

**American College of Radiology
ACR Appropriateness Criteria®**

Clinical Condition: Metastatic Bone Disease

Variant 1: Stage 1 carcinoma of the breast. Initial presentation: asymptomatic.

Radiologic Procedure	Rating	Comments	RRL*
X-ray radiographic survey whole body	1		Med
Percutaneous biopsy area of interest	1		NS
MRI area of interest with or without contrast	1		None
Tc-99m bone scan whole body	1		Med
Myelography and post myelography CT spine	1		High
FDG-PET whole body	1		High
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 2: Stage 2 carcinoma of the breast. Initial presentation, with back and hip pain.

Radiologic Procedure	Rating	Comments	RRL*
Tc-99m bone scan whole body	9	To be done first to evaluate for presence of lesions suspicious for metastatic disease.	Med
X-ray spine and hip	9	Radiographs obtained after bone scan if needed for further lesion characterization.	Med
FDG-PET whole body	5	If bone scan is negative and the results of the PET examination will influence the use of systemic treatment.	High
Tc-99m bone scan with SPECT hip and spine	1		Med
Myelography and post myelography CT spine	1		High
CT hip and spine with or without contrast	1		Med
X-ray radiographic survey whole body	1		Med
MRI hip and spine with or without contrast	1		None
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Metastatic Bone Disease****Variant 3:****Breast carcinoma. Follow-up bone scan reveals single “hot” lesion in spine.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
X-ray spine hot area(s)	9		Low
MRI spine without contrast	9	If radiographs are negative.	None
FDG-PET whole body	5	If results of the PET examination will influence the use of systemic treatment.	High
MRI spine with contrast	1		None
Myelography and post myelography CT spine	1		High
Percutaneous biopsy spine	1		NS
X-ray radiographic survey whole body	1		Med
CT spine with or without contrast	1		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 4:**Breast carcinoma. Three “hot” areas in spine revealed by bone scan. No back pain.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
X-ray spine hot area(s)	9		Low
MRI spine without contrast	9	If radiographs are negative.	None
FDG-PET whole body	5	If results of the PET examination will influence the use of systemic treatment.	High
SPECT spine	5	SPECT added to bone scan in equivocal lesions.	Med
MRI spine with contrast	1		None
Percutaneous biopsy spine	1		NS
Myelography and post myelography CT spine	1		High
CT spine hot area with or without contrast	1		Low
X-ray radiographic survey whole body	1		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Metastatic Bone Disease****Variant 5:****History of treated breast carcinoma. Now has single “hot” lesion revealed by bone scan in sternum.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
CT sternum without contrast	9		Med
MRI sternum without contrast	8	If patient can tolerate prone imaging. Use of opposed-phase sequence helpful to assess for marrow obliterating process.	None
X-ray sternum	5	Difficult area to image with radiographs.	Low
FDG-PET whole body	5	If results of the PET examination will influence the use of systemic treatment.	High
SPECT sternum	5		Med
X-ray radiographic survey whole body	1		Med
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 6:**Patient with known bone metastatic disease (carcinoma of the breast). Presenting with pathological fracture of left femur on radiography.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
Tc-99m bone scan whole body	9		Med
FDG-PET whole body	5	If bone scan is negative and the results of the PET examination will influence the use of systemic treatment.	High
SPECT femur	1		Med
X-ray radiographic survey whole body	1		Med
CT femur without contrast	1		Low
MRI femur without contrast	1		None
X-ray femur	1		Min
Percutaneous biopsy femur	1		NS
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 7:**Prostate nodule on physical examination proven to be a well- or moderately differentiated carcinoma and PSA <20 mg/ml. Patient asymptomatic.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI area of interest without contrast	1		None
CT area of interest without contrast	1		NS
X-ray radiographic survey whole body	1		Med
Tc-99m bone scan whole body	1		Med
FDG-PET whole body	1		High
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Metastatic Bone Disease****Variant 8:****Prostate nodule on physical examination proven to be a poorly differentiated carcinoma or PSA ≥ 20 mg/ml. Patient asymptomatic.**

