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# Imaging Studies in Metastatic Urogenital Cancer Patients Undergoing Systemic Therapy: Recommendations of a Multidisciplinary Consensus Meeting of the Association of Urological Oncology of the German Cancer Society

## Key Words

Bladder cancer · Computed tomography · Germ cell tumors · Magnetic resonance imaging · PET-CT · Prostate cancer · Renal cell cancer · Skeletal scintigraphy · Testis cancer · Therapy response assessment

## Abstract

***Introduction:*** Imaging studies are an integral and important diagnostic modality to stage, to monitor and follow-up patients with metastatic urogenital cancer. The currently available guidelines on diagnosis and treatment of urogenital cancer do not provide the clinician with evidence-based recommendations for daily practice. ***Objectives:*** To develop scientifically valid recommendations with regard to the most appropriate imaging technique and the most useful time interval in metastatic urogenital cancer patients undergoing systemic therapy. ***Methods:*** A systematic literature review was performed searching MedLine, Embase and Web of Science databases using the terms prostate, renal cell, bladder and testis cancer in combination with the variables lymph node, lung, liver, bone metastases, chemotherapy and molecular therapy, and the search terms computed tomography, magnetic resonance imaging and positron emission tomography were applied. A total of 11,834 records were retrieved from all databases. The panel reviewed the records to identify articles with the highest level of evidence using the recommendation of the US Agency for Health Care Policy and Research. ***Conclusions:*** Contrast-enhanced computed tomography remains the standard imaging technique for monitoring of pulmonary, hepatic and lymph node metastases. Bone scintigraphy is still the most widely used imaging technique for the detection and follow-up of osseous lesions. For clinical trials it might be replaced by either PET-CT or MRI of the skeletal axis. Response assessment for patients treated with cytotoxic regime is best performed by the RECIST/WHO criteria; treatment response to molecular triggered therapy is best assessed by CT evaluating decrease in tumor size and density. Cross-sectional imaging studies for response assessment might be obtained after each 2 cycles of systemic therapy to early stratify responders from non-responders.



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## Introduction

Imaging studies of metastatic urogenital malignancies are an integral part of initial staging, response assessment and follow-up after systemic therapy. The currently available guidelines on diagnosis and treatment of urogenital cancer do not provide evidence-based or practical recommendations for routine practice [1–5]. In particular, the clinically important question of the most accurate method to monitor therapeutic response during cytotoxic therapy or treatment with molecular approaches has been much neglected.

It was the purpose of the interdisciplinary consensus meeting comprising specialists of the German Cancer Society involved in the fields of oncological urology, oncology, radiation oncology, radiology, nuclear medicine and epidemiology to develop a consensus with regard to (1) the most accurate imaging modality at time of initial staging, and (2) the most appropriate radiological method and its optimum frequency to monitor treatment response.

## Material and Methods

A systematic review of the literature was performed by the panel members searching MedLine, Embase and Web of Science databases to identify original articles, review articles, and editorials addressing the relationship between the response to systemic treatment of metastatic urogenital cancer and imaging studies. All articles published up to September 2009 were considered for the review process. We applied a 'free-text' protocol using the terms prostate, renal, bladder and testis cancer in combination with the variables lymph node, lung, liver, bone metastases, chemotherapy, molecular triggered therapy, multitarget tyrosine kinase inhibitors, and the search terms computed tomography, magnetic resonance imaging and positron emission tomography. All of the key words were contained within the Medical Subject Headings (MeSH) database. A total of 11,834 records were retrieved from all databases. The panel of the consensus group reviewed the records to identify the articles with the highest evidence based on the recommendation of the US Agency for Health Care Policy and Research (table 1), thereby focusing on the issue of staging and restaging during systemic therapy for metastatic urogenital cancer.

