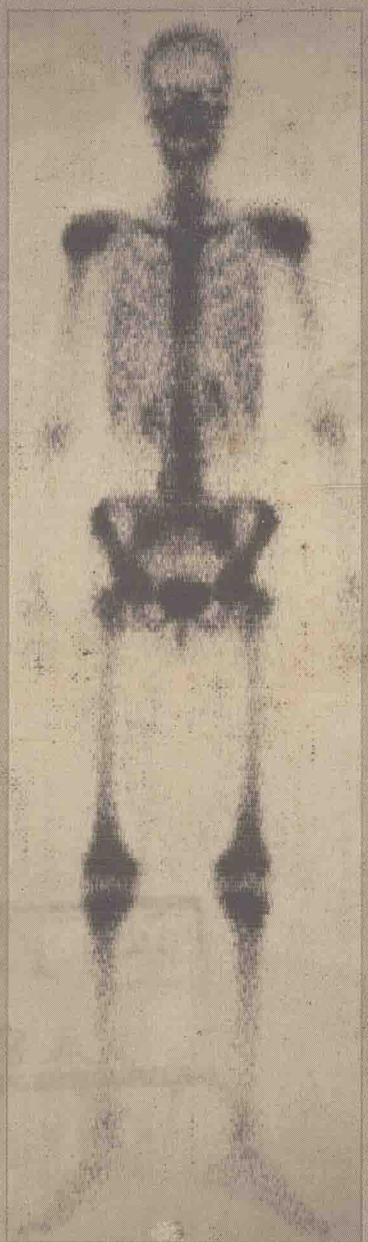
Atlas of Nuclear Medicine

Volume 4

BONE



DIBOS
AND
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to Esther, Luis, Paul, Lydia

FOREWORD

The clinical value of bone scanning was established in the 1960's despite restrictions imposed by suboptimal radiopharmaceuticals. The development in the present decade of phosphate compounds labeled with technetium-99m removed previous drawbacks and improved the quality of the skeletal images, increasing the usefulness and broadening the spectrum of clinical applications of bone scanning. Today bone scanning is a simple, safe, readily available, and widely accepted diagnostic procedure. This atlas is intended to serve as an illustrative reference for nuclear medicine physicians, radiologists, internists, oncologists, general surgeons, orthopedic surgeons, rheumatologists, and pediatricians. We hope that it will also be of value to physicians training in nuclear medicine and radiology. The cases are presented as clinical problems; the reader's diagnostic ability may be challenged by attempting to interpret the scans prior to reading the stated interpretation and the final diagnosis. The reader will notice that the technical quality of some of the earlier studies is poor when judged by today's standards. These older cases have been included because of their interesting clinical features.

P.E.D.
H.N.W.

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CONTENTS

General Principles of Bone Scanning

Bone is a complex structure of protein and minerals. Bone collagen is a fibrous protein that makes up the organic matrix of bone. Osteocytes and vascular structures are suspended in this matrix, and bone mineral is deposited in the collagen by osteocytes which are derived from osteoblasts. Bone mineral accounts for approximately 70 per cent of bone mass. About two thirds of bone mineral is a calcium-magnesium-phosphate complex of hydroxyapatite crystals. Bone mineral has a surface area of approximately 100 square meters per gram of inorganic material where active ion exchange may take place. Increased bone turnover is present at sites of growing bone and of bone injury. In addition to bone collagen and calcium hydroxyapatite crystals, bone contains ions of sodium, magnesium, strontium, fluorine, barium, lead, gallium, and cerium in trace amounts.

Radiography has been the traditional method for studying the structural integrity of the skeleton. Changes of 30 to 50 per cent in the calcium content of bone have to take place in order to produce radiographic differences in bone. Radioactive tracers of normal constituents of bone or their analogues are used for studying the regional metabolic activity in normal and injured bone. Radionuclide images reveal the regional metabolic activity of bone. Past and present bone scanning agents are listed in Table 1.

In recent years, technetium-labeled phosphate compounds have been developed and proven effective for skeletal imaging, replacing earlier agents, such as Sr-85 and Sr-87m. These compounds are the polyphosphates, pyrophosphates, and diphosphonates, of which the latter group appears to be the best. The advantages of these compounds over Sr-85 and Sr-87m are the more suitable gamma energy of 99m-technetium, its greater availability, lower radiation dose, relatively lower cost, and the better anatomical detail it affords of the images.

