solving technique for equivocal CT findings<sup>[19]</sup>.

Recently, MR imaging with lymphotropic nanoparticles (LNMRI) has been shown to be an effective method for evaluating lymph nodes in cancers<sup>[49–55]</sup>. Lymphatic targeting has been shown to result from slow extravasation of nanoparticles into the interstitial space, from which they are transported to lymph nodes by lymphatics. Within lymph nodes, these nanoparticles are internalized into macrophages, resulting in intracellular trapping and subsequent changes in magnetic properties by MR. A recent study showed that lymphotropic nanoparticle-enhanced MRI demonstrated higher sensitivity and specificity for detecting nodal metastases when compared with plain MRI alone. Many nodes larger than 10 mm were benign (32%) and were accurately characterized by LNMRI. The two nodes in that study that were falsely positive were larger than 10 mm and had >50% foci of hyalinization. These areas of hyalinization appeared as focal defects on LNMRI, mimicking metastatic nodes. It was also shown that LNMRI showed a high degree of accuracy in detecting metastases in nodes smaller than 10 mm which would otherwise be considered benign on the basis of traditional size criteria<sup>[50]</sup>.

### *Positron emission tomography (PET)*

PET scanning utilises the differentially greater uptake of fluorine-18-labelled fluorodeoxyglucose (<sup>18</sup>FDG) in malignant cells (owing to their higher metabolic rate) than normal tissue to enable tumour detection. Aside from mature differentiated teratomas (which have a

relatively low metabolic rate) most tumours (and their metastases) demonstrate avid <sup>18</sup>FDG uptake. With respect to testicular tumours it has been shown that seminomatous lesions have a significantly higher FDG uptake than non-seminomatous germ cell tumours, as expressed by the standard uptake values (SUV)<sup>[56,57]</sup>.

The use of PET is widely advocated as it has been shown that the sensitivity of PET is greater than CT (but with similar specificity)<sup>[58,59]</sup>. In one study the sensitivity and specificity of PET was reported to be 87% and 94%, respectively, compared to 73% and 94% for CT<sup>[60]</sup>. It has also been stated that the use of PET can alter management in up to 57% of patients<sup>[61]</sup> although this is not a universally held view<sup>[62]</sup>.

The role of PET in primary staging is minimal if metastatic disease has already been diagnosed. However, as PET images include a greater body area, it may define sites of disease outside the scope of that seen on routine CT scanning. This can have repercussions on management<sup>[59]</sup>. Identification of sites of metastases have been shown repeatedly to be more accurately performed by PET than CT<sup>[63]</sup>. However, its poor detection of small volume (sub-centimetre) disease remains a concern.

A possible use of PET is in those patients with raised tumour marker levels but no definite disease on conventional imaging. Hain *et al.* reviewed cases of patients with raised marker levels (including those with residual mass)<sup>[64]</sup>. They found that in all but one case PET identified the site of disease. In their study, five false negative PET results were found. Out of these, three cases had no abnormality on any imaging modality. During follow-up of these patients, it was found that PET scans were the first imaging modality to identify the site of recurrence. As a result of this it was suggested that in the presence of raised marker levels and negative imaging (including negative PET), the most appropriate follow-up imaging may be repeat PET. The use of PET to predict relapse in patients with clinical stage I non-seminomatous germ cell tumour has been investigated by the Medical Research Council (MRC) in the UK in the TE22 study. The study showed that PET identified a proportion of patients with disease not detected by CT; however, the relapse rate among PET-negative patients remains high. The study results therefore suggest that <sup>18</sup>FDG-PET scanning is not able to identify patients at sufficiently low risk of relapse to replace other treatment options in this setting<sup>[65]</sup>.

## **Surveillance**

In patients with stage I disease surveillance is a common management pathway. Overall, approximately 30% of patients will relapse<sup>[66–68]</sup>. Vascular or lymphatic invasion is the most powerful predictor of relapse; the absence of yolk sac elements and the presence of undifferentiated cells are also independent prognostic

variables<sup>[69]</sup>. In the prospective TE04 trial, 45% of those that relapsed did not have raised markers at the time of discovery of recurrent disease. Sixty-one percent of relapses occurred in the para-aortic nodes and 10% in mediastinal or supraclavicular nodes. Ninety-five percent of those who did relapse were in the IGCCCG good prognostic group and overall survival free from germ cell tumour was 99%<sup>[11]</sup>. As relapse is most frequent in the first year after diagnosis (up to 80%) the number of scans is maximal during this time. Surveillance is performed rigorously with clinical follow-up, chest radiography, serum marker analysis and CT. Serial imaging of the thorax and abdomen is routinely performed.

