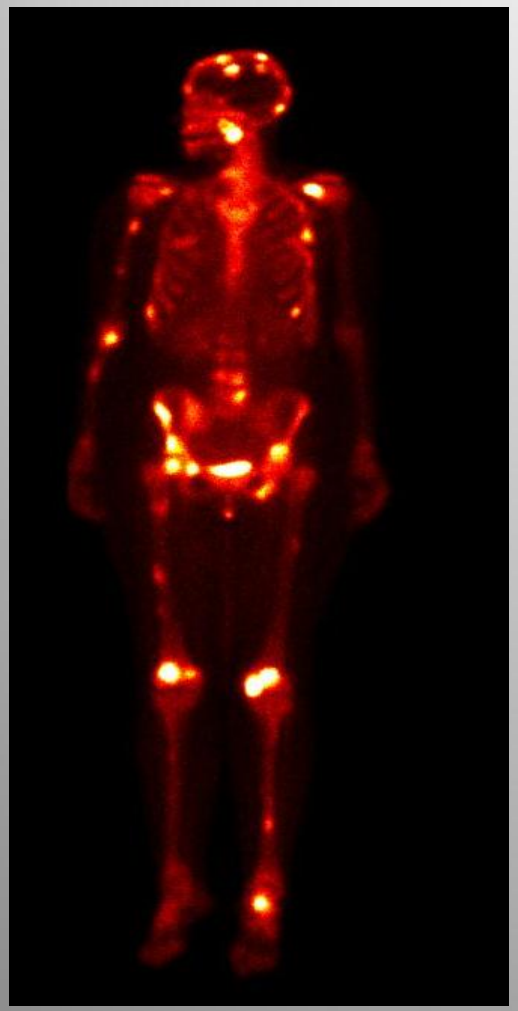
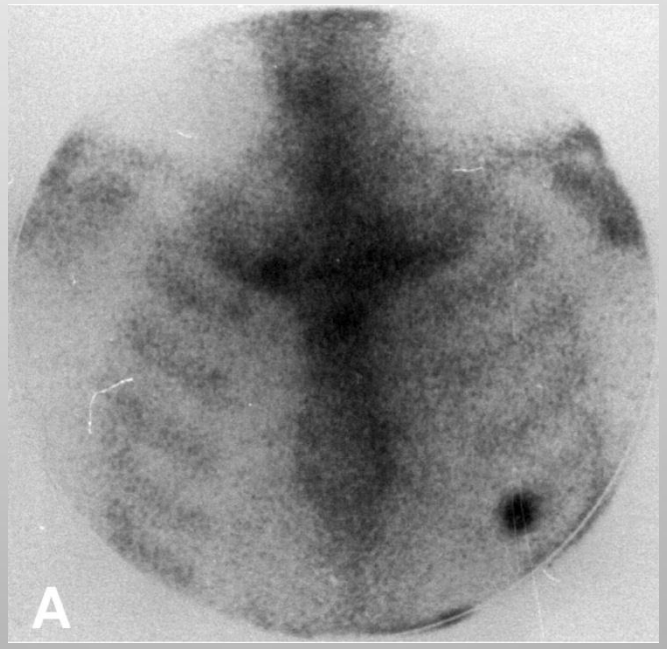
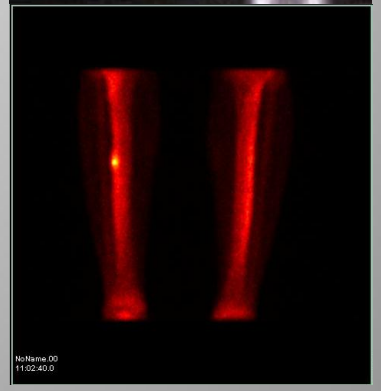
Examinations of skeletal system







Assoc. prof. V. Marković, MD., PhD.

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I. Zebić, MD., nucl. med. spec.

Bone and joint scintigraphy

- Bone and joint scintigraphy is nuclear medicine diagnostic imaging that uses radiopharmaceuticals that accumulate in skeletal tissue.

- Radiopharmaceuticals: bisphosphonate compounds labeled with Tc-99 pertechnetate:
  - methylen diphosphonate (MDP),
  - ethylen-hydroxy-diphosphonate (EHDP) and
  - dicarboxypropane-diphosphonate (DPD)

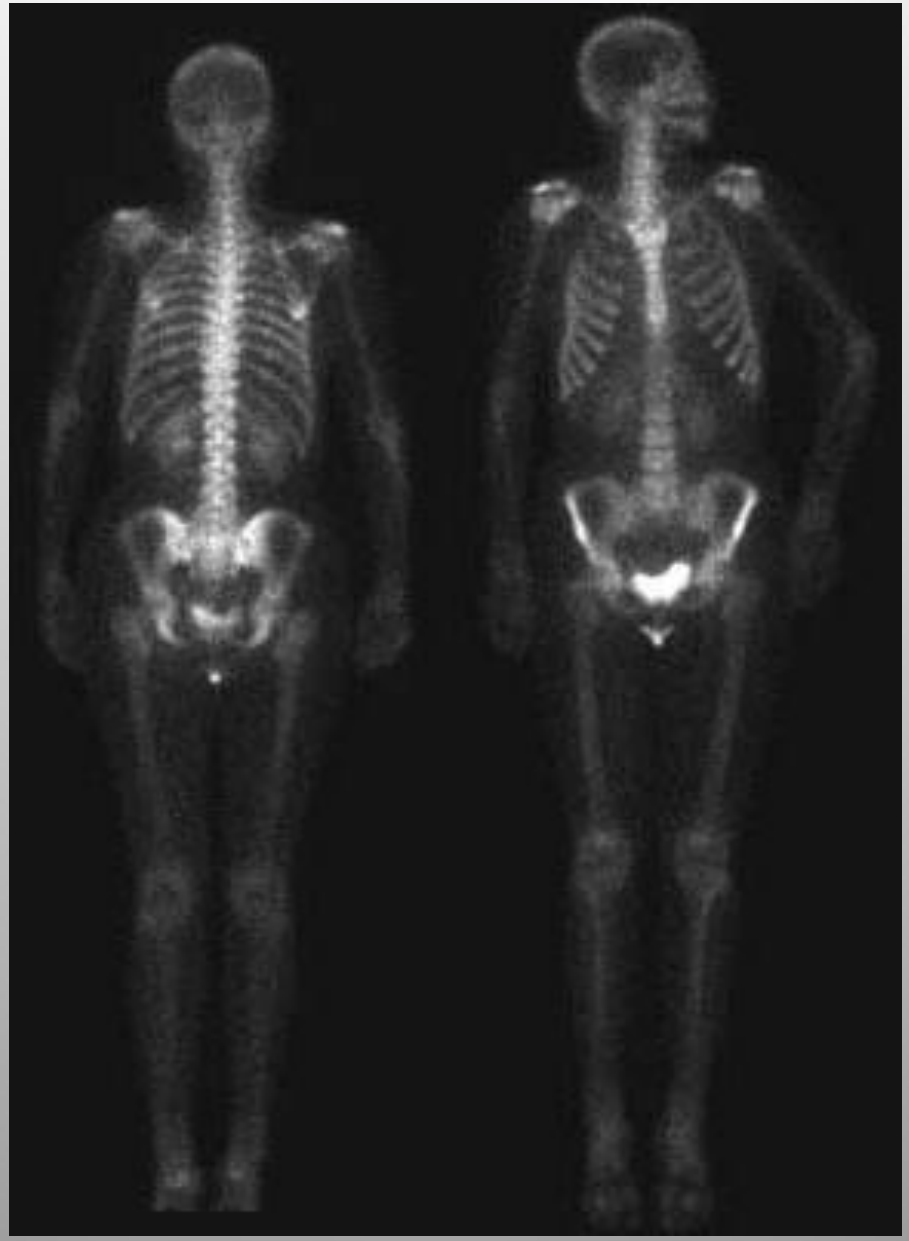
- Bind to the hydroxyapatite crystal (crystal salt calcium phosphate), wich is an integral part of the bone

Factors affecting the accumulation of bone-seeking radiopharmaceuticals:

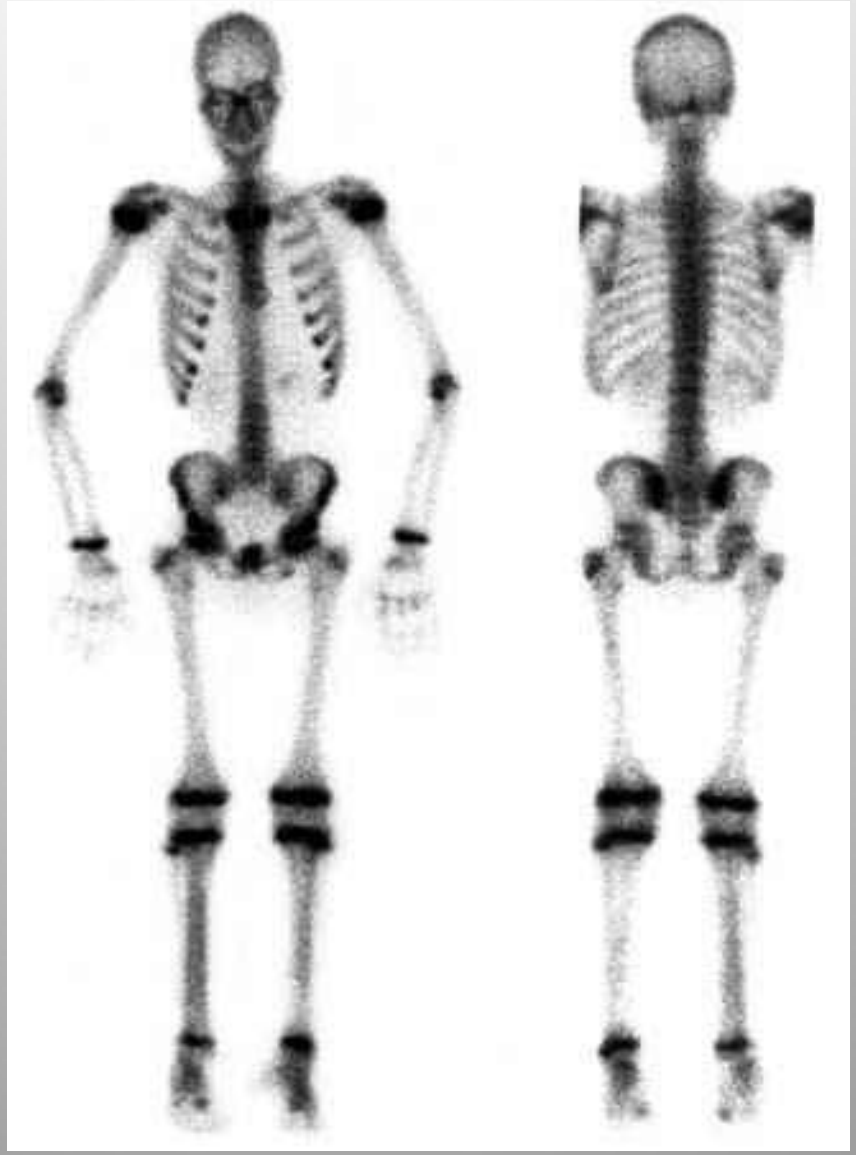
- Blood supply
- Metabolic activity of the lesion (accelerated bone turnover: osteogenesis and "reactive" osteogenesis or osteoblastic response)
- Concentration of the drug in circulation
- Capillary permeability
- Exchange surface

Imaging protocol:

- 555-740 MBq (15-20 mCi) is injected iv.
- In children 37 MBq (1 mCi) per 10 kg. TT
- 3 hours after application the skeletal scintigraphy is done and/or SPECT
- In some lesions three-phase bone scan is done: flow phase, blood pool (tissue phase) and skeletal phase.