In addition to becoming localized in the skeleton, technetium–phosphorus compounds may also accumulate in normal structures, in soft tissue abnormalities, and in the kidney and urinary bladder. At times, this localization may provide clinically useful information when unsuspected renal, bladder, or pelvic disease is detected.

Protein binding affects bone uptake and urinary excretion of Tc–phosphorus compounds. If the protein binding is great, there is a delay in bone uptake and urinary excretion. The blood clearance rate of intravenously injected bone-imaging agents is dependent upon the rate of renal clearance; agents with slower blood clearance have a higher concentration of activity in soft tissue. At one hour after injection, the protein-bound fractions for polyphosphates and pyrophosphates are almost twice those for diphosphonates, methylene diphosphonate (MDP) and ethylene hydroxyphosphonate (EHDP). Bone scans performed with technetium-labeled methylene diphosphonate have a lower concentration of activity in the soft tissue than those performed with polyphosphates and pyrophosphates. A bone scan performed at two hours after the injection of ^{99m}Tc-MDP is comparable to a scan performed at three to four hours with ^{99m}Tc-EHDP or ^{99m}Tc pyrophosphate or to a scan at four to five hours with polyphosphate. The bone to blood ratio of ^{99m}Tc-MDP has been found to be higher than that of the other agents; that of ^{99m}Tc-EHDP, although not as good as ^{99m}Tc-MDP, is higher than that of ^{99m}Tc-pyrophosphate (Fig. 1.)

Variability has been observed in different commercial products of the same compound from the same manufacturer. ^{99m}Tc-MDP appears to have less batch-to-batch variation than ^{99m}Tc-EHDP; variability is most marked in polyphosphates.

The toxicity of ^{99m}Tc-MDP, ^{99m}Tc-EHDP, ^{99m}Tc polyphosphate, and ^{99m}Tc pyrophosphate is low, as evidenced by acute toxicity experiments and the absence of adverse reactions clinically.

TABLE 1. RADIOPHARMACEUTICALS USED FOR BONE SCANNING*

RADIOPHARMACEUTICAL	HALF-LIFE	SCANNING DOSE	RADIATION DOSE (MRAD)	
			Bone	Whole Body
Strontium-85 nitrate**	65 days	100 μCi	3600	500–1000
Strontium-87m carbonate	2.8 hours	500 μCi	50	10
Fluorine-18 fluoride	110 minutes	1.5 mCi	300	60
Technetium-99m polyphosphate	6 hours	10 mCi	500	150
Technetium-99m pyrophosphate	6 hours	10 mCi	500	150
Technetium-99m ethylene hydroxyphosphonate	6 hours	10 mCi	500	150
Technetium-99m imidodiphosphonate	6 hours	10 mCi	500	150
Indium-113m ethylenediamine tetra (methylene phosphonic acid)	90 hours	10 mCi		
Indium-113m diethylenetriamine penta (methylene phosphonic acid)	90 hours	10 mCi		
Technetium-99m methylene diphosphonate	6 hours	10 mCi	500	150

*Technetium-99m imidodiphosphonate, indium-113m ethylenediamine tetra (methylene phosphonic acid) and indium-113m diethylenetriamine penta (methylene phosphonic acid) are currently under investigation; clinical experience with these agents is limited. On the other hand, technetium-99m polyphosphate, technetium-99m pyrophosphate, and technetium-99m diphosphonate have been used extensively since the early 1970's.

