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review

Bone scintigraphy in clinical routine

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Background. *In 1971, bone scintigraphy was performed the first time using ^{99m}Tc-labeled polyphosphonates. Since that time, bone scintigraphy has become one of the most frequent diagnostic procedures in nuclear medicine departments. However, in the last decade, indications for this skeletal imaging procedure have been changing continuously. This paper, therefore gives a concise review of the current spectrum of indications for bone scintigraphy and its realization.*

Conclusions. *Just as many other nuclear medicine procedures, the bone scintigraphy has a high sensitivity, and the changes of the bone metabolism are seen often earlier than the changes in bone structure developing after x-ray. Therefore, occult lesions in the whole skeleton might be detected early by bone scintigraphy. On the other hand, bone turnover is increased in various bone diseases. Consequently, bone scintigraphy usually has a low specificity, and differential diagnosis of the underlying etiology is often not feasible. However, three-phase bone scintigraphy and SPECT can significantly increase the specificity in some skeletal areas.*

Key words: Bone diseases-radionuclide imaging; technetium; diphosphonates; bone neoplasms; bone scintigraphy, ^{99m}Tc-diphosphonates, indications

Introduction

Since 1961 bone turnover has been examined using various radio-labeled substances. In 1971 bone scintigraphy was performed the first time using modern ^{99m}Tc-labeled polyphosphonates, e.g. ^{99m}Tc-hydroxyethylenephosphonate(HDP) or ^{99m}Tc-methoxyethylenephosphonate (MDP). After intravenous injection, these radiopharmaceuticals are adsorbed at the bone surface within some hours. The amount of adsorption depends both on the perfusion of the bones and the intensity of bone metabolism. Moreover, bone-seeking radiopharmaceuticals are excreted by the kidneys, and the kidneys and bladder can be seen routinely on a bone scan. Thus, total bone uptake depends not only on the perfusion and metabolic turnover, but also on renal function. In regions with a high bone metabolism, e.g. epiphyseal plates of children or mechanically stressed regions, e.g. ileosacral

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joints, the radiopharmaceutical uptake is increased physiologically. Additionally, in several pathophysiological conditions, even extraskeletal accumulation of tracer can be seen, e.g. in scars, myositis ossificans, liver metastases or tumors.[1-3] On the other hand, fat patients (high absorption of radiation) and patients with renal failure show a reduced bone-to-background contrast resulting in degraded images.

Since the first bone scans using ^{99m}Tc-labeled polyphosphonates by Subramanian and Mc Affee[4] in 1971, the radioactive load has decreased continuously for the patient due to radiopharmaceutical and technological advantages, and bone scintigraphy has become a routine method in clinical nuclear medicine. However, in the last decade, the indications for bone scanning have changed dramatically. Therefore, the current spectrum of indications for bone scintigraphy and its realization are reviewed concisely in this paper.

Indications in benign bone diseases

In inflammatory joint diseases, both soft tissue and bone metabolism can be affected. The three-phase bone scintigraphy can image the activity of both processes. Increased perfusion, higher blood pool and raised activity of osteoblasts may be demonstrated by bone scan. Moreover, bone scan may contribute to the differential diagnosis of rheumatical joint diseases due to specific distribution patterns of several joint affections.

Fractures are seen primarily in radiographic images. Nevertheless, fractures in radiographically unclear regions can be excluded sufficiently by bone scintigraphy, and bone scanning also allows establishing the vitality of bone grafts or the loosening and infections of prostheses.

Current clinical indications for bone scintigraphy in benign bone diseases are listed in Table 1.

