The Skeletal System

Bone scanning evaluates bone physiology and skeletal anatomy and is one of the most common applications of nuclear imaging. SPECT provides improved sensitivity and even greater anatomic detail in a three-dimensional format. With continued technologic advances, the role of nuclear imaging is changing in patient workup and should be viewed as complementary to plain x-rays, CT and MRI in effective patient diagnosis. This chapter examines nuclear imaging as it relates to neoplasia, bone pain, skeletal trauma, bone viability and systemic diseases. Osteomyelitis is discussed in Chapter 6, Infection Imaging.

SCANS AND PRIMARY CLINICAL INDICATIONS

I. Bone scan

- To detect and follow up bone metastases
- To determine if a fracture is present
- To investigate the cause of unexplained bone or back pain
- To evaluate the significance of a bone lesion discovered on plain x-rays
- To diagnose avascular necrosis
- To investigate possible child abuse or the cause of limping in a child
- To determine the cause of joint prosthesis pain
- To establish viability of a bone graft
- To find the cause of delayed fracture healing
To help diagnose and follow up activity of Paget’s disease
To ascertain if reflex sympathetic dystrophy is present
To gauge the maturity of heterotopic ossification for surgical excision

II. Tumor imaging: Thallium, sestamibi, or fluorodeoxyglucose (FDG)
To follow up the activity of a bone or soft-tissue tumor after therapy

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I. BONE SCAN

A. Background

The radionuclide bone scan is the cornerstone of skeletal nuclear imaging. Although the appearance of bones on plain x-rays depends on the skeletal mineral content, radionuclide bone scanning provides physiologic information, depicting blood flow to bone and bone metabolism or turnover. High sensitivity coupled with the ability to survey the entire skeletal system without added radiation give the radionuclide bone scan broad clinical utility. Although the bone scan lacks specificity, a specific diagnosis often can be made when the bone scan is correlated with plain films and other imaging. The standard bone scan typically is used for whole-body surveys such as those performed for metastatic disease. The three-phase bone scan can evaluate blood flow and soft-tissue uptake, in addition to bone uptake, and is used primarily to evaluate focal areas for suspected osteomyelitis, fracture and tumor.

B. Radiopharmaceuticals

Technetium-99m-diphosphonates are the agents of choice for bone imaging. The radiopharmaceutical is injected intravenously and is distributed via blood flow throughout the body. It passively diffuses into the extravascular and extracellular spaces and binds to the hydration shell around the bone crystal. Unbound radiotracer clears from the plasma via urinary excretion. Delayed images will demonstrate the radionuclide bound to the bone crystal, depicting the skeletal system. Imaging is delayed for 2–3 hr after injection to obtain the high bone-to-background ratio needed for optimal image quality. The greater the
blood flow and metabolic activity of a particular bone region, the higher the uptake of radionuclide.

C. How the study is performed
There are two types of bone scans: the standard delayed scan and the three-phase scan. Typically, for both types of scans, the patient is encouraged to drink liquids and urinate frequently between the time of injection and delayed imaging to increase soft-tissue elimination of radiotracer. The patient also will be asked to empty the bladder before delayed whole-body imaging and will be given wipes to prevent urine contamination of skin and clothing.

Standard bone scan. The radiotracer is injected intravenously (20–30 mCi [740–1110 MBq] adult dose), and delayed views of the entire skeleton are obtained 2–5 hr later.

Three-phase bone scan. As the radiotracer is injected, rapid sequence flow images are obtained of the area in question (angiographic phase). Only one region can undergo flow imaging per scan (i.e., foot or hand, but not both). Ten-minute delayed static images are then acquired, which are called “blood pool” or “soft-tissue uptake” images. These first two phases usually take no longer than 30 min to complete. Delayed images of the region in question are then obtained, typically 2–5 hr later. It is not unusual for the entire skeleton to be imaged 2–5 hr later in addition to the area of clinical concern. Imaging may take as little as 10–20 min to complete or up to 2 hr if SPECT or other special views are required. Occasionally, further delayed images up to 24 hr later may be required.

D. Patient preparation
No special preparation is required, and there are no dietary restrictions. Good hydration may improve image quality, and the patient should be encouraged to drink fluids. In addition, he or she should be informed that this is not a quick examination and that a 2–5 hr delay between injection and imaging should be expected. As always, outside correlative studies should be made available to the nuclear medicine physician.

