



Chapter 30

NUCLEAR IMAGING OF THE SKELETAL SYSTEM

Yong Whee Bahk

Introduction

Bone may well present as a mere inert weight-bearing scaffold of the human body to those who acquired the anatomical knowledge of the skeleton with the aid of dried bone specimens. Nevertheless, like all other active organ systems, the bone changes dynamically as it undergoes incessant turnover with modelling and remodelling through the physiological and metabolic activities of osteoblasts and osteoclasts. The principal roles played by these bone cells are the maintenance of the skeletal and calcium homeostasis by balancing between the ratio of bone collagen production and its resorption or destruction, and governing the mineralization processes. Collagen production is common to various connective tissues but mineralization is unique to bone cells.

Bone scintigraphy is one of the most valuable nuclear imaging procedure, especially remarkable for its high sensitivity in disclosing bone metastasis of cancer long before radiographic demonstration. Bone scintigraphy is also useful in the diagnosis of covert fracture, occult trauma, bone contusion, early acute osteomyelitis, acute pyogenic arthritis and avascular bone necrosis. Measurements of bone clearance of radiopharmaceuticals, absorptiometry and quantitative bone scintigraphy are applied to the study of metabolic bone disorders such as osteoporosis and osteomalacia.

Physiology of bone

The living bone undergoes ceaseless turnover that is mediated by bone production and absorption through the activities of osteoblasts and osteoclasts, respectively. Bone turnover is well balanced and in a state of equilibrium unless disturbed by disease. When bone production is superseded by bone destruction (absorption), as in acute pyogenic infection or invasive malignant neoplasm, osteolysis ensues. In a reverse situation, osteoblastic reaction in the form of bony sclerosis or increased bony density may result.

There are five types of bone cells in the skeletal tissue. They are osteoprogenitor cells, osteoblasts, osteocytes, osteoclasts and bone-lining cells. All the bone cells are contained in bone matrix. Bone formation or osteogenesis is accomplished by the mineralization of organic matrix or osteoid tissue, which is composed of collagen (90%) and surrounding mucopolysaccharides. Bone formation is stimulated by physical stress and strain to the skeletal system, calcium regulatory hormones (parathormone, calcitonin), growth hormone, vitamins A and C and calcium and phosphate ions.

Bone resorption sets forth as the bone matrix has been denatured by the proteolytic action of collagenase which is secreted by osteoclasts. Then phagocytic ingestion and clearing of disintegrated organic material and freed inorganic mineral constituents come into play.

Factors that stimulate osteoclastic activity include physical disuse, hyperaemia, parathormone, active metabolites of vitamin D, thyroid hormone, heparin, interleukin-1 and prostaglandin E.

Bone scanning agents

The first radionuclide successfully used for the photoscanning of bone lesions was ^{85}Sr . Strontium acted as a substitute for calcium; hence its easy incorporation into the hydroxyapatite crystal rendered bone scanning possible. Inconveniently, however, ^{85}Sr had a long physical half-life of 65 days. Moreover, disturbing excretion of the agent after intravenous injection by the gut and kidneys during the first 24-48 hours distracted considerably the quality of scan image. Strontium-87m had a much shorter physical half-life (2.8 hours), but this was too slowly cleared from the blood resulting in prolonged high background activities with consequent low bone to background activity ratio. Fluorine-18 was a useful alternative to strontium but for its limited availability in ordinary nuclear medicine laboratories which were not located within easy reach of medical cyclotron or nuclear reactor.

It was not until the introduction of $^{99}\text{Tc}^m$ labelled stannous triphosphate complex that bone scanning became widely accepted. Within a short period of time, $^{99}\text{Tc}^m$ polyphosphate, pyrophosphate and diphosphonate were developed for general use. Chemically, the phosphate compounds contain as many as 46 phosphate residues (P-O-P), and its simplest form is pyrophosphate with two residues. The phosphonate is a compound with P-C-P bonds instead of P-O-P bonds. Of these the diphosphonates are the most widely used. They are now available in the form of $^{99}\text{Tc}^m$ hydroxy ethylene diphosphonate (HEDP) and $^{99}\text{Tc}^m$ methylene diphosphonate (MDP). The phosphonate compounds have strong avidity for hydroxyapatite crystals in the mineral phase of bone, especially at the sites where new bone is actively formed as in epiphyseal plates of growing long bones.

Following intravenous administration, $^{99}\text{Tc}^m$ labelled phosphates and diphosphonates become rapidly distributed in the extracellular fluid space throughout the body, approximately half of the injected radiopharmaceuticals are then fixed by bone while the rest excreted into the urine by glomerular filtration. The amount of the radiopharmaceuticals accumulated in bone at one hour after injection is 58% with MDP, 48% with HEDP and 47% with pyrophosphate.

Mechanism of bone adsorption

The mechanism of $^{99}\text{Tc}^m$ phosphate complex deposition in bone has not been fully clarified. However, it is known that the uptake and retention of $^{99}\text{Tc}^m$ diphosphonate complex are strongly influenced by such factors as metabolic activity, blood flow, surface bone area available to extracellular fluid and calcium content of bone. It has been demonstrated by autoradiography that the deposition of diphosphonate takes place almost exclusively on the surface of the inorganic calcium phosphate.

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Imaging instruments

Gamma camera is now the most commonly utilized scintillation detection system for nuclear imaging of bones and joints. Normally for a whole body skeletal survey, parallel hole collimators are used but for amplifying the details of the suspected area, pinhole and low energy converging collimators are indispensable adjuncts. The pinhole collimator with 3-mm aperture seems the collimator of choice for image quality with high resolution for this purpose.

Before the gamma-camera era, the rectilinear scanner was used for radionuclide imaging in the diagnosis of bone and joint diseases. This instrument is still used in many nuclear medicine departments of the developing countries but unless one has a fast moving whole body version, it is almost impossible to do a skeletal survey with a rectilinear scanner. Fig. 30.1 is a typical example of the black-and-white photostan image made with a rectilinear scanner in 1960s. The rectilinear scanner is now nearly extinct. On the other end of development, is SPECT, which permits the separation of a selected plane or a small volume of tissue from other overlapping structures both in foreground and background. The separation of tissue in a thin slice can reveal detailed information regarding the distribution of radiopharmaceutical in bone and joint. SPECT is now commonly used in the study of complex structures of the skull, face, spine, pelvis and hip.

Bone scan technique

For static views, it is better to wait for three to four hours to let the non-target radioactivity get excreted in the urine. During this period, the patient is encouraged to drink plenty of fluids to promote rapid clearance of the radiopharmaceutical. The patient is instructed to void the bladder just before starting the scanning, otherwise the bladder activity will be very prominent in the pelvic view. Scrupulous attention should be given to avoid contamination of clothes and the limbs while passing urine.

The usual practice is to obtain first a single-pass or double-pass view of the whole skeletal system (Fig. 30.2). Upon inspection of the whole-body scintigraph, spot views using low energy converging collimator or pinhole collimator are to be taken to detail the region of interest or equivocal findings. In most instances, anterior and posterior views, supplemented by a lateral or oblique view in special situations, are sufficient. It should be emphasized that pinhole collimator scintigraph is not only geometrically magnified but also provides high resolution of anatomy. (Figs. 30.3A and 30.3B).

The three-phase dynamic scintigraphy is another important technique. By this, vascularity of a bone lesion can be quantitatively evaluated. Its typical application is in the differential diagnosis of infectious and non-infectious bone lesions. A recommended protocol includes an immediate nuclear angiography (16 consecutive frames of 2-4 second image), a blood-pool image at two minutes and a delayed static image at 2-4 and 24 hours after intravenous administration of 30 mCi(1.1 GBq) of $^{99}\text{Tc}^{\text{m}}$ -MDP.

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NORMAL BONE SCAN

Logically, abnormality is an antithesis of normality. It is, therefore, essential to be thoroughly familiar with normal findings and the factors that affect normal findings to recognize true abnormalities. Abnormality in a bone scan is seen either as increase or decrease in radionuclide accumulation (RA), euphemistically described as "hot" or "cold" respectively. Of the many factors that distort scan findings, asymmetry about the mid-sagittal plane of the body with tilting of the image to one side is probably the most important. Even a slight difference in the target-detector distance produced by such a tilt can result in significant alteration of the scan image giving fallacious impression. (Figs. 30.4A and 30.4B).

In normal subjects, greater RA occurs in the cranial vault, facial bone around nasal cavity, sternum, spine and around pelvis and hip. Prominent RA is also observed in the large joints of the extremities.