Normal whole body bone scan



Normal whole body scan in child-growth centers

Clinical aplication of skeletal scintigraphy

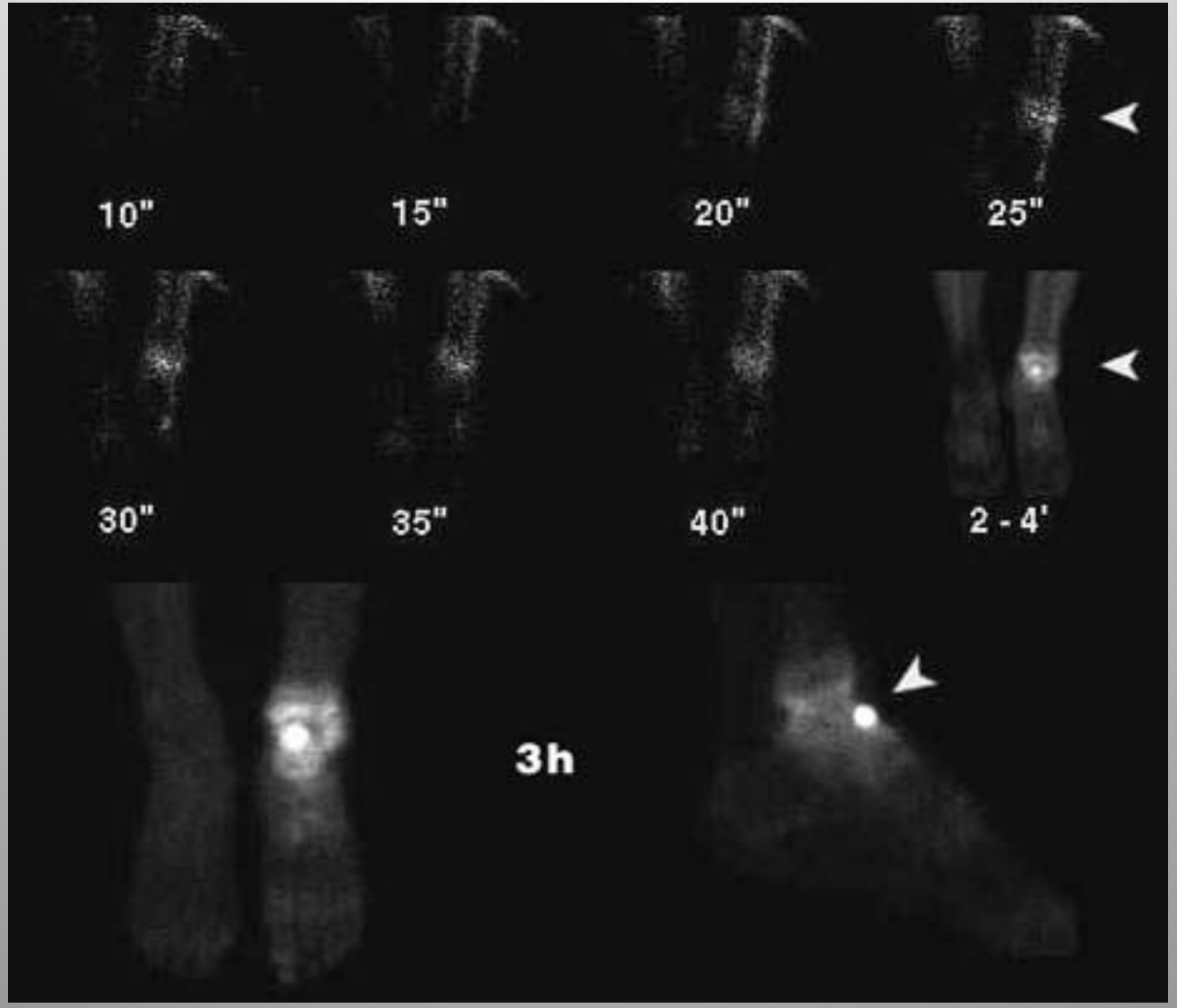
- **Bone tumors:**

- Benign and malignant: although malignant have avid uptake of the bone-seeking radiopharmaceuticals, it is not possible to differentiate them

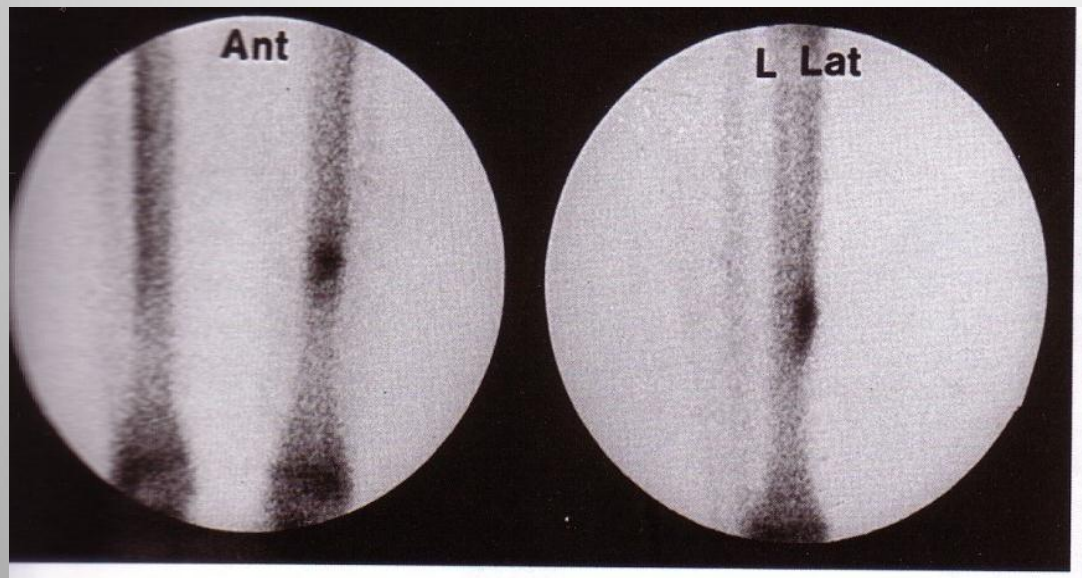
- benign tumors and tumor like lesions: osteoma, Paget-disease, hypertrophic osteoarthropathy, ossifying fibroma, enchondroma, osteochondroma, chondroblastoma- increased accumulation of the radiopharmaceutical

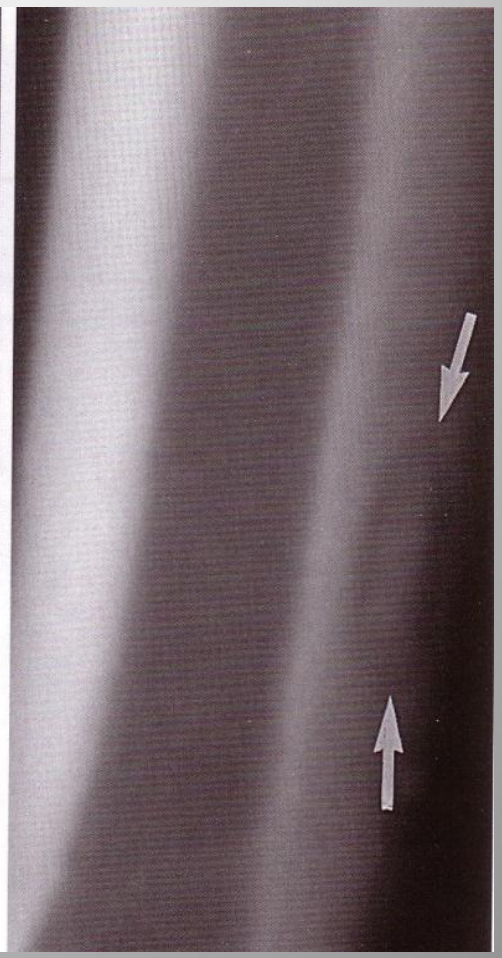
Benign bone tumors

- The patient feels pain and radiographic recordings can be negative
- Poor accumulation of rf initially, except osteoid osteoma (osteoid osteoma had poor visualisation on X-rays but excellent on bone scan)
- Osteoid osteoma intensive focal uptake with "double density" sign.
- On delayed images accumulate more activity: osteoblastoma, chondroblastoma, giant cell tumors, osteoid osteoma.
- Enchondromas can be "hot" and "cold".
- Chondroblastomas demonstrate medium intense uptake on bone scan
- Bone cysts are usually "cold" in the central area, and have a "warm" ring around.
- Fibrous dysplasia also showing increased activity.
- Paget's disease and fibrous dysplasia must be differentiated from metastatic disease-BEWARE!
- Hypertrophic osteoarthropathy, ossifying fibromas, osteochondromas, chondroblastomas, enchondromas – „HOT” lesions



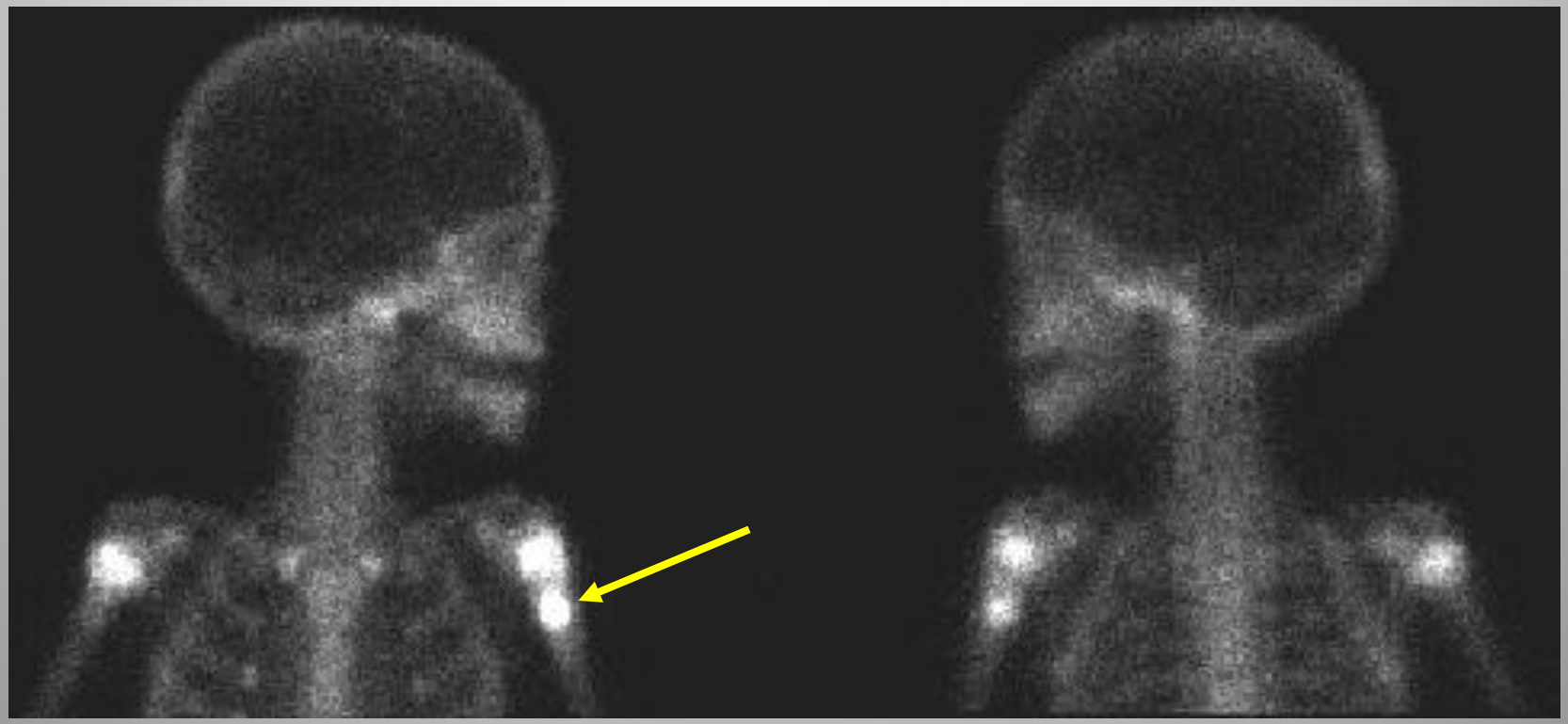
Osteoma



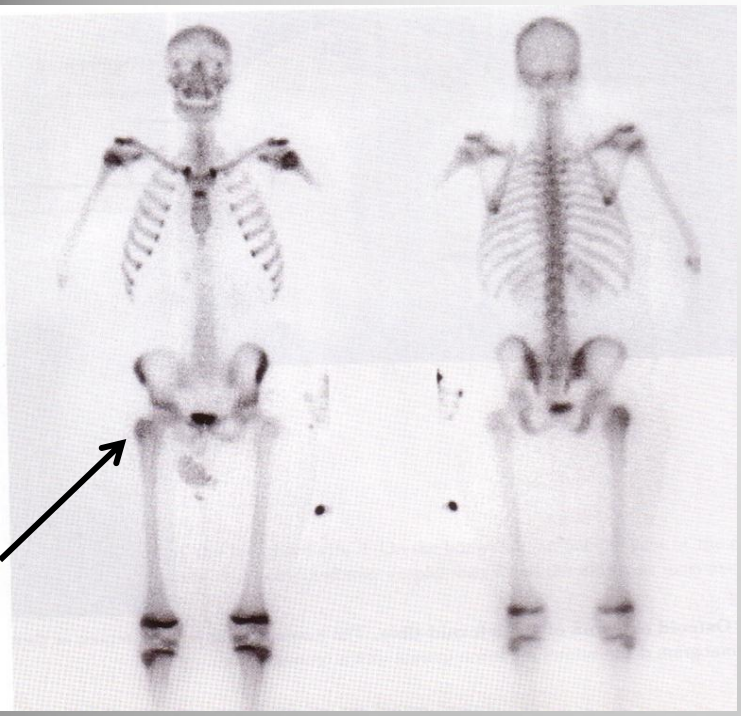


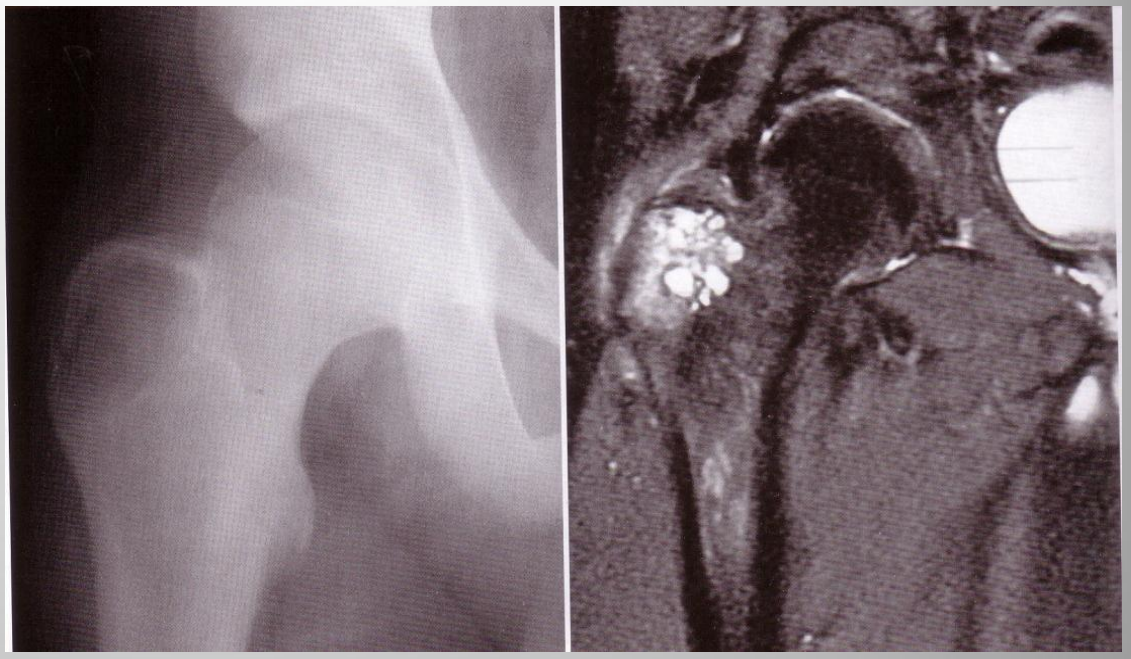
Osteoma

Osteoblastoma



A rare bone tumor (14% of benign bone tumors), similar to osteoid osteoma but larger, usually benign, rarely can be malignant.
The most common (40%) in the spine and long bones; in 80% of cases at a younger age (up to 30 years of age).





