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Pinhole Scintigraphic Diagnosis of Bone Tumors

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Introduction

Imaging modalities presently available for the clinical diagnosis and basic research of bone tumors are versatile including radiography, conventional x-ray tomography, angiography, CT scan, MR imaging, ultrasonography and nuclear bone scan. Of these, radiography and high resolution CT scan are the two most useful means to image bone morphology both in normal and pathologic conditions. However, these two modalities are unable to provide any useful metabolic or chemical information in bone diseases as nuclear bone scan does. ^{99m}Tc-phosphate bone scan has unique capability to disclose both the morphologic and metabolic profile of most bone pathologies including tumors. Bone scan is useful not only for morphologic diagnosis but also for chemical profile studies in almost whole spectrum of bone diseases including metastasis in the preradiographic stage (Fig. 1), cryptic tumor invasion (Fig. 2), disseminated metastasis (Fig. 3) and multiple familial exostosis [1-3]. It is, however, to be mentioned that the ordinary planar bone scan obtained using a parallel hole collimator has limited image resolution due to the miniaturizing of image to 1/15 of the life size. Fortunately, this critical drawback can be remedied by pinhole scan which can readily restore image to an appropriate size, tremendously enhancing the image quality and hence the sensitivity and specificity[1-7].

Thus, pinhole scan has been amply shown to be a new potential diagnostic tool in skeletal oncology[1-7]. Indeed, many subtle morphologic and metabolic alterations, which are not seen on the ordinary planar or even SPECT images, are portrayed in an amazing detail by pinhole scan. Some of the typical applications of pinhole scan are the delineation of metabolic profile of various tumors and tumorous conditions[1-3,5,7], precise localization of nidus in osteoid osteoma[5], the detection of intramedullary skip metastasis in giant cell tumor and osteosarcoma[8] (Fig. 4), the differential diagnosis of osteosarcoma, giant cell tumor, simple and aneurysmal bone cyst and ossifying and non-ossifying fibromas[1] and unexplained bone pains (Fig. 1).

Thus, it follows that more systematic and widespread use of pinhole scan is to be

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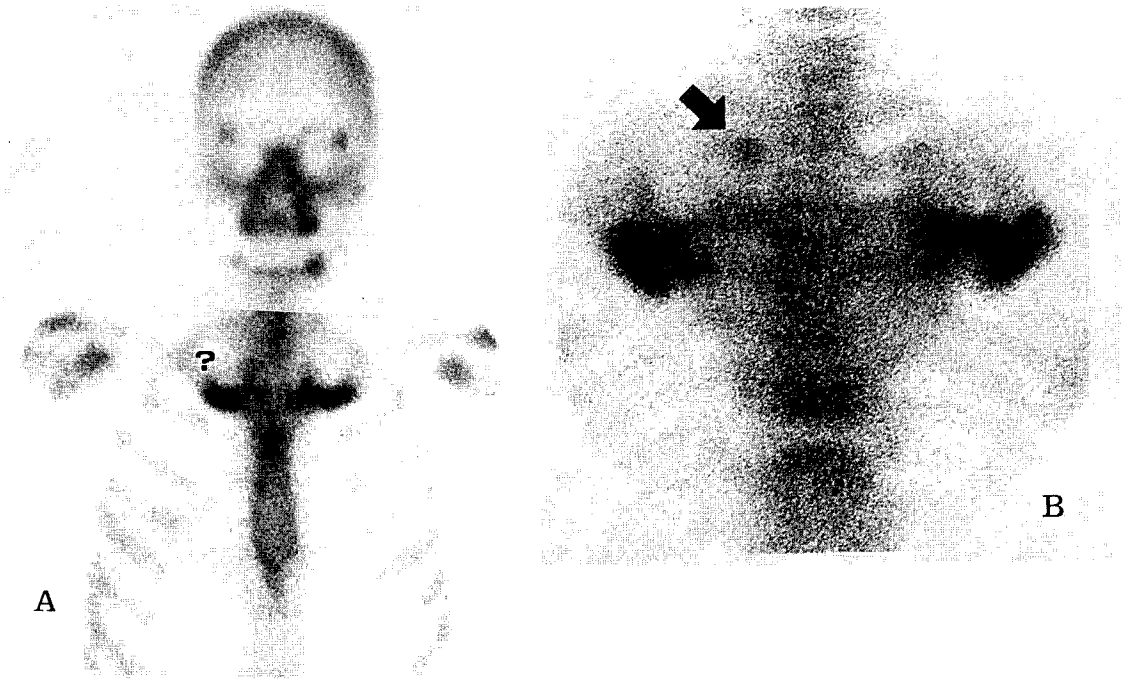

Fig. 1. Difference in sensitivity between planar scan and pinhole scan.
A. Planar scan fails to show abnormality(?).
B. Pinhole scan distinctly visualizes a small hot area in the right transverse process of T2 denoting metastasis(arrow). Note physiological increased tracer uptake in costosternal junctions(CS).

encouraged with the anticipation of founding a new domain of combined anatomic and metabolic diagnosis of tumors and tumorous conditions of bone. This article describes the scope and practical applications of pinholescan in skeletal oncology.

