715381

BERKELEY: DONNER LABORATORY

19 February 1981
Refer to 81RM053

Dobie Jenkins
Committee for the Protection
of Human Subjects
A & E Building
Campus

RE: CPHS #80-9-15

Dear Dobie:

Enclosed is the revised version of the referenced consent form for patients involved in both our protocol ("Brain Tumor Localization and Blood Brain Barrier Studies Using Rb-82") and Dr. Fabrikant's protocol ("Investigation of Charged-Particle Beams for Radiological Neurosurgery in Treatment of CNS Disorders"). Section 2.b. of the consent form is revised so that patients are informed that they are receiving an additional exposure of radiation.

I hope this modification is satisfactory to the Committee.

Sincerely,

Chi-Kwan Yen, M.D.
Principal Investigator

CKY:mg
Enclosure

cc: LBL Human Use Committee

Rev. 2/81
A/V

CONSENT TO ACT AS SUBJECT

FOR

TRANSVERSE SECTION AND TOMOGRAPHIC IMAGING USING RUBIDIUM-82

The diagnostic procedure of imaging the brain in transverse section is a new method for determining the health of brain tissue. The isotope, rubidium-82, goes into brain if the brain tissue is damaged. This procedure may aid a physician in evaluating the extent and location of the blood vessel abnormalities. There is little discomfort from the injection of the isotope as the radiation dose is far less than that received from angiographic or other nuclear medicine procedures. Only a few places in the world have the instrumentation and isotopes available for this new procedure.

Subject's name _____

Date _____

1. I hereby authorize _____
(name of person(s) who will perform diagnostic procedures)

and/or such qualified assistants as may be selected by him to perform the following:

Radiographs of the brain will be made using a rubidium isotope. This isotope will be injected intravenously using saline (salt water) for the infusion. I will rest comfortably on my back and may have EKG electrodes on both arms or chest during this procedure. The information from the brain will be detected by a ring of crystal detectors. A few injections might be necessary. The entire procedure will take 1 1/2 to 2 hours.

2. I understand that the procedure described in Paragraph 1 involves the following risks and discomforts:

   a. Slight discomfort associated with placement of the indwelling intravenous needle.

   b. The radiation received in this study is in addition to the radiation associated with therapeutic irradiation. There is some risk associated with any radiation exposure. The dosage involved in these procedures is small and is equivalent to the dose from routine nuclear medicine procedures for examination of the heart, lungs, brain or kidneys. The whole-body dose from the isotope is only 0.073 rad or equivalent to 1/2 the natural background dose for one year. The kidneys receive the maximum dose which is 4.3 rads (less than that received from a comprehensive x-ray kidney study).

3. I understand the the possible benefits of the procedure(s) and/or investigation(s) are as follows:

   a. Information will be obtained about blood vessels in the brain. This type of information cannot be obtained by other methods.

L.L. Saenger, M.D.
M. Fernandez, M.D.
E.B. Silberstein, M.D.
R. David, M.D.
J. Graham, D.O.
Radioisotope Laboratory
University of Cincinnati College of Medicine
1981

File under Bergen Scanners
Radiopharmaceuticals
Need to staff 1st
Cannot read scans as one reads X-Ray. Info too incomplete
Need for quality Scans Pinhole + converging collimators
Speech material

BONE IMAGING

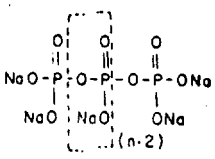
I. RADIOPHARMACEUTICALS

A. ^{99m}Tc LABELLED PHOSPHATE COMPOUNDS

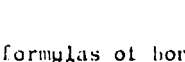
These include a number of compounds but the following preparations are most frequently used:

Done

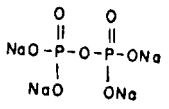
1. ^{99m}Tc-Ethanehydroxy Diphosphonate (^{99m}TcEHDP)
2. ^{99m}Tc-Polyphosphate (^{99m}TcPoly)
3. ^{99m}Tc-Pyrophosphate (^{99m}TcPyro)
4. ^{99m}Tc-Methylene Diphosphonate (^{99m}MDP)
5. ^{99m}Tc-Hydroxymethylene Diphosphonate (^{99m}HMDP)



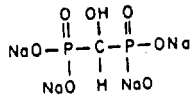
POLYPHOSPHATE
(No longer available)



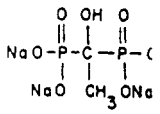
METHYLENE DIPHOSPHONATE



PYROPHOSPHATE



HYDROXY METHYLENE DIPHOSPHONATE



ETHANE-1-HYDR
1-DIPHOSPHONAT

FIG. 1 Chemical formulas of bone seeking phosphates and diphosphonates forming complexes of ^{99m}Tc. Although these are shown as tetrasodium salts, in solution at neutral pH they are probably disodium salts.