CHONDROBLASTOMA

Bone scan: the focus of increased activity in the large trochanter of the right femur.

X-rays: lytic lesion in the same area

MR: chondroic matrix

Benign tumor of bone (extremely may be malignant); 1% of all bone tumors

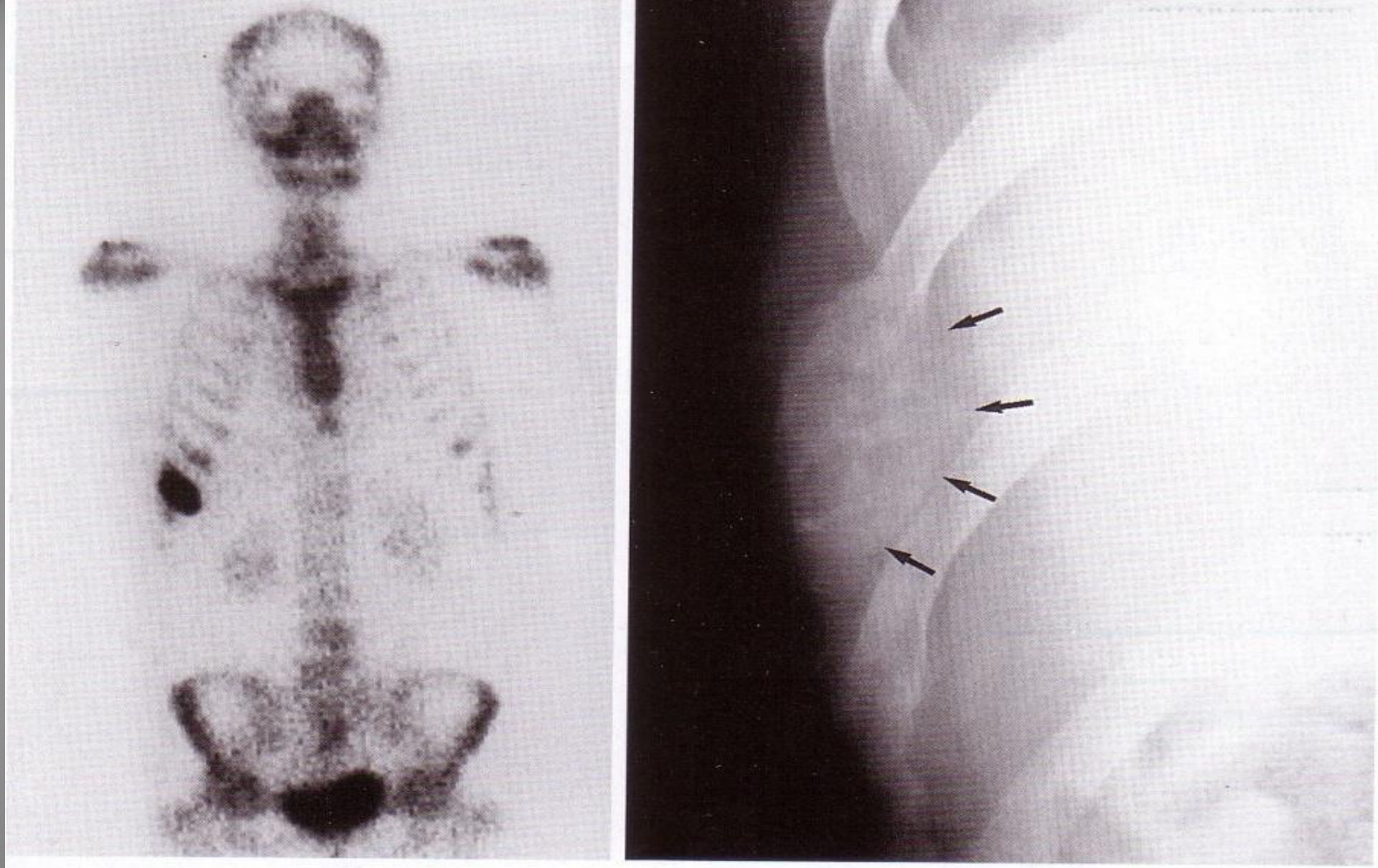


FIGURE 9–14. Multiple enchondromas. *Left,* On the anterior bone scan, areas of increased activity are noted, including in the ribs. *Right,* A rib radiograph shows a characteristic expansile lesion with central matrix.

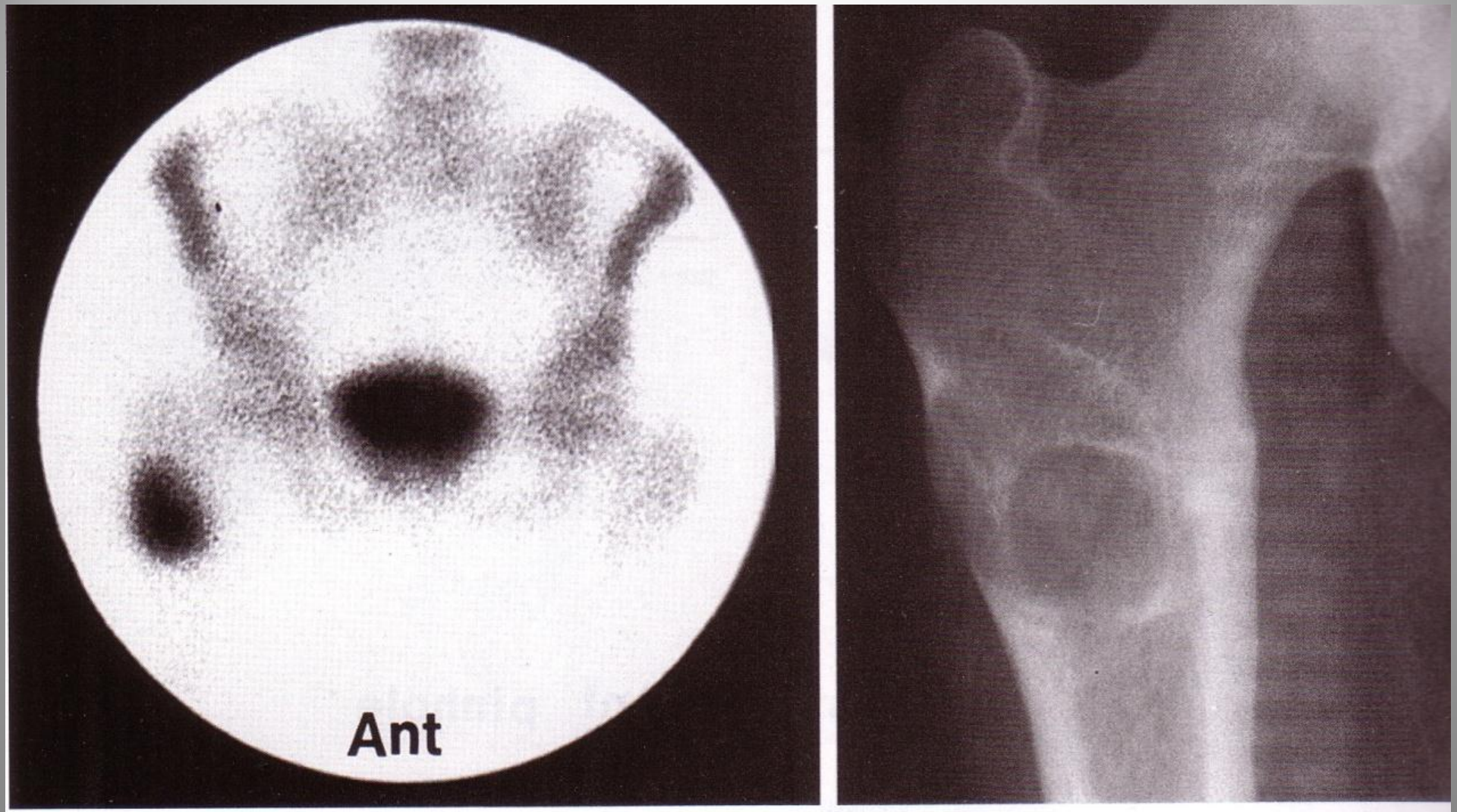
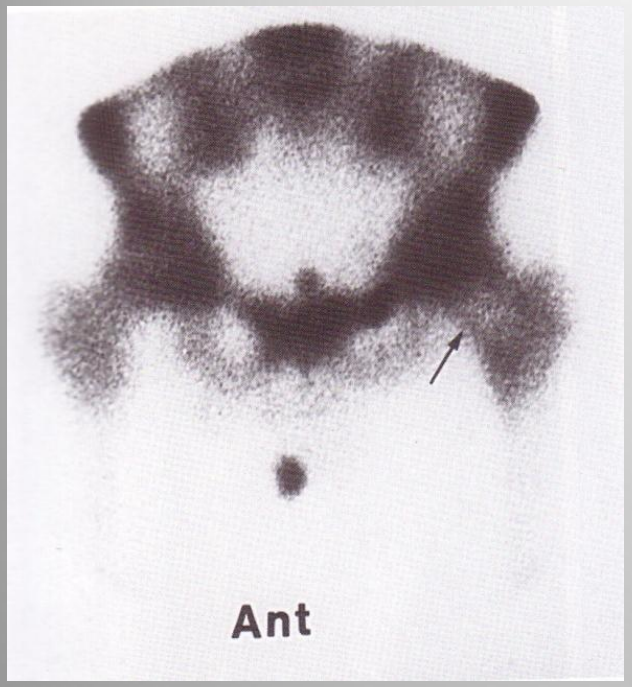
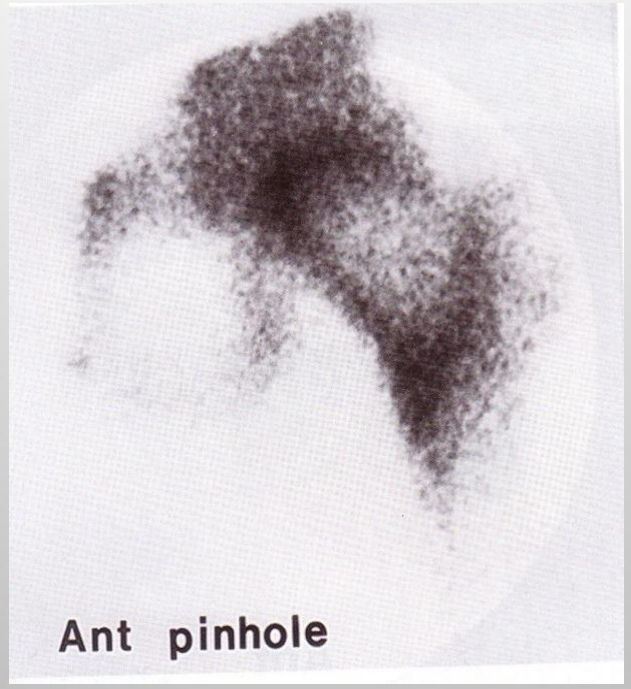
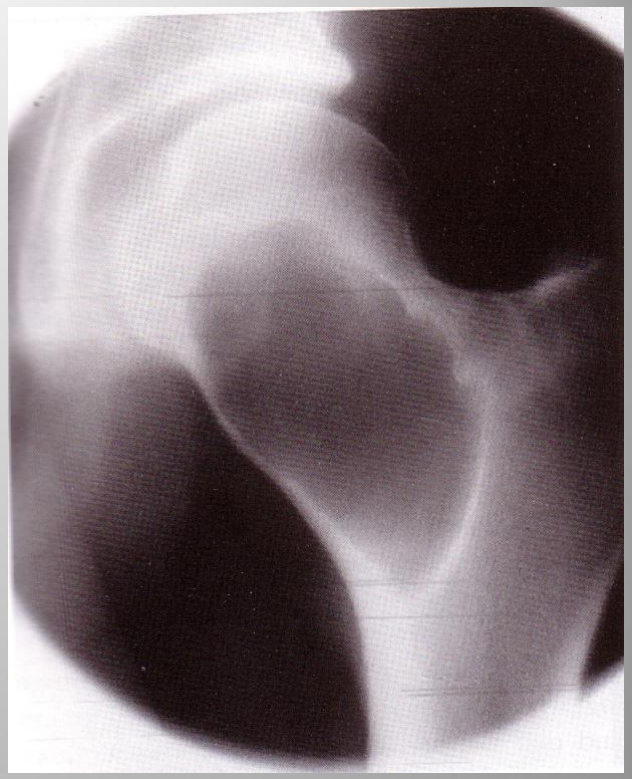


FIGURE 9–17. Fibrous dysplasia of the proximal right femur. *Left,* The anterior view of the pelvis shows markedly increased activity in the metaphysis of the promixal right femur. *Right,* The radiograph shows a well-demarcated, expansile, lucent lesion.