E. Understanding the report
A normal bone scan will demonstrate the axial and appendicular skeletal system. The nuclear medicine physician will be familiar with the expected appearance, including normal patterns in children who have increased uptake in physeal growth centers. In addition, thyroid cartilage, kidneys and bladder usually are seen (Fig. 1).

If the patient had a three-phase scan, angiographic blood flow and soft-tissue activity are described. The delayed bone uptake, which is imaged at 2–5 hr, de-
Interpretative criteria. Interpretation depends on the clinical question to be answered and often relies on specific patterns of uptake. The report will delineate areas of increased or decreased uptake, correlate with other imaging if available (or recommend other imaging for correlation) and come to a conclusion about the clinical question. Soft-tissue or extra-osseous uptake, if present, also will be
described. Soft-tissue uptake is caused by a host of factors, including inflammation and calcification, mucinous and other neoplasia, muscle necrosis, and myositis.

Another pattern that may be described is the so-called superscan in which there is intense diffuse abnormal uptake throughout the skeletal system, giving the appearance of a super-normal scan. This pattern may be caused by diffuse widespread blastic metastases such as from prostate cancer or metabolic bone disease such as hyperparathyroidism.

F. Potential problems
1. Lack of specificity. Although the bone scan is highly sensitive, increased uptake is the result of blood flow and osteoblastic activity. These are nonspecific processes that may be increased because of neoplasia, infection, trauma and arthritides. Pattern recognition by a trained nuclear medicine physician and correlation with other examinations transforms nonspecific uptake to a specific diagnosis.

2. Persistent uptake. Because bone scanning is sensitive, increased uptake may persist for years after trauma, infection and surgery. This potential for an abnormality to persist on bone scanning may make evaluation of that same region difficult if a baseline scan is not available for comparison.

3. The young and the old. Elderly patients may take 2–7 days to manifest a positive bone scan after fracture because of delayed osteoblastic response. Infants younger than 1 mo of age do not have as avid skeletal tracer uptake compared with older children and adults.

4. Flare phenomenon. In the period of 3–6 mo after chemotherapy, hormonal therapy or radiation therapy for bone metastases, increased uptake in known lesions and even foci of new uptake may be seen because of a healing response rather than worsening disease. This is most commonly seen in breast and prostate cancer. Serial scanning and correlating scan findings with the patient’s condition will allow differentiation of the flare phenomenon from increased disease.

5. Etidronate. This bisphosphonate may block uptake of the bone imaging radiopharmaceutical and lead to a poor quality or nondiagnostic bone scan.

II. TUMOR IMAGING: THALLIUM, SESTAMIBI OR FDG
A. Background
Thallium and sestamibi have been used to evaluate tumor extent and response to therapy, taking advantage of their propensity to localize in high-grade neoplastic cells and not in tumor necrosis. Sestamibi results in more detailed images, but there is more clinical experience with thallium scanning in tumors.
FDG scanning probably will replace thallium and sestamibi for tumor evaluation. Although PET scanning is only available at limited locations, coincidence SPECT systems adapted to gamma cameras and centralized delivery of FDG are making this technology more widely available. FDG is a glucose analog that localizes to a greater extent in active tumor and not in necrotic regions but suffers from a certain lack of specificity. Uptake has been described with inflammation, fracture and other benign processes. Absolute quantitation can be performed that can characterize and stage tumors. (See Chapter 15, Introduction to Cancer and FDG Imaging for more details.)

**CLINICAL QUESTIONS**

1 and 2. **Should I order a standard bone scan or a three-phase scan? Should I get a whole-body scan or a scan of a limited area?**

The answer to these questions is specific to each clinical situation and may depend on particular institution protocols. In general, a whole-body scan is indicated in a patient with a history of neoplasia, multiple sites of trauma or unexplained bone pain in patients older than 50 yr of age. With problems such as possible focal osteomyelitis, a three-phase scan clearly is indicated. For focal local trauma or pain, a three-phase scan often is helpful but not critical because the important information will be present on delayed images. A whole-body scan does not expose the patient to any additional radiation but requires a little extra time and is more expensive than a limited-area scan.

3 and 4. **Does a patient have skeletal metastases? When should I get a bone scan for cancer staging?**

Thirty percent of patients with cancer will develop skeletal metastases. This is the most common indication for the radionuclide bone scan. There is no better examination for rapidly and cost-effectively surveying the entire skeletal system for the presence of osseous metastases. It is an easy test to undergo, has no contraindications and is sensitive. Most metastatic processes will manifest an abnormality on bone scan, either increased or decreased uptake. Yet, bone scanning is not necessary or indicated in all neoplastic evaluations.