Metastasis

Unlike in primary bone tumors, radiography plays a relatively unimportant role in the diagnosis of metastatic bone tumors because significant bone destruction is to be present before the lesion is radiographically visible. It is also true that pathology cannot be seen if it occurs in a complex or thin and small bone such as the vertebra, scapula, sternum and rib especially when the bones are porotic and faint. Moreover, the radiographic diagnosis of metastasis or polyostotic disease can be incomplete because the film sizes are such that radiography can visualize the skeleton only in part at one time. In contrast, bone scan is able to visualize the whole skeleton from the vertex to the toes in a single-pass scanning (Fig. 2). For example, if only the skull is examined radiographically for the local swelling in widespread metastasis the disseminated lesions may easily disguise as local pathology, whereas bone scan can disclose the true state of widespread metastases (Fig. 2). The small lesions in complex and small, thin and porotic bones can be effectively diagnosed. Pinhole scan and SPECT are useful in the study of metastasis especially in the thoracic and sacral bones whose anatomy is complex and overlaps with other structures in the

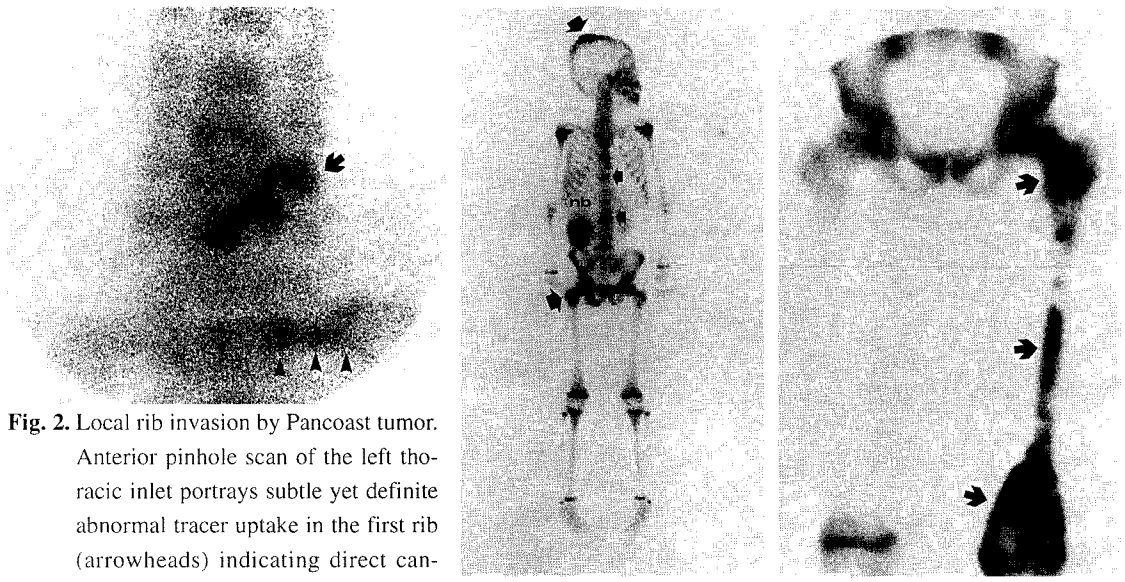

Fig. 2. Local rib invasion by Pancoast tumor. Anterior pinhole scan of the left thoracic inlet portrays subtle yet definite abnormal tracer uptake in the first rib (arrowheads) indicating direct cancer invasion. This finding was not shown on planar image (not shown here). In addition, there is the demonstration of quite unexpected distant metastasis in the lower cervical spine (arrow)

Fig. 3. Usefulness of panoramic whole-body scan in tumor diagnosis. Anterior whole-body scan shows a hot area in the vertex (topmost arrow) to be one of many metastatic lesions of neuroblastoma (nb). Initially, the cranial bone lesion was thought to be a focal sclerotic reaction to meningioma on radiograph.

Fig. 4. Usefulness of bone scan in the detection of intramedullary skip metastasis in osteosarcoma. Composite anterior pinhole scan of the pelvis and left femur shows primary osteosarcoma in the distal femur (lowermost arrow) and skip intramedullary metastases in the upper and middle thirds (other two arrows).

mediastinum and pelvis, respectively (Figs. 1, 4). What is further advantageous is that bone scan is a sensitive test permitting early preradiographic diagnosis of metastasis.

It has been shown that planar scans including the planar SPECT is more often than not deceptively normal and discouragingly low in specificity[9-12] (Fig. 1). Pinhole scan is an easily practicable breakthrough and effective remedy[1,4,6] (Figs. 1, 2, 5-8). A typical case of false negative planar scan result is shown in Fig. 1. Indeed, planar scan fails to demonstrate the small cancer metastasis in the right transverse process of T2 vertebra but pinhole scan portrays it so distinctly. One screening study reported the incidence of false negative bone scan test in metastasis to be less than 3%[13] which is not acceptably low. Judicious use of pinhole scan can significantly reduce false negative results and greatly enhances the specificity at the same time (Figs. 1, 2).