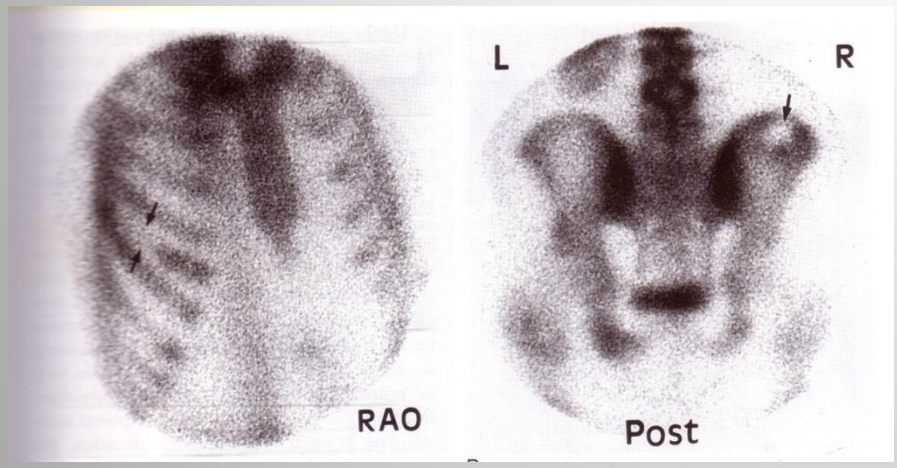




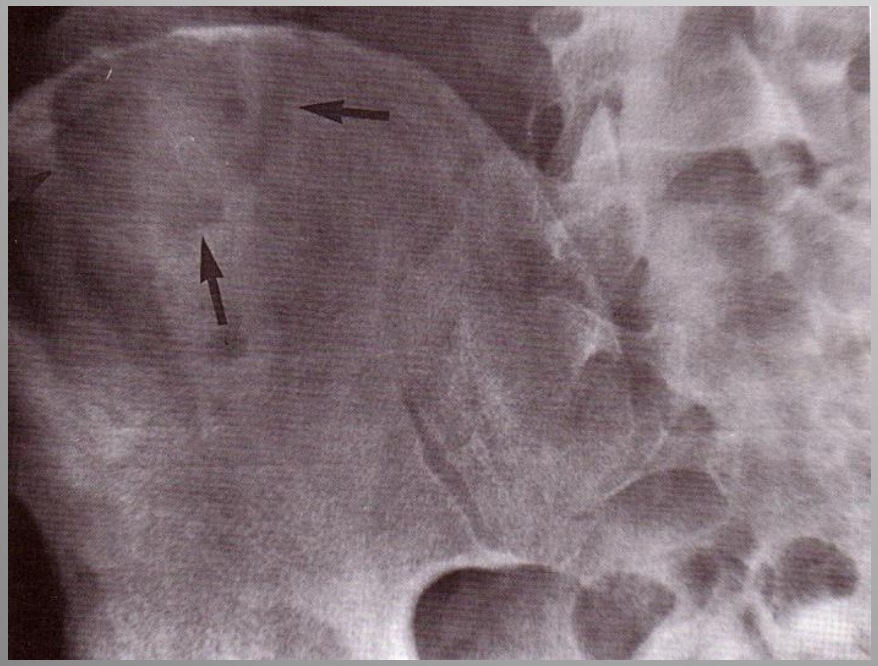


CYST

Scintigraphically "cold" zone of left femoral neck with peripheral ring of increased activity, better visible with the pin-hole collimator



„cold” spots caused by the lytic metastasis of kidney cancer



RTG: lytic lesion in same place

Clinical aplication

- **Malignant bone tumors:**

  - **osteosarcoma:** within area of increased accumulation there are parts of reduced accumulation

  - **Ewing's sarcoma:** homogeneously increased uptake with blurred border to healthy bone

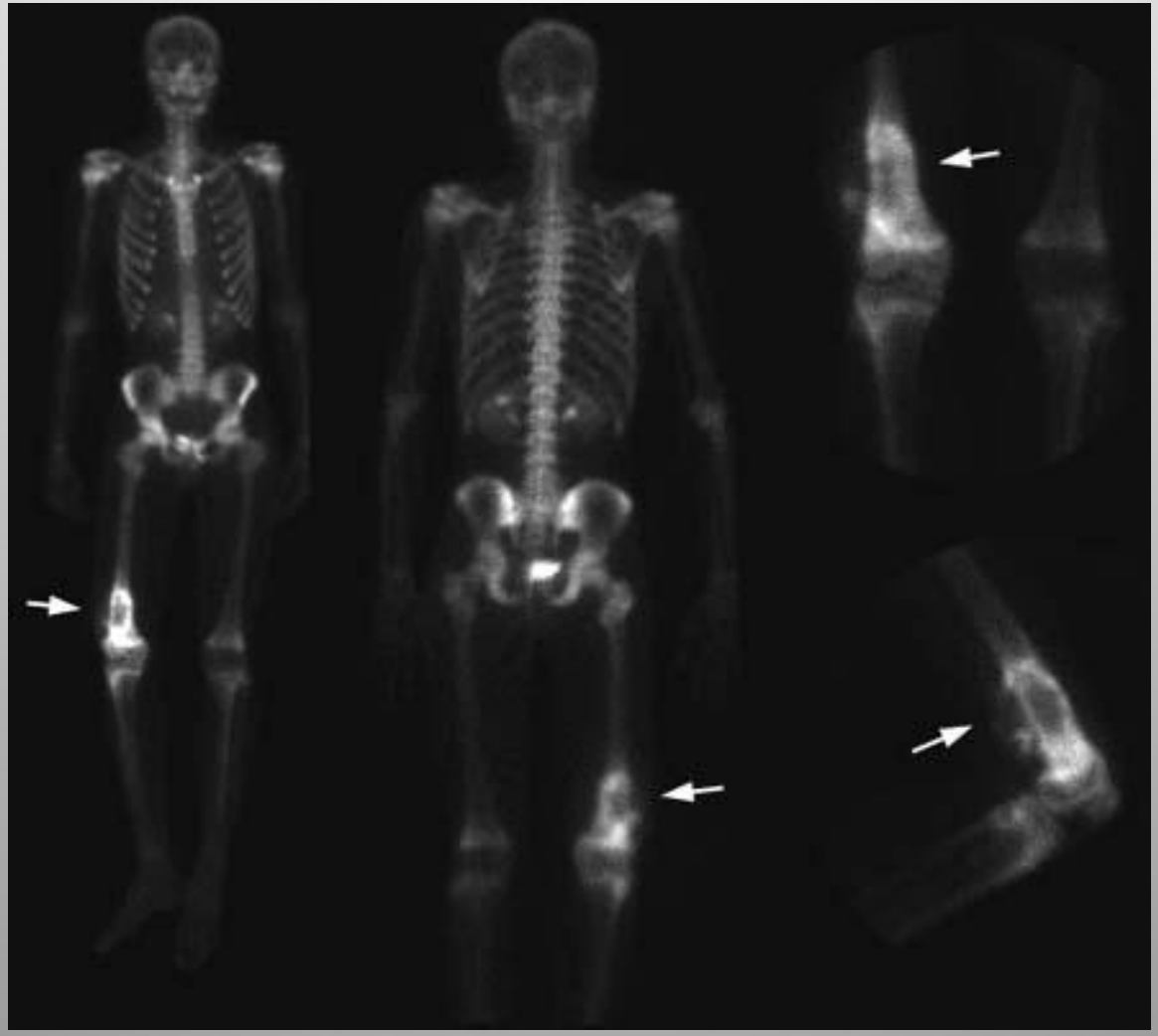
  - **chondrosarcoma:** less intensive uptake with „hot" zones inside of the bone and clear border to healthy bone

  - **On three-phase bone scan: increased perfusion and increased uptake on immediate static (blood pool images) and delayed static images**

OSTEOSARCOMA

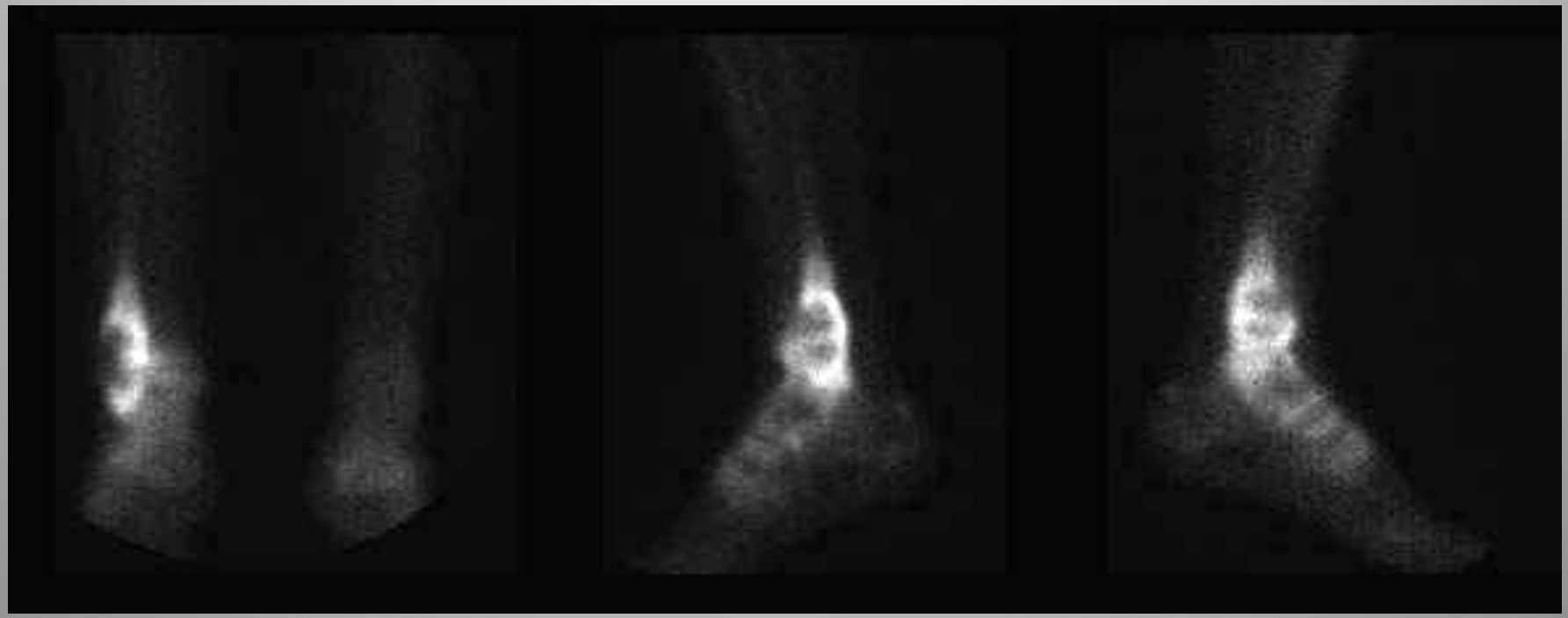
The most common primary bone tumor, in 50% of cases occurring in the knee, but also in other parts of the skeleton (pelvis, humerus, spine), hematogenous spread, most commonly metastasizes to the liver and lungs

Osteosarcoma of the femur



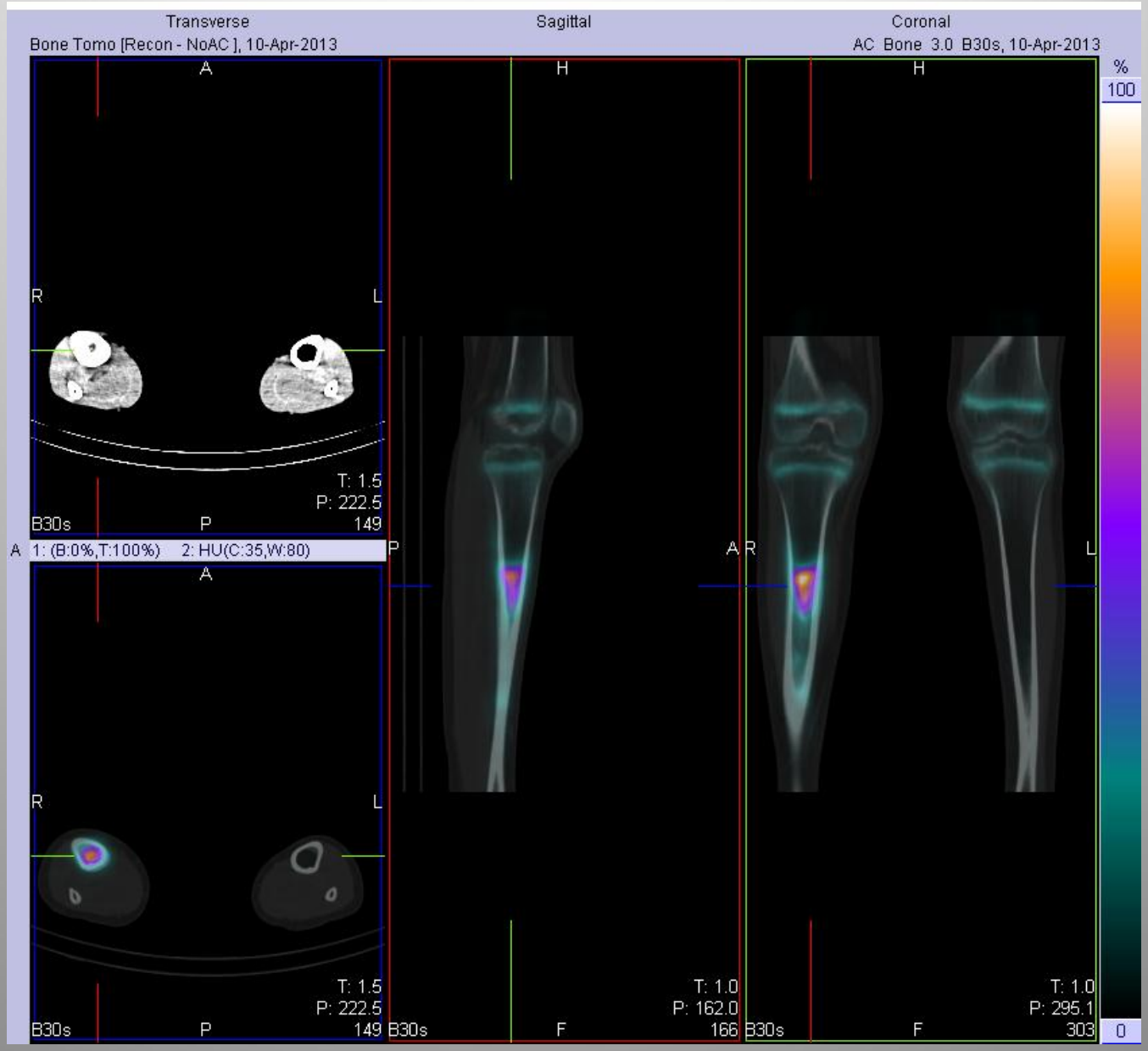
Within the area of increased uptake there are zones of reduced accumulation