Table 1. Bone scanning in benign bone diseases

Disease	To be mentioned
Osteomyelitis	In 3-phase bone scintigraphy, the activity of the process and other bone lesions can be seen early in acute osteomyelitis.[9-11] In newborn the sensitivity is as low as 50 %.[1,2] In children with acute osteomyelitis MRI has the highest sensitivity (90%).[12] In diabetic foot, 3-phase bone scintigraphy should be first in the diagnostic cascade.[13] However, 3-phase bone scintigraphy is sensitive but not specific in osteomyelitis of diabetic foot.[14]
Evaluation of prostheses	Normal 3-phase bone scintigraphy excludes infection or loosening of hip prostheses.[1,2] Sensitivity of 3-phase bone scintigraphy in knee prostheses is low.[15]
Arthritis or rheumatoid diseases Psoriatic arthritis Ankylosing spondylitis Reiter's syndrome	Bone scintigraphy can be used to confirm arthritis if x-ray is normal. Scintigraphy may show arthritis earlier, may explore the severity of arthritis and may be used for evaluation of therapy.[2,16-18] Distribution of joint diseases may allow differential diagnosis.[16,19] 3-phase bone scintigraphy can be used to evaluate the therapeutic success after radiosynoviorthesis.[20]

Degenerative joint diseases - osteoarthroses	Bone scintigraphy is uncommon
Avascular necrosis Perthe's disease Osteonecrosis	3-phase bone scintigraphy may help, if MRI is not predicative.[1,2,21] MRI is the method of choice for avascular necrosis of the hip.[22]
Bone fractures and stress fractures	Normal bone scan can exclude bone fractures after distinct time intervals,[1,2,23] especially in carpal bones[24,25] and tarsal bones, in scapula, vertebrae, proximal femur, sternum, pelvic bones,[26] sacrum.[27]
Reflex sympathetic dystrophy	3-phase bone scan is of major importance for establishing the diagnosis, in staging and to control results of therapy.[28]
Child abuse	Bone scan provides an overview over the whole skeleton, and periostal lesions can be seen.[1,2,29] Metaphyseal lesions in younger children, multiple fractures in different stages of healing, posterior rib fractures, long-bone fractures in younger children are typical signs.
Frostbite and ischemic injuries	Bone scan may help to specify the need and the line of amputation.[2,30]
Paget's disease	Normal 3-phase bone scintigraphy excludes dedifferentiation, helps to screen both regions and extent of bone involvement.[2,11]
Plantar fasciitis, archilles tendinitis, osteitis pubis	Normal 3-phase bone scan excludes inflammation in patients with clinical symptoms and negative x-ray.[2]
Heterotopic ossification	Bone scan is abnormal before radiographic lesions show up.[2]
Osteoporosis	Bone scan is usually used to exclude stress and compression fractures.[2,31]
Osteomalacia	Bone scan excludes pseudofractures earlier than x-ray.[2]
Benign bone tumors (enchondroma, chondroblastoma, giant cell tumors, eosinophilic granuloma, fibrous dysplasia, brown tumors of hyperparathyroidism, osteoid osteoma, aneurysmal bone cyst, vertebral hemangioma)	Normal 3-phase bone scintigraphy excludes any bone involvement if radiographically no lesion is shown. However, bone scan has low specifity since most lesions will accumulate radioactive tracer. Characteristic findings are rare, e.g. in osteoid osteoma.[11] Usually, vertebral hemangioma show normal uptake in planar scintigraphy.[32] Malignancy cannot be excluded by bone scintigraphy.[2]
Bone infarction	Bone scan has a high sensitivity but is less specific.
Erdheim-Chester disease	Scintigraphic patterns of involved skeletal sites may lead to the diagnosis.[33]
"Bone" pain of unknown origin	Bone scan allows the differential diagnosis between soft tissue and bone lesion.[2] In patients older than 50 years a bone scan is useful to exclude occult malignancy or metastases.[34]
Myositis ossificans	3-phase bone scan may demonstrate the activity of the process.

Indications in malignant bone diseases

In primary bone tumors, the three-phase bone scintigraphy is often used to evaluate the primary lesion and to search for other occult bone lesions. In oncology, bone scintigraphy is used to exclude bone metastases of various malignancies. Current recommendations for bone scanning in daily clinical nuclear medicine are given in Table 2.