Radiologic Procedure	Rating	Comments	RRL*
Tc-99m bone scan whole body	9		Med
CT area of interest without contrast	1		NS
X-ray radiographic survey whole body	1		Med
MRI area of interest without contrast	1		None
FDG-PET whole body	1		High
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 9:**Patient with known malignancy, with back pain and partially collapsed vertebra on radiography. Otherwise healthy.**

Radiologic Procedure	Rating	Comments	RRL*
MRI spine without contrast	9	To differentiate osteoporotic collapse from destructive lesion.	None
Tc-99m bone scan whole body with SPECT spine	8	To detect additional lesions.	Med
FDG-PET whole body	5	If bone scan is negative and the results of the PET examination will influence the use of systemic treatment.	High
MRI spine with contrast	1		None
CT spine without contrast	1		Med
Percutaneous biopsy spine	1		NS
X-ray radiographic survey whole body	1		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 10:**1 cm lung nodule. Non-small-cell at needle biopsy. Now coming for staging and resection.**

Radiologic Procedure	Rating	Comments	RRL*
FDG-PET whole body	9		High
Tc-99m bone scan whole body	9	Not needed if PET imaging performed for initial nodule workup.	Med
MRI chest without contrast	1		None
X-ray radiographic survey whole body	1		Med
CT chest without contrast	1		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Metastatic Bone Disease****Variant 11:****Patient with multiple myeloma presenting with acute low back pain.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
X-ray lumbar spine	9		Med
MRI lumbar spine without contrast	8	Important if neurologic symptoms are present. Better defines lesion characteristics and adjacent marrow.	None
X-ray radiographic survey whole body	2	If long interval since last bone survey.	Med
Tc-99m bone scan whole body	1		Med
CT lumbar spine without contrast	1		Med
MRI lumbar spine with contrast	1		None
FDG-PET whole body	1		High
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 12:**Young patient with osteosarcoma of long bone coming for staging. Chest CT normal. Looking for bone metastases.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
Tc-99m bone scan whole body	9		Med
MRI area of interest with or without contrast	9	MRI of surrounding region to evaluate for small skip metastases. See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body	5	If bone scan is negative and MRI is equivocal, and if results of the PET examination will influence the use of systemic treatment.	High
Tc-99m bone scan with SPECT area of interest	1	SPECT added to nuclear medicine in equivocal lesions.	Med
CT area of interest without contrast	1		NS
X-ray radiographic survey whole body	1		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Metastatic Bone Disease****Variant 13:****Osteosarcoma, resected clear margins. Chemotherapy, asymptomatic. Six-month follow-up after treatment to rule out bone metastases.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
Tc-99m bone scan whole body	9		Med
CT area of interest with or without contrast	1		NS
X-ray radiographic survey whole body	1		Med
MRI area of interest with or without contrast	1		None
Tc-99m bone scan with SPECT area of interest	1		Med
FDG-PET whole body	1		High
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 14:**Female, 8 weeks pregnant, with known primary, now suspected of having bone metastasis. She wants to continue with the pregnancy.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI whole body without contrast	9	Should be done first due to lack of ionizing radiation.	None
X-ray area of interest	9	With appropriate shielding. Helpful to evaluate risk of pathologic fracture.	NS
CT area of interest without contrast	2	If involving an extremity. With appropriate shielding.	NS
Tc-99m bone scan whole body	2		Med
X-ray radiographic survey whole body	1		Med
FDG-PET whole body	1		High
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

METASTATIC BONE DISEASE

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Summary of Literature Review

There are several imaging and interventional techniques for the initial detection and follow-up of metastatic bone disease: radiography, radionuclide bone scanning, computed tomography (CT), magnetic resonance imaging (MRI), fine-needle aspiration, and core-needle biopsy. Newer techniques include fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET), FDG-PET/CT, and whole-body MRI [1-4].