A notorious scintigraphic dilemma is that some highly aggressive metastases and myelomatosis do not accumulate tracer presenting as photopenic lesions easily passing undiagnosed[14,15]. The metastasis from renal cell carcinoma is well known for its coldness [16] but there is peripheral tracer accumulation which is sufficient for diagnostic recognition. Other primary tumors which create cold metastasis include cancers of the gastrointestinal tract, breast, nasopharynx and larynx. There are certain scintigraphic patterns which may be linked with metastases. For example, the hot areas in the calvari-

um, scapula, sternum, vertebra, pelvis and long bone shaft have been described to be related with metastases. Of course, multiplicity of such hot areas strongly supports metastases. Metastasis becomes even likelier when lesions are scattered randomly with heavier involvement of the bones having active hematopoietic marrows, producing the "superscan" sign. As in some primary bone tumors the scintigraphic characterization can be attempted at in metastatic bone tumors when one uses pinhole scan[6] (Figs. 5, 6). Occasionally, pinhole scan clearly discloses cold area(s) within a lesion which appears to be hot on planar image, creating the characteristic "ring" or "frame" sign. The sign has been observed in the metastases from carcinomas of the lung, breast, stomach and kidney and pathologically related to necrosis, hypovascularity and aggressive invasion. Conversely, pinhole scan can delineate septum-like or mottled areas of increased tracer uptake in an apparently cold metastatic lesion[6] (Fig. 5). These two contrasting situations attest to the fact that pinhole scan is

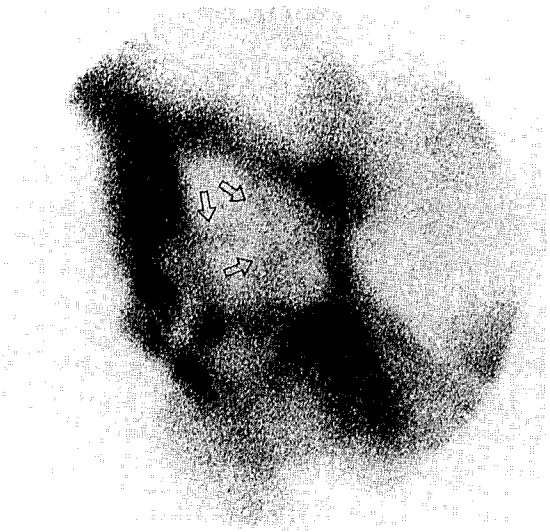

Fig. 5. Septated photopenic presentation of follicular thyroid carcinoma metastasis. Anterior pinhole scan of the right iliac bone shows a large irregular photopenic defect with septation (open arrows). The septation was not seen on the planar scan which presented the lesion simply as a cold defect (not shown here).

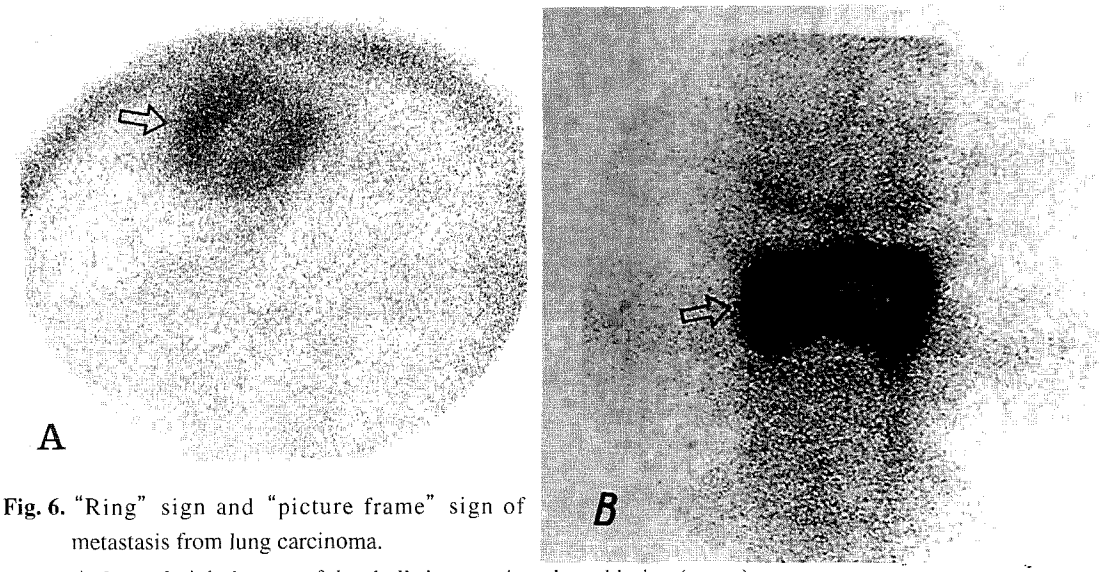

Fig. 6. "Ring" sign and "picture frame" sign of metastasis from lung carcinoma.