These five preparations have been shown to have biologic differences apparently related to their chemical structures. The mechanism of bone uptake of these compounds is not perfectly elucidated but they seem to bind strongly to the bone surface by absorption ("chemisorption"). A recent report suggests that these compounds, and especially pyrophosphate, have a greater affinity for non-osteoid organic matrix than the crystal surface.

All five agents have a high affinity for bone but they also have biological differences which seem to be related to their differences in chemical structure (4,5).

The blood clearance of the Tc-Phosphates in humans and animals appears to be best for the MDP and HMDP, followed by EHDP, Pyrophosphate, and Polyphosphate.

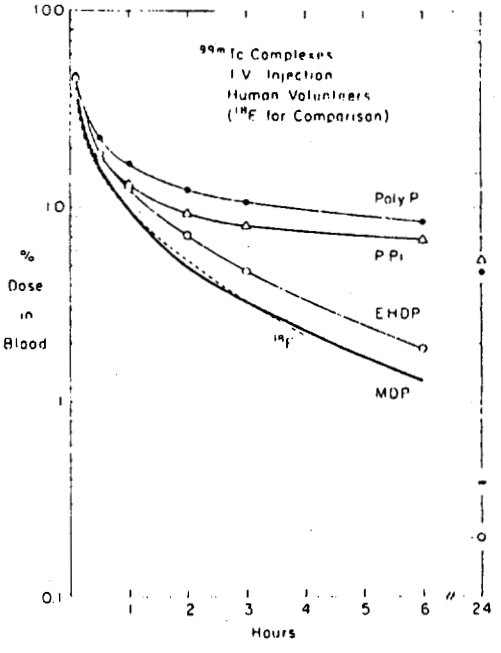


FIG. 2 Blood clearance of MDP in humans compared with three other ^{99m}Tc complexes and ^{18}F (corrected for physical decay), assuming blood volume was 7% of body weight. PPi indicates pyrophosphate and PolyP denotes polyphosphate.

Subramanian et al. J Nuc Med 16: 748, 1975.

The relatively slower clearance of the ^{99m}Tc-Pyrophosphate and ^{99m}Tc-Polyphosphate is explained by the stronger affinity and binding to serum proteins.

Overall, Tc-diphosphonate has been favored as the best agent for clinical use followed by the Tc-pyrophosphate and the polyphosphates (10,11).

As an example, some specific data are given for the labelled diphosphonate.

B. TECHNETIUM LABELLED DIPHOSPHONATES (P-C-P Bonds [Pyrophosphonates have P-O-P bonds which lead to some minor differences]).

1. Actions
   a. Increased blood flow
   b. Chemisorption
   c. Displacement of orthophosphate
2. Localization
   a. Amount and type of calcium and phosphorus present
   b. Increased vascularity of area (i.e., epiphyses)
   c. Increased surface area
   d. Increased turnover
3. Physiology and Pharmacology
   a. Optimum scan time - 2-3 hours, depending on the pharmaceutical 50% in bone - 50% excreted. Patient should void at 1 hour and at time of imaging.
   b. Diphosphonate - chelate excreted via GFR (bladder is critical organ)
   c. High ratio bone/soft tissue
   d. High ratio lesion to normal bone
   e. Low radiation dose