Osteosarcoma of the fibula



Within the area of increased uptake there are zones of reduced uptake

OSTEOSARCOMA



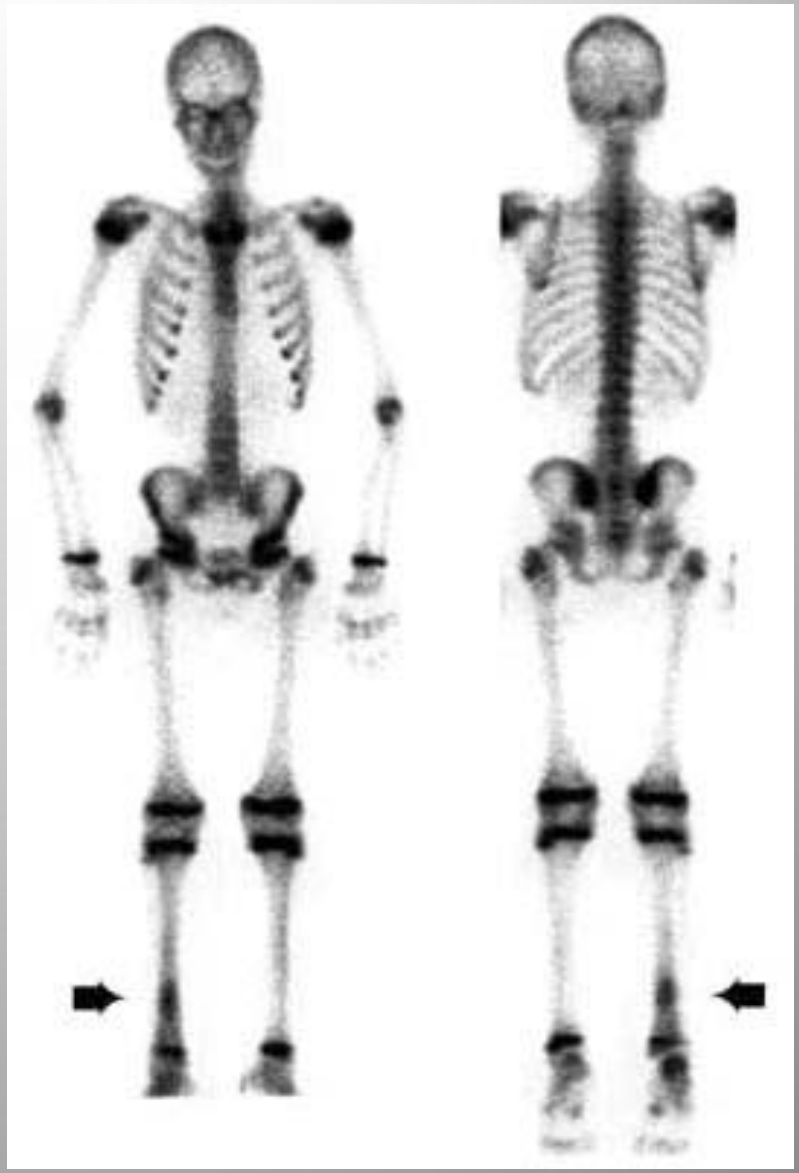
OSTEOSARCOMA

EWING'S SARCOMA

Most commonly in the pelvis, femur, tibia, humerus, ribs.

It occurs most often in children age 10-20 years.

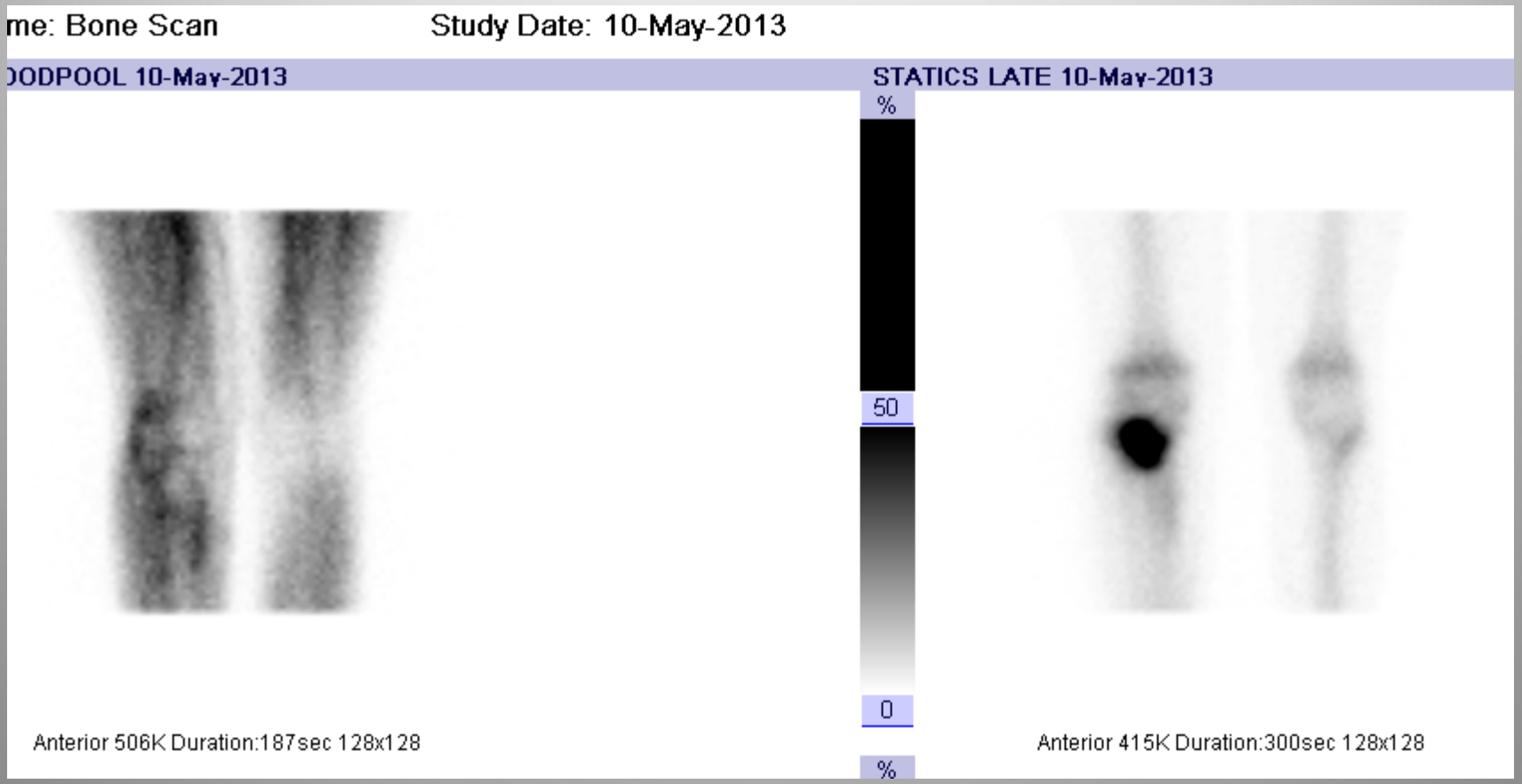
Homogeneous uptake with blurred border to healthy bone**.**