A. Lateral pinhole scan of the skull shows a ring-shaped lesion (arrow).

B. Posterior pinhole scan of T10 shows a classic "picture frame" sign (arrow). These lesions were presented as hot areas on the planar scan (not shown here).

not only sensitive to portray inhomogeneity of an apparently homogeneous lesion but virtually indispensable for the accurate assessment of bone tumors. Pinhole scan is also useful for the detection of intramedullary skip metastasis in osteosarcoma (Fig. 4).

The direct invasion of local bone is another mode of metastasis. Some of typical examples are Pancoast tumor in the thoracic inlet with direct invasion of the regional rib (Fig. 2), rectal cancer with contiguous spread to the sacrum and nasopharyngeal cancer with spread to the regional bone including the clivus[1]. It is to be emphasized that tracer uptake in direct invasion site is often inconspicuous on planar bone scans, necessitating pinhole scan to prevent false negative study (Fig. 2).

Primary Bone Tumors

As mentioned already radiography is simple yet the most useful diagnostic tool of primary bone tumors. However, in spite of the resolution which is lower than that of radiography, bone scan has been used rather extensively in the studies of a large variety of primary bone tumors with accumulation of a substantial volume of valuable information. One important reason is probably that bone scan, pinhole scan in particular, can provide the information regarding the metabolic or chemical alterations of bone tumors which is obtainable by no other imaging modalities available at present.

The primary malignant bone tumors of scintigraphic interest include osteosarcoma, chondrosarcoma, Ewing's sarcoma, fibrosarcoma, chordoma and myeloma. On the other hand, the benign bone tumors originated from bone, cartilage, fibrous tissue, vessels and unknown tissue make up another group of relative indication of bone scan[1]. The benign group embraces osteochondroma, enostosis, osteoma, osteoid osteoma, enchondroma, chondroblastoma, fibroma, fibrous conversion defect, simple bone cyst, aneurysmal bone cyst and giant cell tumor. Of these osteoid osteoma, osteochondroma, bone cysts and giant cell tumor are of scintigraphic interest[1,5].

Malignant Bone Tumors

Osteosarcoma

Osteosarcoma is characterized by its capability to produce neoplastic bone tissues, hence osteogenic sarcoma. This is the most common variety of malignant bone tumors in the pediatric and adolescent age groups. The most common site of involvement is the bones about the knee and the next most common site is the proximal humerus[8]. Bone scan is characterized by either hyper- or hypovascularity, intense tracer uptake with photopenic component, bone distortion and moderately well defined margin. Pinhole scan reveals some specific findings, disclosing the true nature of the tumor. Indeed, while planar bone scan shows simple "bone distortion" in osteosarcoma pinhole scan can separate the simple alteration into the main host bone reaction and neoplastic osteogenesis in the periosteum and adjacent soft tissue which is known as the "sunburst" sign (Fig. 7). Also, pinhole scan is able to delineate the characteristic acute rupture of periosteal reaction, the well-known Codman's triangle sign of malignacy (Fig. 9). The telangiectatic subtype of osteosarcoma strognly resemble aneurysmal bone cyst in so far as the radiographic and scan findings are concerned. Unlike ordinary osteosarcoma, however, the telangiectatic varient does not concentrate