TABLE I

DOSIMETRY OF BONE IMAGING AGENTS

(in 70 kg Adult - Rads/mci Administered) (Data from package inse

	Radiopharmaceutical				
ORGAN	^{99m}TcMDP	^{99m}Tc Pyrophosphate	^{99m}Tc EHDP	^{18}F	^{67}Ga Citrate
Skeleton	.035	.034	.039	.15-.29	.44
Bone Marrow	.028	.028-.036	.028	.04	.58
Kidneys	.031	.028-.14	.14		.41
Liver	.008	.001	----		.46
Total Body	.0065	.009	.009	.05	.26
Bladder				2.0	
2-3 h voiding	.13	.04-.1	.1		----
4.8-6 h voiding	.31	.07-.23	.23		----
Testis					.24
2-3 h voiding	.008	.004-.01			
4.8-6 h voiding	.01	.007-.015			
Ovaries					.28
2-3 h voiding	.012	.004-.009			
4.8-6 h voiding	.017	.007-.015			
Heart					----
Normal		.007	.007		
Impaired		.014	.02-.03		
Gastroenteric Tract					
Stomach					.22
Small bowel					.36
Upper large bowel					.56
Lower large bowel					.9

Doses 10 - 20 Mci
Blood pool esp $\bar{c}$ infection
Average 3-5 hrs, 24 hrs.
35 rads/mCi of administered activity to bone
Reduces dose 2X
marrow " 1/2
TB dose 10 rads/mCi
Bladder wall > 10 rads/study
hydrate + Void

C. OLDER BONE SEEKING AGENTS

1. ^{18}F - short T1/2 (1.8 hr). High energy (511 KeV) annihilation photons are not ideal for gamma camera.

^{18}F has very favorable biologic characteristics. It is absorbed by the GI tract and can be given orally. The mechanism of uptake appears to be that of ion exchange at the level of the hydroxyapatite crystals. Extraction efficiency is excellent and approaches 100% depending on bone flow.

^{18}F is rapidly secreted by kidney (20-60% at 2 hours) a factor to keep in mind since overlapping of the kidneys and bladder with structures may occur.

2. ^{85}Sr - long T1/2 (64 days) requires low administered dose for low patient doses. This leads to low photon flux, long scanning time, and low resolution. Obsolete.

3. ^{87}Sr - short T1/2 (2.8 hours) does not allow for adequate soft tissue clearance. Higher photon energy (388 KeV) not ideal for gamma cameras. Obsolete.

BONE IMAGING

85 Sr Scan Hodgkins

II. PATHOPHYSIOLOGY

It appears that several factors are implicated and determine the degree of concentration of bone seeking agents in the osseous tissue. These factors are:

1. Vascularity and blood flow
2. Deposition at the level of the mineral phase (hydroxyapatite)
3. Deposition at the organic phase (osteoid matrix)
4. Degree and level between osteoblastic and osteolytic activities
5. Finally the mechanism of deposition in some non-osteoid forming tissues like tumors and ischemic and necrotic tissues (e.g. myocardial infarction), is not fully understood but intracellular metabolic changes appear to be involved.

The relationship between osteolytic and osteoblastic activities is a very important factor in determining deposition of radionuclides in bone. Radionuclide uptake is associated with osteoblastic activity. * Since most of the pathologic processes are associated with osteoblastic activity (tumor, infection, trauma, etc.) bone scanning is a non-specific procedure. Final diagnosis should be attempted on other clinical grounds. One expects to find positive bone scans when osteoblastic activity is the prominent event and conversely negative studies if absent. This finding is the common one, but there are many exceptions to this observation.

III. INTERPRETATION - NORMAL

A. The Spine

Some difference due to tomographic effect of focused collimators used with rectilinear scanners versus gamma cameras must be considered.

1. Vertebral Bodies

   a. Best on posterior position where lumbar region is seen as being of uniform density. Hip and femoral heads are well seen especially with large patients.

B. The Skull

1. Cranial vault and facial structures are well seen (sutures seen in children).
2. Base of skull
3. External occipital protuberance
4. If positive image is seen, obtain vertex view to exclude intracranial disease.

3 slides [illegible]

3006018

C. The Thoracic Region

1. Inferior angle and spine of scapula are well seen. Sternum and ossification centers and sternoclavicular joints (watch for assymetry. Occasionally, costo chondral junctions are well seen.

D. The Long Bones

1. Small bones in wrists, hands, and feet are frequently easily visible due to large proportion of cancellous to cortical bones. Good detail achieved with pinhole collimator.