The value of chest CT above chest radiography has been studied. In a series of 168 stage I NSGCT patients on surveillance in whom chest X-ray rather than chest CT was performed<sup>[70]</sup>. Nineteen percent (42 patients) of these patients relapsed of which 8/42 relapsed with chest disease. Seven out of eight of these latter patients had evidence of disease elsewhere which was identified on abdominal CT. The one patient in this series who had only chest disease at relapse was clearly diagnosed by chest radiography. This led the authors to conclude that chest imaging with CT would not have changed the prognosis of those that relapsed in the chest in their study<sup>[69]</sup>.

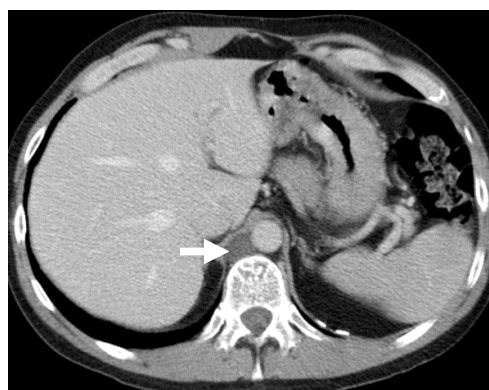
The role of pelvic CT has also been called into question. In one series of patients with testicular germ cell tumours pelvic lymphadenopathy was seen in 16 of 167 patients (9.6%). The presence of bulky para-aortic lymphadenopathy was the only significant predictor for pelvic disease and was present in 11 of 16 patients. In the absence of this or other risk factors for pelvic disease (previous scrotal or inguinal surgery, maldescent, tunica vaginalis invasion, retroperitoneal lymph node dissection or bulky abdominal nodes), routine pelvic CT for patients on surveillance for stage I disease may constitute unnecessary radiation<sup>[25]</sup>.

Centres vary in their preference, but most will scan patients between two and six times during the first year. As yet no consensus on optimal management has been derived but it is seen that those centres that scan more frequently do not detect relapse at a significantly earlier stage. Indeed in one study of 46 patients, all relapses detected after the 3 month CT were picked up by clinical suspicion, raised tumour markers or chest X-ray<sup>[71]</sup>. The question of whether more frequent CT results in earlier diagnosis of relapse and whether this has any outcome on survival still remains to be conclusively answered. Indeed, early results of the MRC TE08 study have not detected any advantage for a five scan schedule over a two scan schedule (NCRI meeting, October 2005).

The potential benefit of repeated scanning must be weighed against the financial and health costs of more frequent scans. A thoracic CT gives a radiation dose equivalent to 400 chest radiographs (8 vs. 0.02 mSv), while for a chest and abdomen CT the dose is increased to approximately 20 mSv (a dose equivalent to 1000

chest radiographs). This results in a 1:1000 lifetime risk of a second cancer/leukaemia in a 25-year-old over the subsequent 40 years. Another approach to reducing radiation exposure is to use alternative technology. The use of ultrasound and magnetic resonance imaging (MRI) has therefore been suggested in surveillance programmes. Ultrasound is not as reliable as CT or MR imaging in the assessment of abdominal para-aortic nodes. Limited data suggest that MR imaging may be used instead of CT for abdominal disease<sup>[46]</sup>.

Positron emission tomography (PET) is an attractive alternative modality to improve surveillance but as discussed above the MRC TE22 protocol suggests the added value of PET scan may be limited<sup>[65]</sup>.