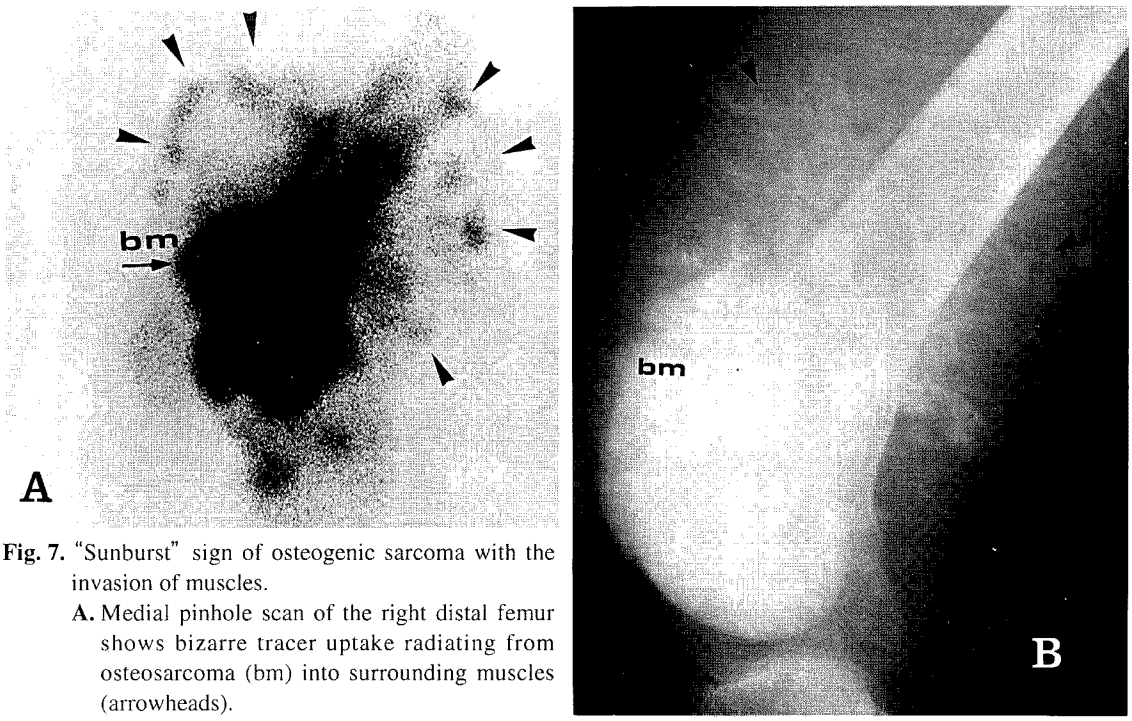

Fig. 7. "Sunburst" sign of osteogenic sarcoma with the invasion of muscles.

A. Medial pinhole scan of the right distal femur shows bizarre tracer uptake radiating from osteosarcoma (bm) into surrounding muscles (arrowheads).

B. Radiograph shows typical "sunburst" sign of spicular bone formation which haphazardly invade the muscle layers (arrowheads). bm denotes primary osteogenic sarcoma.

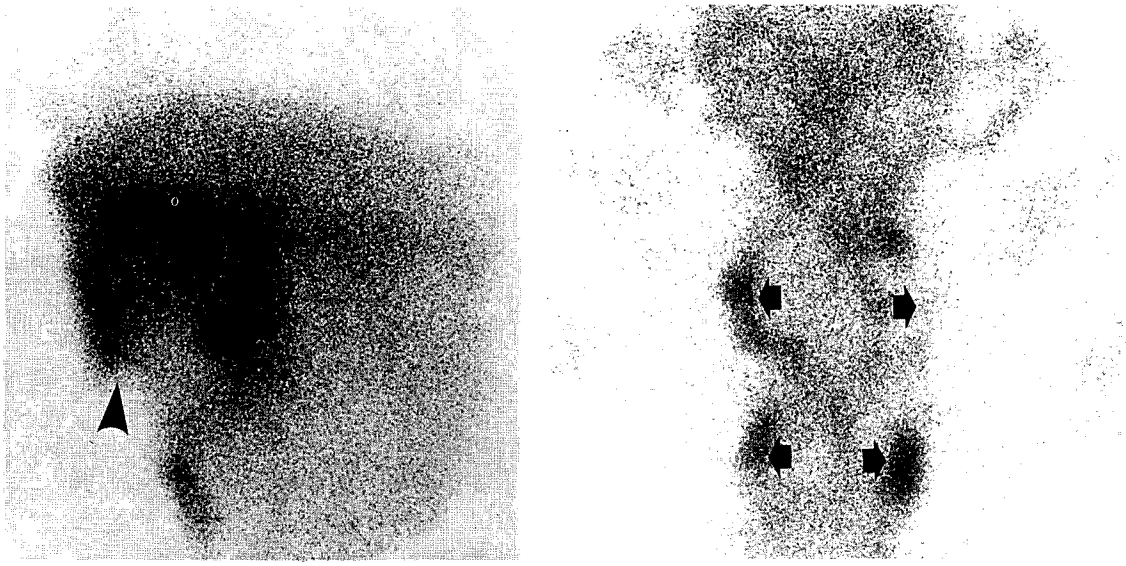

Fig. 8. Pinhole scan version of Codman' s triangle in osteogenic sarcoma. Anterior pinhole scan of the right proximal tibia shows a photopenic lesion surrounded by reactive hot area and disrupted elevated periosteum representing the classic triangle sign (arrowheads).

Fig. 9. "Broken egg-shell" sign of plasmacytoma in the sternal body. Anterior pinhole scan shows expansile photopenic lesions with scalloped margin and dotted hot areas in ruptured cortex (arrows).

tracer manifesting a cold lesion.

Chondrosarcoma

The basic tissue is cartilaginous which may become either myxomatous, calcified or even ossified. The cell differentiation ranges from nearly benign one to highly malignant. The tumor is either primary in form or transformed from a preexisting benign tumor such as osteochondroma, enchondroma or exostoses. The incidence of the primary type is 76-90%[8] . This is the tumor of middle to old ages with male predilection. The femur, humerus and axial skeleton are affected in more than 75%. Bone scan findings are increased blood flow, decreased tracer uptake, mild bone distortion and sharp demarcation. Pinhole scan reveals the tumor to be basically photopenic with watershed. Correlation with radiograph shows the photopenic area to correspond with osteolysis which is hypodense cartilaginous tissue on CT scan. The hot area represents hyperdense bone tissue.