E. Other Normal Sites of Increased Uptake

1. Epiphyses and apophyses in juveniles.
2. Joints - variable and sometimes assymetric.
   a. Sacro-iliac joints usually show increased uptake. Sacral tubercle normally prominent (~4%). [Blei L., et al., The Sacral Tubercle - A Cause for Hot Spots on Bone Scan. Clin Nuc Med 3: 351-354, 1978].
   b. Skull - petrous pyramids and facial bones
   c. Cartilage - watch for thyroid cartilage
   d. Shoulder uptake corresponding to handedness and/or position.
3. Organs
   a. Kidney and bladder
   b. Breast
   c. Myocardium
4. Free $^{99m}Tc\ O_4^-$
   a. Thyroid
   b. Salivary Gland, Sinuses
   c. Stomach
   d. Bowel
   e. Liver (rare)
5. Technical - change in distance of spine from collimator

IV. INTERPRETATION - ABNORMAL

A. Non-specificity of Bone Scans - cannot distinguish benign from malignant disease.

B. Soft Tissue Injury

Post-operative sites, myocardial infarction, CVA.

C. Vertebral Bodies

Most common sites for bony metastasis.

D. Delayed Scanning

1. In patients who cannot empty bladder; to increase target/non-target ratio.

Voiding

D. Delayed Scanning (continued)

2. In patients with questionable densities at 2-3 hours. At 12-24 hours occasionally an abnormality will appear better visualized than at the earlier time.

E. Spot Images using pinhole or other collimator (converging or diverging) as indicated is often useful. Oblique and lateral views are often helpful. The opposite side should be imaged for comparison. *

F. Metastases

Metastases to the skeleton may show as single or multiple areas of increased uptake. Practically any bone of the skeleton may be involved, but spine, ribs, and pelvis are the most frequently observed.

The most frequent tumors with bone metastases found in clinical practice are cancer of the breast, lung and prostate gland (12).

A clear decision for preoperative bone scans in patients with operable Breast Cancer is not entirely resolved. Patients with lesions < 2 cm in diameter tend not to have positive scans. With increase in lesion size and the presence of positive axillary nodes rates of true positive scans range from 6% to about 25%. The variation is due to several factors: size of tumor, differences in hospital populations, differences in technique, problems of FP and FN interpretation. FN include early very small metastases, lack of an osteoblastic response, lesions of pubis and ischium. FP include the many other causes of positive bone scans. CT, observation and biopsy may be needed to resolve this problem. The subsequent development of metastases is related to the size and extent of the original tumor.

References: Bone scanning in breast cancer, Brit. M.J. 2: 180-181, 15 July 1978.

Galasko CSB. Problems associated with the detection of skeletal metastases. J. Roy. Soc. Med. 71: 38-41, 1978.

McNeil BJ et al. Preoperative and follow up of bone scans in patients with primary carcinoma of the breast. Surg, Gynec and Obst 147: 745-748, 1978.

Clark DG et al. Indications for bone scans in preoperative evaluation of breast cancer. Am J Surg 135: 667-670, 1978.

G. The Patient With Single Bone Lesions

Single bone lesions in bone scanning are frequently found (13). The most common causes are:

1. Metastatic tumor (lung, breast, prostate)
2. Post thoracotomy (surgery scar)
3. Fracture of vertebral body
4. Normal variants (shoulder, sternum)

H. The Patient with Diffuse Increase Uptake in Skeleton (14,15,16)

Diffuse or symmetric increase uptake is not a rare situation. The importance of this possibility stems from the fact that a symmetric diffuse uptake may be easily overlooked.

This finding has been noted in metastatic cancer of the prostate and diffuse lymphoma and cancer of the renal pelvis. It is also expected in metabolic bone disease due to hyperparathyroidism and osteomalacia. In our lab we have found Paget's of the skull and hypertrophic pulmonary osteoarthropathy present with symmetric bone involvement. It can occur in hypervitaminosis D and also in renal osteodystrophy where it may represent secondary hyperpara thyroidism. [Fogelman et al. Bone scan findings in hypervitaminosis D: Case report, J Nuc Med 18: 1205-1207, 1977].

I. Presence of "Cold" Lesions in Bone Scanning (17,18,19)

A cold lesion may occur as the sole abnormality in a bone scan and it has been recognized most frequently in the vertebra and long bones. It has been described in the following conditions:

1. Metastatic disease of different sources
2. Post-traumatic aseptic necrosis
3. Sickle cell anemia with bone infarction
4. Chronic renal failure

Pathogenesis of this type of condition has not been elucidated but interruption of blood supply appears to be a prominent factor. Conceivably a poor osteoblastic reaction surrounding an area of necrosis or tumor would result in a "cold" area.