Bone scanning

The injected activity of ^{99m}Tc-polyphosphonates varies from 700 to 800 MBq. In children, the activity is adapted to body weight, with a minimum of 80 MBq. Younger children should get a sedative during image acquisition in order to reduce movement arti-

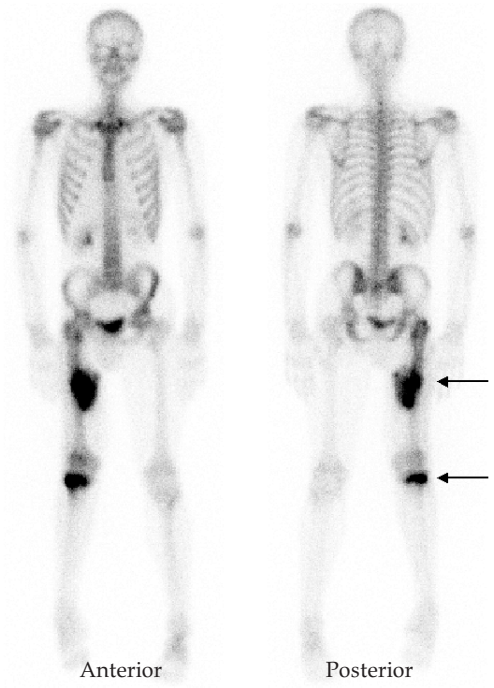

Figure 1. Recurrent osteosarcoma in the right femur in a 17-year-old boy and metastatic disease in the right tibia (arrows).

Table 2. Bone scanning in malignant bone diseases

Disease	To be mentioned
Primary bone tumors (Osteosarcoma, Ewing's Sarcoma, Chondrosarcoma)	Bone scan is not useful to exclude primary bone malignancies. Bone scan is helpful to search for bone metastases or to exclude a local recurrence after treatment.[2,35,36] 3-phase bone scan is useful to evaluate treatment efficacy[37] or viability of bone grafts.
Screening for metastases	Bone scan allows screening of the whole skeleton with a high sensitivity.[38,39]
Prostate cancer	Bone scan is useful in preoperative staging when PSA is increasing ≥30 ng/ml or in patients with clinical evidence of bone metastases. Control of progression of known bone metastases with scintigraphy.[40-42] Evaluation of therapeutic effects in bone metastases following endocrine therapy.[43]
Breast cancer	Bone scan is indicated in primary staging of high-risk patients (axillary lymph nodes positive), clinical evidence of bone metastases or if CA 15-3 is elevated.[44,45] In known skeletal metastases bone scan allows to look for potential pathological fractures.[3] Treatment control is also possible by bone scan, if flare phenomenon is taken into account.[46] About 5% of metastases are missed due to pure osteolyses.[1]