The finding of multiple asymmetric foci of increased uptake in the axial and appendicular skeleton is characteristic of osseous metastases (Fig. 2). Other processes may have multifoci of increased uptake that can be mistaken for metastatic disease. Correlation with plain x-rays and other imaging modalities, pattern recognition and the judicious use of follow-up studies are important in arriving at the proper diagnosis.
Bone scanning in prostate, breast, lung and other cancers. The initial evaluation of prostate cancer traditionally has included bone scanning because of its high sensitivity. With the advent of prostate-specific antigen (PSA) serum testing, the role of the bone scan has changed. If the PSA is $< 10$ ng/ml, there is a low likelihood of bony metastases. The recommendation is to obtain a bone scan...
to exclude metastatic disease if the PSA is >10, if there is a high Gleason histologic grade, a high clinical stage or symptoms suggestive of metastatic disease. A baseline bone scan can be helpful in patients with a history of trauma or arthritis to enable comparison with subsequent bone scans that may be obtained because of new pain or rising PSA.

Breast cancer also metastasizes frequently to bone, including local invasion of the sternum. The role of the bone scan in this disease has been somewhat controversial. The recommendation is not to obtain a bone scan in an asymptomatic patient with a small, low-stage, primary tumor. If the patient has bone pain, has laboratory values suggestive of metastatic disease or is in clinical stage 3 or 4, a bone scan should be obtained.

In non–small-cell bronchogenic cancer, a bone scan is recommended if curative surgery is contemplated and there is no evidence of other metastatic disease or if there is clinical or laboratory evidence of bone metastases. Small-cell lung cancer frequently metastasizes to bone, and a bone scan often is included as part of the routine workup.

For renal cell cancer, routine bone scanning in the absence of clinical and laboratory findings is not indicated but should be used when the patient is symptomatic or when a change in therapy is contemplated. Many surgeons advocate nephrectomy even in the presence of bone metastases.

Neuroblastoma is another nonprimary bone neoplasm in which bone scanning commonly is performed for screening in conjunction with the use of metaiodobenzylguanidine (MIBG) or Octreoscan (see Chapter 16, Neuroendocrine Tumors). If there is focal skeletal pain, plain x-rays should first be obtained, followed by CT or MRI as necessary.

The possibility of thyroid cancer bone and soft-tissue metastases is investigated routinely with $^{131}$I. Bone scanning may be useful in specific clinical situations. Bone scanning is not routine for lymphoma or leukemia. Gallium or FDG scanning is more useful to detect osseous and soft-tissue lesions for lymphoma. The bone scan is standard in the metastatic workup of Ewing’s sarcoma and osteosarcoma. (Multiple myeloma is discussed in Clinical Question 6, below.)

**Bone scanning versus MRI in the evaluation of bone metastases.** Each has advantages and disadvantages, and they should be considered complementary, rather than competing modalities. The most important advantage of bone scanning is that the entire skeletal system can be surveyed with ease and little expense. This cannot be done with MRI. Bone scanning can be performed when there are contraindications to MRI such as a pacemaker and certain vascular clips. Bone scanning more easily evaluates the skull, ribs and extremities. MRI is considered more sensitive and specific for most marrow processes, although other imaging modalities as well as biopsy may be required. In scanning the spine and pelvis, MRI is more accurate in differentiating benign from malignant abnormalities. For patients with acute neurologic deficits and a history of
cancer, urgent MRI is necessary to evaluate for spinal cord compression, which may require emergency radiotherapy or surgery.

**Summary.** Bone scanning should be used routinely to aid in the evaluation of stage 3 and 4 breast cancer, prostate cancer with PSA >10, non–small-cell bronchogenic cancer when curative surgery is considered, neuroblastoma, Ewing’s and osteosarcoma and small-cell lung cancer. It is also useful and efficient for any clinical stage cancer in a patient with nonlocalizable or diffuse bone pain or laboratory findings suggestive of bone metastases. If the patient has focal bone pain or local back pain or neurologic symptoms, primary evaluation with plain x-rays or MRI is probably more cost-effective. MRI may be required urgently to determine if spinal cord compression is present. For cancer that can spread to bone, a negative bone scan has important prognostic implications and can serve as a baseline in case of future bone pain, especially in patients with a history of trauma or arthritis.