Except for a few limitations, radionuclide bone scanning remains the primary imaging examination used to detect osseous metastasis. It has been repeatedly shown to be more sensitive than radiography [5]. Bone scans are sensitive in detecting osseous abnormalities, but they are nonspecific. After an abnormality has been detected, it should be radiographed to make sure it does not represent a benign process such as osteoarthritis, inflammatory

arthritis, or fracture [6]. One of the major advantages of radionuclide bone scanning is that it allows for a total body survey. This is important because approximately 13% of metastatic lesions occur in the appendicular skeleton in regions that are usually not included on a skeletal survey [7]. Krishnamurthy et al [7] pointed out that most metastatic skeletal lesions could be asymptomatic and that the serum alkaline phosphatase level is a poor indicator of early metastases. Highly aggressive metastases may show “cold” or photopenic areas on a bone scan. Multiple myeloma can frequently show photopenic lesions or a negative bone scan [8,9]. Bone scans are also insensitive in detecting skeletal lesions due to Langerhans cell histiocytosis (histiocytosis X), and radiographic surveys are recommended for patients with this disease [10,11]. Diffuse bony metastasis may present with a pattern of intense uniform radionuclide uptake (superscan), which can be misinterpreted as a negative examination.

Solitary sites of increased radionuclide uptake in patients with known malignancy are a common occurrence, and they could pose a diagnostic problem because of the nonspecific nature of these abnormalities on bone scintigraphy. On the other hand, Boxer et al [12] reported that approximately 21% of patients with breast cancer relapsed with a solitary bone lesion, most commonly in the spine. The spine was the commonest site for both solitary and multiple metastases. Tumei et al [13] reported that a solitary rib metastasis in cancer patients is uncommon and that 90% of “hot” rib lesions on bone scan are due to benign causes. A solitary sternal “hot” lesion in a patient with breast carcinoma has an 80% probability of being due to metastatic disease [14]. When a patient with a known primary tumor develops a solitary lesion on a bone scan, further diagnostic evaluation should be undertaken, starting with radiography and, if that is not diagnostic, proceeding to CT, MRI, or even biopsy [15,16]. Some authors advocate single-photon emission CT (SPECT) imaging as an effective method for differentiating malignant from benign lesions in the spine [17].

Breast Cancer

In stage 1 breast carcinoma where bone scintigraphy is usually negative, most authorities believe that routine baseline and follow-up bone scans are probably unwarranted because of the very low true positive yield [18,19]. The panel does not recommend any imaging studies of the skeleton in asymptomatic patients with stage 1 carcinoma of the breast when they present initially. Bone scanning, FDG-PET [20,21] and PET/CT [22,23] have been shown to be useful in the preoperative staging and postoperative follow-up of stages 2, 3, and 4-breast carcinoma.

If a patient with stage 2 breast carcinoma presents with back and hip pain, the panel recommends radiography of the back and hip and radionuclide bone scan. Other

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studies may be needed depending on the results of the radiographs and bone scan. In patients with known breast carcinoma who are discovered to have a single “hot” area in the spine on bone scan, the panel recommends radiography of the “hot” area. If radiography is negative, the panel recommends MRI. For lesion localization and needle guidance, a CT scan is recommended if a needle biopsy is warranted. The panel recommends adding SPECT imaging if the planar radionuclide bone scan is equivocal. In patients discovered to have multiple “hot” lesions in the spine, the panel recommends radiography of these “hot” lesions; MRI is also recommended if the radiographic examination is negative. A CT scan becomes necessary if a needle biopsy is to be performed.

For a “hot” lesion of the sternum in a patient with known breast carcinoma, the panel recommends radiography, followed by MRI, to help in the diagnosis. MRI should be performed with the patient prone to minimize respiratory artifact, and the use of an opposed phase (also referred to as in and out of phase) sequence is suggested to best assess for marrow replacement by tumor. CT is useful for localization if fine-needle aspiration or core biopsy is required.

Long Bone Fracture

In a patient with known metastatic carcinoma presenting with a pathological fracture of a long bone on radiography, the panel recommends a radionuclide bone scan to look for other metastatic sites in the skeleton.

Prostate Cancer

Studies have shown that for staging and follow-up of patients with prostate carcinoma, radionuclide bone scans are not necessary unless the prostate specific antigen (PSA) is ≥ 20 ng/ml or the primary tumor is poorly differentiated [24-27]. For routine staging purposes (no bone pain), the panel agrees with these studies. However, the panel recommends a radionuclide bone scan for patients with a PSA no greater than 20 ng/ml or a poorly differentiated primary tumor.