See Table III.

J. The False Negative and False Positive Bone Scan

False negative bone scans may result when radioactivity in the lesion is not intense enough, when the lesion is mostly osteolytic (e.g., 50% of multiple myeloma) or when the disease process involves the skeleton in a diffuse or symmetric fashion.

False positive scans are seen mainly as a consequence of contamination with urine and at the site of injection. If the technetium label is poor, uptake by the thyroid gland and the stomach may be a source of confusion. Increased uptake in the area of radical mastectomy presumably due to decreased attenuation of γ rays by removed soft tissue has been observed. Increased uptake in areas of post-surgery scars, biopsy sites, normal or pathologic breast tissue, soft tissue, inflammation and myocardial and cerebral infarcts occurs.

K. Increased Concentration in Extraskeletal Tissues

This condition has been found in many circumstances. The causes and conditions can be listed as follows:

1. Uptake in Osteoid Forming Tissues

K. Increased Concentration in Extraskeletal Tissues (con't.)

a. Myositis ossificans
b. Diffuse calcinosis
c. Metastatic osteosarcoma
d. Osseous metaplasia in soft tissues or lymph nodes
e. Ectopic calcification in paraplegic patients
f. Metastases of bladder (with osseous metaplasia)
g. Calcific tendonitis

In the above conditions concentration of bone seeking agents is expected and probably related to the presence of hydroxyapatite as well as immature collagen matrix.

2. "Non-osteoid" forming tissues

a. Thoracotomy and post-surgery scars
b. Soft tissue inflammation
c. Brain infarction
d. Brain astrocytoma
e. Brain metastases from lymphoma
f. Myocardial infarction

The mechanism of uptake is not known but increased blood flow and concentration of the isotope by the collagen and intracellular structure could be involved.

L. The Significance of Kidney Abnormalities Incidentally Found During Bone Imaging (20-23)

This point has been recently brought to attention since many of the bone seeking radioisotopes, specifically the Tc-Phosphate compounds, are avidly concentrated by the kidneys enabling us to observe some anatomic detail of the kidneys and excretory system. The following points should be emphasized:

1. There is no good correlation between kidney concentration of ^{18}F-Fluoride and renal function.

2. Hence, kidney asymmetry during ^{18}F-Fluoride bone scanning is unreliable to predict renal disease.

3. The overall accuracy and the level of confidence when kidneys are found morphologically abnormal are high.

4. In general, information regarding kidney morphology and function appears to be similar with all four currently used Tc-Phosphate compounds.

5. The most common conditions that can be detected during bone imaging in general clinical practice are -

a. Bilateral decreased visualization due to:
1. bilateral kidney disease
2. increased bone uptake ("steal phenomena")

L. The Significance of Kidney Abnormalities... (con't)

b. Small kidney due to unilateral disease
c. Space occupying lesions: tumors, cysts, dilated calyces
d. Absent kidney: congenitally, surgically, destruction by encroaching process
e. Obstructive uropathy with dilated excretory system
f. Displacement of bladder by pelvic tumor
g. Ectopic location

M. Bone Scanning in Pediatrics

Some pertinent points are to be considered when dealing with the pediatric age group.

1. The presence of normal variants inherent to this group such as the increased uptake in juxta-articular areas.

2. Positive bone scans due to metastatic disease of pediatric neoplasms, i.e. Wilms Tumor, neuroblastoma, leukemia, rhabdomyosarcoma. Valuable in following course of disease and evaluating treatments. In neuroblastoma bone imaging may miss the lesion although x-ray may be positive. [Reference - Kaufman RA et al. False negative bone scans in neuroblastoma metastatic to ends of long bones. Am J. Roentgenol. 130: 131-135, 1978].

3. Frequency of solitary lesions are more likely to be associated with primary bone tumors. Benign tumors take up less activity than do malignant ones. Imaging is useful in determining extent of osteoblastic tumors.