5. **Can the bone scan be used to follow up the activity of skeletal metastatic disease?**

The activity of metastatic disease can be followed up with bone scanning. Plain x-rays may demonstrate lesions even after successful treatment because the bone may continue to remodel. If there is absent activity on a formerly positive bone scan after treatment, this is a strong indicator of disease regression. Irradiated bone initially may show increased uptake due to osteitis but then decreased uptake in the radiation port for up to several years afterward. (See Potential Problem 4, Flare Phenomenon, above.)

Follow-up intervals are usually institution- and protocol-specific. After radical prostatectomy for prostate cancer, PSA should drop to near zero. Thus, routine follow-up bone scanning usually is performed only in face of a rising PSA or new bone symptoms. Also, PSA may not be a reliable indicator of progressive disease when the patient is on hormonal therapy. For other types of cancer including that of the breast, bone scanning is the first choice for routine follow-up in asymptomatic patients, as well as in those with diffuse bone pain or abnormal laboratory values. In a patient with focal back pain or neurologic symptoms, MRI should be the initial modality.

6. **Is bone scanning appropriate for multiple myeloma?**

The bone scan is most sensitive in detecting hot lesions with an osteoblastic component. Yet, multiple myeloma lesions tend to be lytic, and many lesions elicit little, if any, osteoblastic response. These cold multiple myeloma defects are less conspicuous on bone scanning. Thus, the plain x-rays are still considered most appropriate for multiple myeloma. A bone scan may be helpful for local pain when plain x-rays are negative, but MRI is considered far more sensitive for focal questions. MRI is also the best method to evaluate the spine.
7 and 8. What is the significance of an incidentally discovered bone lesion on plain x-rays? What is the likelihood that a solitary lesion on bone scan represents a metastasis in a patient with a known or suspected malignancy?

X-rays, CT and MRI are the mainstays of noninvasively diagnosing a bone tumor. The likelihood that a solitary lesion on bone scan represents a metastatic focus varies with clinical history, as well as location and appearance of the abnormality. Correlation with plain x-rays is important in making this distinction. For example, in a patient with a known malignancy, a solitary lesion on a bone scan in a vertebra or in the pelvis will represent metastatic disease 60–70% of the time, but this likelihood decreases to almost zero if the abnormality correlates to a benign finding on plain x-rays such as degenerative disease.

Benign and malignant bone lesions run the gamut from faint to intense uptake on bone scanning. Although bone scanning alone may not distinguish a benign from malignant process, it can be helpful in evaluating a potential abnormality and in determining if there are single or multiple lesions. For example, a bone scan may be performed to differentiate a bone island that has little or no uptake from a blastic metastasis that will exhibit greater uptake and often presents as one of many lesions.

9. Is nuclear imaging helpful in the staging and follow-up of primary bone tumors?

Primary bone tumors such as osteosarcoma and Ewing’s sarcoma are more common in the pediatric age group. MRI is considered the procedure of choice in preoperative staging of local bone and soft-tissue involvement. Although the three-phase bone scan is sensitive because of intensely increased flow, soft-tissue and delayed uptake, it overestimates local extent of disease. Because bone scanning is sensitive in detecting skip lesions and metastatic foci, it is included as part of the standard workup.

Bone scanning may demonstrate nonspecific increased uptake in the tumor bed after surgery, chemotherapy or radiation therapy. Flare phenomenon also may occur. (See Potential Problem 4, Flare Phenomenon.) Persistent increased uptake at the treatment site 6–12 mo after therapy, compared with a post-therapy baseline, is considered suspicious for local recurrence. A negative scan has good prognostic implications. CT and MRI are not optimal for monitoring local recurrence because of the difficulty in distinguishing necrosis and fibrosis from recurrent tumor. Thallium, sestamibi or FDG tumor imaging seem to provide an excellent means to monitor response to therapy, in conjunction with a pretherapy baseline scan. Successful treatment and decreased tumor burden correlates with decreased to absent uptake on these tumor-imaging scans.