Chondrosarcoma

30% of bone tumors, in all age groups, more often in the elderly

Synovial sarcoma



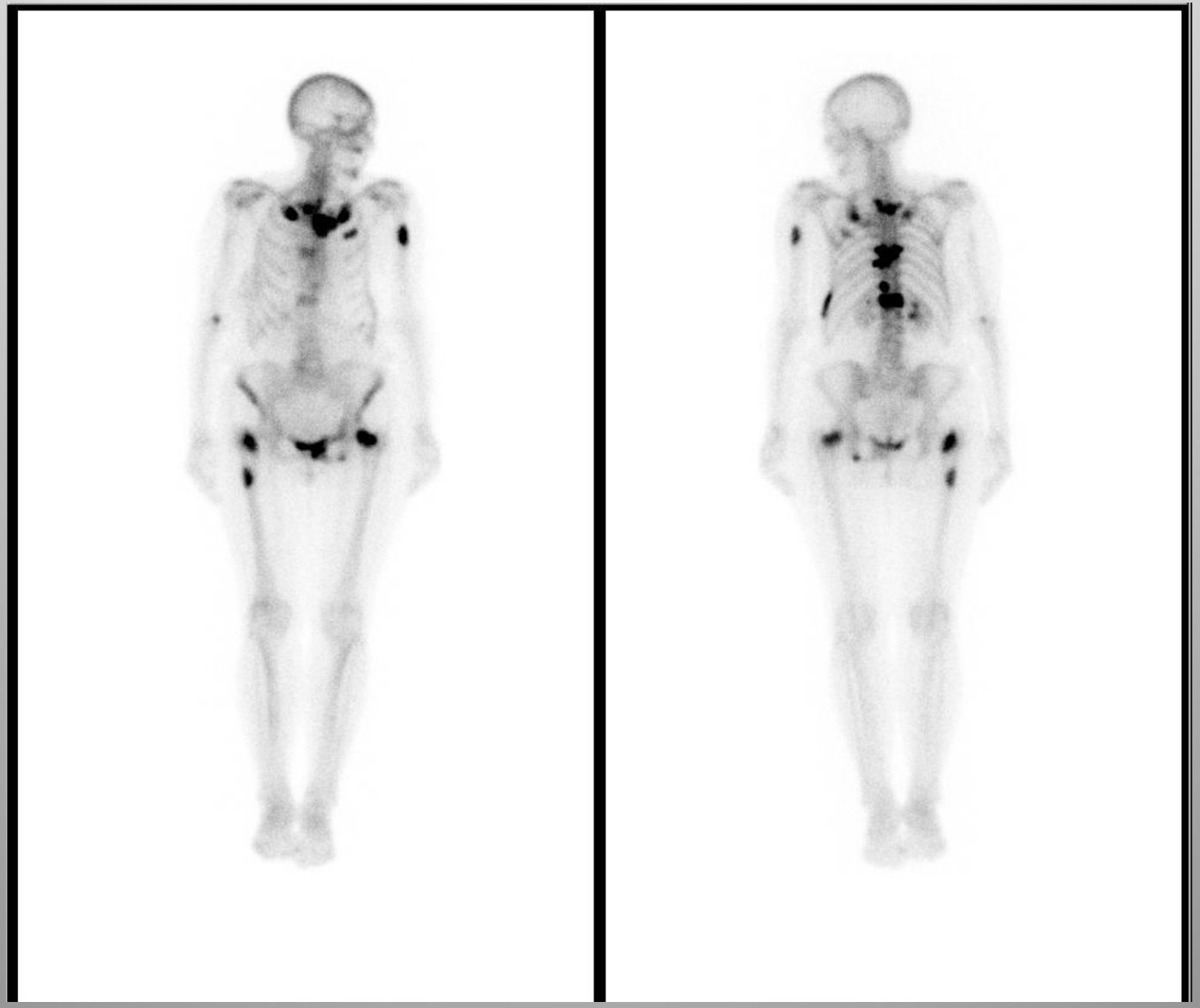
Synovial sarcoma

Clinical aplication of skeletal scintigraphy

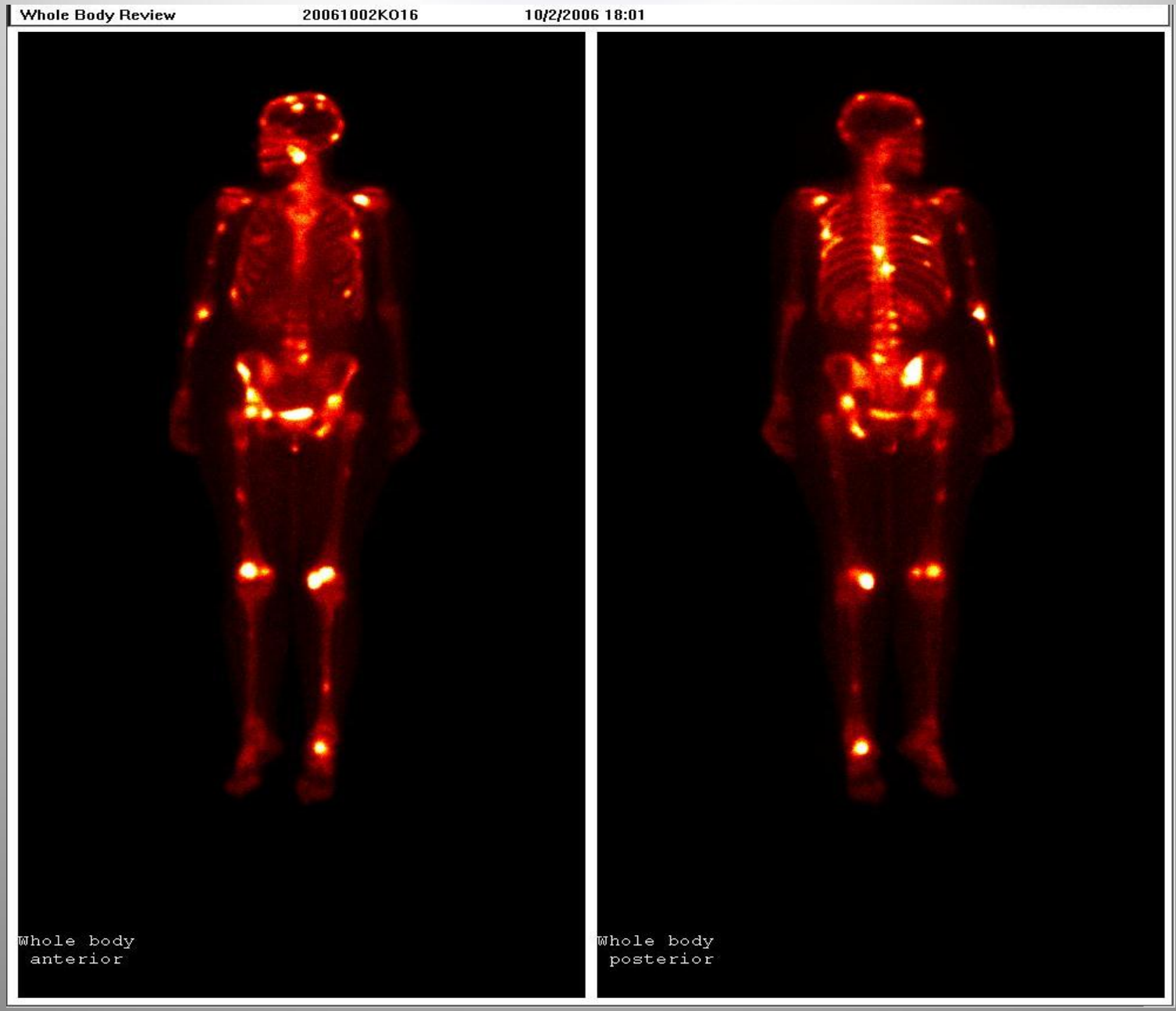
- **Metastatic bone disease**:
  - Provoke osteoblastic bone reaction even in cases where the lesion is osteolytic
  - Scintigraphic patterns are multiple focal lesions
  - The most common carcinoma who metastasise in bones: breast ca, prostate ca, lung ca, gastric ca
  - Bone scan may be used for staging, restaging and
  - **„super scan"** - in the case of diffuse involvement of the skeleton there will be a very high accumulation of activity in the skeleton (80% of the inj. dose) with an intense skeletal uptake and the absence of activity in the kidney and bladder, and very low activity in the circulation and soft tissues.

Bone metastases

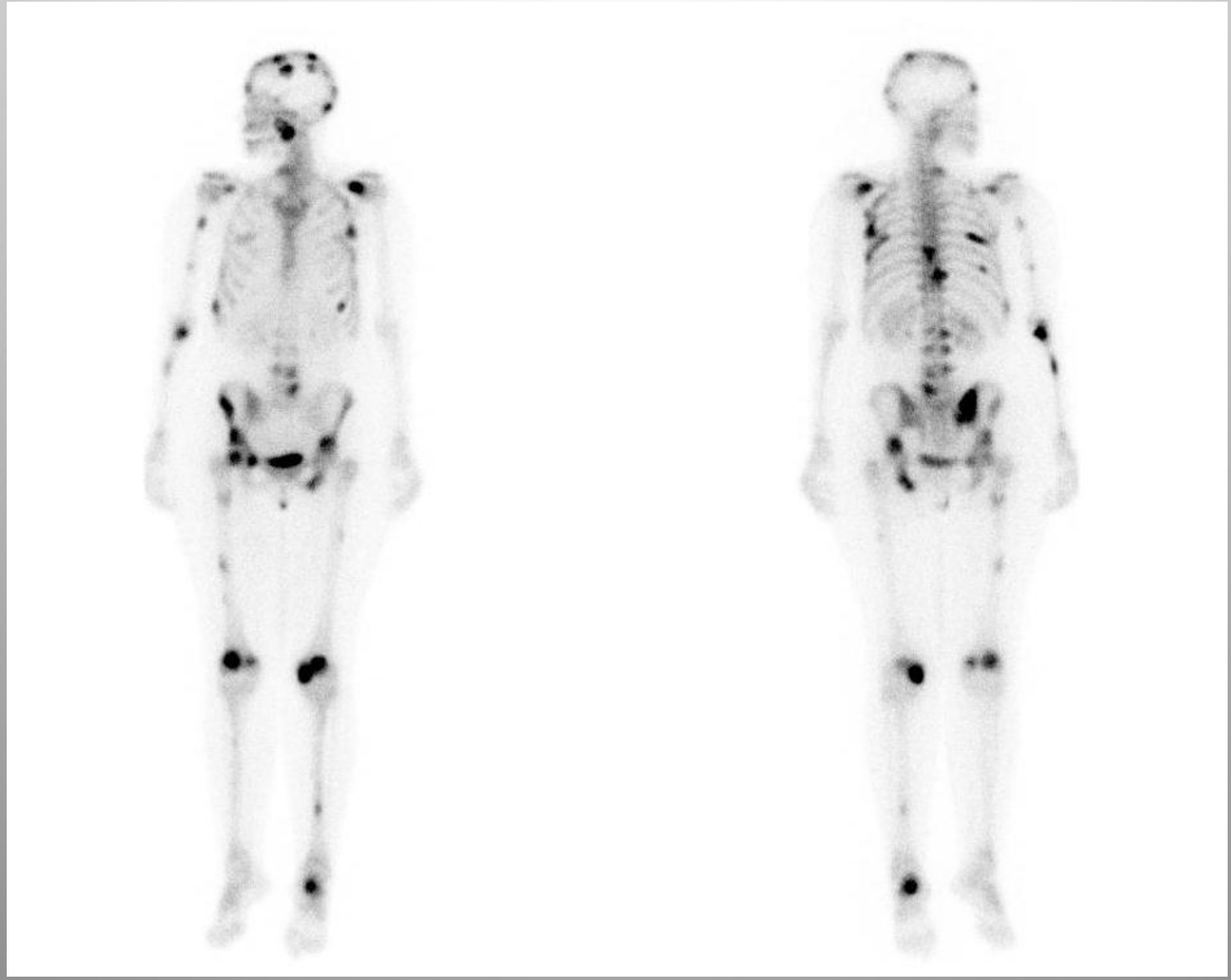
- 80% in the axial skeleton: the spine, chest, pelvis
- 10% in the skull
- 10% in the long bones
- we describe: the number of lesions, size and intensity of uptake