**Table 1.** Levels of scientific evidence as defined by the US Agency of Health Care Policy and Research

| Level | Sources and characteristics of evidence |
|---|---|
| IA | Evidence obtained from meta-analysis of randomized clinical controlled trials and systematic review |
| IB | Evidence obtained from at least one randomized clinical controlled trial |
| IIA | Evidence obtained from at least one well-designed controlled study without randomization |
| IIB | Evidence obtained from at least one other type of well-designed quasi-experimental study |
| III | Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies |
| IV | Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities without transparent proof |

## Assessment of Tumor Response with Standard Imaging Techniques

Metastases of solid tumors and their response to medical treatment are assessed with the use of the Response Evaluation Criteria in Solid Tumors (RECIST; table 2) [6–11] in clinical trials, whereas the WHO criteria are used in daily practice. According to RECIST up to 5 lesions in a single organ and up to 10 lesions in total should be evaluated. Tumor lesions will be defined as measurable disease if they are ≥20 mm on conventional studies or ≥10 mm on helical CT scans in at least 1 dimension. All baseline evaluations have to be performed as close to the start of medical treatment as possible, but never more than 4 weeks prior to treatment start.

For better correlation and interpretation, the same method of assessment and the same technique should be used at baseline and during follow-up to characterize each lesion. CT scans and MRI are currently the best available and reproducible imaging studies for measuring target lesions with regard to their response to medical treatment. It is currently a challenge to assess tumor response to molecular triggered therapies with only minimal changes in tumor volume but maximum changes in tumor density and vascularity. In these cases $^{18}$F-FDG-PET/CT has been shown to be able to identify patients with a good response to therapy despite the presence of residual masses on CT [6–11]. Furthermore, $^{18}$F-FDG-PET/CT has been shown to allow earlier treatment response monitoring in a variety of solid tumors, thereby offering the opportunity to predict patient outcome after the first or second cycle of treatment [9–11].

**Table 2.** Response criteria as defined by RECIST and the WHO

| | RECIST | WHO |
|---|---|---|
| Complete remission | disappearance of all disease | disappearance of all disease |
| Partial remission | decrease ≥30% in the sum of the greatest dimension of all measurable disease | decrease ≥50% in the sum of the cross products |
| Stable disease | decrease <30% and increase <20% in the sum of the greatest tumor dimensions | decrease <50% and increase <20% in the sum of the cross products |
| Progressive disease | increase ≥20% in the sum of the greatest tumor dimensions | increase ≥50% in the sum of the cross products |

## Radiation Exposure and Side Effects in Cancer Imaging

It is estimated that the annual global per caput effective ionizing radiation dose was slightly less than 3 mSv in the year 2000, with somewhat higher values for developed countries [12].

The introduction of helical and multidetector CT scanners has resulted in a significant increase in the number of indications to perform CT scanning for staging and follow-up purposes [13, 14]. Depending on the type of radiation procedure and the type of CT scanning, there are significant differences between the procedures with regard to effective doses (table 3). Young age at exposure (e.g. monitoring of testis cancer patients) appears to enhance the risk of radiation-related tumors of many sites and radiation-related risks persist throughout life, so that the frequency and dose of diagnostic radiation procedures should be minimized [12, 14].

Contrast-induced acute kidney injury (CIAKI) is a significant complication of contrast-enhanced CT and it develops in up to 10% of the patients [15]. CIAKI is associated with an increased mortality risk and medical response use. CIAKI can be prevented by pre- and postprocedure intravascular volume expansion with isotonic fluid, discontinuation of NSAID's and prophylactic administration of N-acetylcysteine.

Contrast reactions such as anaphylctoid urticaria, bronchospasm, laryngeal edema, hypotension and tachycardia are infrequent and occur in 5–10% of patients for high osmolality contrast media and 1–3% for low osmolality contrast media [16].

Nephrogenic systemic fibrosis is a sclerosing disorder found exclusively in patients with impaired renal function [17]. An association with gadolinium contrast agents in the development of nephrogenic systemic fibrosis has been suggested, although other factors such as recent surgery, inflammatory disease, or granulomatous disease might also contribute to the development.