Non-Small-Cell Lung Cancer

In patients with non-small-cell carcinoma of the lung, bone is one of the most common sites for early extrathoracic spread. Some of these bony metastases are asymptomatic. The exclusion of bone metastases is important in the initial preoperative staging of lung cancer, although it is not clear from the literature whether bone scans should be performed routinely or only when clinical indicators suggest skeletal metastases [28-30]. The panel currently recommends a radionuclide bone scan of the skeleton in patients coming for staging after needle biopsy of a lung nodule revealed a non-small-cell carcinoma. However, in patients with non-small-cell carcinoma of the lung who have received or will be receiving an FDG-PET study as part of their initial workup, a radionuclide bone scan is not necessary [1,2]. The current PET literature has significant variability due to differing study quality and imaging techniques used, but this technique has the potential to improve the

accuracy of non-small-cell lung carcinoma tumor staging, especially for bone metastases [31].

Primary Bone Tumors

Bone metastases are very uncommon at initial presentation in patients with primary malignant bone tumors; therefore radionuclide bone scan is not indicated. Bone scanning has been shown not to be useful in differentiating between benign and malignant lesions or in defining the local extent of a malignant tumor reliably [32,33]. Osteosarcoma is probably the only exception; although the yield of imaging for metastases at the time of diagnosis is small, the presence of an occasional metastasis could substantially affect the treatment of the patient [34,35]. The panel concurs with these reports, and it recommends a radionuclide bone scan for patients with osteosarcoma at presentation for staging. In patients with osteosarcoma who have received adjuvant chemotherapy, 16% may develop asymptomatic osseous metastasis before lung metastasis; therefore some authors suggest bone scans for routine follow-up [34,35]. The panel concurs with these reports, and it recommends a radionuclide bone scan for patients with osteosarcoma at follow-up and after tumor resection with clear margins and chemotherapy. FDG-PET has not been proven to replace chest CT and bone scanning as a staging modality for osteosarcoma [36].

Other Cancers

In patients with cancers that rarely metastasize to bone — such as cervical, endometrial, bladder, and gastrointestinal tract tumors — baseline scans are obtained only when the disease is advanced [37]. There is no consensus in the literature about the timing of follow-up scans in asymptomatic patients. Some authors suggest a bone scan every 6 months for 1 year and then every 2 years. In clinical practice, most medical and radiation oncologists request follow-up bone scans only a) in asymptomatic patients with evidence of progressive disease (ie, rising carcinoembryonic antigen or alkaline phosphatase values), b) for restaging the disease in patients with local recurrence, and c) in patients with symptoms that are potentially of osseous origin [37].

Radiography is frequently used to screen for metastatic sites in multiple myeloma and Langerhans cell histiocytosis (histiocytosis X), but generally it is considered insensitive to screen for asymptomatic metastases [8-11]. In patients with multiple myeloma who present with acute low-back pain, the panel recommends radiographs of the lumbosacral spine or bone survey if the interval since the last bone survey is long. MRI is useful in patients with neurological findings or to better characterize the bone marrow. The panel believes that the only time when radionuclide bone scan (with or without SPECT) would be needed in cases of multiple myeloma is when strontium 89 treatment is being considered.

Vertebral Column

The vertebral column deserves special consideration. It is the most common site of skeletal metastasis, and cord

compression from metastasis is among the most dreaded complications of cancer [12]. MRI has proven advantages over all other imaging modalities, including myelography and CT myelography [6,16]. One limitation of MRI has been its inability to consistently differentiate an acute traumatic or acute osteopenic compression fracture from a pathologic fracture. The use of diffusion-weighted MRI has been shown to be effective in differentiating benign osteopenic vertebral collapse from malignant collapse, but the efficacy of this technique is still controversial and it has not gained widespread use [38-42]. The role of FDG-PET and FDG-PET/CT has been assessed in metastatic disease of the spine. In patients with lung cancer, studies have shown that FDG-PET has better specificity than bone scans using Tc-99m methylene diphosphonate (MDP) tracer, but similar sensitivity for detecting osseous metastatic disease [1,2]. Additionally, FDG-PET/CT has better specificity for detecting metastatic involvement of the spine than FDG-PET. FDG-PET/CT allows precise localization of bone lesions and associated soft-tissue involvement with potential neurologic significance [4].