**Of historic interest only.

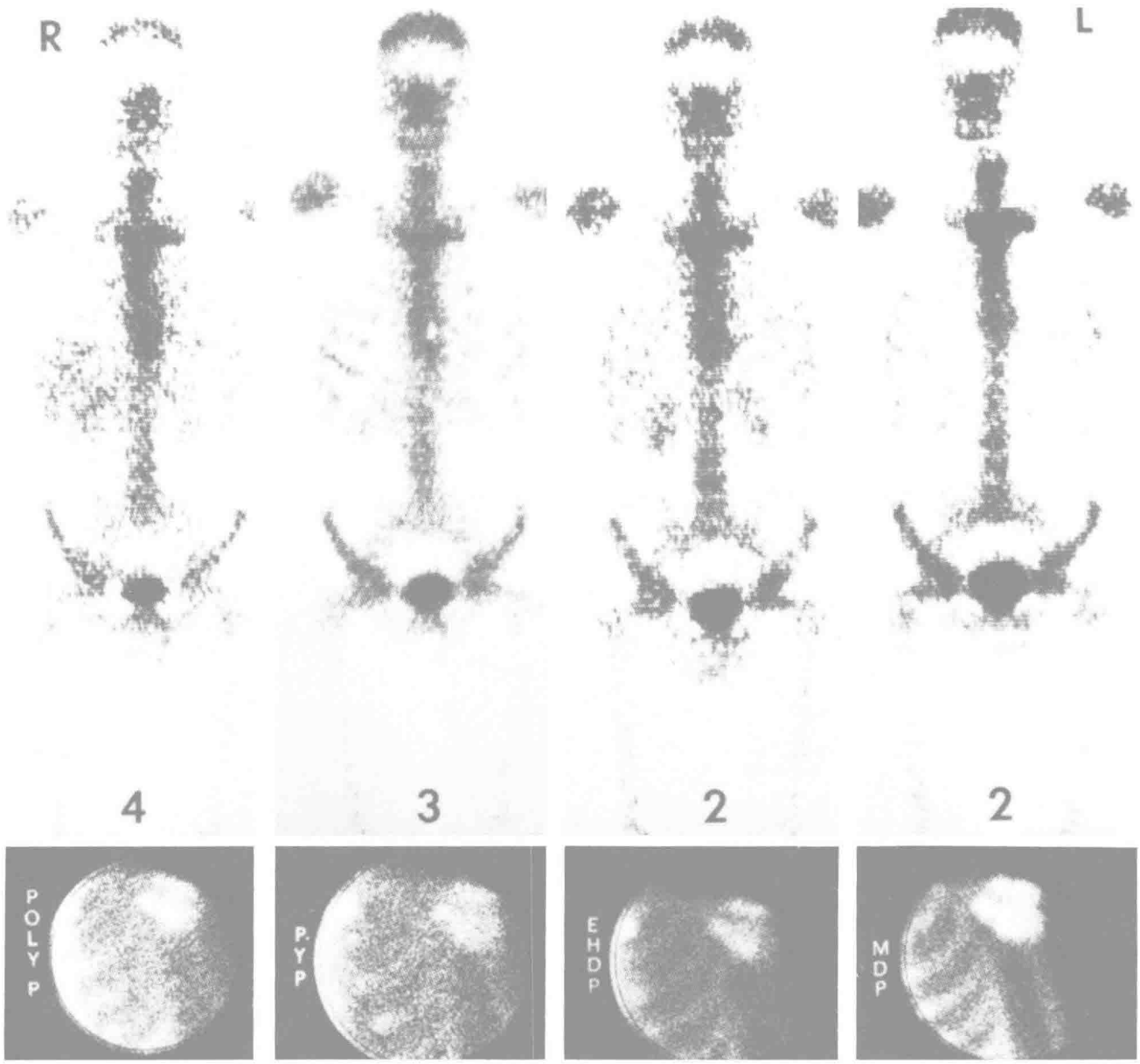
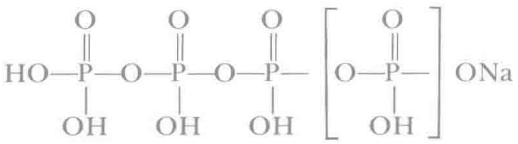
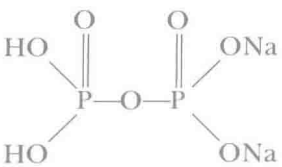


Figure 1 Anterior rectilinear scan images (top) and spot camera images (bottom) of left upper chest and shoulder obtained in the same normal individual after administration of 15 mCi of each of four technetium-99m bone scanning agents: polyphosphate (Poly P), pyrophosphate (PYP), ethane-1-hydroxy-1, 1-diphosphonate (EHDP), and methylene diphosphonate (MDP). The numbers indicate the number of hours between injection and initiation of the scan. The target (bone) to nontarget (soft tissue) ratio appears to be highest with methylene diphosphonate. Conversely, the highest amount of soft tissue activity is seen with polyphosphate and pyrophosphate. (*From*: Subramanian, G., McAfee, J. G., Blair, R. J., et al.: J. Nuclear Med., *16*:744, 1975.)