Breast carcinoma metastases

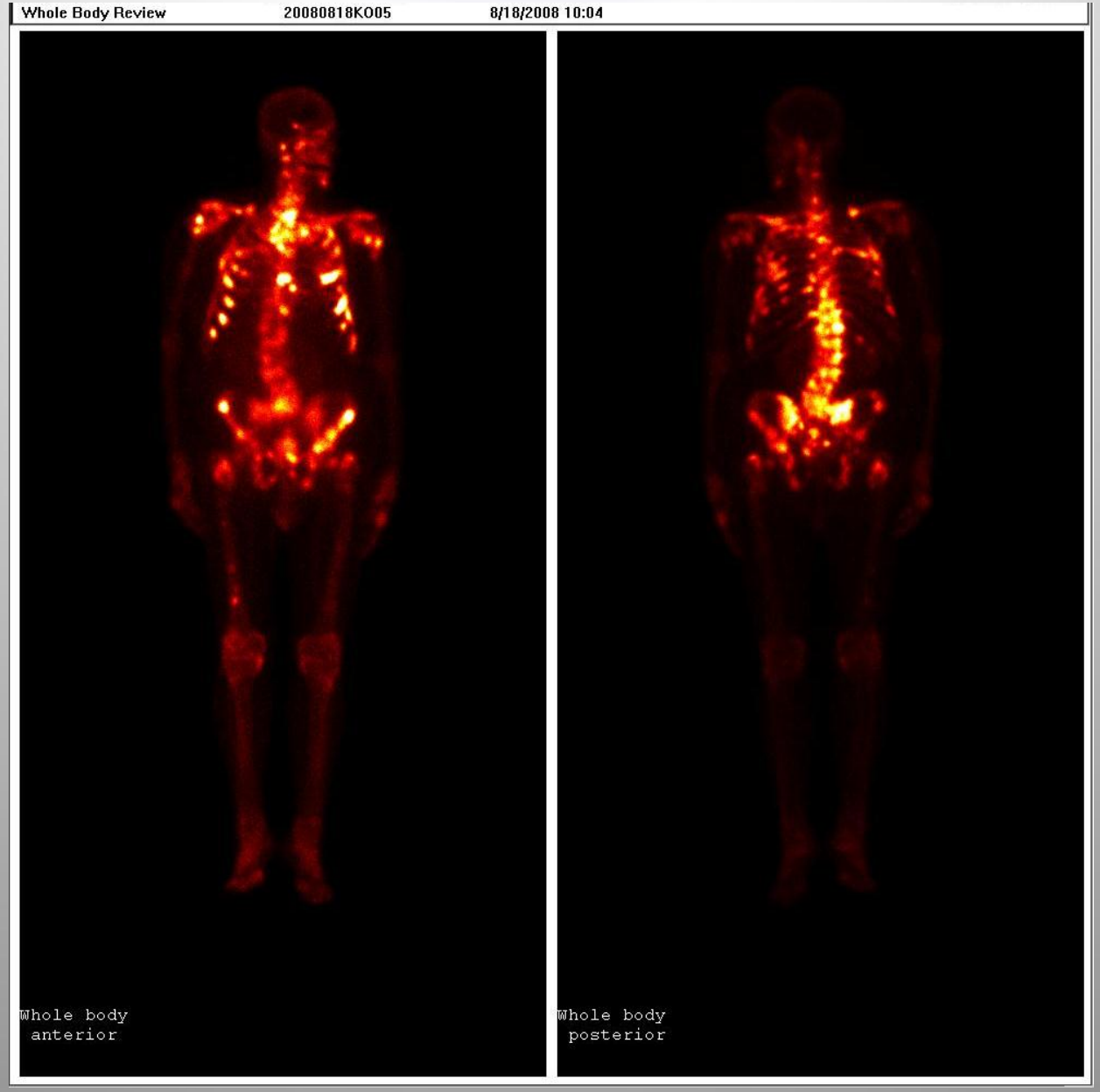


Breast carcinoma metastases

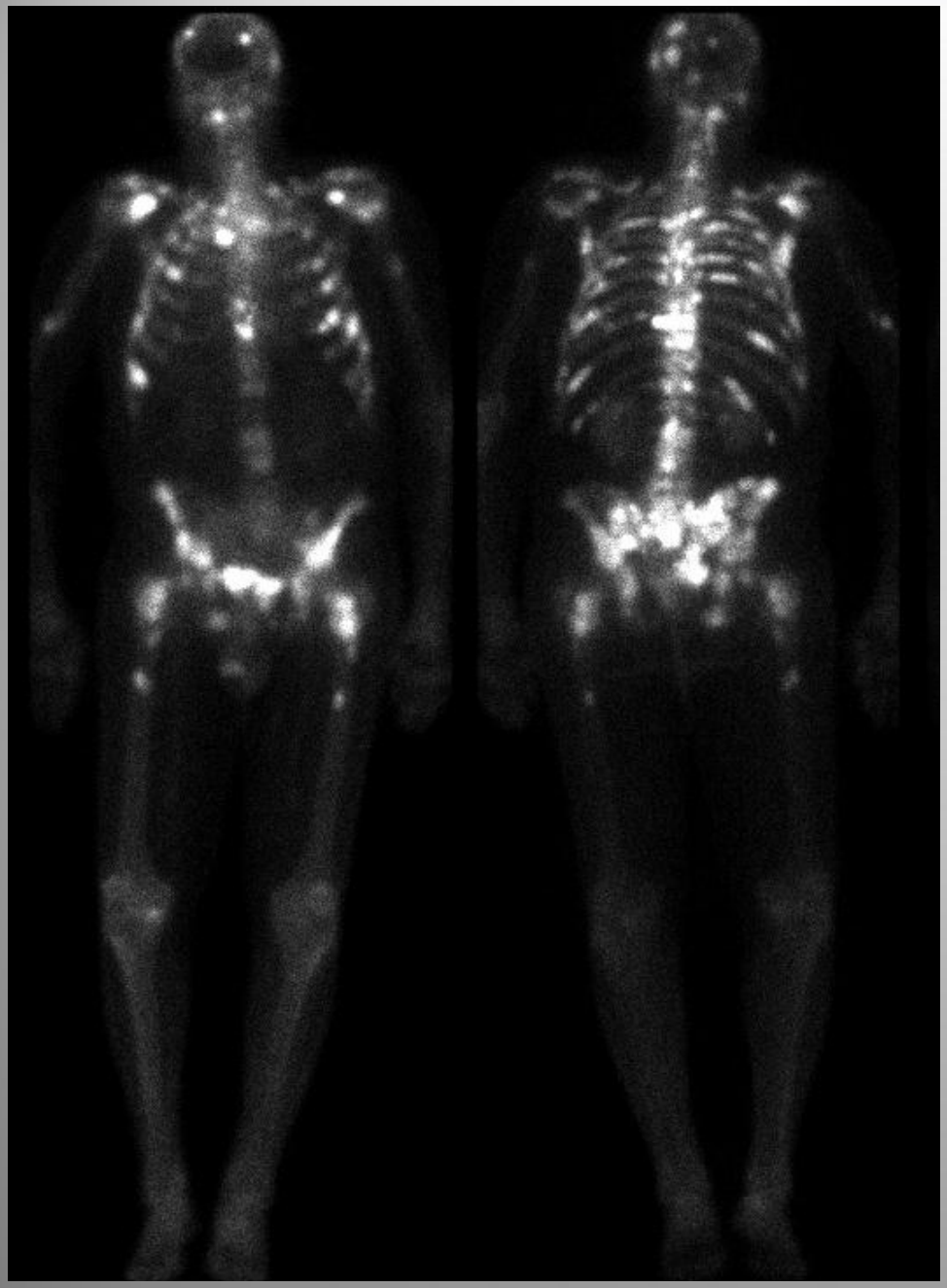


Breast carcinoma metastases

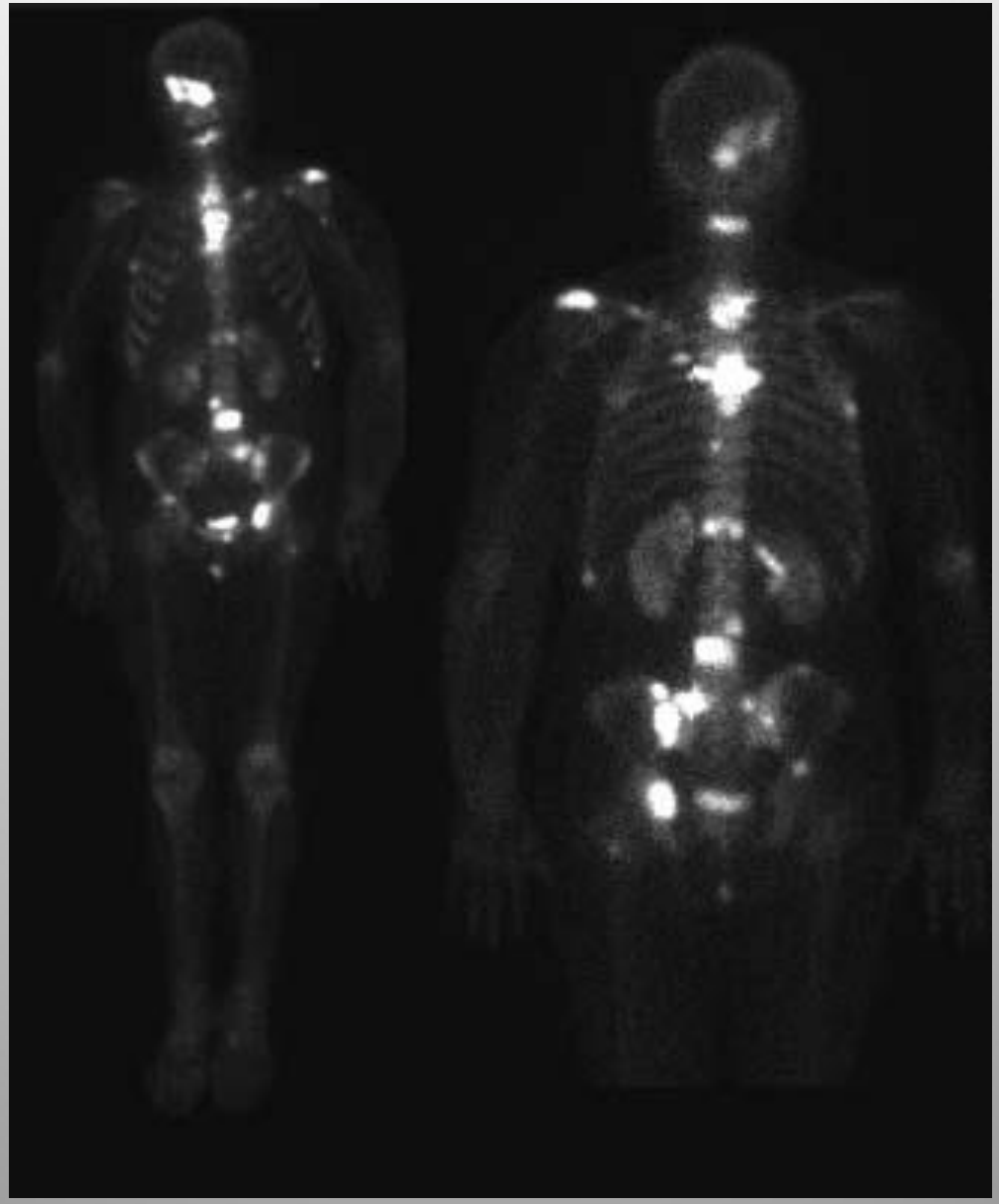
Prostate carcinoma metastases



Prostate carcinoma metastases

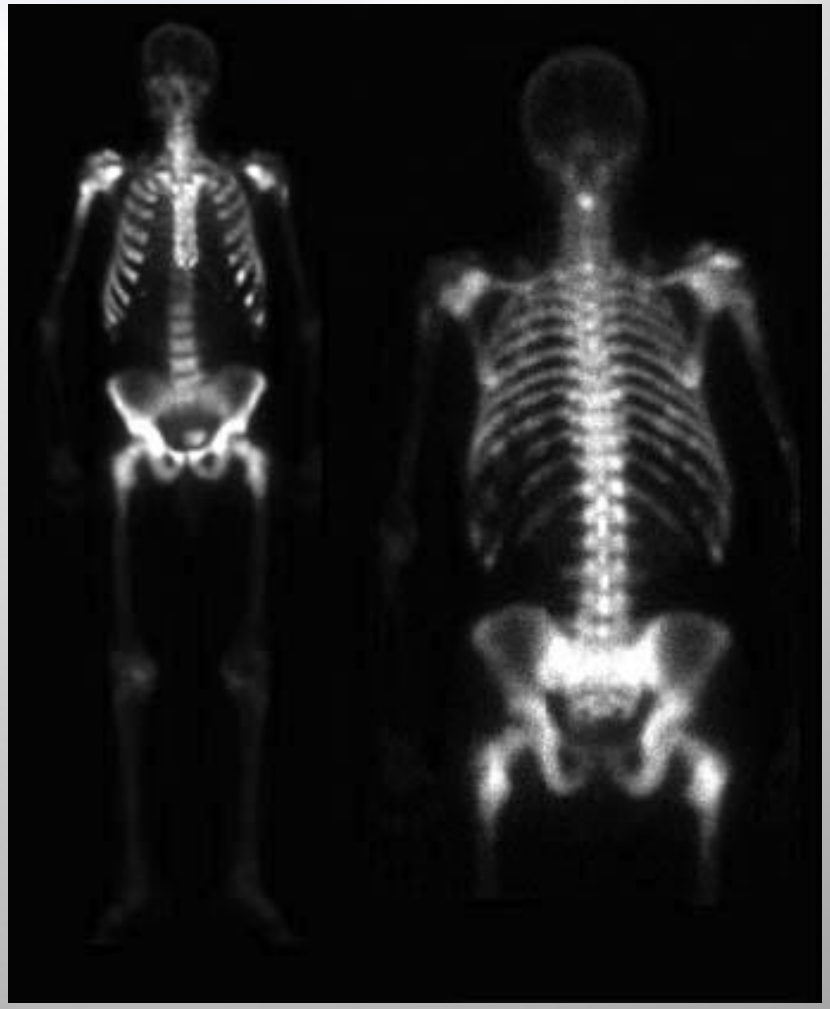


Prostate carcinoma metastases



Metastases

„Superscan”



„Super scan "- diffuse involvement of the skeleton with metastases, bone scan demonstrates markedly increased skeletal radioisotope uptake relative to soft tissues, in association with absent or faint urinary tract activity.

OSTEOMYELITIS

Detection, monitoring of therapeutic effect or exacerbation.

The most commonly located in the diaphysis of long bones (hematogenous-staphylococc).
X-rays- pos. only for 10-14 days after onset.

Scintigraphy: positive in all three phases of the three-phase scintigraphy

Increased perfusion of the affected bone, AND SURROUNDING TISSUE (as opposed to the tumor), intense uptake in lesions on early static scintigraphy (tissue phase) and even more intense (and more localized to the bone) in the late static scintigraphy

Cellulitis showing increased radiotracer uptake on early sc. (I, II phase) while on the late static sc. activity decreases.

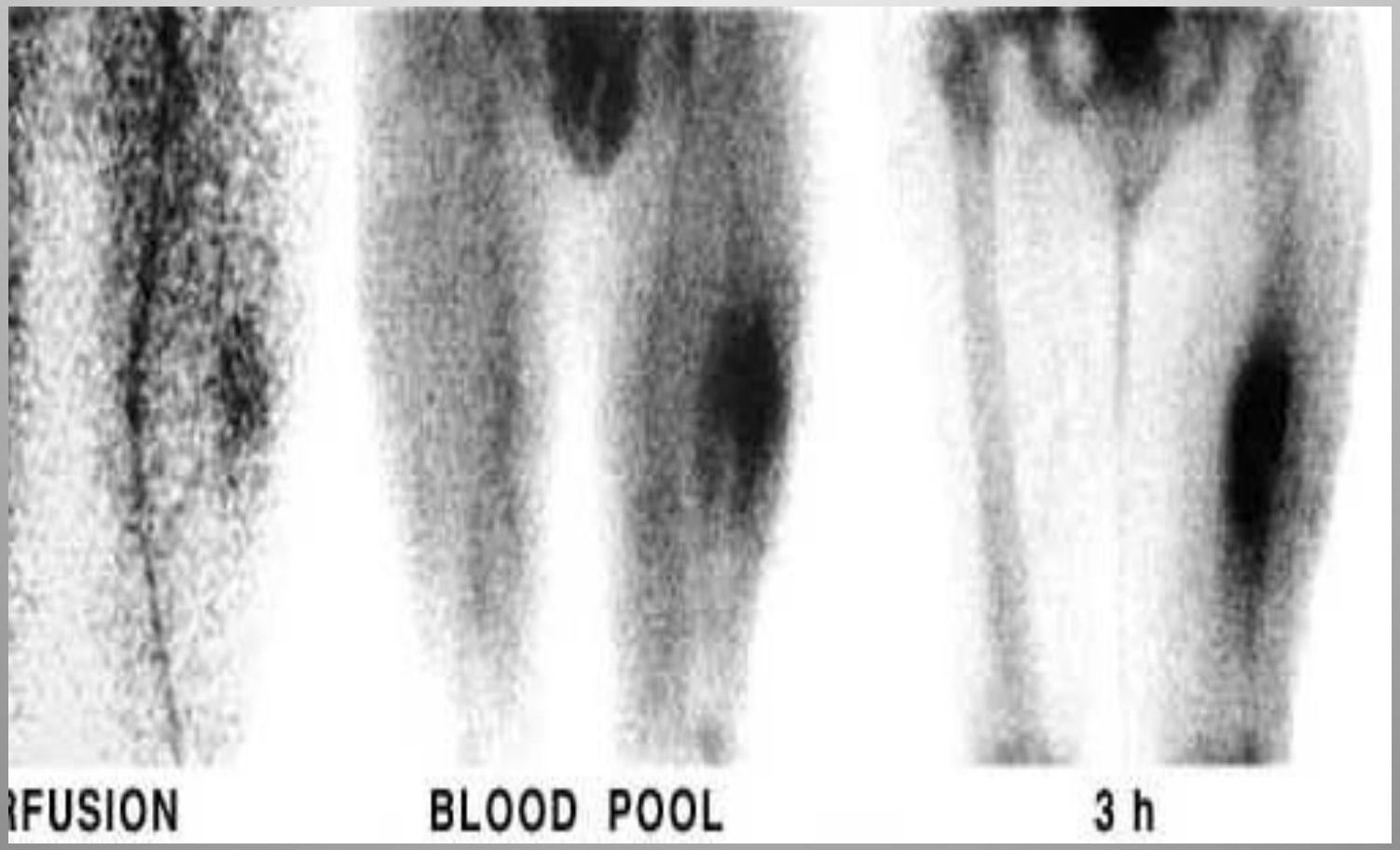
Septic arthritis - increased accumulation of radiotracer on both sides of the joint (proximal and distal).