4. Differential diagnoses between osteomyelitis and cellulitis. This is a frequent situation which poses a difficult problem since clinical and radiologic findings may not be conclusive. In this regard, comparing early "blood pool" pictures with the conventional delayed scan is often helpful. In soft tissue inflammation or infection, the early blood pool scans show a greater concentration of the radioisotope when compared with the delayed scan. The reverse is usually found in cases of osteomyelitis. High sensitivity and pinhole collimators are often helpful when dealing with small children. Septic arthritis, discitis (spondylarthritis), bone infarcts in sickle cell disease require consideration in the differential diagnosis.

5. Aseptic necrosis. If imaged early, may show decreased uptake. Later uptake will be increased. In Perthe's disease osteotomy may decrease uptake. Attention to technique important for bilateral disease and to follow course. Quantitative technique may be valuable.

[References: Morley TR et al. Femoral head activity in

M. Bone Scanning in Pediatrics (con't)

Perthe's disease: Clinical evaluation of a quantitative technique for estimating tracer uptake, J Nucl Med 19: 884-890, 1978.

Sty JR. Panner's disease (Osteonecrosis of the capitellum). Clin Nuc Med 3: 117, 1978].

[redacted]

VI. GALLIUM 67 FOR BONE IMAGING

^{67}Ga may be useful in circumstances where ^{99m}Tc phosphorus compounds appear to give normal images as occasionally in osteomyelitis, septic arthritis. In primary bone tumors it correlates well with ^{99m}Tc compounds. It may be more useful in showing the extent of soft tissue extension. Its chief drawbacks are the high energy of its photons resulting in poor resolution. It is superior to radiography but generally not as reliable as ^{99m}Tc compounds. In selected cases where ^{99m}Tc appears equivocal or at variance with expectation it should be utilized. (Reference - Handmaker H et al. Gallium imaging in pediatrics. J Nuc Med 18: 1057-1063, 1977).

VII. DISEASES OF JOINTS

Joint abnormalities frequently show increased activity with ^{99m}Tc phosphorus compounds. Osteoarthritis joints are frequently visualized in the course of bone surveys. It is prudent to examine these joints clinically or by x-ray to exclude other causes for visualization.

In rheumatoid arthritis bone scanning agents usually show more joints to be involved than are found clinically and other forms of arthritis show similar findings. Septic arthritis is readily visualized. The peri-articular activity is usually increased due to increased blood flow and local reaction. Symmetrical abnormal increased in activity of involved joints is sometimes difficult to resolve especially with involvement of sacro-iliac joints. Although some investigators find obtaining joint to sacrum count ratios to be valuable in finding and staging sacro-iliac disease (Dequeker et al. Scintigraphic investigation of sacro-iliac disease. J Nuc Med 19: 119-120, 1978), and others (Lentle BC et al. J Nuc Med 19: 120, 1978) disagree in its usefulness for the diagnosis of ankylosing spondylitis.

A painful total hip or knee prosthesis suggests possibility of loosening of one or more components. Imagine with a Tc phosphate complex is an effective screening procedure to determine loosening or other complications. The bone scan alone lacks specificity but approaches 100% sensitivity for loosening and or infection. If the bone scan is negative, no further work-up is necessary at that time. Recent interest has been directed to the combined use of Tc-MDP and gallium in the evaluations of a painful total hip prosthesis. Both studies are needed as the interpretation depends on the presence of abnormal uptake plus the pattern of abnormal uptake, that is to assess the congruity or incongruity of the patterns of abnormal uptake.

EVALUATION OF TOTAL JOINT REPLACEMENT WITH TC-PHOSPHATES AND GALLIUM

	BONE SCAN		GALLIUM SCAN	CONGRUENT	INCONGRUENT
LOOSENING	+		-	-	-
INFECTION	+		+	-	+
OR	+	(INTENSE)	+	+	-
TRAUMA	+		+	+	-

VIII. QUANTITATIVE TECHNIQUES

Among these methods currently utilized is that using probes (Park et al, A quantitative evaluation of rheumatoid arthritis activity with Tc 99m HEDP, J Nuc Med 18: 973-976, 1977) with counts over affected and normal areas at specific times after

review of earlier images to evaluate treatment in rheumatoid arthritis. Another method uses regions of interest and external standards to estimate the amounts of activity taken up in various parts of the skeleton in Paget's disease [Lurye DR et al. An improved method for quantitative bone scanning, J Nuc Med 18: 1069-1073, 1977]. A third method uses serial measurements at frequent intervals up to 24 hours with a shadow shield whole body monitor [Fogelman et al. The use of whole body retention of Tc 99m diphosphonate in the diagnosis of metabolic bone disease J Nuc Med 19: 270-275, 1978; see also Holmes RA, editorial, Quantification of skeletal Tc-99m labeled phosphates to detect metabolic bone disease, J Nuc Med 19: 330-331, 1978]. This technique differentiated patients with renal osteodystrophy, Paget's disease, osteomalacia and primary hyperparathyroidism from normal subjects. Patients with osteoporosis did not differ from normals.