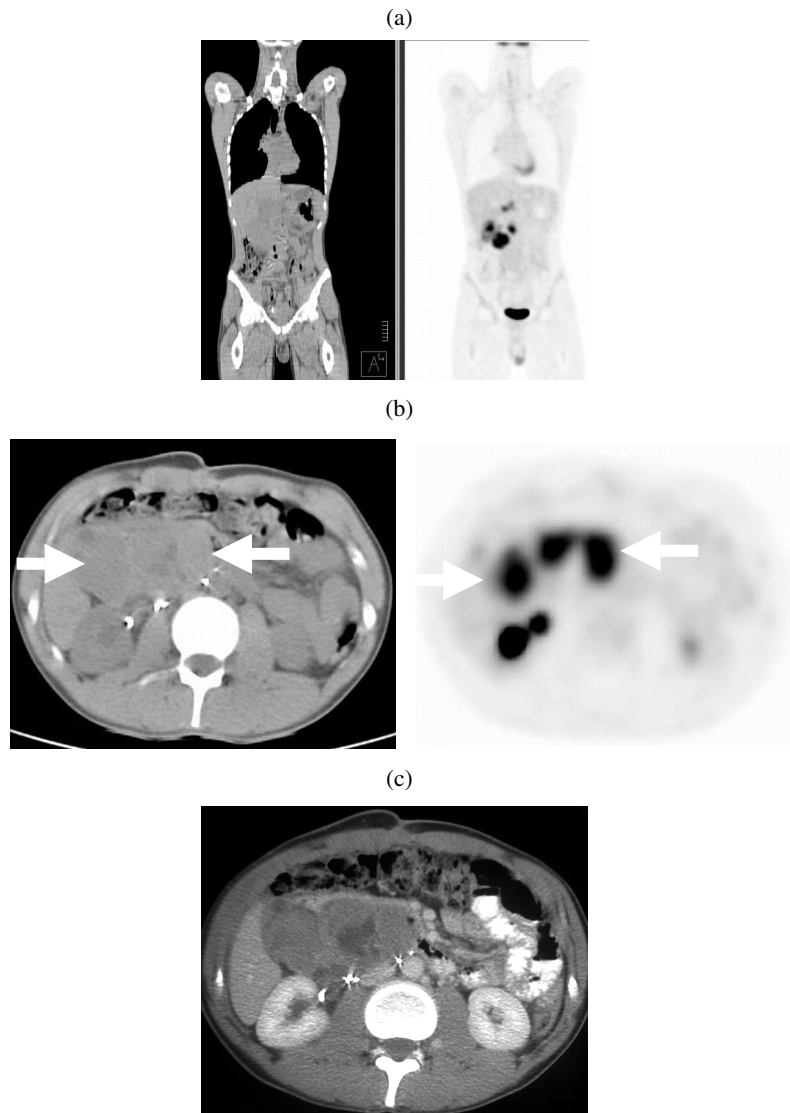
**Figure 6** Mature teratoma differentiated in retrocrural node (arrow). Contrast-enhanced CT shows low density lesion in the right retrocrural region.

### Assessing response to therapy

The EGCCCG guidelines state that radiological restaging must be performed after completion of first-line chemotherapy. However, in patients with slow tumour marker decline or clinical evidence of progression, restaging should be performed earlier.

Chest radiographs are useful screening tools and are often used in the routine follow-up of early-stage patients and those in complete remission following chemotherapy<sup>[72]</sup>. They enable detection and surveillance of lung parenchymal nodules 1 cm (or greater) in size, pleurally based masses and effusions and mediastinal masses. In a study designed to investigate the predictive capacity of chest radiography, 288 patients were retrospectively studied. Thirty-three cases of relapse were found but none were identified by chest radiography<sup>[73]</sup>. Despite this, their relatively low radiation burden and cost continue to make them attractive tools for follow-up studies.

CT is the primary imaging modality for assessing response of disease to treatment. Reduction in size of metastases is the primary change found on CT indicating response to therapy even if malignant cells persist within the residual tissue (Fig. 5). In addition to size, CT can help assess residual masses post-chemotherapy by



**Figure 7** Non-seminomatous germ cell tumour. (a) Coronal and (b) axial images on 18-FDG enhanced PETCT and (c) iodinated contrast enhanced CT showing a large metabolically active retroperitoneal mass (arrows).

assessing changes in appearance. Cystic and fatty change which is well assessed using CT have been associated with mature differentiated teratoma and may indicate the need for surgical removal (Fig. 6)<sup>[74–76]</sup>.