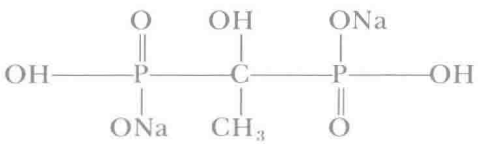
Chemical Structure of Bone Scanning Pharmaceuticals



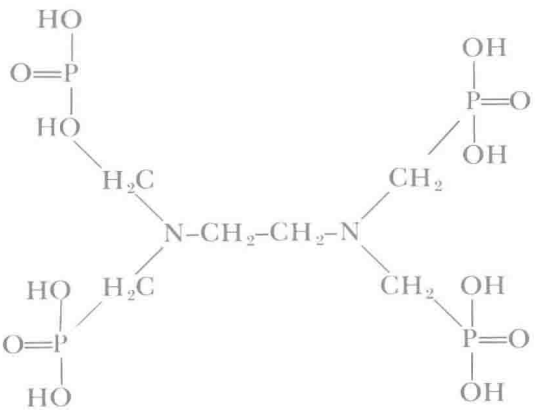
Polyphosphate (monosodium polyphosphate)



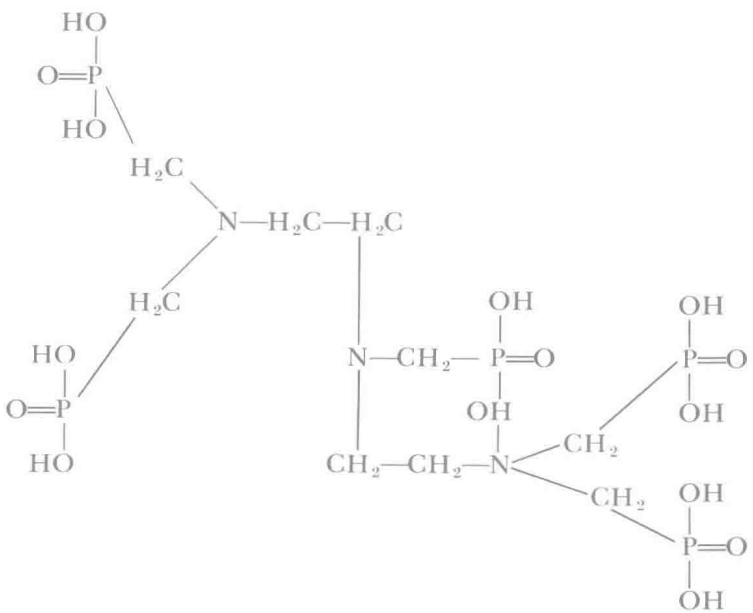
Pyrophosphate (disodium pyrophosphate)



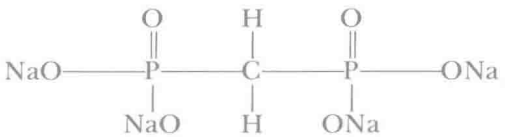
Diphosphonate 1-hydroxy-ethylidene-
1, 1-disodium phosphonate (HEDSPA)



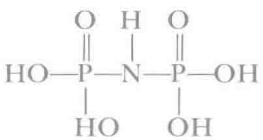
Ethylenediamine tetra (methylene phosphonic acid)



Diethylenetriamine penta (methylene phosphonic acid)



Methylene diphosphonate



Imidodiphosphonate

The precise mechanism of bone localization of the radiopharmaceuticals employed in bone scanning has not been well defined. It is the thought that bone blood flow, ion exchange between ionic tracers and the ions within bone, diffusion of the tracer within bone tissue, and surface absorption to bone (which may be increased in diseased areas) may all play a role.

Factors Affecting Bone Localization of Scanning Radionuclides

1. Bone blood flow.
2. Extracellular fluid space of bone.
3. Ion exchange (between ionic tracers and ions within bone).
4. Diffusion of tracer within bone tissue.
5. Increased surface absorption to bone.

The instruments utilized in bone scanning are: (1) moving detector scanners capable of producing whole-body images, (2) stationary gamma cameras with standard-size or large crystal detectors, and (3) cameras with moving beds or moving detectors. With technetium-99m phosphorus complexes, either the scanner or camera is suitable, whereas with fluorine-18, which has a high gamma energy, better images are obtained with the rectilinear scanner because of better detector efficiency.