IX. MISCELLANEOUS

Careful evaluation of jaws and related structures can reveal positive images associated with extraction sites, pulp and peridontal infections and local irritation [Tow DE et al. Bone scan in dental disease, J Nuc Med 19: 845-847, 1978].

The use of single photon emission tomography of facial bones using a special collimator and Tc Pyrophosphate compounds gives improved resolution of facial bones and improves the study of tumors, infections, bone grafts and post irradiation osteonecrosis [Brown ML et al. Facial bone scanning by emission tomography, J Nuc Med 18: 1184-1188, 1977].

X. GAMUT APPROACH AND REFERENCES

The gamut approach to roentgenology has been applied to nuclear medicine. Though scintiscan abnormalities are less specific than roentgen lesions, the approach has been useful.

A recent gamut prepared by one of our residents is included. It contains a comprehensive list of references.

TABLE II

SINGLE LOCALIZED AREA OF INCREASED RADIONUCLIDE UPTAKE ON A BONE SCAN

COMMON

1. Metastatic tumor (lung, breast, prostate) (26,67)
2. Post thoracotomy/surgery scar (26,28)
3. Vertebral body compression fracture (26)
4. Normal variants (shoulder, sternum) (29)

TABLE II (con't)

LESS COMMON

1. Metastatic tumor (cervix, neuroblastoma in children) (27,30)
2. Primary bone tumor (Ewing's sarcoma, osteosarcoma, ostrochondroma) (26,31)
3. Lymphoma (26,27)
4. Monarticular degenerative disease (26)
5. Trauma - fracture other than vertebral body, biopsy site, prosthesis site) (26)
6. Osteomyelitis, pyogenic (26)
7. Peridontal disease (33) and post tooth extraction
8. Paget's disease (26,27)

RARE

1. Metastatic tumor (thyroid, renal, melanoma, pancreas, other gastrointestinal) (27)
2. Primary bone tumor (fibrosarcoma, chondrosarcoma, giant cell tumor, fibrous dysplasia, enchondroma, osteoid osteoma, bone cyst, hemangioma) (26, 32-35)
3. Multiple myeloma (27)
4. Aseptic necrosis (32)
5. Osteitis pubis (32)
6. Osteomyelitis, TB (26,36) coccidiomycosis (27)
7. Extra skeletal calcified and non-calcified tissue uptake [breast carcinoma (29,34), neuroblastoma (37,38), neurofibroma (39), brain metastasis from lung carcinoma (34), cecal/rectal carcinoma (34), nasopharyngeal carcinoma (34), fibrosarcoma (34), soft tissue abscess (40), brain infarction (41), myocardial infarction and other areas of tissue necrosis, Hodgkin's involving spleen (42), leukemic infiltrates (35), myositis ossificans (43), calcific tendonitis (32), thrombophlebitis (29)]. Also in lung, stomach, liver, kidneys in metastatic melanoma and chronic renal disease [Veukatesh et al. Metastatic calcification: the role of bone scanning, Radiology 129: 755-758, 1978; Rosenthal DI, Uptake of bone imaging agents by diffuse pulmonary metastatic calcification, Am J Roentgenol 129: 871-874, 1977; Oren VO et al., Liver metastases of oat cell carcinoma of lung detected on ^{99m}Tc diphosphonate bone scan, Clin Nuc Med 3: 355-357, 1978 - has a good table of soft tissue uptake with ^{99m}Tc bone imaging agents].