As MRI sequences continue to become faster, there is emerging evidence showing that whole-body MRI is feasible and that it can replace bone scintigraphy for detecting metastatic bone disease. Proponents of this technique indicate that whole-body MRI is more sensitive and more specific than bone scintigraphy or PET [43,44]. In addition to bone metastases, whole-body MRI can demonstrate silent metastases in the brain, lungs, and liver [45]. Whole-body MRI is also comparable in cost to bone scintigraphy [46]. No ionizing radiation is involved with whole-body MRI, making it especially suited for pregnant patients with suspected bony metastasis [3].

Depending on whether the lesion is lytic, blastic, or associated with a soft-tissue mass, fine-needle aspiration or core biopsy can be used to arrive at a definitive diagnosis in patients suspected of having metastasis of known or unknown origin. Needle biopsy is also helpful in suspected tumor recurrence and to differentiate metastasis from osteonecrosis in previously irradiated bone [47-50].

Summary

- Radionuclide bone scanning is the most widely used primary imaging examination for detecting osseous metastasis.
- After an abnormality has been detected, radiographs should be obtained to make sure the abnormality does not represent a benign process.
- If radiography is not diagnostic, additional lesion workup with MRI, CT, SPECT, or FDG-PET/CT is highly variable and should be based on the clinical situation and lesion location.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both

underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, <30 mL/min/1.73m²), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m². For more information, please see the [ACR Manual on Contrast Media](#) [51].

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level*	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv
*The RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, the region of the body exposed to ionizing radiation, the imaging guidance that is used, etc). The RRLs for these examinations are designated as NS (not specified).	

Supporting Document(s)

- [ACR Appropriateness Criteria® Overview](#)
- [Evidence Table](#)

References

1. Bury T, Barreto A, Daenen F, Barthelemy N, Ghaye B, Rigo P. Fluorine-18 deoxyglucose positron emission tomography for the detection of bone metastases in patients with non-small cell lung cancer. *Eur J Nucl Med* 1998; 25(9):1244-1247.
2. Gayed I, Vu T, Johnson M, Macapinlac H, Podoloff D. Comparison of bone and 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography in the evaluation of bony metastases in lung cancer. *Mol Imaging Biol* 2003; 5(1):26-31.
3. Lauenstein TC, Goehde SC, Herborn CU, et al. Whole-body MR imaging: evaluation of patients for metastases. *Radiology* 2004; 233(1):139-148.