Lung cancer	Bone scan in primary staging only in resectable tumors[47,48] or in clinical evidence.[46,49] About 10% of metastases are missed due to pure osteolyses.[1]
Renal cell or bladder carcinoma	Bone scan should be done in patients with clinical evidence of bone metastases only.[2,50]
Differentiated thyroid cancer	In advanced follicular thyroid tumors or increasing Tg-levels without any correlates in 131I-scan or in bone pain. About 30-50% of metastases may be missed due to pure osteolyses.[1] Patients with elevated serum calcitonin and patients with medullary thyroid carcinoma should undergo bone scintigraphy.[2]
Gastrointestinal cancer	Only in patients with advanced regional tumors and clinical evidence of bone metastases or in patients in whom an infiltration of sacrum is possible.
Malignant Melanoma	In patients with clinical evidence of bone metastases or in patients with advanced regional tumors or histological positive lymph nodes. Bone scan cannot exclude bone metastases.[2]
Squamous-cell carcinoma of the upper aerodigestive tract	Only in patients with an advanced-stage disease, local and regional recurrences, and in second primaries located below the clavicle.[51]
Cervical carcinoma, endometrial carcinoma, ovarian carcinoma	Only in patients with clinical evidence of bone metastases or with advanced regional or histologically poorly differentiated tumors.[2]
Testicular carcinoma	Only in patients with stage IV seminoma with bone pain.[2]
Neuroblastoma	^{123}I-MIBG-scintigraphy is more sensitive.[2] Bone scan can show MIBG-negative metastases.[52]
Lymphoma	Useful in primary lymphoma of the bone and in reticulum cell sarcoma.[3]
Multiple Myeloma	Not useful since metastases are missed in 60-80% due to pure osteolyses.[1]
Systemic Mastocytosis	Bone marrow scintigraphy is more sensitive.[2] The degree of uptake and progress in serial scans marks more aggressive bone marrow disease.[53]
Langerhans cell histiocytosis	Bone scan may detect additional regions of bone involvement.[54]
Palliative pain-therapy with osteotrope radiopharmaceuticals.	Bone scan is a prerequisite for palliative pain-treatment with ^{186}Re-HEDP or ^{153}Sm-HDTMP
Soft tissue tumors	Bone scintigraphy can establish the activity and perfusion of soft tissue processes. Screening for bone metastases or postoperative recurrences is also possible.

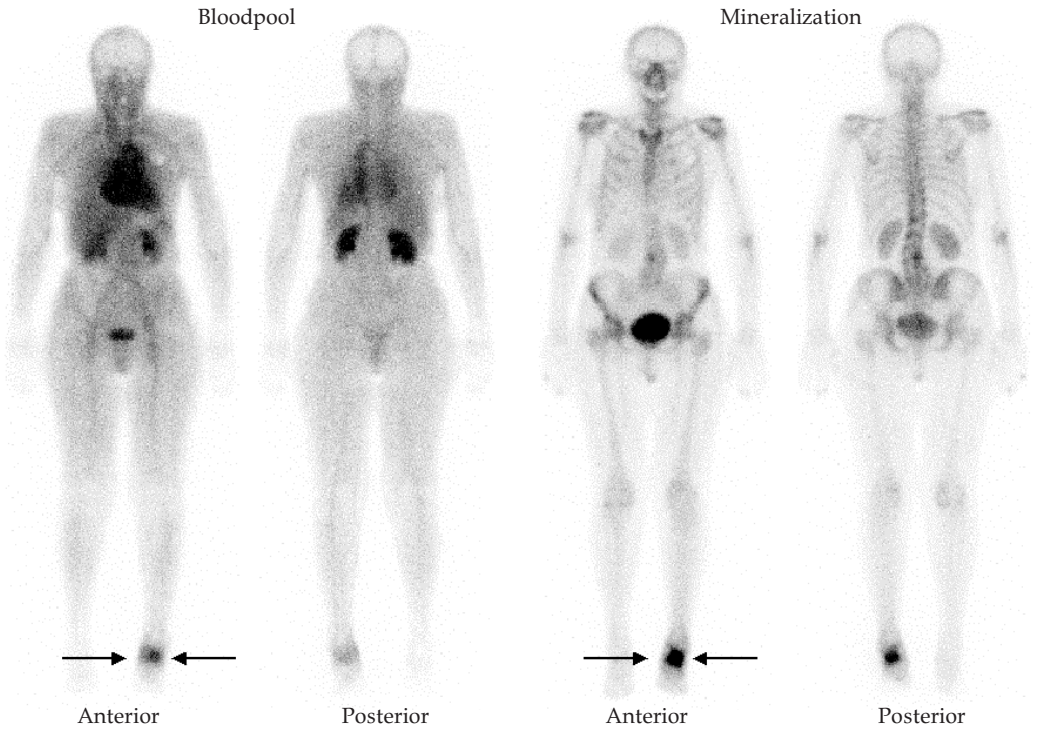

Figure 2. Bloodpool and late whole body images in a 75-year-old women with diabetes. Images show active osteomyelitis of the talus (arrows) and degenerative disease in the lumbar spine due to scoliosis. Artificial photopenia in the left thorax is caused by a pacemaker.

facts. In standard bone scintigraphy, images are acquired approximately 3 hours after injection. In the interim period, the patients should drink at least 1 liter of fluid. Immediately before image acquisition, the patients are asked to empty their bladder. In order to reduce the radiation burden of physicians and nurses, bone scintigraphy should be performed directly after dialysis of the patients with renal failure.