The sacroiliac joints show the greatest RA and this is due to constant, strenuous weight bearing.

Skull and Neck

Prominent RA can be seen in the cranium along the cranial tables and suture lines, around orbits and paranasal sinuses and in the unfused occipitospheoid synchondrosis. Often the maxilla and mandible with a denture show increased RA. Various parts of the vertebra lie on the same transverse plane in the cervix (in the thoracic and lumbar regions, the vertebral body and posterior structures are on the different transverse plane) making their separation difficult on bone scintigraphy. The thyroid cartilage is not infrequently visible due to ^{99m}Tc -MDP uptake simulating the thyroid gland that has concentrated unbound ^{99m}Tc -pertechnetate. Occasionally, the hyoid bone can be also seen.

Thoracic Cage and Shoulders

The sternum is regularly visible. Greater RA can be noted in the sternoclavicular joint, manubriosternal junction and calcified costochondral junctions. Prominent accumulation can also occur in the coracoid process, acromioclavicular joint, glenoid process and inferior angle of the scapula. The clavicles are visible on the anterior view, whereas the rib cage and scapulae are more clearly visible on the posterior view.

Vertebral Column

Individual vertebra along with its small parts such as the pedicles, laminae, apophysial joints and spinous process can be visualized only by pinhole collimator. The kyphotic thoracic spine is more clearly seen in the posterior view, whereas the lordotic lumbosacral spine is well visualized in the anterior view.

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Pelvis and Hips

The sacrum and iliac bone overlap at the sacroiliac joints, but they can be portrayed as separate structures along the joint space in the butterfly view. The iliac bone accumulates more radionuclide than the sacral part. RA in the pelvis and hips is symmetrical along the mid-sagittal line. The adult hip joints also present a problem of overlapping. The acetabular roof and femoral head superimpose each other. The RA is highest along the acetabular roof.

Extremities

The long bones are visible in scintigraph unless the subject is very old with advanced osteopaenia. RA is comparatively great in the bones around the shoulders, elbows, hips, knees and ankles. Pinhole collimator scintigraphy can image the small bones of hands and feet. The patella often shows greater RA. The growing bones of infancy and adolescence accumulate more radionuclides, particularly along epiphyseal lines. The greatest accumulation is seen in the long bones of the late teens before epiphyseal fusion takes place.

ABNORMAL BONE SCAN

Basically, the scintigraphic manifestations of bone abnormality can be described from three different view points viz. anatomy, RA patterns and vascularity. The anatomical changes are expressed in terms of size, shape and position, and RA or vascularity is either increased, unaltered or decreased. The majority of bone lesions show increased RA or "hot spot" and only a small fraction presents as photopaenic or "cold spot". Typical lesions that manifest as photopaenic area are avascular bone necrosis, photopaenic cancer metastases and multiple myeloma.

Altered biodistribution of radiopharmaceuticals

Significant dehydration, ascites, anasarca and renal and/or hepatic failure cause increased RA in the soft tissues of the body resulting in low bone-to-background ratio and poor bone image (Fig. 30.5). Unlabelled free $^{99}\text{Tc}^{\text{m}}$ -pertechnetate and oxidation of the $^{99}\text{Tc}^{\text{m}}$ -phosphate complex may increase background activities, and cause thyroid or liver uptake and alimentary tract excretion. Anticancer chemotherapeutic drugs, steroid and iron have been shown to suppress RA in bones. It is interesting to note that chemotherapy makes some bone lesions in the healing stage "flare up".

It should not be forgotten that normally kidneys and breasts show some concentration of the radiopharmaceutical. Abnormal accumulation in the soft tissues may also be seen in contused muscles, brain infarct, myocardial infarct, calcified lymph nodes and metastatic calcification of soft tissues in hypercalcemic states.

CLINICAL APPLICATIONS

General Considerations

Nuclear bone imaging was initially utilized for the demonstration of metastatic cancer and fracture of bone. Since then, the scope of bone scintigraphy has enormously expanded, and the imaging techniques have become highly refined and versatile, both qualitatively and quantitatively. This is now the method of choice for screening, localizing and specifying many bone and joint diseases. The sensitivity and specificity can be significantly increased when scintigraphy is supplemented with nuclear angiography (three-phase test), pinhole collimator imaging and SPECT. Bone scintigraphy is particularly indicated in the diagnosis of cancer metastases, septic conditions of bones and joints, multiple trauma, occult fractures, diseases involving multiple bones such as fibrous dysplasia, enchondromatosis, Paget's disease, myelomas and patients with bone pain or fever of unknown origin. The arthritis that affect more than a single joint also constitute an important indication. The scintigraphic examination in combination with augmenting techniques is useful in assessing the extent and activity of rheumatoid or rheumatoid-related arthritis, osteoarthritis and spondylosis. The pinhole collimator scintigraphy has been shown to be of great value in the differential diagnosis of metastases, fractures, infections and degenerative diseases of the spine (Fig. 30.6).

Metastatic Bone Tumours

Bone metastasis of malignant neoplasms of both extra- and intra-osseous origin is the most widely accepted indication of bone scintigraphy. The purposes are the early diagnosis, evaluation of disseminated area, staging of the primary disease, prognostication and for follow-up of patients on therapy.

The majority of metastatic bone lesions are multiple, around 7% being solitary. Regarding the site of predilection, approximately 80% of cases involve the axial bones and the remaining 20% involve the skull and long bones in equal frequency. It has been known that cancers of the breast and prostate tend to disseminate via the vertebral veins to the spine, while lung cancer and thyroid spread haematogeneously to random sites in the skeleton. Some metastatic bone lesions from anaplastic carcinomas of the kidney, breast and lung produce photopaenic or "cold spot". The incidence of cold-spot metastases was reported to be around 2% but with application of pinhole techniques, this incidence may be found to be higher. (Figs. 30.8A and 30.8B). Extensive skeletal metastases with diffuse increased RA give rise to the "superscan" sign (Fig. 30.9).

Bone scintigraphy is highly sensitive in detecting bone metastases. A positive bone scan predates negative radiograph by months. Nevertheless, there are cases with false negative scan. A painful focus with radiographically visible osteolytic change may not be visible in bone scan. Bone is reported to be normal in approximately 5% of skeletal metastases with radiographically evident osteolysis.

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Certain scintigraphic features are helpful in distinguishing cancer metastases from benign conditions. Multiple vertical band-like hot spots in the ribs lined in a row represent fractures (Fig. 30.10), while an elongated transverse accumulation of RA in the rib is highly suggestive of cancer metastasis (Fig. 30.11). A solitary hot spot in a rib is malignant only in 1.4%, and 90% of solitary lesions have a benign etiology such as trauma or postoperative irradiation. In contrast, 68% of solitary lesions in the axial skeleton are malignant. A solitary hot spot in the sternum in patients with known primary malignant neoplasm indicates metastasis when trauma can be excluded. A short segmental RA in the vertebral end plate or diffuse homogeneous uptake throughout the body of the vertebra suggests metastases (Figs. 30.6 and 30.12), while a long arcuate uptake along the whole length of the end plate is rather characteristic of compression fracture (Fig. 30.7).

Rationale for Bone Scintigraphy in Metastases

Ever since its initial clinical applications, bone scanning has been utilized for the diagnosis, evaluation of therapeutic effects and for prognosis of both extraosseous and intraosseous malignancies. There are still many unanswerable questions regarding the appropriate utilization and reasonable indications of this diagnostic modality in cancer patients. Of these questions, indication for bone scintigraphy in patients with known primary malignancy in the non-skeletal organs is probably the central issue. In spite of innumerable publications, there exist still much confusion and controversy over whether or not bone scintigraphy should be a routine procedure in cancer patients and how often a follow-up study should be performed. In particular, the utilization of bone scan for the detection of bone metastases in an early cancer is a subject of diverse opinion. These questions are of particular importance for the developing countries. Bone imaging is a time consuming procedure. Most of the nuclear medicine units in these countries have a single gamma camera and the perpetual question is how much time should be spared for bone scintigraphy on this one instrument. Whatever prescriptions arrived at on the basis of the Western data are not going to be practical for the developing countries.

Nonetheless, there are a few useful guidelines. The most important indication is bone pain in patients with known malignancy, especially when the tumour has a high propensity to metastasize to bone. Such tumours include cancers of the breast, lung, kidney and prostate. Probably the next most important indication is a baseline documentation before starting an anticancer regimen.

Bone scintigraphy as a part of tumour staging constitutes another important indication. This indication, however, is valid only for tumours with a tendency to metastasize to the bones.