4. Metser U, Lerman H, Blank A, Lievshitz G, Bokstein F, Even-Sapir E. Malignant involvement of the spine: assessment by 18F-FDG PET/CT. *J Nucl Med* 2004; 45(2):279-284.
5. Schaffer DL, Pendergrass HP. Comparison of enzyme, clinical, radiographic, and radionuclide methods of detecting bone metastases from carcinoma of the prostate. *Radiology* 1976; 121(2):431-434.
6. Algra PR, Bloem JL, Tissing H, Falke TH, Arndt JW, Verboom LJ. Detection of vertebral metastases: comparison between MR imaging and bone scintigraphy. *Radiographics* 1991; 11(2):219-232.
7. Krishnamurthy GT, Tubis M, Hiss J, Blahd WH. Distribution pattern of metastatic bone disease. A need for total body skeletal image. *JAMA* 1977; 237(23):2504-2506.
8. Ludwig H, Kumpan W, Sinzinger H. Radiography and bone scintigraphy in multiple myeloma: a comparative analysis. *Br J Radiol* 1982; 55(651):173-181.
9. Woolfenden JM, Pitt MJ, Durie BG, Moon TE. Comparison of bone scintigraphy and radiography in multiple myeloma. *Radiology* 1980; 134(3):723-728.
10. Parker BR, Pinckney L, Etcubanas E. Relative efficacy of radiographic and radionuclide bone surveys in the detection of the skeletal lesions of histiocytosis X. *Radiology* 1980; 134(2):377-380.
11. Siddiqui AR, Tashjian JH, Lazarus K, Wellman HN, Baehner RL. Nuclear medicine studies in evaluation of skeletal lesions in children with histiocytosis X. *Radiology* 1981; 140(3):787-789.
12. Boxer DI, Todd CE, Coleman R, Fogelman I. Bone secondaries in breast cancer: the solitary metastasis. *J Nucl Med* 1989; 30(8):1318-1320.
13. Tumeh SS, Beadle G, Kaplan WD. Clinical significance of solitary rib lesions in patients with extraskelatal malignancy. *J Nucl Med* 1985; 26(10):1140-1143.
14. Kwai AH, Stomper PC, Kaplan WD. Clinical significance of isolated scintigraphic sternal lesions in patients with breast cancer. *J Nucl Med* 1988; 29(3):324-328.
15. Braunstein EM, Kuhns LR. Computed tomographic demonstration of spinal metastases. *Spine* 1983; 8(8):912-915.
16. Smoker WR, Godersky JC, Knutzon RK, Keyes WD, Norman D, Bergman W. The role of MR imaging in evaluating metastatic spinal disease. *AJR* 1987; 149(6):1241-1248.
17. Even-Sapir E, Martin RH, Barnes DC, Pringle CR, Iles SE, Mitchell MJ. Role of SPECT in differentiating malignant from benign lesions in the lower thoracic and lumbar vertebrae. *Radiology* 1993; 187(1):193-198.
18. Coleman RE, Rubens RD, Fogelman I. Reappraisal of the baseline bone scan in breast cancer. *J Nucl Med* 1988; 29(6):1045-1049.
19. Kunkler IH, Merrick MV, Rodger A. Bone scintigraphy in breast cancer: a nine-year follow-up. *Clin Radiol* 1985; 36(3):279-282.
20. Cermik TF, Mavi A, Basu S, Alavi A. Impact of FDG PET on the preoperative staging of newly diagnosed breast cancer. *Eur J Nucl Med Mol Imaging* 2008; 35(3):475-483.
21. Uematsu T, Kasami M, Yuen S. Comparison of FDG PET and MRI for evaluating the tumor extent of breast cancer and the impact of FDG PET on the systemic staging and prognosis of patients who are candidates for breast-conserving therapy. *Breast Cancer* 2008.
22. Groheux D, Moretti JL, Baillet G, et al. Effect of (18)F-FDG PET/CT imaging in patients with clinical Stage II and III breast cancer. *Int J Radiat Oncol Biol Phys* 2008; 71(3):695-704.
23. Iagaru A, Masamed R, Keesara S, Conti PS. Breast MRI and 18F FDG PET/CT in the management of breast cancer. *Ann Nucl Med* 2007; 21(1):33-38.
24. Kosuda S, Yoshimura I, Aizawa T, et al. Can initial prostate specific antigen determinations eliminate the need for bone scans in patients with newly diagnosed prostate carcinoma? A multicenter retrospective study in Japan. *Cancer* 2002; 94(4):964-972.
25. O'Sullivan JM, Norman AR, Cook GJ, Fisher C, Dearnaley DP. Broadening the criteria for avoiding staging bone scans in prostate cancer: a retrospective study of patients at the Royal Marsden Hospital. *BJU Int* 2003; 92(7):685-689.
26. Sandblom G, Holmberg L, Damber JE, et al. Prostate-specific antigen for prostate cancer staging in a population-based register. *Scand J Urol Nephrol* 2002; 36(2):99-105.
27. Leibovici D, Spiess PE, Agarwal PK, et al. Prostate cancer progression in the presence of undetectable or low serum prostate-specific antigen level. *Cancer* 2007; 109(2):198-204.