Although bone scanning is being used more and more in other diseases, it is performed most often for the early detection of bone metastases. Cancers of the breast, prostate, lung, kidney, and thyroid commonly metastasize to bone; bone metastases are also found in many other types of tumor. Bone metastases are generally detected by scanning techniques one to six months prior to the development of radiographic bone abnormalities. However, there are rare instances when the scan is normal in the presence of metastatic disease. Foci of active bone metabolism detected by bone scanning are not specific and at times need to be further investigated by appropriate radiographs or even by biopsies of the suspected area(s). Thus, bone scanning and bone radiographs are complementary diagnostic studies. In benign conditions, such as osteomyelitis, the scan may indicate the presence of increased mineral metabolism several days prior to radiographic changes. The multiple conditions that may produce abnormalities in bone scans are shown in the following section.

Causes of Increased or Decreased Activity in Bone Scans

I. Increased activity
   A. Normal states
      Growing metaphyses and epiphyses, costochondral junctions, facial bones, spine, sternoclavicular joints, scapulae, shoulders, sacroiliac joints, elbows, and knees.
   B. Normal variants of skeletal structure
      Persistent ossification centers (e.g., sternum).
   C. Soft tissue abnormalities
      Myositis ossificans, calcinosis cutis, calcific tendinitis, healing wounds (e.g., surgical), sites of intramuscular injections, sites of bone marrow aspiration or biopsy.
   D. Pathologic conditions of bone
      Benign: Bone tumors, hyperostosis, congenital fusion of vertebrae, fibrous dysplasia, eosinophilic granuloma (histiocytosis), hypertrophic osteoarthropathy, regional migratory osteoporosis, arthritis, fractures, osteomyelitis, gout, Paget's disease, hyperparathyroidism, ischemic necrosis of hip, systemic mastocytosis, bone infarction.
      Malignant: Primary and metastatic bone tumors, multiple myeloma, lymphomas.
II. Decreased activity
   A. Pathologic conditions
      Bone cysts, gangrene.
   B. Nonpathologic conditions
      Artifacts such as gold teeth, prostheses, and pacemakers.
   C. Other
      Radiation therapy sites.

Clinical Uses of Bone Scanning

1. Detection of primary and metastatic bone tumors.
2. Evaluation of patients with possible osteomyelitis, particularly at early stages with negative radiographs.
3. Preoperative evaluation of patients with breast masses or pulmonary neoplasms.
4. Evaluation of patients with prostatic nodules.
5. Monitoring of response to therapeutic procedures.
6. Diagnosis of stress fractures.
7. Differential diagnosis of active versus chronic or inactive arthritic processes.
8. Early detection and determination of the extent of Paget's disease of bone.
9. Evaluation of patients with possible ischemic necrosis of bones, such as the hip.
10. Detection of breast lesions, such as neoplasms or fibrocystic disease.
11. Selection of sites for bone biopsy.
12. Planning of radiation therapy ports.