A follow-up period after the initial negative bone scan has been variously prescribed from one year to five years. The follow-up period should be shorter for cancer that metastasize rapidly, haphazardly and with high frequency.

Primary Malignant Bone Tumours

As far as specific and differential diagnosis of primary bone tumours is concerned, the yield of bone scintigraphy is much lower than that of radiography. This is simply due to the difference between the resolution in imaging achieved with these two modalities. Scintigram can not replace or substitute radiography particularly when definition of fine structures, such as trabeculae and periosteum, is required. Nevertheless, bone scintigraphy can demonstrate altered bone turnover which is not evident on radiograph permitting early diagnosis of metastasis. This may also help distinguish some bone tumours from inflammatory processes. Another advantage is that bone scintigraphy can detect bone-to-bone metastasis and assess local extent of primary neoplastic focus. Osteogenic sarcoma and Ewing's tumour are well known indications in this respect.

The use of bone scintigraphy may be encouraged in the study of suspected multiple myeloma since a negative bone scan in the presence of multiple punched-out osteolytic lesions in bone radiograph strongly suggest myeloma.

Benign Bone Tumours

Bone scintigraphy can not play a decisive role in the diagnosis of bone tumours because of its low specificity. However, it may have helpful findings in some benign tumours. One important indication is detection of suspicious pathological fracture.

Among the bone tumours that may be indications of bone scintigraphy are bone cyst, enchondroma, osteoid osteoma and giant cell tumour (osteoclastoma). In general, there are no pathognomonic findings of benign bone tumours or tumorous conditions in scintigraphy. Nevertheless, the diagnosis may be suggested by bone scintigraphy in some diseases. For example, ring-like RA along the periphery of photon deficient area in the end of a long tubular bone is highly suggestive of bone cyst. Hot spots within hot area is pathognomonic of Osteoid osteoma. This pattern can indeed be well demonstrated in pinhole scintigraphy (Fig. 30.13). Bone islands or pacchionian depressions in the skull may sometimes impose the problem of differential diagnosis from metastatic bone lesions. Neither of them concentrates radiopharmaceutical. Eosinophilic granuloma, the most common and benign variety of histiocytosis X, shows considerable RA.

Traumatic Bone Lesions

It may be justified to state that one of the most widely accepted indication of bone scintigraphy is traumatic and sports injuries of the musculoskeletal system. This statement is particularly valid for stress fracture, bone contusion, covert fracture of the ribs, sternum, lumbosacral spine and acute skeletal muscular injuries. Most of these lesions are either elusive or invisible in a radiograph.

The ordinary spot scintigraphy made with general purpose low-energy converging collimator is sufficient for the detection of stress fracture or covert fracture. For the

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demonstration of more specific features of injuries, however, pinhole collimator scintigraphy is necessary. Fig. 30.14 is a case of stress fracture accompanied by periosteal reaction in the tibia. Acute bone contusion may be defined as blunt trauma to bone without fracture so that condition will not be diagnosed by radiography. Bone scintigraph is of great value in this condition since it reveals intense RA uptake in the contused bone (Figs. 30.15A and 30.15B).

OSTEONECROSIS AND RELATED DISEASES

Avascular Bone Necrosis

This is one of the frequent indications of bone scintigraphy. Bone necrosis is a state in which the bone cell is devitalized along with its neighbouring bone marrow cells resulting from deprivation of blood supply. Hence, the process is termed avascular or aseptic. The single most important mechanism of avascular bone necrosis is vascular injuries, causes of which are either direct or indirect. Among the direct causes are trauma, embolism, thrombosis, elevated bone marrow pressure and vasculitis. Caisson disease, sickle cell anaemia and radiation necrosis are well known clinical entities. Indirect or probable associations have been related to steroid therapy, minor trauma, collagen disease, alcoholism and pancreatitis. The third category is osteochondrosis and ischemic necrosis, the aetiology of which is obscure.

Scan findings are rather specific when the dead bone is visualized as a photopaenic area within normal or reactive bone of, for example, the femoral head in Legg-Perthes disease (Fig. 30.16). Pinhole collimator image is particularly suited for the study of bone necrosis as there will be a greater possibility of demonstrating even a small cold spot. As bone necrosis recovers and is revascularised, photopaenic area will begin to concentrate the radionuclide. Thus, the bone scintigraphy is a valuable tool in assessing recovery in bone necrosis.

Avascular bone necrosis is an annoying and disabling complication of kidney transplantation. The incidence has been reported to range from 2% to 17%. It is presumed to result from exogenous use of corticosteroids. Bone necrosis in transplant patient affects most frequently the femoral head. Rarely are the bones of the knee involved.

METABOLIC AND RELATED BONE DISEASES

Metabolic diseases of bone result from vitamin deficiency or excess, endocrinopathy, disturbed calcium and phosphate metabolism and malnutrition. Osteomalacia and osteoporosis are two examples of metabolic disorders which are of special relevance to the developing countries. The former is a failure of calcium deposition in bone matrix, whereas the latter represents deficient matrix formation. Rickets is a special form of osteomalacia that affects

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growing bones of infants and children due to vitamin-D deficiency. Osteoporosis is either generalized or regional. There is a third form of osteoporosis which is associated with endocrine disorders like hyperparathyroidism, hyperthyroidism and acromegaly.

Bone scintigraphy is significantly more sensitive than radiography in detecting osteomalacia, renal osteodystrophy and primary hyperparathyroidism. The relative sensitivity is, however, reverse in case of osteoporosis. On the whole, the high specificity and accuracy of radiography in the diagnosis of metabolic bone diseases are usually not achieved by bone scintigraphy.

Osteomalacia.

Osteomalacia is marked by softening of bone due to poor mineralization and excessive osteoid accumulation. The causes of osteomalacia include vitamin D deficiency or impaired intestinal absorption of calcium and phosphorus. The deficiency of vitamin D and minerals leads to inadequate calcification of osteoid, the net effect of which is demineralization and consequent bone fragility. In essence, osteomalacia is a disease of mature bone of adults, and its counterpart in infancy is rickets. Unlike rickets that occurs in unfused growing bones, osteomalacia affects the bones which have already been formed. In osteomalacia, uncalcified osteoid accumulates within fused bone resulting in diffuse osteopaenia. Thus, malacic bone easily sustains infraction or pseudofracture.

Bone scan shows diffuse increase in RA in skeletal system along with occasional focal hot areas indicating generalized osteopaenia and infarction & pseudofractures respectively (Fig. 30.17).

Rickets

Histologically, uncalcified osteoid accumulates luxuriously in the metaphyseal end of actively growing long bones. The affected bone becomes cupped, widened and flared due to weight bearing.

At this stage, bone scan shows characteristic "chicken bone" appearance due to intense RA both in the epiphyseal ossification centre and widened metaphysis. As the condition improves, scan changes return slowly to normal over a period of months.

Osteoporosis

In osteoporosis the bone mass is reduced. It may be classified clinically into senile (postmenopausal) form, idiopathic form in males and idiopathic juvenile form. Senile osteoporosis in women is clearly related with the loss of stimulation by oestrogen, but definite hormonal relationship has not been established in men. Idiopathic osteoporosis of males has probable association with alcoholism and liver cirrhosis, which are commonly present. Idiopathic juvenile osteoporosis is an uncommon disease of self-limited nature. In osteoporosis, the spine and limb bones are easily fractured. Regional osteoporosis includes

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disuse osteoporosis, reflex sympathetic dystrophy syndrome, transient regional osteoporosis and regional migratory osteoporosis. Other forms of osteoporosis are osteoporosis due to hyperparathyroidism, hyperthyroidism, acromegaly and multiple myeloma.

In general, bone scan is insensitive and nonspecific in the diagnosis of osteoporosis. Occasionally, however, "washed out" pattern of generalized osteoporosis can be seen. This pattern is encountered in patients with little or no osteoblastic activity. For quantitative analysis, radiograph or more sophisticated methods like single or dual photon absorptiometry are to be resorted to.

Bones are brittle and prone to fracture in osteoporosis. In bone scintigraph, fractured bone shows marked RA. Osteoporotic vertebra is particularly liable to compression fracture, which produces characteristic pathognomonic sign of arcuate "hot end plate" in pinhole collimator scintigraph (Fig. 30.7).

Disuse Atrophy of Bone

When a limb is immobilised for a certain period of time, bone mass becomes reduced due to increased endosteal bone resorption from the loss of stimulation. Disuse atrophy is a type of osteoporosis, in which remodelling is accelerated. Disuse atrophy of bone is a frequent occurrence in hemiplegia, paralysis or immobilization. Bone scan shows increased RA in the bones around large joints, which have been in disuse.