28. Merrick MV, Merrick JM. Bone scintigraphy in lung cancer: a reappraisal. *Br J Radiol* 1986; 59(708):1185-1194.
29. Michel F, Soler M, Imhof E, Perruchoud AP. Initial staging of non-small cell lung cancer: value of routine radioisotope bone scanning. *Thorax* 1991; 46(7):469-473.
30. Erturan S, Yaman M, Aydin G, Uzel I, Musellim B, Kaynak K. The role of whole-body bone scanning and clinical factors in detecting bone metastases in patients with non-small cell lung cancer. *Chest* 2005; 127(2):449-454.
31. Ung YC, Maziak DE, Vanderveen JA, et al. 18Fluorodeoxyglucose positron emission tomography in the diagnosis and staging of lung cancer: a systematic review. *J Natl Cancer Inst* 2007; 99(23):1753-1767.
32. Hudson TM, Chew FS, Manaster BJ. Scintigraphy of benign exostoses and exostotic chondrosarcomas. *AJR* 1983; 140(3):581-586.
33. Simon MA, Kirchner PT. Scintigraphic evaluation of primary bone tumors. Comparison of technetium-99m phosphonate and gallium citrate imaging. *J Bone Joint Surg Am* 1980; 62(5):758-764.
34. Goldstein H, McNeil BJ, Zufall E, Jaffe N, Treves S. Changing indications for bone scintigraphy in patients with osteosarcoma. *Radiology* 1980; 135(1):177-180.
35. McKillop JH, Etcubanas E, Goris ML. The indications for and limitations of bone scintigraphy in osteogenic sarcoma: a review of 55 patients. *Cancer* 1981; 48(5):1133-1138.
36. Volker T, Denecke T, Steffen I, et al. Positron emission tomography for staging of pediatric sarcoma patients: results of a prospective multicenter trial. *J Clin Oncol* 2007; 25(34):5435-5441.
37. Holder LE. Clinical radionuclide bone imaging. *Radiology* 1990; 176(3):607-614.
38. Baur A, Stabler A, Bruning R, et al. Diffusion-weighted MR imaging of bone marrow: differentiation of benign versus pathologic compression fractures. *Radiology* 1998; 207(2):349-356.
39. Park SW, Lee JH, Ehara S, et al. Single shot fast spin echo diffusion-weighted MR imaging of the spine; Is it useful in differentiating malignant metastatic tumor infiltration from benign fracture edema? *Clin Imaging* 2004; 28(2):102-108.
40. Spuentrup E, Buecker A, Adam G, van Vaals JJ, Guenther RW. Diffusion-weighted MR imaging for differentiation of benign fracture edema and tumor infiltration of the vertebral body. *AJR* 2001; 176(2):351-358.
41. Karchevsky M, Babb JS, Schweitzer ME. Can diffusion-weighted imaging be used to differentiate benign from pathologic fractures? A meta-analysis. *Skeletal Radiol* 2008; 37(9):791-795.
42. Nakanishi K, Kobayashi M, Nakaguchi K, et al. Whole-body MRI for detecting metastatic bone tumor: diagnostic value of diffusion-weighted images. *Magn Reson Med Sci* 2007; 6(3):147-155.
43. Ghanem N, Uhl M, Brink I, et al. Diagnostic value of MRI in comparison to scintigraphy, PET, MS-CT and PET/CT for the detection of metastases of bone. *Eur J Radiol* 2005; 55(1):41-55.
44. Schmidt GP, Reiser MF, Baur-Melnyk A. Whole-body imaging of the musculoskeletal system: the value of MR imaging. *Skeletal Radiol* 2007; 36(12):1109-1119.
45. Thomson V, Pialat JB, Gay F, et al. Whole-body MRI for metastases screening: a preliminary study using 3D VIBE sequences with automatic subtraction between noncontrast and contrast enhanced images. *Am J Clin Oncol* 2008; 31(3):285-292.
46. Eustace S, Tello R, DeCarvalho V, et al. A comparison of whole-body turboSTIR MR imaging and planar 99mTc-methylene diphosphonate scintigraphy in the examination of patients with suspected skeletal metastases. *AJR* 1997; 169(6):1655-1661.
47. Edeiken B, deSantos LA. Percutaneous needle biopsy of the irradiated skeleton. *Radiology* 1983; 146(3):653-655.
48. El-Khoury GY, Terepka RH, Mickelson MR, Rainville KL, Zaleski MS. Fine-needle aspiration biopsy of bone. *J Bone Joint Surg Am* 1983; 65(4):522-525.
49. Ghelman B, Lospinuso MF, Levine DB, O'Leary PF, Burke SW. Percutaneous computed-tomography-guided biopsy of the thoracic and lumbar spine. *Spine* 1991; 16(7):736-739.

50. Murphy WA, Destouet JM, Gilula LA. Percutaneous skeletal biopsy 1981: a procedure for radiologists--results, review, and recommendations. *Radiology* 1981; 139(3):545-549.

51. American College of Radiology. *Manual on Contrast Media*. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/contrast_manual.aspx.

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.