**Table 3.** Effective doses of different imaging modalities

| Imaging study | Effective dose (mSv) | Number of chest X-rays with equivalent effective dose |
|---|---|---|
| Chest X-ray | 0.02 | 1 |
| X-ray skull | 0.07 | 3.5 |
| Osseous pelvis | 0.7 | 35 |
| Renal scintigraphy | 0.8 | 40 |
| Lumbar spine | 1.3 | 65 |
| Skeletal scintigraphy | 4.4 | 220 |
| PET | 7.2 | 360 |
| Chest CT | 8 | 400 |
| Abdominal CT | 10 | 500 |
| Whole-body PET | 25 | 1,250 |

## Standard Imaging Studies for the Evaluation of Metastases

*Lung Metastases*

Pulmonary metastases typically present as multiple and bilateral, well-defined, non-calcified pulmonary nodules with predominantly basal and peripheral location [18].

Helical CT represents the standard imaging technique of choice to detect lung metastases (table 4) [18] and it should be performed by use of a 5-mm contiguous reconstruction allowing a minimum-sized lesion of 10 mm to be detected. The sensitivity of helical CT to detect pulmonary metastases varies between 78 and 88% when helical

**Table 4.** Current standard imaging studies for metastatic lesions at different organ sites

| | Standard | Interval | Experimental/alternative | Interval |
|---|---|---|---|---|
| Lymph node metastases | helical CT with contrast dye | 8 weeks | MRI with/without superparamagnetic iron oxide (SPIO) contrast dye | 8 weeks |
| Lung metastases | helical CT | 8 weeks | MRI, dynamic MRI, FDG-PET/CT | 8 weeks |
| Liver metastases | multidetector helical CT with contrast dye | 8 weeks | MRI, dynamic MRI, MRI with liver-specific contrast agents (SPIO), FDG-PET/CT | 8 weeks |
| Bone metastases | bone scintigraphy | 12 weeks | MRI axial skeleton, FDG/choline-PET/CT | 8 weeks |

CT findings are compared with intraoperative findings [19–21].

If the nodules are larger than 10 mm in diameter, a contrast material-enhanced examination may be performed with 3 mm collimation before and after administration of a weight-related dose of intravenous contrast material. Contrast-enhanced examinations are performed at 1-minute intervals up to 4 min after the injection of contrast dye. Morphologic features such as shape, margin, cavitation, attenuation and size are helpful to identify those pulmonary nodules that are most likely to represent malignancy.

The risk of malignancy is strongly associated with nodular size, and nodules larger than 1 cm are highly suspicious for metastatic disease. However, even nodules smaller than 5 mm are malignant in up to 42% of the cases. The risk of harboring lethal cancer is less than 1% in nodules ≤4mm, about 10–20% in nodules up to 8 mm and more than 50% in nodules larger than 1 cm. Nodule enhancement following intravenous administration of contrast dye might help to differentiate malignant from benign lesions. Absence of significant enhancement of ≤15 HU is strongly predictive of benignity [16–21].

MRI has a limited role in the diagnosis of pulmonary metastases due to (1) its limited spatial resolution as compared with multidetector CT, (2) its high susceptibility to differences between airspaces and the pulmonary interstitium, and (3) its high susceptibility to respiratory and cardiac motions resulting in artifacts [16, 22].

PET/CT for identification of metastatic pulmonary disease has been demonstrated to have a sensitivity and specificity of 96 and 88%, respectively. with the lower specificity being related to the inability to differentiate infectious and inflammatory changes from malignant disease.

Based on the widespread availability, the cost effectiveness and the lower susceptibility to artifacts, dynamic or multidetector CT represents the cross-sectional imaging study of choice to detect and monitor pulmonary nodules.

*Liver Metastases*

10–20% of patients with urogenital cancer will develop liver metastases during the progression of their disease. On the other hand, 20–25% of all liver lesions smaller than 2 cm are benign [23], so that imaging techniques of the liver in patients with cancer do not only need high sensitivity, but also the ability to differentiate benign from malignant lesions.