Reflex Sympathetic Dystrophy Syndrome

The syndrome is known also as Sudeck's atrophy or causalgia. Aetiology is usually trauma with or without bone fracture. Infection and peripheral or central nervous system abnormalities may precipitate the disorder. Clinical symptoms include pain, often severe and incapacitating, and skin atrophy with glistening appearance. In 69% of cases, radiograph demonstrates patchy and mottled pattern of deossification or osteopaenia which is similar to the bone changes seen in severe disuse atrophy. Bone scan is characterized by marked RA in the affected joint representing hypervascularity. Radionuclide angiography reveals increased blood flow to the lesion.

Bone Irradiation

Irradiation can induce vasculitis and vascular stenosis, which, in turn, leads to osteitis and osteonecrosis. The ischemic bone becomes photopaenic in scintigraph, as early as few months after radiation therapy, and after a cumulative dose as low as 2000 rad.

Another possible effect of irradiation in bone are on osteoblasts. Damaged bone cells may die causing osteonecrosis. Radiation osteitis is considered to be secondary to a combination of irradiation, infection and trauma. The mandible, clavicle, humeral head, rib and femur are usual sites of such osteitis. Scintigraph reveals intense RA in the afflicted bone.

INFLAMMATORY BONE DISEASES

Osteomyelitis, cortical bone abscess, osteitis and bone tuberculosis constitute major inflammatory bone diseases. Osteomyelitis is an acute febrile bone disorder of infancy and childhood. Inadequate or even properly treated acute osteomyelitis may persist or recur as chronic form. In some patients, acute osteomyelitis is walled off by reactive bone to form abscess. Cortical bone abscess is a special type of pyogenic bone infection in which infectious focus is harboured within the bone cortex. Osteitis is either infective or noninfective. Infective osteitis is usually concomitant to osteomyelitis. Noninfective osteitis includes condensing osteitis, radiation osteitis and others. Tuberculous osteomyelitis is predominantly a problem of the developing countries. It usually affects the spine and joints. Fungi, parasites and viruses also produce osteomyelitis. In drug addicts, pseudomonas, Klebsiella and enterobacters are prevailing offenders.

Acute Osteomyelitis

This is primarily a pyogenic infection of bone marrow with subsequent spread to periosteum, cortex and neighbouring soft tissue. The lesion is associated with frank osteolysis. The unmatched value of bone scintigraph in early detection of acute osteomyelitis has been well documented. Nuclear angiography demonstrates increased blood flow and blood pool (Fig. 30.18A). Static bone image reveals prominent RA in the affected bone (Fig. 30.18B). Such triple-phase bone scintigraphy can be utilized as an excellent discriminator between osteomyelitis and cellulitis which is not attended by bone infection. In the latter condition, blood flow and blood pool are increased but there is no significant RA in the bone. Chronic osteomyelitis has been related to the persistence of infective organism in the haversian system. In adults, acute haematogenous osteomyelitis frequently affects the spine, and pyogenic spondylodiscitis ensues. Typically, pyogenic spondylodiscitis involves the end plates of two opposing vertebrae with the disc sandwiched in between. Although infrequent, acute haematogenous osteomyelitis can involve multiple bones.

The sensitivity of bone scintigraph in the diagnosis of acute osteomyelitis approaches 100%. However, the examination is not so much sensitive in early infancy or neonatal period probably because suppuration progresses so rapidly and aggressively that there is not enough time for bone to resist and react. Another problem is associated with the fact that the predilected site of acute osteomyelitis viz. the metaphysis is closely placed to the epiphyseal line. Thus, in unmagnified view, the two bands of intense RA may often be seen as a single band. This problem can be resolved when pinhole collimator image is obtained.

Labelled Leucocytes and ^{67}Ga Scan in Osteomyelitis

Leucocytes labelled with ^{111}In or $^{99\text{m}}\text{Tc}$ or ^{67}Ga have been used in the diagnosis of osteomyelitis. The rationale of this examination is that leucocytes are taken up by inflammatory tissues. When granulocytes and lymphocytes are selectively labelled, the former can be localized by acute inflammatory focus having granulocytic infiltration, whereas the latter by chronic inflammatory focus having lymphocytic infiltration. The sensitivity and

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specificity of ^{111}In leucocyte scan have been reported to range between 50%-100% and 69%-100%, respectively.

Recently, $^{99}\text{Tc}^{\text{m}}$ -HMPAO (hexamethyl propylene amine oxime) was introduced to label leucocytes. The quality of the $^{99}\text{Tc}^{\text{m}}$ image in terms of detail was found to be comparable or superior to that of ^{111}In image. The sensitivity is reported to be 100% and the specificity 95%.

The usefulness of ^{67}Ga scan in the study of acute bone infections has been questionable because ^{67}Ga is localized not only by infectious bone diseases but by neoplastic conditions, making the test nonspecific. However, it has been demonstrated that ^{67}Ga uptake is rather intense in acute bone infection compared to neoplasm. ^{67}Ga uptake is greater than $^{99}\text{Tc}^{\text{m}}$ -MDP uptake in acute bone infection.

Bone Tuberculosis

Clinically, bone tuberculosis consists of spondylitis (spine tuberculosis) and tuberculous osteomyelitis of other bones. Spondylitis is far more common than other osseous tuberculosis. Joints are also frequently affected with tuberculosis.

Bone tuberculosis is characterized by a destructive process with minimal reactive bone formation. In long tubular bone, destruction takes place typically at the metaphysis as in acute pyogenic osteomyelitis. As tuberculous process advances, a cystic lesion accompanied by marginal osteosclerosis and periosteal reaction can be produced.

Bone scan findings of tuberculosis are not specific. Affected bone simply shows increased RA. Occasionally, photopaenic area can be portrayed within intense RA due to necrosis.

Tuberculous spondylitis is still not a rare disease in many developing countries. It is characteristic of spine tuberculosis to involve simultaneously two neighbouring vertebrae and the intervertebral disc interposed between them. This is due to the presence of freely anastomosing rich venous network within two vertebrae. In established spondylitis, the affected vertebrae and disc are destroyed as a block.

Bone scan shows diffuse irregular RA within the vertebral body. Disc space becomes narrowed and obliterated. Pinhole image is valuable in differentiating spine tuberculosis from pyogenic spondylitis, compression fracture and cancer metastases.

ARTHRITIS

With accumulation of knowledge in nuclear imaging of various arthritides, the categorization of arthritis into two groups viz. inflammatory and non-inflammatory has become warranted. The inflammatory type is attended by synovitis so that the RA is diffuse

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within the articular confinement, whereas the non-inflammatory type is characterized by degeneration of articular cartilage and associated subchondral bone reaction with focal or compartmental RA.

Among the common inflammatory arthritides are rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, infectious arthritis and Reiter's syndrome. Osteoarthritis is probably the most common non-inflammatory arthritis. For the nuclear imaging of arthritis, ^{99m}Tc -MDP, ^{67}Ga citrate and radiolabelled leucocytes can be utilized. Nuclear angiography is of great value in septic arthritis.

Acute Pyogenic Arthritis

This is one of the excellent indications for nuclear imaging. Frequent offenders are staphylococci, streptococci, pneumococci and gonococci. As is the case with acute osteomyelitis, acute pyogenic arthritis is difficult to detect in its early phase by radiography. However, bone scan demonstrates increased blood pool and intense RA in the septic joint already in its early stage (Figs. 30.19A and 30.19B). Pinhole scintigraph may disclose diffuse RA in periarticular bones.

Synovitis

Highly vascular synovial membrane becomes markedly congested when inflamed, and shows marked concentration of radionuclide especially in the vascular phase of the scintigram. In acute synovitis, periarticular bones also concentrate radionuclide due to concomitant bone inflammation. Moreover, nuclear angiograph and blood-pool image may well reveal hypervascular state of the lesion. Pinhole image may prove that periarticular bones are not the site of primary infection. Thus, the discrepancy between a "hot joint" in standard scintigraph and normal or only slight RA by periarticular bone in pinhole image can be used as a differential finding.

Osteoarthritis

Osteoarthritis is essentially a degenerative disease of joints characterized by histological derangement of cartilage and subchondral bone without obvious inflammation. Synovitis is not a prominent feature.