10. What is the cause of a patient’s bone pain?

Bone scanning is an excellent screening examination for bone pain, especially diffuse pain or ill-defined symptoms. Yet it should not be used in isolation. Each
situation must be judged on the basis of individual history and physical examination. With focal pain, especially after trauma, it is mandatory to begin the evaluation with a plain x-ray. A plain x-ray is relatively inexpensive and may obviate bone scanning. If the plain x-ray is not revealing, bone scan may be an appropriate next study to evaluate for traumatic fracture, stress fracture, avascular necrosis, primary tumor, occult metastasis (especially in patients over 50 years old), infection, shin splints, avulsion fractures and a host of other possibilities. MRI may be more accurate and cost-effective in some situations, especially if a soft-tissue component is strongly suspected. CT may allow definitive characterization of an abnormality on plain x-rays.

A bone scan is uniquely suited to determine the true cause of the patient’s pain in the presence of other possible causes such as degenerative disease or old trauma discovered on plain x-rays. For example, pain often is referred to the pelvis region and upper chest/shoulders. Just because a patient has degenerative disease of the hips, does not mean that a sacral insufficiency fracture may not be present that can be classically defined with bone scan. In summary, although one generally should begin with plain x-ray evaluation, the bone scan is an excellent tool for screening because of its sensitivity and may suggest other studies.

11. Bone pain: Is a post-traumatic fracture present?

The nuclear bone scan is highly sensitive in the evaluation of fractures, yet it is not the optimal examination for the rapid and efficient workup of acute trauma. In the setting of acute trauma, plain x-rays should be obtained first. Yet fractures may not be immediately apparent on plain films; the patient can be treated clinically and a follow-up x-ray obtained in 3–5 days.

If a definitive diagnosis is needed immediately, such as establishing the presence of a hip fracture in an elderly patient, MRI is the next logical test. It is sensitive and specific for not only cortical fracture but also bone bruising, as well as soft-tissue injury. If MRI cannot be performed, a bone scan is an excellent choice. Potential false-negative results must be kept in mind though. Although the majority of fractures will manifest a positive three-phase bone scan immediately, it may take up to a week for the scan to become positive in a small percentage of the elderly. The best route of evaluation must be decided on a case by case basis with an understanding of the mechanism of injury.

In a polytrauma situation, bone scan provides excellent whole-body screening and may reveal fractures that initially were missed in the heat of the acute workup (Fig. 3). In addition, bone scanning is more helpful in the regional survey of certain problem areas such as the pelvis and lower extremities, which may be difficult to evaluate because of referred pain. CT scanning also can be useful when plain x-rays are not definitive and is often used in the secondary evaluation of spine and hip fractures, as well as for presurgical planning.
Figure 3. Injured hiker with complaint of “hurting all over.” At initial emergency room evaluation, a left ankle fracture was diagnosed with plain x-rays. After experiencing multifocal pain days after the trauma, the patient underwent bone scanning. Anterior (A) and posterior (B) views revealed additional fractures at L2 (arrows), proximal left fibula (curved arrows), left foot (small arrowheads) and right ankle (large arrowheads).
12 and 13. Delayed fracture healing: Is bone scan helpful? Can bone scanning be used to date fractures?

With the clinical question of nonunion, the appearance of the bone scan can help the orthopedic surgeon plan therapy. Reactive nonunion will demonstrate intense activity at the fracture site and predicts a good response to electrical stimulation. A photon deficient gap may represent atrophic nonunion (which does not respond well to electrical stimulation) and may indicate pseudoarthrosis, interposed soft-tissue or infection, or an impaired blood supply.

Although not usually indicated, the three-phase bone scan can be used to date fractures. The first phase should be positive for the first 3–4 wk, the second phase is positive for the first 8–12 wk, and the delayed phase may be positive for many years after healing, but typically normalizes by 2 yr.

14 and 15. Bone pain: Is a stress or insufficiency fracture present? Bone pain: Is a tibial stress fracture or shin splints present?

In the clinical setting of suspected stress or insufficiency fracture, bone scanning is nearly 100% sensitive and specific and is the preferred whole-body and regional screening choice. If there is focal pain, plain x-rays should be obtained first and may obviate bone scanning. MRI is highly sensitive but less specific. CT is less sensitive and is not a practical method for an extensive regional survey. CT and MRI are excellent problem-solving modalities when the bone scan is equivocal.