Various radiological procedures are employed for the (differential) diagnosis of liver tumors. CT should be performed with native images as well as after using modern nonionic, iodine-containing water-soluble contrast agents; multidetector helical CT is today's standard [24–27]. For helical CT, 5 mm reconstructions should be used allowing a minimum-sized lesion of 10 mm to be detected.

Multisplice spiral CT has a sensitivity for the detection of liver metastasis of 65–85% [24–27], thus making it the method of choice for staging urogenital cancer. Contrast-enhanced MRI increases the sensitivity for detecting metastases to 90% as compared to only 70% of unenhanced MRI [26, 27]. There is currently some debate whether enhanced MRI with liver-specific superparamagnetic iron oxide (SPIO) contrast agents even improves the diagnostic accuracy of contrast-enhanced CT [26, 27]. The comparative studies performed so far did not identify significant differences in the sensitivity of detection of hepatic metastases between contrast-enhanced CT and SPIO-MRI. Because MRI is more expensive and less widely available than CT, it is not considered as a practical routine screening tool.

The value of $^{18}$F-PET/CT for the detection of liver metastases is controversial. Various groups have demonstrated that PET is equivalent to MRI and CT for the identification of liver metastases, and currently there is no evidence that PET would do better than MRI and CT.

*Lymph Node Metastases*

The majority of lymph node metastases originating from urogenital cancer are located in the retroperitoneum. CT scans of the abdomen and the pelvis are the imaging procedures of choice. On these cross-sectional modalities, nodal metastases are usually suspected according to location and size criteria (i.e. a maximum short axis diameter ≥1 cm is considered malignant [28]). However, CT scans of the abdomen and pelvis might give false-negative results in up to 30% of cases due to difficulties in the interpretation of lymph nodes based on morphology and size alone [29, 30]. MRI scans of the abdomen and pelvis do not provide additional information and should be restricted to patients with contraindications to CT [29, 30]. MRI lymphangiography is a promising technique, but needs further evaluation in staging and monitoring of patients with metastatic urogenital cancer [31, 32]. Based on available data, PET has not been conclusively demonstrated to improve sensitivity in patients with metastatic urogenital cancer over staging by CT scanning alone [33].

*Skeletal Metastases*

Bone scintigraphy (BS), conventional radiographic techniques, $^{18}$F-FDG-PET/CT and whole-body MRI represent potential imaging studies to diagnose and to monitor skeletal metastases [34–36]. Skeletal scintigraphy is still used as the most common procedure to assess bone metastases due to its comparatively low cost and its general availability, although it suffers from suboptimal specificity in the accurate differential diagnosis of malignant versus benign processes.

Whole-body MRI within a single examination has been demonstrated to visualize bone metastases earlier and with higher sensitivity than conventional BS [37–41]. In a prospective study MRI predicted the origin of a bony lesion with a sensitivity of 92% (BS 93%), a specificity of 91% (BS 82%) and an accuracy of 91% (BS 82%). In patients with high-risk or androgen-independent prostate cancer, MRI of the axial skeleton (MRIas) was shown to be superior to BS and bone scans completed with targeted X-rays. MRIas altered the clinical management of high-risk prostate cancer (PCa) in 30% of the patients due to the finding of skeletal metastasis. Sensitivities were 46% for BS, 63% for BS plus targeted X-ray, 83% for BS plus targeted X-ray combined with MRI and 100% for MRIas [39]. When compared to whole-body MRI, sensitivity of FDG-PET/CT was significantly lower (78 vs. 94%), specificities were not significantly different (80 vs. 76%), and the diagnostic accuracy was significantly better (91 vs. 78%) for whole-body MRI [40]. In another comparative study focusing on staging of PCa, sensitivity, specificity and diagnostic accuracy of $^{11}$C-choline-PET/CT (96.6, 76.5, and 93.3%, respectively) and whole-body MRI (78.4, 94.1 and 81%, respectively) did not differ significantly [41].

In summary, MRIas and $^{18}$F-choline PET-CT are more sensitive and specific to detect and to monitor skeletal lesions, and they should be further explored in clinical trials.