Bone scan shows RA which is typically focal or compartmental in distribution. Compartmental, segmental or focal nature of RA can be clearly depicted in pinhole image (Fig. 30.20). This finding may be confused with spontaneous osteonecrosis when it occurs in the knee joint. Distinction is, however, possible because the hot spots in the latter condition tend to localize within the osseous portion (Fig. 30.21).

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Rheumatoid Arthritis

Bone scan has been shown to be useful in the diagnosis of rheumatoid arthritis and assessment of its activity. Multiarticular involvement can be clearly portrayed by whole body bone imaging. In magnified view, inflammatory changes in small bones and joints of hands and feet can be detailed. Nuclear angiography may provide information regarding the lesional vascularity, and, in turn, the activity of the pathologic process. In remission, vascularity reverts to normal. Pinhole scintigraph shows obliteration of joint space due to ankylosing process which is characteristic of rheumatoid arthritis.

Ankylosing Spondylitis

It is well known that ankylosing process of the spine is usually preceded by sacroiliitis. Bone scan reveals characteristic features of the obliteration and bridging of vertebrae giving rise to the appearance of "square vertebrae in unsegmented spinal column". Pinhole image permits to recognize that ankylosis involves not only the longitudinal ligaments and interspinous ligaments, but small apophysial joints.

CONCLUSION

Skeletal imaging is one area where nuclear medicine has an edge over other imaging modalities. Its importance in the early diagnosis of metastases and its unequivocal role in the overall management of cancer are unquestionable. Gradually this mode of imaging is establishing its usefulness in other non-malignant conditions of bones and joints. This Chapter also emphasizes the extensive information that can be obtained with the use of pin-hole collimator, which is bound to be available in a nuclear medicine department of the developing countries because of their traditional obsession with thyroid imaging. What is not available is time to do many bone scans in a day in these monogamous (mono-gamma camera) units of the developing countries. Ideally, and rationally from the point of view of health care benefits, each nuclear medicine centre should have one gamma camera exclusively devoted to bone imaging.

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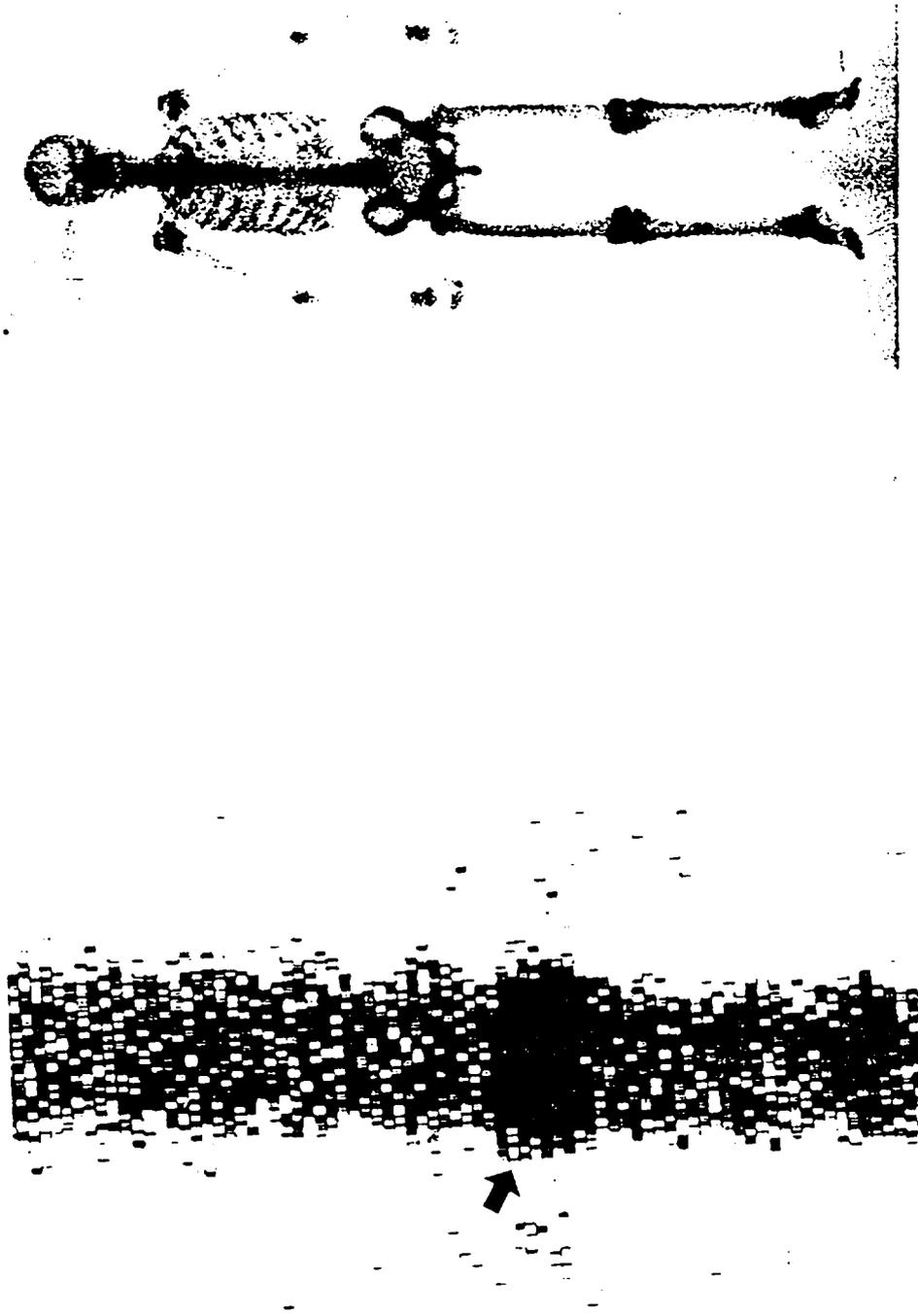


Fig. 30.2 Anterior single-pass view of the whole skeletal system.

Fig. 30.1 An anterior black-and-white photoscan of the thoracolumbar spine made with a rectilinear scanner. Intense radiouclide accumulation is seen in the body of D12 representing gastric cancer metastasis (arrow).



Fig. 30.3 A. Anterior low-energy converging collimator view of the chest showing a questionable hot area in the right suprasternal region (?).

Fig. 30.3 B. Anterior pinhole view of the area in question clearly localizing the hot spot in the costovertebral junction of D2 vertebra (arrow).

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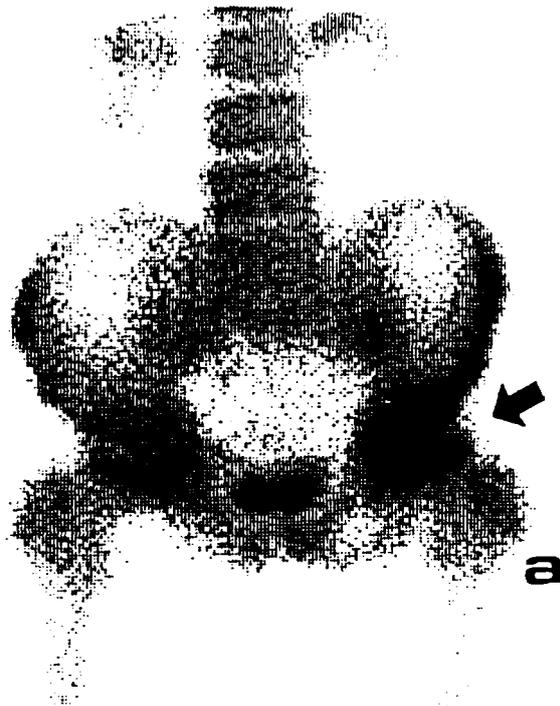


Fig. 30.4 A. Anterior view of the pelvis, tilted left anteriorly, showing fallacious increase in radionuclide accumulation in the left hip (arrow).

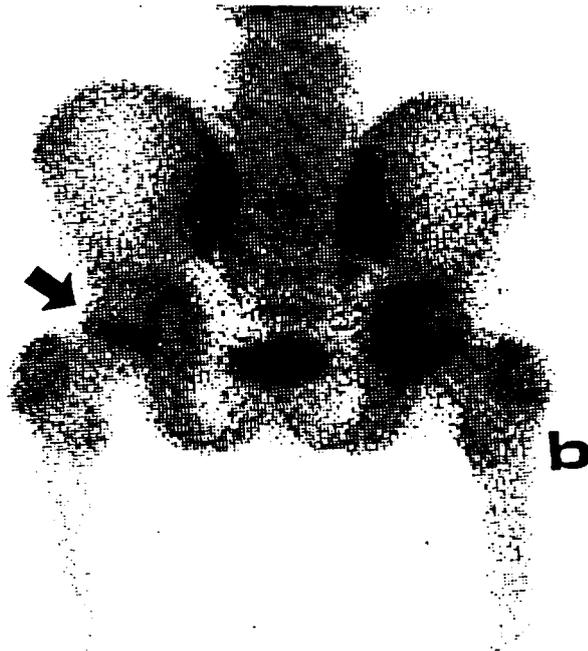


Fig. 30.4 B. Posterior view of the same hip showing normal left hip (arrow).