Fibrosarcomas

Malignant fibrous tumors of bone are primary and secondary fibrosarcomas and malignant fibrous histiocytoma which has been established as a distinct entity. The primary form may originate from medullary space, periosteum or soft tissue with extension to adjacent bone. Histologically, tumor cells are spindle shaped producing no bone. The cell differentiation varies from low one to highly malignant. This is a tumor of the middle age without gender predilection. Slightly more than 50% are found in the knee bones and humerus. Secondary fibrosarcomas imply the sarcomatous transformation of pagetoid bones, bone infarcts or irradiated bones. Bone scan is nonspecific simply showing photopenic defect surrounded by an irregular rim of intense tracer uptake. Infiltrative variants may present patchy areas of tracer uptake intermixed with irregular cold area. Pinhole scan can effectively detect intramedullary spreads. The basic scan manifestations of malignant fibrous histiocytoma with bone destruction are essentially the same as those of osteolytic primary fibrosarcoma but the "bubbly" form may show septations.

Plasma Cell Diseases

Histology is characterized by the neoplastic proliferation of abnormal plasma cells in the hematopoietic marrow. When diagnosed first the lesions may be multiple (over 50%), generalized or diffuse (15%) or solitary (25%), but the solitary form eventually develops to either the multiple or generalized form. Radiographically, the last named form often disguises as simple osteoporosis. The spine, pelvis, skull, sternum, and shoulder bones are commonly involved. Peak incidence is in the middle age. Bone scan is of limited value because myelomas usually do not accumulate tracer regardless of type. In some clinical situations, however, bone scan is useful. The most important indication of a bone scan is pathologic fracture of myelomatosis in an aged subject with osteoporosis. Its radiographic detection is extremely difficult because of osteoporosis. As well known, fractures avidly concentrate tracer helping its easy recognition. The next important indication is perhaps plasmacytoma in a small or thin bone such as the sternum and rib. In these bones, even a sizable lesion can easily be overlooked radiographically. Pinhole

scan, however, can often show findings which indicate the disease (Fig. 9). The third indication is the diagnosis of the radiographically invisible lesions which are rare.

Chordoma

Chordoma is a slow-growing, low malignancy tumor which originates from the pri-mitive notochordal remnants. Histologically, the tumor is characterized by the lobule formation of highly vacuolated cells and mucoid intercellular material[8]. Typically, it involves the caudal sacrum and the clivus near the sphenooccipital synchondrosis. Incidence ranges from 1% to 4% and is nearly twice as much common in men as in women. The majority of cases occur between the fourth and seventh decades of life. Clinical manifestations relate closely to the location of the tumor. Initially, the symptoms are mild and nonspecific. The sacrococcygeal involvement is characterized by progressive perineal pain, constipation, urinary difficulty and bleeding. The skull base tumor may increase the intracranial pressure and compress the adjacent structures manifesting headaches, blurred vision, memory loss and emotional instability. When the vertebra is involved, the tumor gradually invades the spinal cord and nerve roots, causing pain, numbness, motor weakness and paralysis. Bone scan is useful for the portrayal of expansile cold defect in the central caudal sacrum. The defect can be outlined by irregularly interconnected hot areas of reactive and destructive bones around the tumor, resembling the solitary plasmacytoma in irregular bones[1].

Benign Bone Tumors

Osteoid Osteoma

Osteoid osteoma is a painful tumor richly innervated with nerve fibers. Histologically, the tumor is characterized by the presence of nidus and prominent osteoblastic reaction. The nidus is a variously mineralized meshwork of osteoid and woven bone with osteoclasts and dilated vessels. This is a tumor of the second to third decades of life with 2-3 times higher incidence in men. Incidence in a Mayo Clinic series was 12.1% of all benign bone tumors[17]. More than one half of cases involve the femur and tibia. The vertebral arches are also frequently involved. Bone scan is sensitive and often specific. Pinhole scan is quite unique portraying the "hotter spot within a hot area" sign which is nearly pathognomonic[5] (Fig. 10). The central "hotter" spot and surrounding "hot" area represent respectively the nidus and reactive sclerosis. Bone scan is valuable in detecting the nidus in the early phase or in irregular bones, especially when radiographic findings are equivocal. Bone scan has been utilized for the localization of the nidus during surgery.

Enostosis (Bone Island)

This is an innocuous commonplace bone lesion of adults, being found in any bone but with a predilection for the pelvis, femur, and ribs. Enostosis is made up of compact lamellar bone which contains haversian system. General incidence is unknown but one radiographic study of 189 subjects showed an incidence of 1.1% in the pelvic bone. Both genders are affected nearly equally. The lesion is roundish or elongated in shape and 2 mm to 2 cm in size. Rarely, giant variant can attain a size of 4 cm[18]. It is known to change in size and may even vanish. Its important clinical implication is potential mimicry of metastasis. It is different from

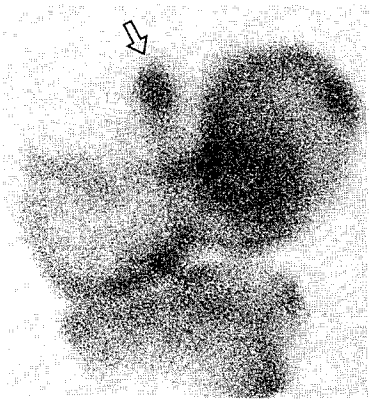

Fig. 10. "Hotter spot within hot area" sign of osteoid osteoma. Anterior pinhole scan of the right proximal tibia shows a small spotty extremely hot area surrounded by less intense tracer uptake in the medial cortex representing the nidus.