## Response Assessment

*Metastatic Renal Cell Cancer*

Molecular triggered therapy with antibodies or multitarget tyrosine kinase inhibitors represents the standard treatment of choice for metastatic renal cell cancer (RCC) [3]. At time of diagnosis of metastatic disease about 55% of patients demonstrate metastases at more than 2 different organ systems [42, 43].

CT is the standard modality for the evaluation of mediastinal and retroperitoneal nodal metastasis from RCC and assessment of extent and location of liver metastases [29, 44, 45]. The role of MRI has not been evaluated in large clinical series [29, 46]. There is a poor agreement for N-staging between MRI and surgical pathological staging [47].

Response of soft tissue metastases to medical treatment is assessed according to RECIST within clinical trials, whereas WHO criteria are recommended for daily routine, although these criteria have been developed for cytotoxic drugs that cause tumor shrinkage, whereas molecular targeted therapy usually results in growth inhibition and necrosis which might be followed by tumor shrinkage at a later phase of treatment [6, 7]. Typically, response to treatment with multitarget tyrosine kinase inhibitors is characterized by an increase of the intralesional necrosis, no change of the tumor diameter and sometimes an increasing partial tumor blood volume as detected by dynamic enhanced MRI [48]. Currently, much controversy exists with regard to the most appropriate timing and technique of image-guided response assessment. There are, however, no randomized or large

clinical studies in RCC so that experiences from other solid tumors have to be considered. In gastrointestinal stroma tumors, various authors have evaluated most accurate imaging modalities for response evaluation following treatment with imatinib mesylate [49, 50]. In a prospective evaluation, Choi et al. [49, 50] analyzed intralesional changes in CT density 8 weeks after treatment and they identified a decrease in tumor size and tumor density of ≥26% and ≥31%, respectively, to be associated with a good response. Tumor density was defined as the CT attenuation coefficient of each tumor in HU by drawing a region of interest around the margin of the entire tumor. None of the poor responders either demonstrated a >10% decrease in tumor size and/or a >15% decrease in tumor density at 8 weeks after treatment.

In metastatic RCC, the potential use of $^{18}$F-FDG-PET/CT imaging for an early assessment of response to sunitinib was described [51] with a good correlation between maximum standardized uptake value ($SUV_{max}$) after 1 cycle of treatment and response and progression rates. In another trial including 10 patients with 52 metastatic lesions, FDG-PET/CT was performed prior to and 1–2 months after initiation of treatment with sorafenib [52]. It was shown that a significant decrease in glucose uptake was already present in all lesions independent of their location – soft tissue or skeletal system – after 1 month of treatment. It was concluded that FDG-PET/CT is advantageous to routine CT imaging, which is limited to soft tissue lesions.

Also the measurement of changes in tumor blood flow evaluated by arterial spin labeling (ASL) magnetic resonance imaging before and at 1 month on treatment with a pan-vascular endothelial growth factor receptor tyrosine kinase inhibitor correlate with response to therapy [53]. Changes in blood flow at 1 month and changes in tumor size measured at 4 months or at time of disease progression were significantly correlated ($p = 0.01$). Patients with progressive disease within 4 months on treatment had a nonsignificant increase in tumor blood flow at 1 month, whereas patients with stable disease or partial response at 4 months had a significant decrease in tumor blood flow at 1 month ($p = 0.02$).

The data of early changes in FDG-PET/CT or ASL-MRI are consistent with a hypothetical functional role for tumor ischemia in the mechanism of response to antivascular endothelial growth factor therapy. Both imaging techniques should be analyzed further with regard to their clinical utility.

The consensus of the group is to perform CT scans every 8 weeks and to analyze tumor response according to a decrease of tumor size (≥25% for good responders) and according to a decrease in tumor density (≥30% in good responders). For the future, $^{18}$F-FDG-PET/CT or ASL-MRI should be included as imaging techniques in clinical trials.