In several focused problems, the three-phase bone scintigrams may give an overview of perfusion, blood pool, and bone mineralization. Dynamic image acquisition is started directly after intravenous injection of ^{99m}Tc-polyphosphonates (perfusion phase). After the first minute, a static image is acquired for 5 minutes (blood pool phase). Late static images (mineralization phase) are performed at least after three hours. Usually, whole-body images are acquired at a double-headed gamma camera with large field-of-view.

The quantification of images may help to establish specific diagnoses, e.g. in sacroileitis, or may help to monitor treatment regimen, e.g. during chemotherapy of primary bone tumors. Additional images may be acquired from unusual angles optimized for best views of distinct bone areas. The images with a pinhole collimator permit clear identifications of small lesions, e.g. of bone infarction in the femoral head of children. Additionally, tomographic image acquisition using single photon emission computed tomography (SPECT) allows to separate overlapping bone structures, e.g. in pelvic, vertebrae, or in hip joints in transaxial, coronal and sagittal projections.

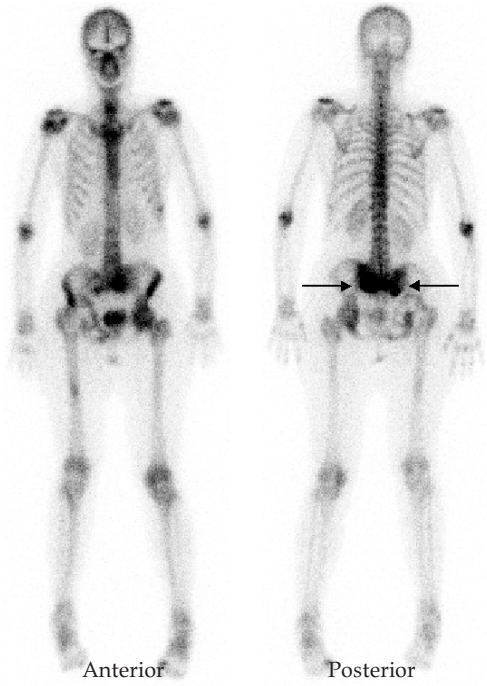

Figure 3. 61-year-old women with radiological obscure findings in the sacrum. Bone scintigraphy performed 6 days after trauma revealed sacrum fracture (arrows). Additionally, hip prosthesis on the right side without any signs of loosening or infection and degenerative changes of bone metabolism in the left hip, both shoulders and in the left big toe can be seen.

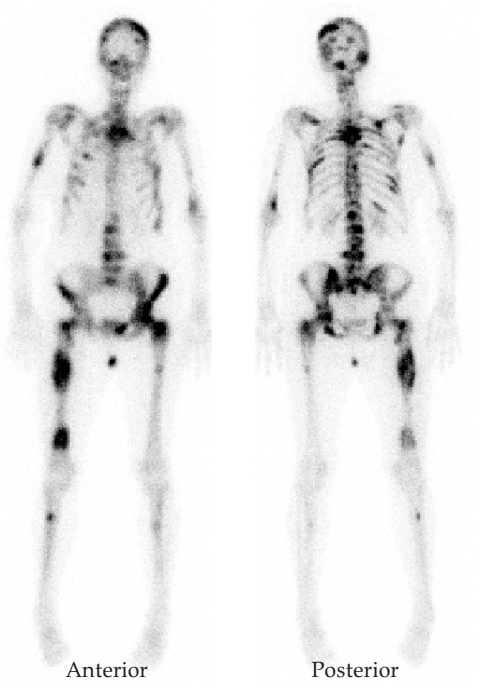

Figure 4. Multilocalar bone metastases in a 73-year-old woman with breast cancer.