Fig. 11. Bone island. Anterior pinhole scan of the distal right femur shows a bean-sized lesion with moderate tracer uptake (arrow). The lesion is discrete and has a vertical orientation within cancellous bones.

osteoma which almost exclusively involves the skull, especially the frontal and ethmoid sinuses. Bone scan shows tracer accumulation in about one half of cases and the remainder invisible. Pinhole scan portrays an enostosis as roundish or void tracer uptake. The contour is fuzzy and characteristically aligned longitudinally when it is in long bones. Pinhole scan is clearly more sensitive than the planar scan showing increased tracer uptake in some enostoses which are cold and invisible on the planar scan (Fig. 11).

Fibrous Cortical Defect and Nonossifying Fibroma

Fibrous cortical defect and nonossifying fibroma are closely related each other and have been described as two different evolutional forms of the same process. The lesions consist of non-neoplastic fibrous tissue characterized by a spindle-cell mesenchymal hyperplasia of transient nature. Clinically, fibrous defect is innocuous and detected by chance in children. It is solitary and affects the cortex of long bones. The vast majority of cases spontaneously regress during childhood and adolescence. However, a small fraction of cases proliferate to become nonossifying fibroma in the medullary space. Occasionally, it may be fractured causing pain. This is a disease of the late childhood or adolescence, and, with age, most of lesions gradually become restored to a normal bone by centripetal host bone replacement. Bone scan is usually not helpful, but pinhole scan can demonstrate the characteristic ring-like tracer uptake encircling an ovoid photopenic lesion within or near the cortex. Tracer is accumulated in the sclerotic margin and its lateral border abuts on the adjacent cortex when the lesion is subcortical (Fig. 12). Fibrous defects may resemble simple bone cysts, but cysts are central in location and concentric in the diaphysis of long bone.

Osteochondroma (Exostosis)

Osteochondroma is a benign cartilage-capped osseous protuberance of the metaph-

ysis, hence exostosis. The tumor consists of regular cortical and medullary bone formed from enchondral ossification of cartilaginous cap. The tumor is either sessile or pedunculated. When multiple the condition is called multiple exostoses. It has a great tendency toward malignant transformation. The incidence ranges from 20% to 35.8% of all benign tumors, comprising one of the most common benign tumors[8]. About 75% of solitary lesions are seen before the age of 30. The vast majority of cases remain as a painless lump. In some cases mechanical irritation, nerve compression, fracture or malignant transformation may produce pain. Radiographic features vary according to whether tumor is pedunculated or sessile. The cartilaginous element of the tumor is radiographically invisible. Bone scan shows tracer uptake in the osseous part but not in the cartilaginous part. Pinhole scan can portray even very subtle change in the aged lesion which cannot be detected by the planar scan[1]. Magnified pinhole scan reveals the characteristic crest-like hot area indicating the zone of active turnover of cartilage into mature bone (Fig. 13).

Primary Bone Cysts

Cysts that primarily originate from marrow space include simple unicameral bone cyst and aneurysmal bone cyst. The former is true cyst containing clear serous fluid and a fibrous lining, whereas the latter consists of multilocular cystic mass containing free flowing blood or fluid with rare endothelial lining. Approximately 95% of **simple bone cysts** involve the metaphysis near the physeal plate in growing long bone[8]. The proximal metaphysis of the humerus and femur are the most frequent sites of involvement.

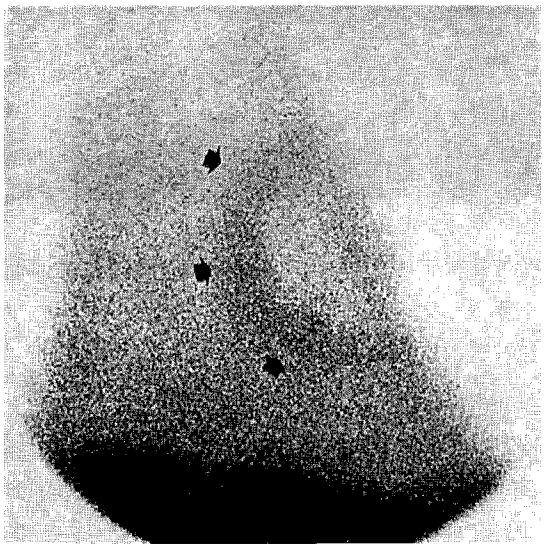

Fig. 12. Fibrous cortical defect. Anterior pinhole scan of the distal right femur shows a photopenic ovoid lesion surrounded by subtle tracer uptake in the periphery (arrows). Note that the lesion abuts to the cortex.