*Urothelial Cancer*

Approximately 50% of all patients with urothelial cancer will relapse after radical cystectomy with the majority of them developing distant metastases [4]. About 10–15% of patients with urothelial cancer initially present with metastatic disease. Cisplatinum-containing combination chemotherapy with gemcitabine/cisplatin (GC) represents the standard of care [54].

With regard to response assessment, the current standard approach is to perform a baseline CT scan of the chest, abdomen and pelvis 2–4 weeks prior to chemotherapy followed by the same imaging studies every other cycle of chemotherapy (level IA) [4]. According to most clinical trial protocols, a validation CT scan of the target lesions should be performed after another 4 weeks. A bone scan usually is only performed in the presence of symptoms or in the case of incidental findings on CT scans.

Taking into account the significant side effects comprising grade 3/4 hematotoxicity and gastrointestinal toxicity in 44 and 33% of the patients associated with the GC regime [54], one has to consider the option to perform CT scans after each single cycle in order to assess treatment response and to spare toxic treatment in nonresponders. In the recent prospective randomized clinical trial comparing the therapeutic efficacy of GC versus MVAC in patients with advanced urothelial cancer, liver, lung and lymph nodes were the predominant sites of progression in 69% of patients and should be targeted with imaging studies. Median time to progression was 1.9 months in patients with progressive disease despite chemotherapy [54].

The consensus of the group was to recommend a slightly intensified monitoring with 5 CT scans of the chest and/or abdomen depending on the location of metastases during a 4-cycle regime of GC or a clinical trial: pretherapeutic, after cycles 2, 3 and 4, and a validation scan 3–4 weeks after completion of chemotherapy. Dynamic contrast-enhanced MRI might help to predict response and failure to systemic chemotherapy after 2 cycles of the MVAC regime [55]. Larger patient cohorts have to be assessed before a transfer of these methods in daily routine is justified.

With regard to the detection of bone metastases, a baseline bone scan should be obtained. In case of positive

findings, one should consider performing an $^{18}$F-FDG-PET or whole-body MRI due to its higher specificity and overall accuracy for the diagnosis of bone metastases (level IIA–B) [36–42].

*Prostate Cancer*

The majority of men with metastatic PCa develop bone metastases, 10 and 3% of the men develop lung and liver metastases [2]. Approximately 40% of patients demonstrate a combination of both osseous and soft tissue lesions [2]. Whereas the imaging studies for diagnosis and therapeutic response assessment of soft tissue metastases are standardized, there are no such standardized criteria available to define response and progression of skeletal metastases. According to its definition, RECIST and WHO criteria do not apply for osseous disease [6, 7].

Quite recently various working groups established a simple technique to quantify the extent of bone metastasis: the percentage of the positive area on a BS (%PABS), which is evaluated automatically using a computer-assisted image analysis [56]. %PABS was indentified as a valid tool to assess response to treatment, and it correlated very well with PSA decrease after initiation of androgen-deprivation therapy. Changes in %PABS with prognostic significance could be observed as early as 3 months after initiation of therapy. %PABS was also identified as a prognostic marker with patients demonstrating a >25% decline surviving significantly longer than those with a <25% decline (52.3 vs. 37 months, $p = 0.0207$). However, %PABS has its limitations due to the low specificity of BS, the difficulty and objectiveness to clearly trace outlines of positive areas and lack of prospective validation.

Quantification models relying on bone scans to monitor the therapeutic response bear the major disadvantage of the well-known 'flare-phenomenon' [57] so that early changes in bone scintigraphy might not represent the best marker to assess objective response to therapy in solid cancer types with metastatic bone disease. In men with castration-resistant PCa (CRPCa) changes of metastatic deposits in imaging studies should always be correlated with changes in PSA and other markers such as alkaline phosphatase, LDH and bone resorption markers which correlate significantly with therapeutic response [2].