Fig. 30.5 Generalised increase in soft tissue radionuclide accumulation due to anasarca from advanced cancer.

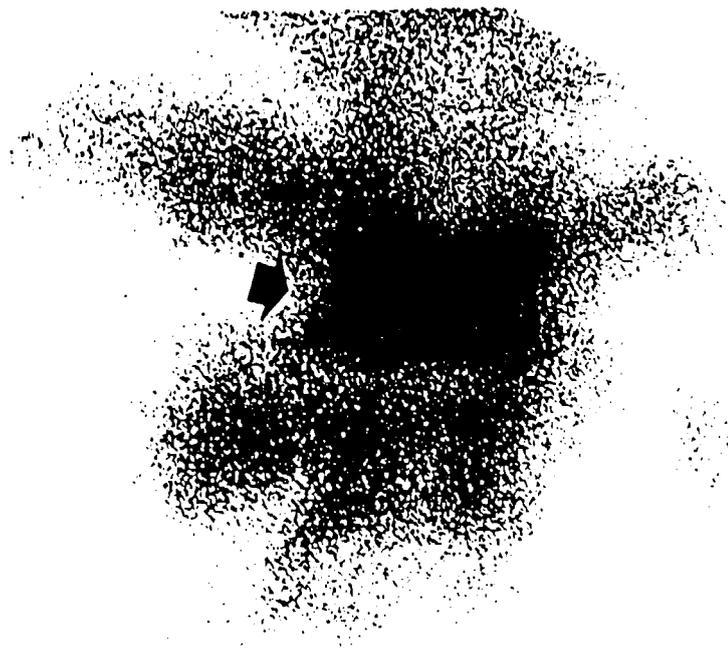


Fig. 30.6 Posterior pinhole view of D12 vertebra showing diffuse radionuclide accumulation due to metastasis from nasopharyngeal carcinoma (arrow).

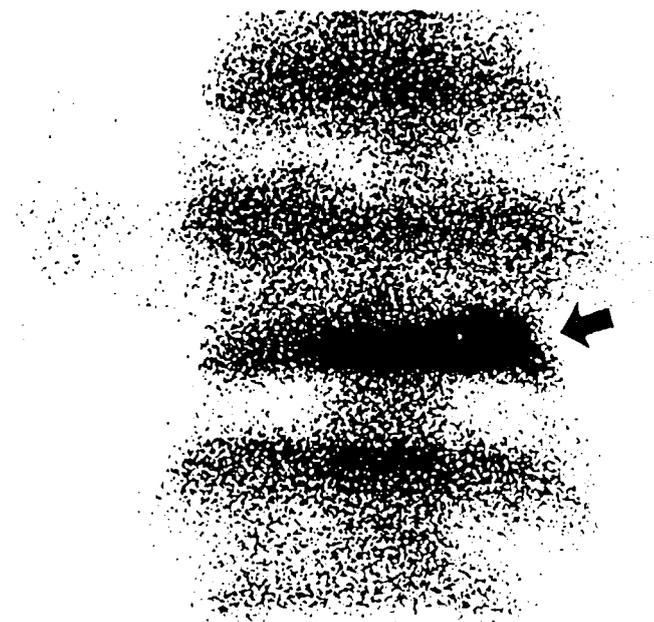


Fig. 30.12 Posterior pinhole view of L2 vertebra showing characteristic segmental radionuclide accumulation in the lower end plate representing breast cancer metastases (arrow).

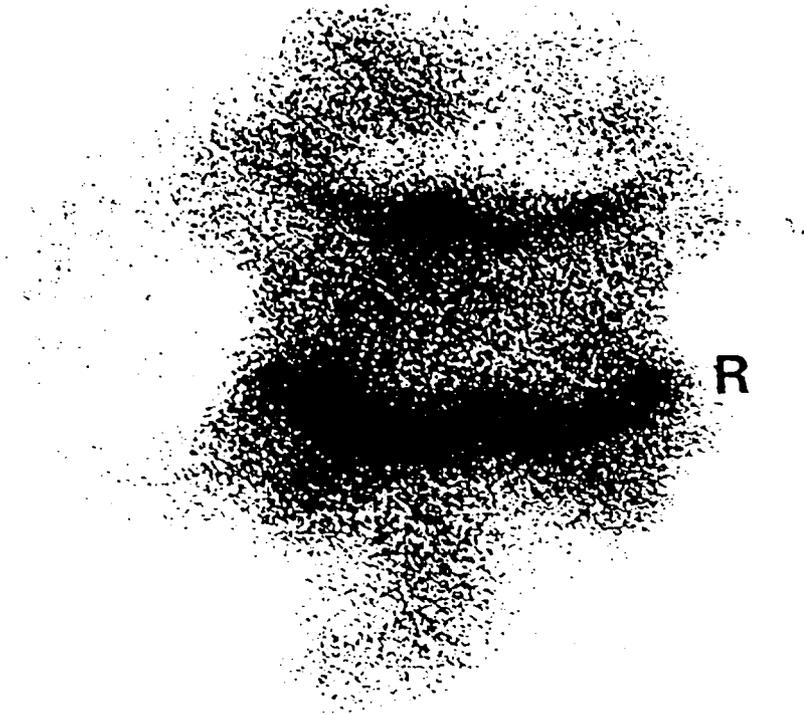


Fig. 30.7 Posterior pinhole view of D12 and L1 vertebrae showing characteristic arcuate radionuclide accumulation along fractured upper plates.

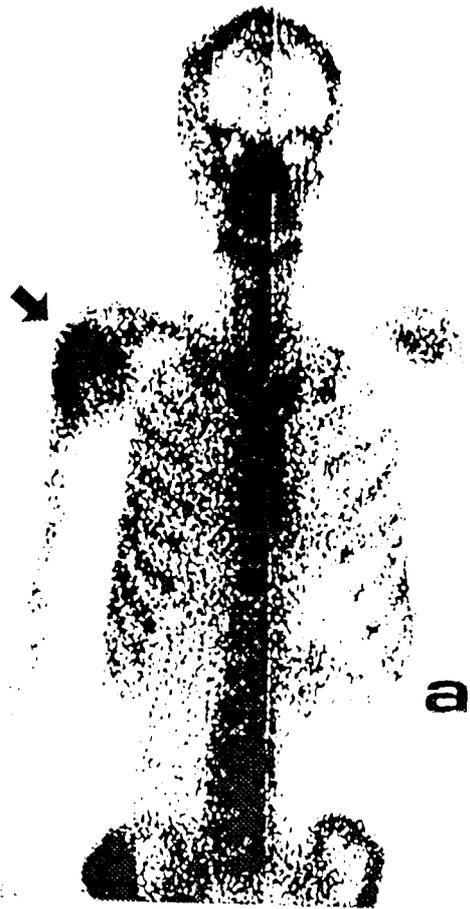


Fig. 30.8 A. Anterior single-pass view of the chest showing an ill defined hot area in the head of the right humerus (arrow). The lesion, does not appear to be photopaenic in this view.

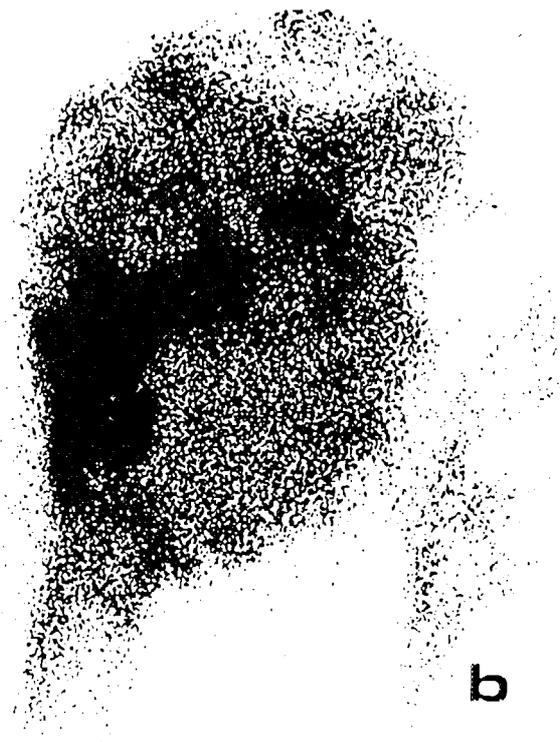


Fig. 30.8 B. Pinhole view of the humeral head showing the lesion to be predominantly osteopaenic with areas of increased radionuclide accumulation indicating pathological fracture.