The term stress reaction may be used to describe bone remodeling and repair covering the continuum of injury from early periosteal reaction to an overt fracture; it usually manifests as uptake in all three phases of the bone scan with focal intense delayed uptake. There also are characteristic patterns of stress injury/fracture depending on location. In the tibia, increased uptake on all three phases with delayed fusiform uptake in the upper tibia, sometimes extending across the bone, allows differentiation of stress reaction from shin splints, which have less intense, superficial and elongated posteromedial uptake on delayed imaging only (Fig. 4). Sacral insufficiency fractures often manifest with an H-shaped delayed uptake extending across the sacral alae. In addition, a whole-body survey can easily be performed with bone scanning, and may uncover unsuspected additional foci of stress injury.

16. Bone pain: Is AVN present?

Both MRI and bone scanning have been used in the evaluation of AVN in the hips. In the first 7–10 days, AVN will demonstrate a cold defect on delayed bone scan images, but will then transition to increased uptake in the reparative phase. (Flow images are generally not helpful.)
In the adult hip, AVN usually becomes symptomatic in the reparative phase. Therefore, increased uptake will be seen. Although bone scanning has high sensitivity, it has poor specificity and suffers from relatively poor spatial resolution. MRI is considered the state of the art in the evaluation and grading of hip AVN. Plain x-rays should be obtained first, because classic findings of AVN may obviate more advanced imaging. If MRI cannot be performed, a negative bone scan can exclude anything but the smallest focus of osteonecrosis. It is a rapid and simple examination to perform in the elderly, many of whom cannot hold still for MRI, and may incidentally discover a fracture or other abnormality elsewhere in the pelvis.

In a child in whom there is suspicion of Legg-Calvé-Perthes disease, symptoms usually manifest early, and classic findings of a perfusion defect in the anterolateral femoral head are sought. Imaging should include pinhole views and be performed at a center experienced in pediatric evaluation. It is easier to perform bone scanning than MRI on a child, and the examination is highly sensitive and specific for not only AVN, but also osteomyelitis. Scanning of the entire lower extremities also can be completed without extra radiation exposure.

MRI or bone scanning may be used elsewhere in the skeletal system depending on body part, age of patient and clinical history.

**17. Back pain: How is spinal pathology determined?**

Bone scanning and MRI play complementary roles in back pain, depending on patient age and clinical presentation. If pain can be localized, initial plain x-rays may be diagnostic. Bone scanning is excellent in evaluating low back, pelvic and hip pain, especially in the elderly, because pain may be referred. It is also use-
ful in surveying the entire back in children, who are more apt to present with nonlocalized pain. Bone scanning with SPECT is highly sensitive in screening for spondylolysis and for osteoid osteoma and can be used to focus subsequent CT and MRI investigations.

For most adult chronic back pain in which disc abnormalities are sought, MRI is the procedure of choice. Bone scanning can be helpful in the differentiation of benign from malignant disease to find if there are multifocal abnormalities characteristic of metastases. CT and MRI are the preferred methods to evaluate individual lesions. In a patient with neurologic symptoms, MRI is also the technique of choice. A myelogram can be performed if MRI is not available or contraindicated.

For the postoperative spine, recurrent or residual disc questions should be evaluated with MRI, but for evaluation of bone grafting and complications such as pseudoarthrosis, bone scan and CT are preferred. Metal fixation devices can interfere with MRI or CT, although they do not present as much of a problem with the bone scan. A normal bone scan is helpful postoperatively. Increased uptake at the lumbar fusion site after 1 yr is consistent with a complication such as pseudoarthrosis. The bone scan also may localize adjacent areas of spinal instability.

18. Bone pain: How can osteoid osteoma be identified?
Bone pain at night relieved with aspirin is the classic history with osteoid osteoma but is not universally present. Plain x-rays should be obtained first, and a positive finding will allow detailed evaluation with CT scanning to look for the nidus. If plain x-rays are unrevealing, a wide region can be surveyed with bone scanning to help focus the search because pain may be referred. This lesion typically demonstrates intense activity on all three phases of a bone scan and may show a focus of more intense uptake within the hot area called the double density sign. Findings should be confirmed with CT before surgery or other intervention is contemplated.

19. How can persistent pain after orthopedic prosthesis be evaluated?
Three-phase bone scanning is useful in the postoperative hip evaluation, although a plain x-ray should be obtained first. The bone scan can help diagnose loosening and heterotopic bone. When combined with radiolabeled white blood cell or gallium scanning, infection also can be investigated (see Chapter 6, Infection Imaging). There are characteristic increased uptake patterns with which the nuclear medicine physician will be familiar. These are based on the type of prosthesis and the time since surgery.