It has been shown in other solid cancers that PET-CT is far more sensitive to assess responses of osseous lesions to systemic chemotherapy as early as 8 weeks following initiation of treatment [9, 10]. The decrease in $SUV_{max}$ of osseous target lesions after systemic treatment was an independent predictor of response and duration of response. However, there are only very few studies with regard to CRPCa and its response to systemic chemotherapy. In CRPCa, $^{18}$F-fluoride and $^{18}$F-choline PET-CT have been shown to have a higher sensitivity than bone scans in the evaluation of treatment response of bone metastases [58]. Although PET-CT is not widely available, it might represent the most reliable imaging modality to monitor therapeutic response to new agents in the management of CRPCa with bone metastases in clinical trials.

Whole-body MRI within a single examination has been demonstrated to visualize bone metastases earlier and with higher sensitivity than conventional bone scintigraphy [37–41]. With regard to the evaluation of chemotherapeutic response in CRPCa with bone metastases, MRIas was significantly more sensitive and specific as skeletal scintigraphy. It was also shown that RECIST criteria could be transposed to MRIas imaging thereby allowing an accurate assessment of complete and partial responses of osseous lesions after 6 months of treatment [38].

In summary, BS is still the most widely used imaging modality to detect and monitor bone metastases in CRPCa, despite its low specificity. If bone scans are to be used to monitor treatment response, an interval of 12 weeks is sufficient considering the flare-up phenomenon in one third of the patients by week 8. If shorter intervals are used, changes in bone scans should not be used as the single marker to define progression but bone scan findings should be assessed together with changes of the tumor markers PSA, LDH and alkaline phosphatase. MRIas and choline PET-CT are more sensitive and specific to detect and monitor skeletal lesions, and these new imaging techniques should be further explored in clinical trials with new agents for the treatment of metastatic prostate cancer.

*Testicular Cancer*

CT of the chest, abdomen and pelvis are required as initial staging investigations [1]. Oral and intravenous contrast media are mandatory [1]. For the evaluation of the lung and mediastinum, chest CT scan is more sensitive than plain X-ray films [59, 60]. However, it should be noted that pulmonary/pleural nodules of <1 cm can represent a false-positive finding in CT scans. Furthermore, CT scans of the abdomen and pelvis might give false-negative results in up to 30% of cases due to difficulties in the interpretation of lymph nodes based on morphology and size alone [28–31]. Magnetic resonance tomogra-

phy scans of the abdomen and pelvis do not provide additional information and should be restricted to patients to whom intravenous contrast media cannot be given [61, 62]. Based on available data, PET has not been conclusively demonstrated to improve sensitivity over staging by doing CT scanning alone [63, 64]. PET scans are not recommended outside clinical trials as part of routine initial staging procedures. Bone scans should be obtained in patients in whom bone metastases are clinically suspected. Imaging of the brain preferably by magnetic resonance tomography is required in patients with clinical symptoms and signs indicating brain metastases.

With regard to treatment during chemotherapy for advanced nonseminomas, it was the consensus of the group that CT/MRI studies of the chest and the abdomen should be performed after 2 cycles and approximately 4 weeks after the last cycle of systemic treatment. In advanced seminomas with residual masses following chemotherapy, a FDG-PET/CT should be performed 6–8 weeks after treatment due to its high sensitivity to detect vital cancer [1, 65].

## Conclusion

Imaging studies are an integral and important diagnostic modality to stage, to monitor and to follow-up patients with advanced or metastatic urogenital cancer.

Based on an extensive review of the literature the following statement can be made: contrast-enhanced CT remains the standard imaging of choice for monitoring of pulmonary, hepatic, mediastinal and retroperitoneal lymph node metastases. In young testicular cancer patients, CT might be replaced by MRI in order to decrease radiation exposure in long-term cancer survivors. BS is still the most widely used imaging technique for the detection and follow-up of osseous lesions despite its low specificity. For clinical trials it might be replaced by either PET-CT or MRI of the skeletal axis. Response assessment for patients treated with cytotoxic regime within clinical trials is best performed by the RECIST criteria; for daily routine WHO response criteria should be used. In patients undergoing molecular triggered therapy, follow-up studies are best performed by $^{18}$F-FDG-PET/CT examinations or the application of the Choi criteria when using CT scans.

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