ANTERIOR VIEW

Child

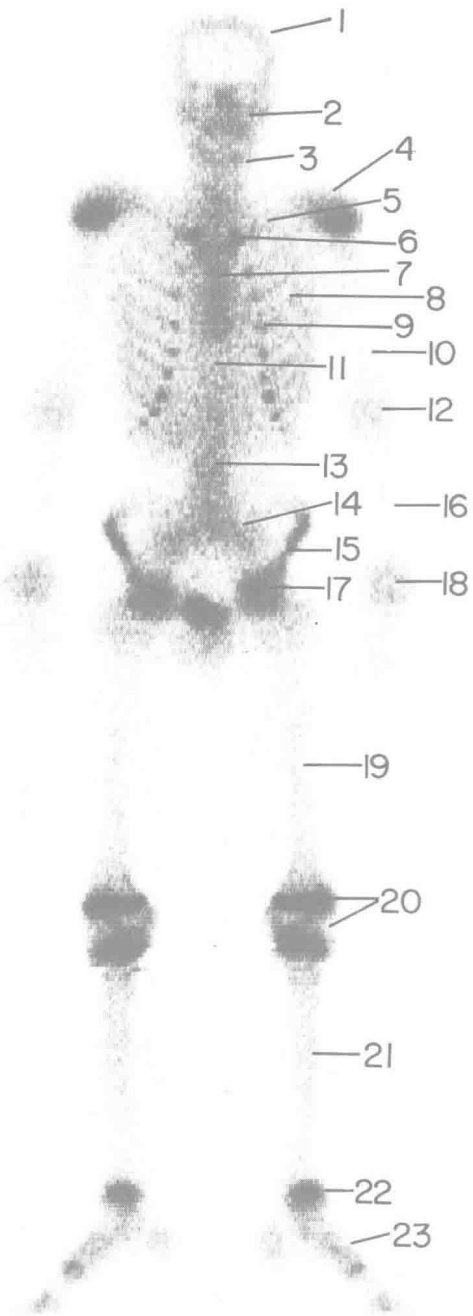


Figure 2a

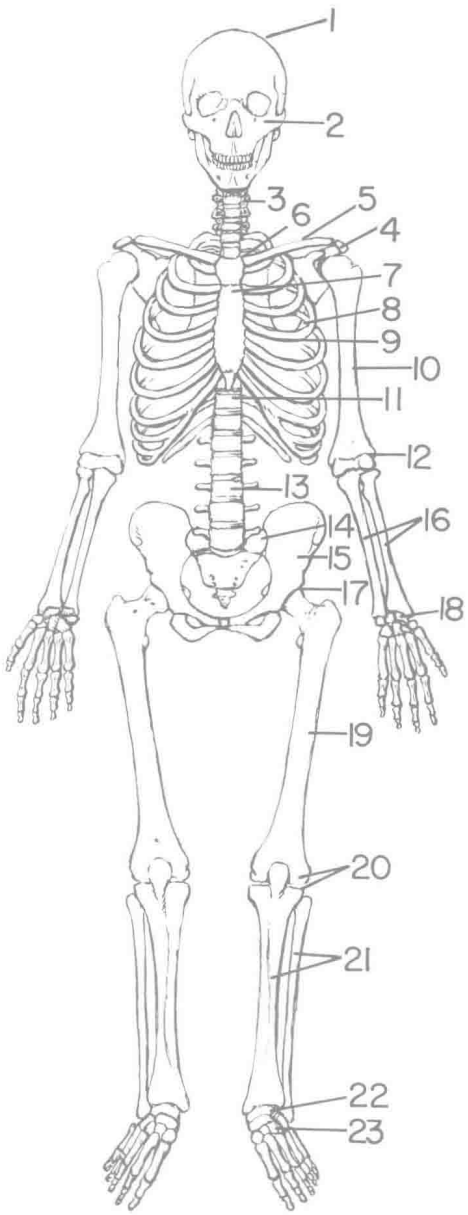


Figure 2b

Adult

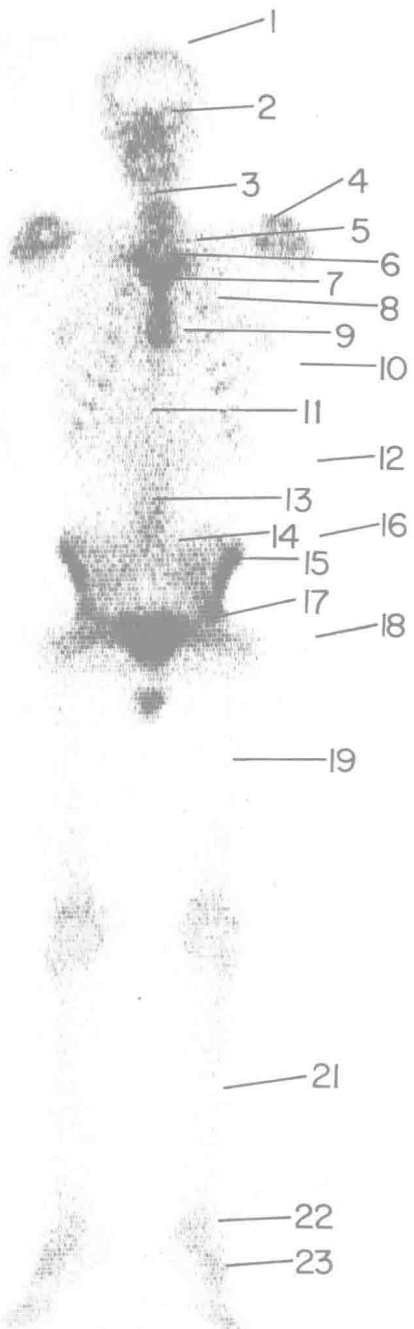


Figure 2c

1. Skull
2. Facial bones
3. Cervical spine
4. Shoulder
5. Clavicle
6. Sternoclavicular joint
7. Sternum
8. Ribs
9. Costochondral junctions
10. Humerus
11. Thoracic spine
12. Elbow
13. Lumbar spine
14. Sacroiliac joint
15. Pelvis
16. Radius and ulna
17. Hip
18. Wrist
19. Femur
20. Knee metaphyses and epiphyses
21. Tibia and fibula
22. Ankle
23. Foot