Uptake involving knee replacements and other prostheses is variable. For example, persistent uptake around normal total-knee replacements has been described for years after surgery. Yet a negative scan correlates with a low likeli-
hood of complication. Serial scanning also may be required in some instances of equivocal studies.

20 and 21. Is a bone graft viable? Is a bone fusion solid?

The three-phase bone scan is an excellent technique to noninvasively monitor graft viability. Autologous grafting with revascularization will demonstrate increased uptake on all three phases and should become uniform to adjacent bone as the graft is incorporated. Allografts usually are photon deficient but will fill in with serial imaging.

22. Can bone scanning help with the presurgical evaluation of heterotopic ossification?

The three-phase scan is useful for tracking the maturity of heterotopic ossification. This process manifests with increased flow and uptake even before plain x-ray evidence of calcifications is present. Surgery is delayed until activity is similar to that of adjacent bone. Once this maturity has been ascertained, resection can be performed with less chance of recurrence. Alternatively, a bone marrow scan can be performed that will show uptake in mature heterotopic bone to indicate timing of surgery.

23. Is child abuse present?

A combination of bone scanning and plain x-rays is critical in the evaluation of potential child abuse. Bone scanning is useful for surveying the entire skeleton without added radiation, especially for difficult-to-evaluate areas on plain x-rays such as scapula, ribs and sternum. Plain x-rays are helpful to date the fractures, determine type and treatment and exclude bone diseases such as osteogenesis imperfecta. Skull fractures are also easier to document on plain x-rays because they may not evoke a significant osteoblastic response. The bone scan is especially useful with infants who cannot communicate areas of pain, and it can be used to direct plain x-ray evaluation. Of course, negative bone scanning and plain x-rays should not deter additional investigations because not all child abuse involves bone damage.

24. The limping child: Is bone pathology present?

Plain x-rays of the area in question should be obtained first. Limping may be caused by a variety of processes including AVN (Legg-Calvé-Perthes disease), stress reactions and post-traumatic fractures from the lower spine to the pelvis, benign and malignant tumors and infections. If plain x-rays are unrevealing, or a suspected area cannot be identified, bone scanning is the best screening method to survey extensive areas easily, inexpensively and with great sensitivity.
25. Is nuclear imaging helpful with metabolic bone disease?

Bone scanning is not useful for the initial diagnosis of metabolic bone diseases of calcium metabolism such as primary or secondary hyperparathyroidism. Yet, such processes can be suggested from a superscan appearance. Bone scanning is best used to survey for suspected complications of these metabolic diseases such as pseudofractures and brown tumors.

26. Is bone scanning helpful with Paget's disease?

Baseline and serial bone scanning is useful in surveying for Pagetic involvement, in screening for complications such as fracture and sarcoma and in monitoring the efficacy of therapy. The bone scan will be hot in the early osteolytic and osteosclerotic active phases and becomes cooler in later osteosclerotic disease. A sudden increase in activity from baseline images is suspicious for fracture or neoplastic transformation. Paget's disease is 70% polyostotic, and bone scanning can be used to find unsuspected sites before disease can be detected on plain x-rays. Bone scanning is also useful in diagnosis when x-rays are equivocal.

27. Is bone scanning useful to evaluate arthritis?

Bone scanning is sensitive for most arthritic processes, but it is not specific. Usually arthritis will cause diffuse periarticular uptake. A whole-body bone scan survey can be performed in one sitting, and it can be used in the identification of areas that represent active disease and in the assessment of response to treatment. Yet nuclear imaging has not found widespread use because most clinicians can assess the arthritides effectively with a combination of clinical history, physical examination, laboratory tests and plain x-rays. The bone scan may be valuable as a problem-solving tool in some situations, such as those that involve documenting joint pain from osteoarthritis even before the joint appears abnormal on plain x-rays.

28. Is reflex sympathetic dystrophy present?

There is no pathological standard or well-defined clinical criteria for reflex sympathetic dystrophy. Bone scan patterns depend on the extremity and the stage of the disease. From 0–6 mo, increased flow and delayed periarticular uptake is characteristic. At 6 mo to a year, perfusion returns to normal, but the delayed uptake pattern persists. After a year, decreased flow and normalization of delayed uptake is described. Plain x-ray evaluation is neither sensitive nor specific, and MRI is of little value. Although the above patterns have been described in the hand, there is much less agreement on diagnostic criteria in the foot and knee. Thus, with early scanning, in appropriately screened patients, the three-phase bone scan has high sensitivity and specificity in diagnosing reflex sympathetic dystrophy of the hand. With longer duration of symptoms and in other
extremities, nuclear imaging is not as helpful, reflecting confusion about this disease process.