Fig. 30.9 Posterior single-pass view of the whole skeletal system showing diffuse radionuclide accumulation in the spine and sacroiliac joint showing "super scan" appearance. Open arrows indicate markedly diminished radionuclide accumulation in the skull and limb bones. This is the case of gastric cancer metastasis.

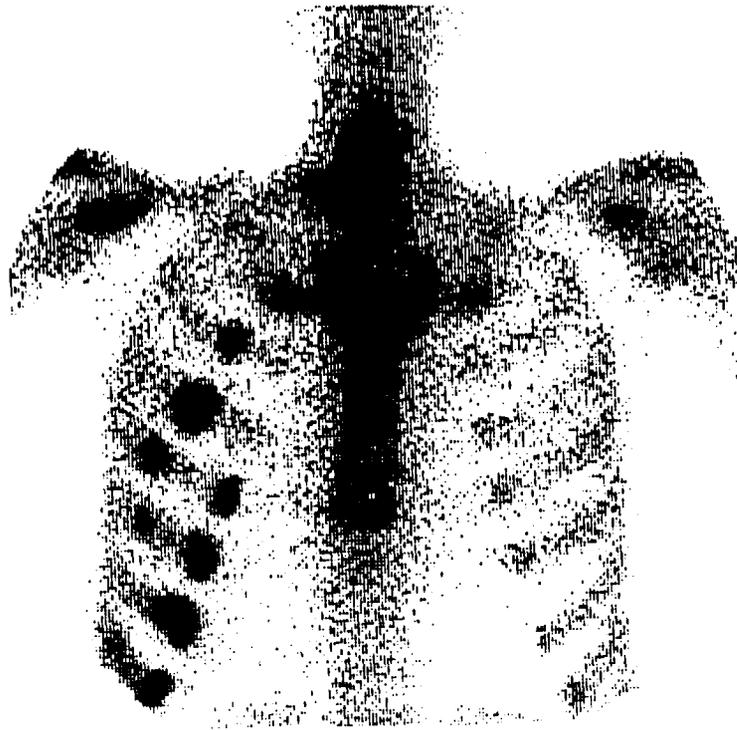


Fig. 30.10 Anterior view of the chest showing multiple rib fractures involving the right hemithorax. Band-like hot spots lined in a row are characteristic of fractures.



Fig. 30.11 Left anterior oblique view of the chest showing multiple elongated transverse hot areas involving many ribs representing breast cancer metastases (arrows).



Fig. 38.13 Pinhole scintigraph of the right proximal tibia showing a hot spot within hot area indicating the nidus surrounded by reactive osteosclerosis in osteoid osteoma.

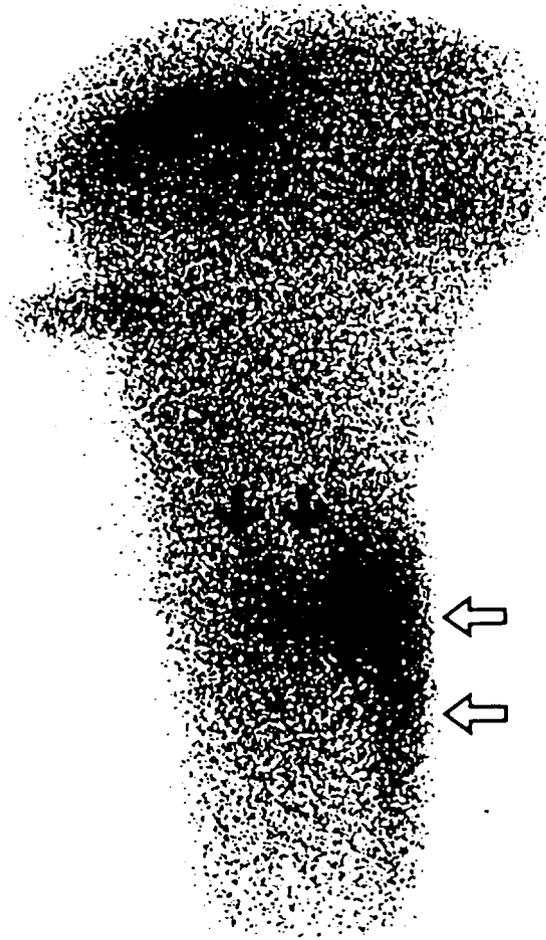


Fig. 30.14 Anterior pinhole view of the right proximal tibia showing radionuclide accumulation along stress fracture (solid arrows) and associated periosteal reaction (open arrows).

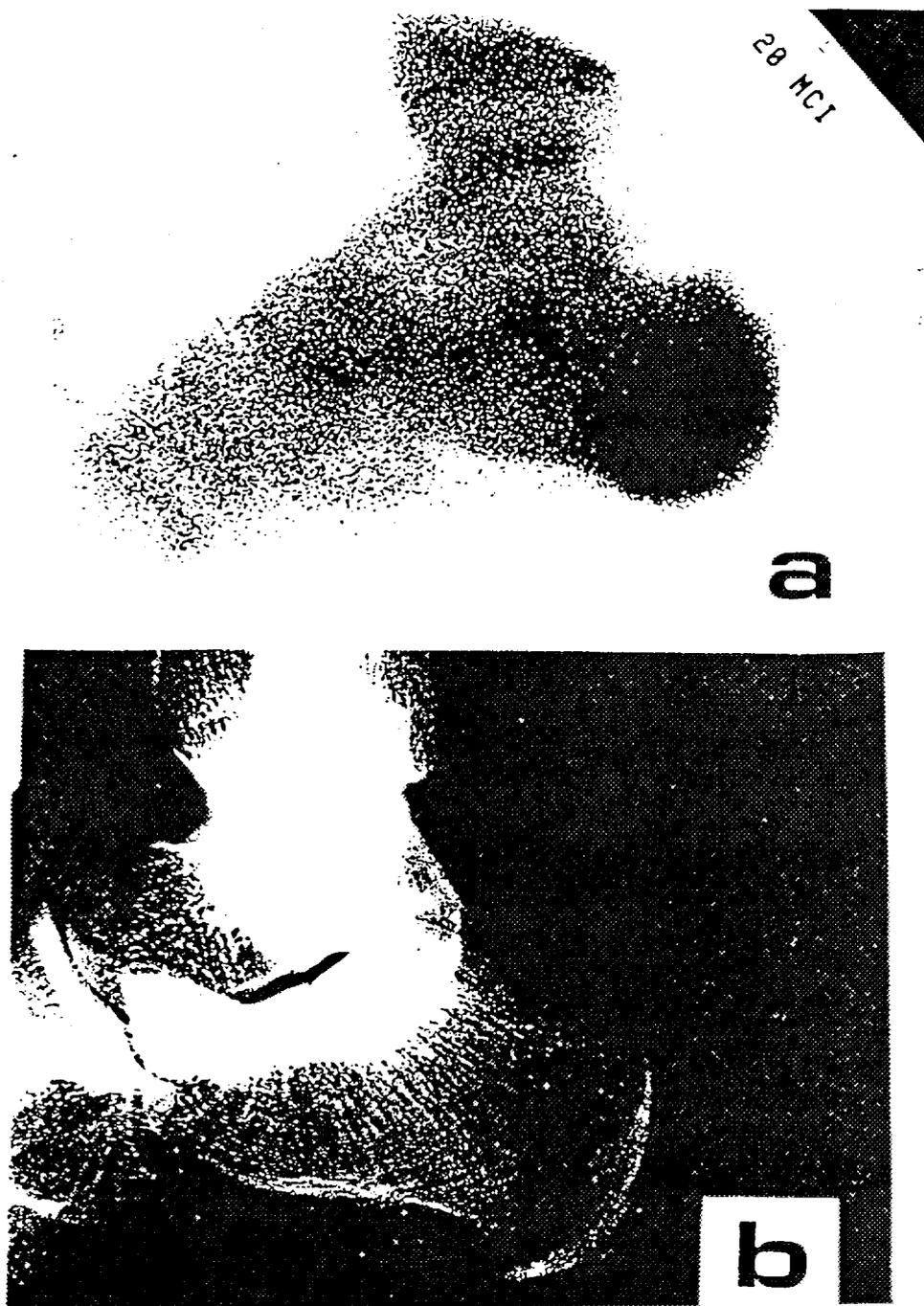


Fig. 30.15 A. Lateral pinhole view of the left os calcis showing diffuse increased radionuclide accumulation in the posterior aspect indicating bone contusion.