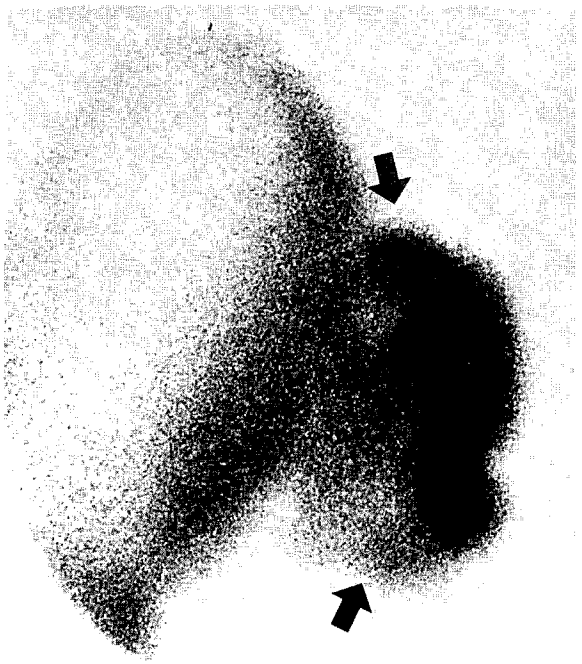

Fig. 13. Young osteochondroma with the "crest" sign. Anterior pinhole scan of the left iliac bone shows very intense tracer uptake in the crest of osteochondroma which is the zone of active bone turnover.

Other limb bones and pelvic bones are also affected. Planar bone scan is not helpful. Pinhole scan, however, can portray specific signs. Cysts which contain fluid or blood are indicated by ring-like tracer uptake in cyst wall (Fig. 14). Old cyst with reparative osteofibrosis may concentrate tracer diffusely obliterating ring-like accumulation. Instead, an "extended" tracer uptake can be seen around the cyst denoting bone reaction. Fallen fragment is not visualized because it is devascularized but undetached fragment may concentrate tracer[1]. **Aneurys-mal bone cyst** is multilocular cystic tumor containing free flowing blood or fluid. It may grow and expand rapidly with haphazard bone destruction strongly mimicking malignant tumor. The etiology may be related with trauma. Thirty-two% of cases occur in relation to giant cell tumor, chondroblastoma, simple cyst and telangiectatic osteosarcoma. In occasional cases prominent periosteal new bone formation is seen about the cyst and in others cyst is osteoblastic or filled with new bones. The cyst occurs virtually in any bone with the long bone and spine being affected in 50-60%. Unlike simple cyst, aneurysmal bone cyst may involve the skull, mandible, maxilla, ribs and patella. Swelling and pain are the presenting symptoms in 85%. Bone scan reveals increased tracer uptake in the periphery of cyst the content of which is photopenic. Peripheral uptake is typically irregular contrasting with smooth ring-like uptake of uncomplicated simple cyst. The tracer uptake is inconspicuous unless it is complicated with fracture. Pinhole scan may visualize septation reflecting the bubbly nature of the lesion.

Giant Cell Tumor

Giant cell tumor is common in adults in the third and fourth decades of life comprising 5% of all bone tumors[8] . Histology is characterized by benign looking osteoclast-like giant cells and stromal cells. The tumor has strong predilection for the long bone ends and is located eccentrically. In more than one half of cases the knee bones are affected and the next most common sites include the distal end of the radius and the sacrum. The clinical features are pain and swelling with occasional pathologic fractures. Bone scan shows ring-like or diffuse tracer uptake which is intense. Pinhole scan may show the caracteristic bubbly appearance

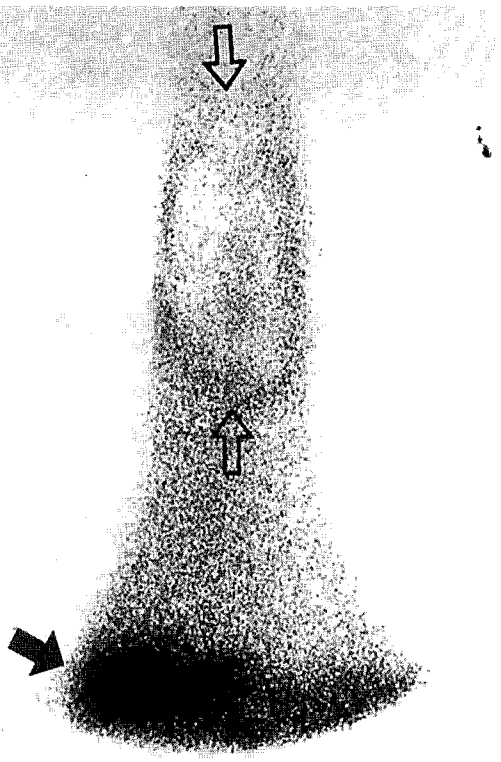

Fig. 14. Simple bone cyst. Anterior pinhole scan of the left distal femur shows a small egg-sized photopenic lesion with faint tracer uptake in the wall (open arrows). There is an intense physiologic tracer uptake in the growing distal femoral metaphysis (solid arrow).

Fig. 15. Giant cell tumor. Anterior pinhole scan of the right distal radius shows a large irregularly expansile photopenic lesion with increased tracer uptake in the wall. Note the bubbly appearance of the lesion.

(Fig. 15). An extended tracer uptake around the tumor is not uncommon.

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