TABLE II (con't)

8. Gout (26)

9. Periostitis (31)

10. Meningiomas (44)

11. Scurvy - [Front D et al., Bone scintigraphy in scurvy, J Nuc Med 19: 916-917, 1978].

TABLE III

DECREASED RADIONUCLIDE UPTAKE ON A BONE SCAN

AVASCULAR AREAS

Aseptic necrosis, bone infarcts
Radiation therapy (late effect)
Lack of weight bearing stress
Metastasis
Sickle Cell C crisis
Chronic renal failure
Acute osteomyelitis
References: Georgen et al., J Nuc Med 15: 1120-1124, 1974
Fordham et al., Sem Nuc Med 4: 411-429, 1974
Quint PA, Radiol 130: 751-752, 1979, #58.

TABLE IV

True Abnormal, False Abnormal and False Normal Abnormalities in Bone Imaging
Silberstein, EB, J Nuc Med 17: 229-232, 1976

Abnormalities generally show increased uptake of radiopharmaceuticals

A. True Abnormal
   1. Tumor, primary or secondary
   2. Fractures and surgical osteotomy
   3. "Metabolic"
      a. hyperparathyroidism
      b. Paget's disease
      c. osteoporosis
      d. osteomalacia and occasional pseudofractures of ribs [Fogelman et al., The role of bone scanning in osteomalacia, J Nuc Med 19: 245-248, 1978; Fogelman et al., Pseudofracture of the ribs detected by bone scanning, J Nuc Med 18: 1236-1237, 1977].
   4. Inflammation of bone
      a. osteomyelitis
      b. abscess
      c. sterile osteitis (e.g. osteitis pubis)
      d. granuloma including sarcoid, eosinophilic granuloma
      e. hyperostosis frontalis interna
      f. fibrous dysplasia
      g. hypertrophic pulmonary osteoarthropathy

TABLE IV (con't)

5. Arthritis
   a. osteoarthritis
   b. rheumatoid arthritis
   c. gouty arthritis
6. Soft-tissue calcifications
   a. myositis ossificans
   b. soft-tissue osseous metaplasia
   c. soft-tissue tumors with calcification or ectopic bone formation
   d. vascular calcification, especially femoral artery
   e. calcific tendonitis
   f. abscess
   g. infarct, cerebral or myocardial
   h. thrombophlebitis
7. Vascular
   a. surrounding the bone infarct
8. Decreased uptake
   a. tumor
   b. disuse of limb (may also be increased with osteoporosis)
   c. vascular obstruction (e.g., sickle cell disease, aseptic necrosis)

B. Falsely Abnormal
   1. Renal artifacts or disease
      a. hydroureter-hydronephrosis with ^{99m}Tc-diphosphonate
      b. contamination of clothing or skin with urine
   2. Recent surgical procedures on bone or soft tissue
   3. Biopsy site
   4. Colloid formation with liver-spleen uptake

C. Falsely Normal
   1. Lesions of smaller size than the resolving power of the system
   2. Purely lytic lesions (e.g., some myelomas)
   3. Jewelry, prostheses, pacemaker overlying a lesion

TABLE V

Bilateral Lower Limb Uptake of Bone Scanning Agents, in R.P. Spencer and J.A. Datu, Sem Nuc Med 10, (#3): 314-316,1980

Some causes of bilateral lower limb uptake of bone imaging agents are:

COMMON

1. "Calcified" femoral vessels
2. Trauma (and battered child)
3. Stress fractures
4. Aseptic necrosis,* osteonecrosis

*increased uptake is likely outside of the affected region.

BONE IMAGING

TABLE V (con't).

5. Multiple small vessel occlusion, as in SS disease*
6. Osteomyelitis (acute or chronic)
7. Hypertrophic pulmonary osteoarthropathy
8. Increased collagen turnover**
9. Paget's disease
10. Arthritides (osteoarthritis, rheumatoid)
11. Multiple metastases+

UNCOMMON

1. Ectopic calcifications
2. Injection sites
3. Polymyositis, myolysis, dermatomyositis
4. Soft tissue infection, infarction
5. Surgically induced (bone grafts, pinning, prostheses)
6. Septic or other emboli*
7. Bilateral sympathectomy
8. Lymphoma
9. Multiple myeloma
10. Gaucher's disease
11. Sarcoidosis++
12. Scurvy
13. Myelofibrosis
14. Joint disorders

*increased uptake is likely outside of the affected region

**Includes hyperthyroidism, acromegaly, thyroid acropachy, hyperparathyroidism, renal osteodystrophy.

+Multiple primary bone tumors can occur but are quite rare.

++Well documented radiographicallu, less well established by bone scans.

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