**WORTH MENTIONING**

1. **Bone marrow (sulfur colloid) scan**
Because bone marrow is so well imaged by MRI, use of the sulfur colloid scan is limited. Some applications include correlation with radiolabeled white blood cell scans for potential prosthesis infection, the differentiation of osteomyelitis from bone infarcts in patients with sickle cell anemia and the evaluation of marrow expansion processes such as myelofibrosis with myeloid metaplasia. Any marrow-replacing process such as tumor, infarct or abscess that is of sufficient size and focalization will result in a cold defect.

2. **Amputation**
Bone scanning can help the surgeon delineate viable from nonviable bone in preparation for amputation.

3. **Rhabdomyolysis**
Bone scanning is a sensitive indicator of muscle death, demonstrating increased uptake in soft tissue. Technetium-99m-pyrophosphate has been used for infarct imaging of the heart and brain. Pyrophosphate imaging also may be helpful to assess the degree of muscle necrosis after electrical injury.

4. **Multiple myeloma**
Thallium, sestamibi and FDG scanning show promise in whole-body evaluation of multiple myeloma lesions.

5. **^{18}F fluoride**
Fluorine-18-fluoride, a positron emitter, was once the most commonly used bone scanning agent but was replaced by the more practical technetium diphosphonates. With the increasing availability of PET and coincidence detection systems, this radionuclide may find more use because it produces higher resolution images and is quantifiable. It can also be combined with FDG scanning.

6. **Osteoid osteoma**
A special nuclear probe may prove useful during surgery to localize the osteoid osteoma nidus, which will concentrate radiotracer.

7. **Radiation synovectomy**
Beta-emitting radiopharmaceuticals have been used for a number of years to alleviate the pain and swelling of rheumatoid arthritis and other arthritides in-
including psoriatic arthritis and hemophiliac synovitis. The procedure consists of a direct injection of the radiopharmaceutical into the joint capsule, where it is in contact with the inflamed, hyperplastic synovium. As the radionuclide decays, the beta particles deliver a therapeutic dose of radiation to the synovium. The response rate is reported to be high and benefits to the patient include increased joint movement and reduced swelling, effusion and pain.

Most of the radiopharmaceuticals are colloids, and leakage from the joint appears to be minimal. No detectable damage to the articular cartilage has been determined from a recent MRI study. A number of different radionuclides and colloid preparations have been studied widely in Europe and Australia and, to a lesser degree, in the United States. The most commonly used agent is $^{32}\text{P}$ chromic phosphate, but as of 2000 no therapeutic agent has been approved by the United States Food and Drug Administration, and this procedure is not widely available in the United States.

**PATIENT INFORMATION**

I. BONE SCAN

A. Test/Procedure

Your doctor has ordered a bone scan to detect possible bone problems.

A small amount of radioactive material called a tracer will be injected into your vein. You will be asked to return 2–5 hr later, and you will be positioned next to a special machine called a gamma camera, which does not produce radiation but detects radiation that is coming from the injected tracer in your body. A series of pictures of your body will then be taken, which typically takes about 30 min but may take up to 2 hr if special views are required. Sometimes, images also are acquired during the initial injection of tracer.

B. Preparation

No special preparation is required. You may eat and drink as usual and take your medications. You will be asked to drink as much fluid as possible before and after the procedure. Most of the radioactive material not going to the bones leaves your body through the urine. You should empty your bladder as often as you can after the injection and again just before the pictures are taken.

C. Radiation and other risks

The amount of radiation used is small and similar to that given by other diagnostic x-ray tests. The effective adult radiation dose to your whole body from this test is approximately the same the dose the average person living in the United States receives in 2–3 yr from cosmic rays and naturally occurring background radiation sources. The radiation dose is about 15% of the yearly dose considered safe for doctors and technologists who work with radiation. Please
urinate frequently for the day after the test to lessen radiation exposure. You can be around other people and use a bathroom normally without risk to others.

D. Pregnancy
If you are pregnant or think you could be pregnant, inform your doctor so that this can be discussed with the nuclear medicine physician.

References