Seminoma is extremely sensitive to chemo- and radiotherapy, such that residual mass post treatment usually only consists of fibrosis and necrosis. Calcification may also be found within post-treatment tissue<sup>[77]</sup>. The CT findings may be allied to reduction in serum marker levels and reduction in avidity of uptake on PET scanning.

Treated lung metastases may resemble irregular scars in the region of the previous metastases. In some cases they may also be seen to cavitate<sup>[78]</sup>. Interval CT scanning during and following completion of therapy is important to assess the response<sup>[79]</sup>. It also allows the selection of patients who may benefit from surgical lymphadenectomy (traditionally those with residual

masses greater than 1 cm)<sup>[80]</sup>. In those patients with large-volume disease the use of CT and MRI has been shown to be useful in planning an operative approach<sup>[81]</sup>.

PET may have a role in the assessment of residual masses after chemotherapy. Cremerius *et al.* reviewed PET scans in patients with seminoma after treatment<sup>[56]</sup>. They reported that PET had 90% sensitivity for detecting residual disease. These results indicate that PET may be of value in selecting patients with seminoma for radiotherapy. The SEMPET trial (where PET was used to assess residual disease in patients with seminoma who were on chemotherapy) showed that PET imaging was more accurate than other assessment modalities<sup>[82]</sup>. In that study, PET was performed in all patients with residual masses  $\geq 1$  cm within 4–12 weeks of completion of chemotherapy. The results were compared to histological analysis of tumour viability or CT evidence of



progression. They reported that PET correctly identified all cases of residual tumour in lesions  $>3$  cm and in 95% of cases with lesions  $\leq 3$  cm. This gave an overall specificity and sensitivity for 100% and 80% respectively for PET, compared with 74% and 70% for CT. A further recent study reported that only 4 of 47 lesions  $<3$  cm (8.5%) were viable, whereas 11 of 27 lesions  $\geq 3$  cm (41%) were viable<sup>[83]</sup>. This led the authors to conclude that using a solely CT-based surgical strategy would have resulted in over-treatment of nearly 60% of the patients. They suggest that, in lesions  $\geq 3$  cm, a negative PET scan may justify surveillance of the patient, since no false negative PET scan was registered in lesions  $\geq 3$  cm in the present study. In lesions  $<3$  cm, only one of four viable lesions showed FDG uptake. As there were no false positive results in this group either, it was suggested that a positive PET scan, even in small lesions, is highly specific for tumour viability.

In NSGCT patients with residual masses PET is less useful. PET can differentiate between viable disease and fibrosis (Fig. 7)<sup>[56,64,84]</sup>. The sensitivity and specificity of PET in the largest (75 scans in 55 men) series was 88% and 95%, respectively, with high negative predictive value (NPV) and positive predictive value (PPV) of 90% and 96%, compared with a PPV for CT in this circumstance of 56%<sup>[64]</sup>. However, its use is limited in this setting as differentiated teratoma (MTD) has variable low or no uptake and cannot be distinguished from fibrosis or necrosis. The crucial decision here is whether a marker response requires surgery or not and PET is unable to help these patients.

The use of PET to predict response to treatment is uncertain. In contrast to salvage treatment one study found that PET was found more sensitive than CT or serum markers, 100% vs. 59% and 48%, respectively<sup>[85]</sup>. Though PET was shown not to be as specific as serum tumour markers for this purpose (78% vs. 100%, respectively) it did correctly predict all patients in this study who failed therapy. The overall accuracies of PET, CT and serum markers for prediction of response to high-dose chemotherapy in this study were 91%, 59% and 48%, respectively. There is little information to suggest that PET has a role in first-line treatment when standard assessment tools are successful.

## Conclusion

Testicular germ cell tumours have been increasing in incidence and now represent 1% of all male tumours. Tumour presence is normally clinically diagnosed and confirmed by raised levels of serum markers. Imaging can confirm tumour presence but is most useful in assessing the sites of metastases. The most common sites of spread are to retroperitoneal lymph nodes and lung parenchyma. Staging of tumours (which is an integral process in establishing prognosis and therapy) is largely performed using CT. Recent studies have shown that the use of

PET in specific scenarios may have significant advantage over CT. MR imaging is used in those patients with neurological disease or where intravenous contrast agent cannot be administered or as an aid to problem solving for equivocal CT.

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