Fig. 30.15 B. Lateral X-ray of the same os calcis showing no bone abnormality.



Fig. 30.16 Anterior pinhole view of the pelvis showing photopaenic area in the left capital femoral epiphysis representing aseptic bone necrosis (Leg-Perthes Disease), (open arrows).



Fig. 30.17 Anterior single-pass view of the whole skeletal system showing generalized increase in radionuclide accumulation and several hot areas (arrows) representing osteomalacia and pseudofractures, respectively.



Fig. 30.18 A. Nuclear angiograph of the left lower extremity showing increased blood flow and blood pool in the distal femur in the site of acute osteomyelitis (arrow).

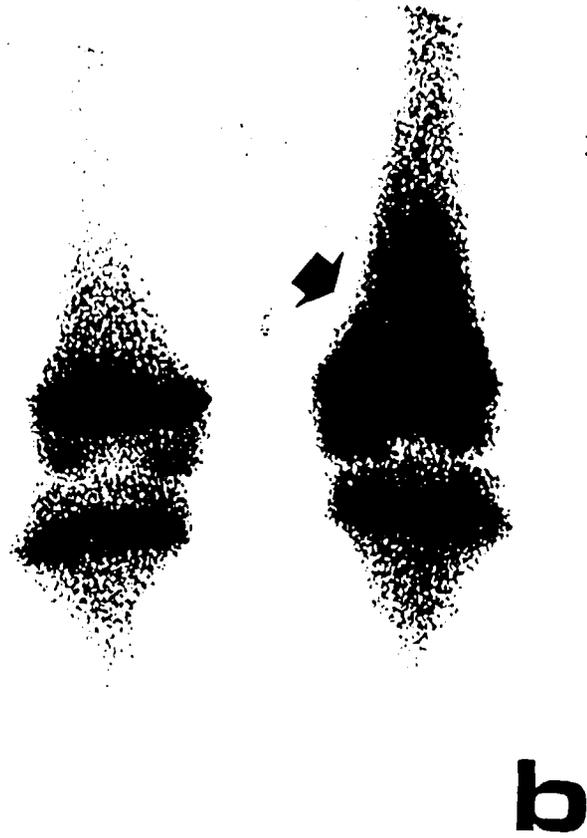


Fig. 30.18 B. Static view showing prominent radionuclide accumulation in the affected left distal femur (arrow).

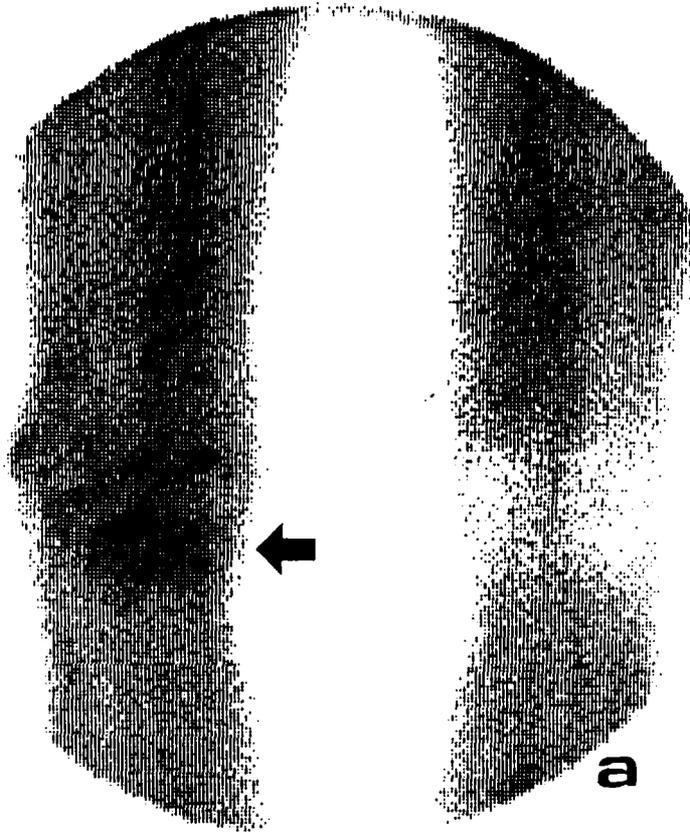


Fig. 30.19 A. Nuclear angiograph of the right lower extremity showing increased blood flow and blood pool in the septic right knee (arrow).

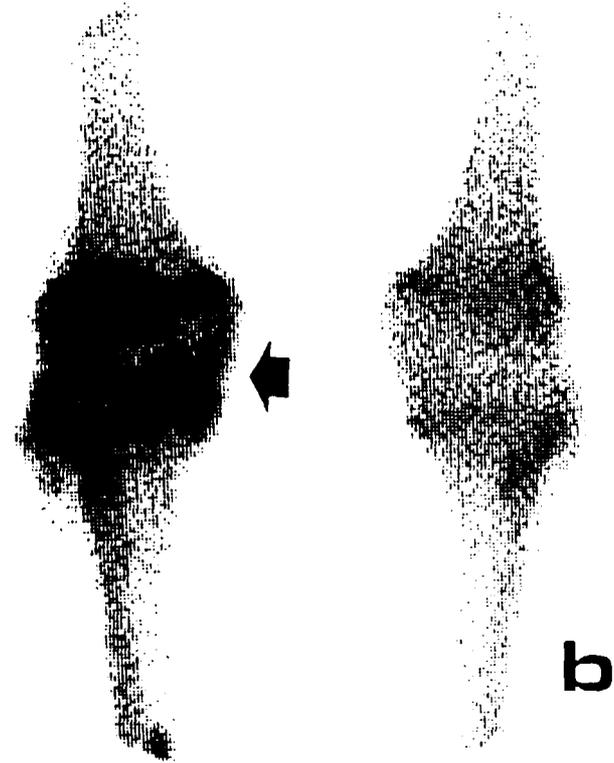


Fig. 30.19 B. Static view showing prominent radionuclide accumulation within the confinement of the joint capsule and periarticular bones (arrow).

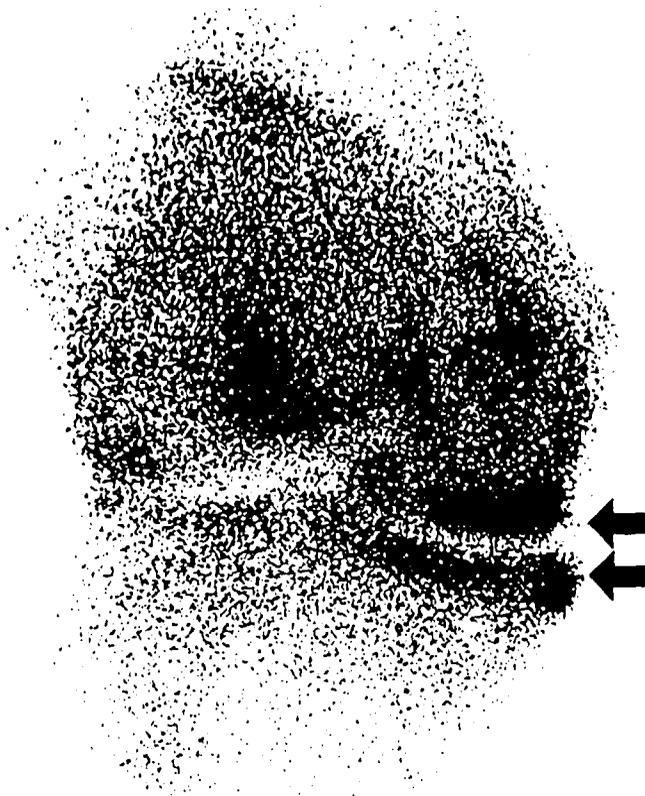


Fig. 3 .20 Anterior pinhole view of the right knee showing characteristic segmental localization of the radionuclide accumulation in subchondral bones of the medial compartment representing osteoarthritis (arrows).



Fig. 3 .21 Anterior pinhole view of the right knee showing intraosseous localization of radionuclide in the distal femur around the condylar fossa representing spontaneous osteonecrosis (arrows).