Contraindications

Bone scintigraphy will usually not be performed during pregnancy, and only life-threatening indications will lead to bone scanning in breast-feeding women. In these patients, breast-feeding should be discontinued for 48 hours after injection. In children, repeated imaging need rigorous indication, particularly because of the higher radioactive load in their epiphyseal plates.

Radiation load

The effective dose in normal bone metabolism and regular renal function amounts to 0.008 mSv/MBq, which is equivalent to 6 mSv per study.[5]

Conclusion

Just as many other nuclear medicine procedures, the bone scintigraphy has a high sensitivity, and changes of the bone metabolism are often seen earlier than the subsequent changes in bone structure in x-ray. Therefore, occult lesions in the whole skeleton might be detected early by bone scintigraphy.[6] On the other hand, bone turnover is increased in various bone diseases. Consequently, bone scintigraphy usually has a low specificity, and the differential diagnosis of the underlying etiology is often not feasible. However, three-phase bone scintigraphy and SPECT[7,8] can significantly increase the specificity in some skeletal areas.

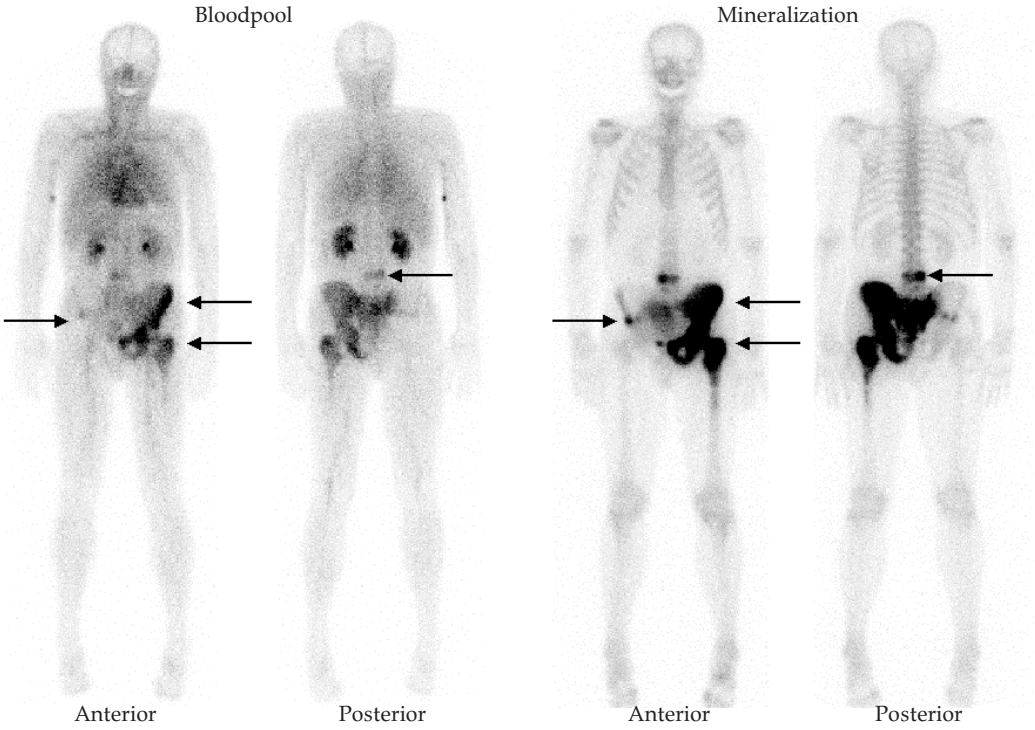

Figure 5. Bloodpool and late whole body images of 67-years-old man with Paget's disease in the pelvis (arrows).

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