Osteomyelitis:

For the diagnosis of osteomyelitis can also be used:

- Ga-68- citrate,
- labeled leukocytes,
- antigranulocyte antibodies,
- marked human albumin nanocolloid particles
- human immunoglobulin
- 18 FDG

Osteomyelitis



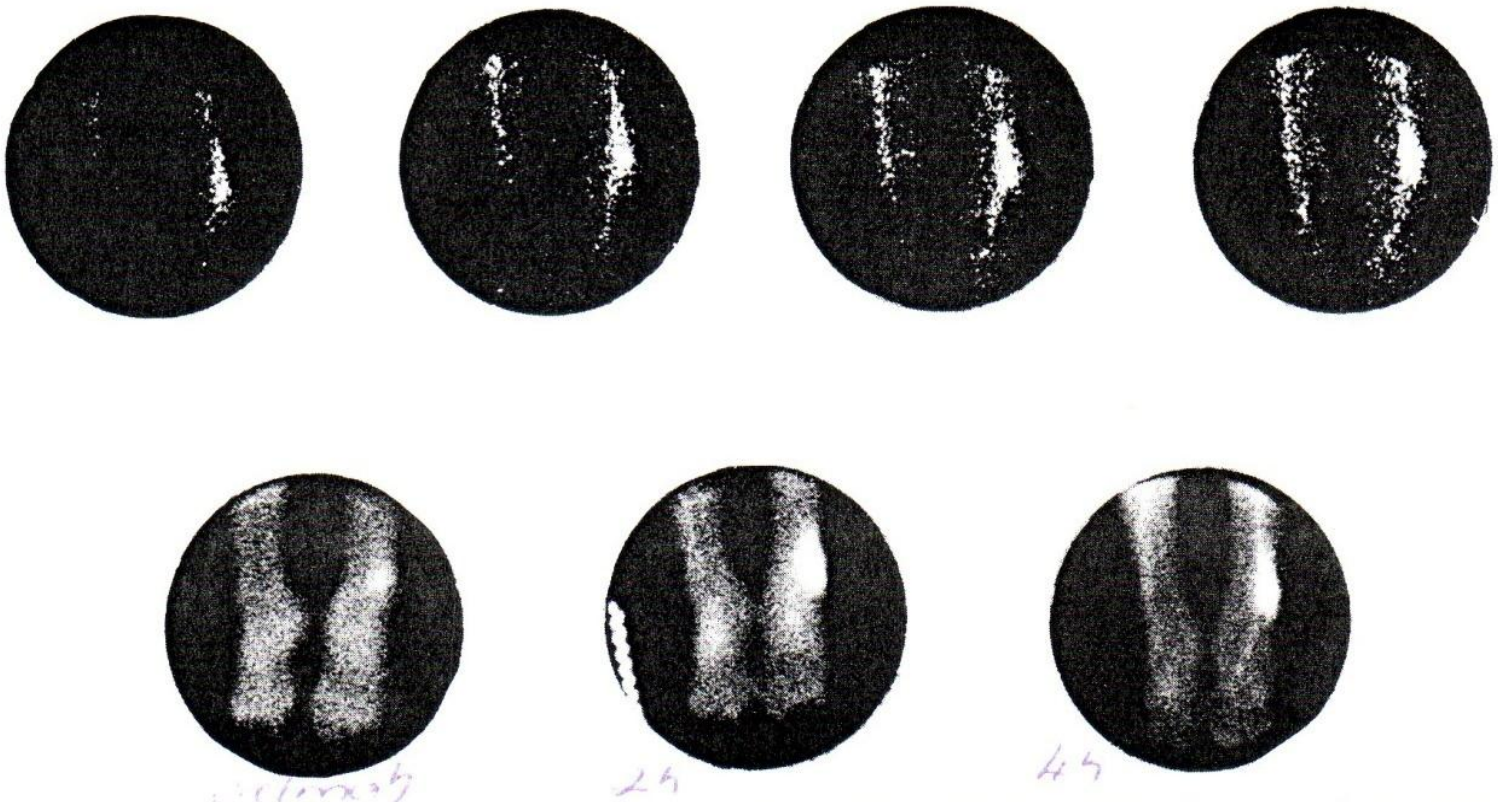


Fig. 8–5. Three-phase bone scan in osteomyelitis of the left distal tibia. Top row: Sequential 5-sec scintiphotos following intravenous injection of 20 mCi (740 MBq) Tc-99m MDP show focal hyperemia in distal tibia. Bottom row: left, immediate blood pool image showing increased perfusion; center, delayed 2-hr image; right, delayed 4-hr image showing increasing bone-to-soft tissue ratio.

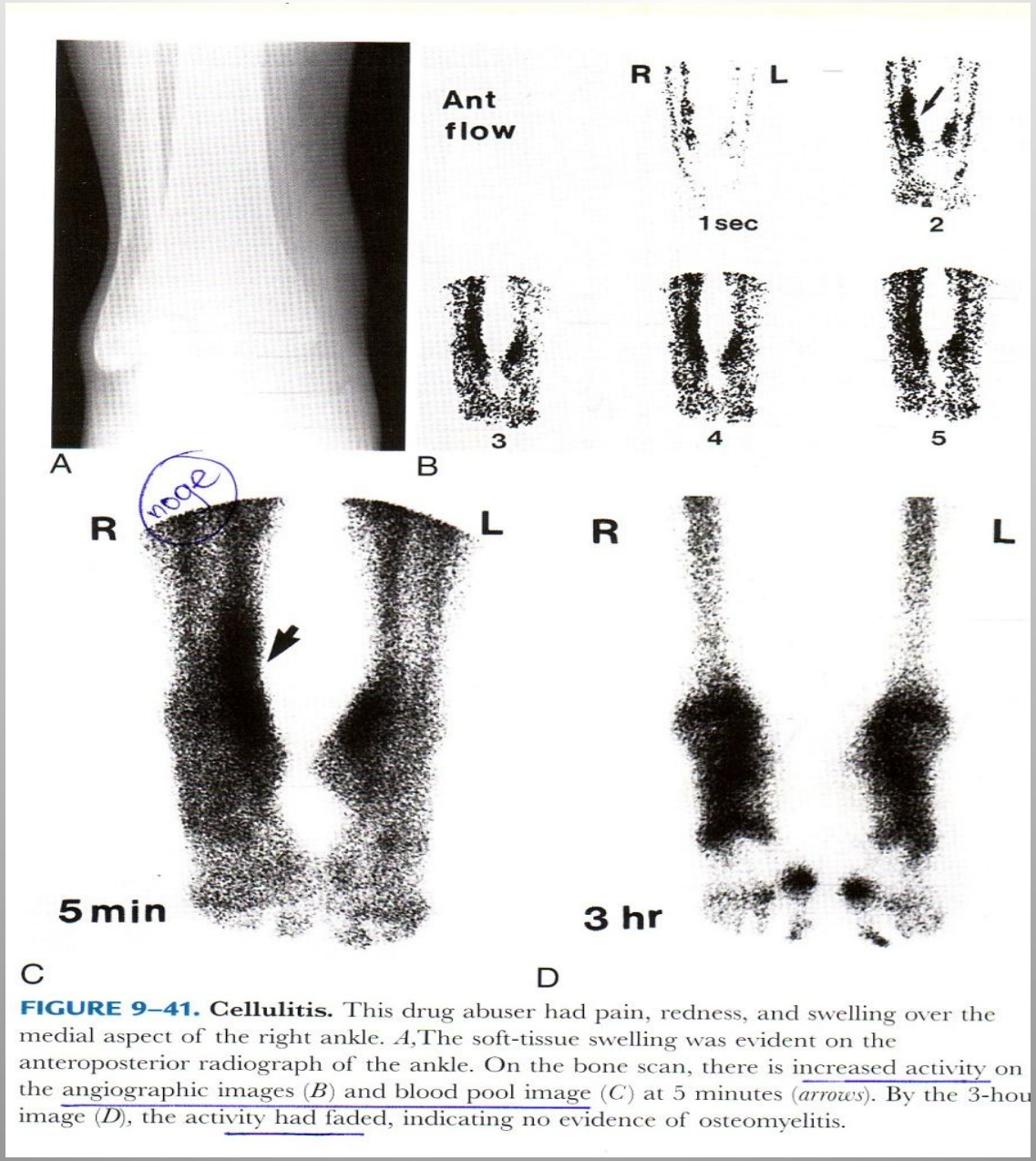


FIGURE 9–41. Cellulitis. This drug abuser had pain, redness, and swelling over the medial aspect of the right ankle. *A*,The soft-tissue swelling was evident on the anteroposterior radiograph of the ankle. On the bone scan, there is increased activity on the angiographic images (*B*) and blood pool image (*C*) at 5 minutes (*arrows*). By the 3-hou image (*D*), the activity had faded, indicating no evidence of osteomyelitis.

Cellulitis

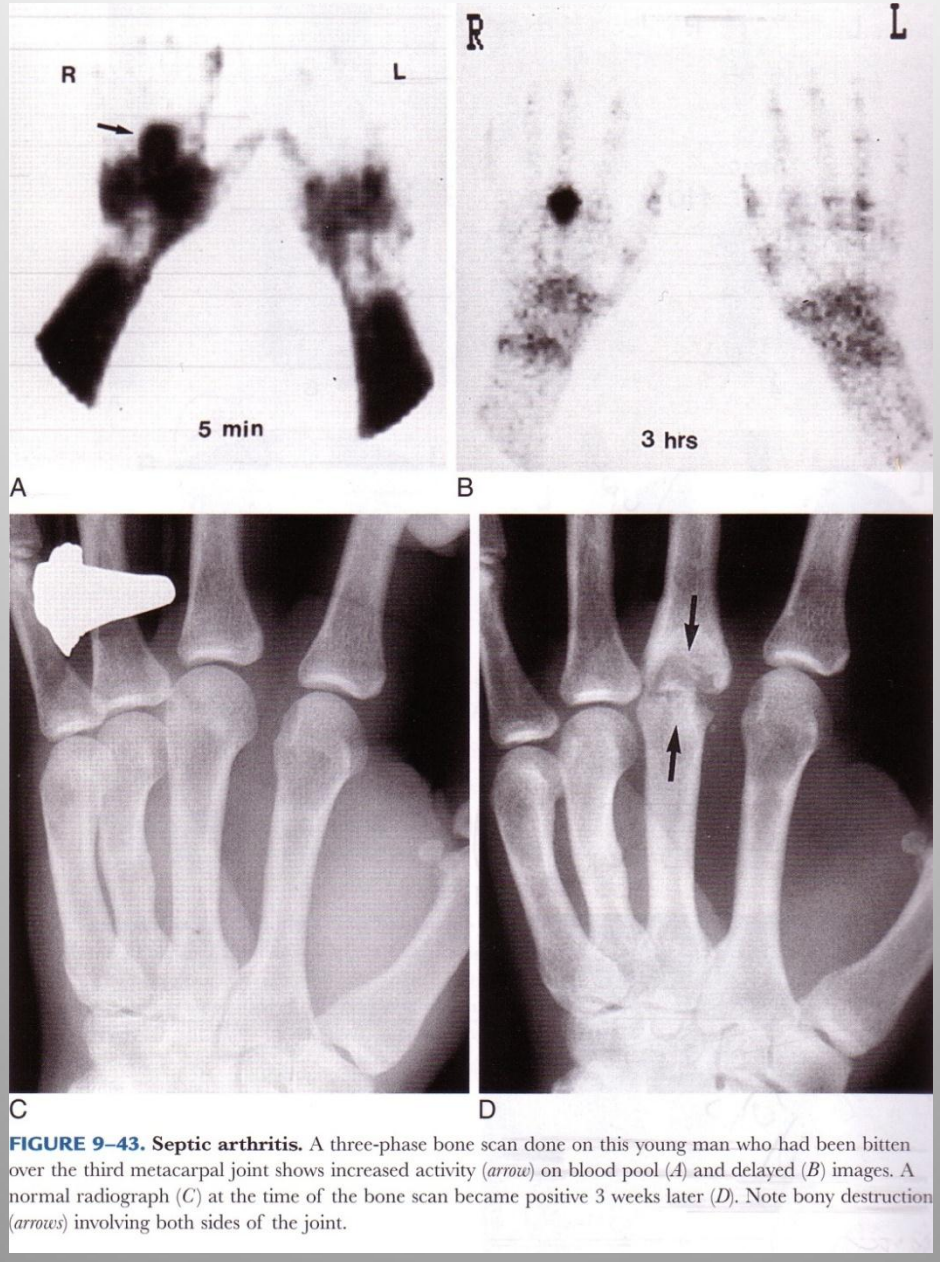


FIGURE 9–43. Septic arthritis. A three-phase bone scan done on this young man who had been bitten over the third metacarpal joint shows increased activity (*arrow*) on blood pool (*A*) and delayed (*B*) images. A normal radiograph (*C*) at the time of the bone scan became positive 3 weeks later (*D*). Note bony destruction (*arrows*) involving both sides of the joint.

Septic arthritis

Joint prostheses: loosening or inflammation

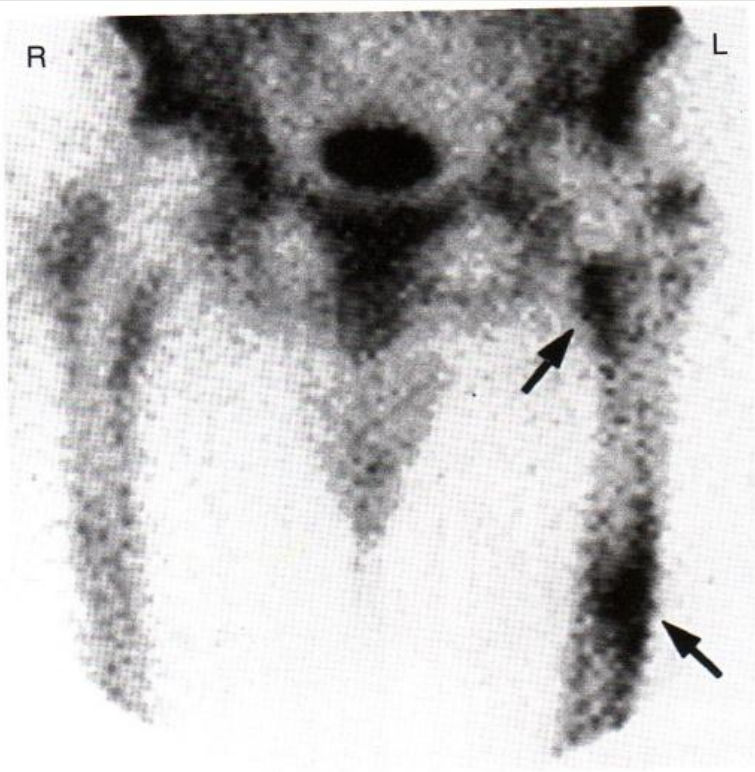
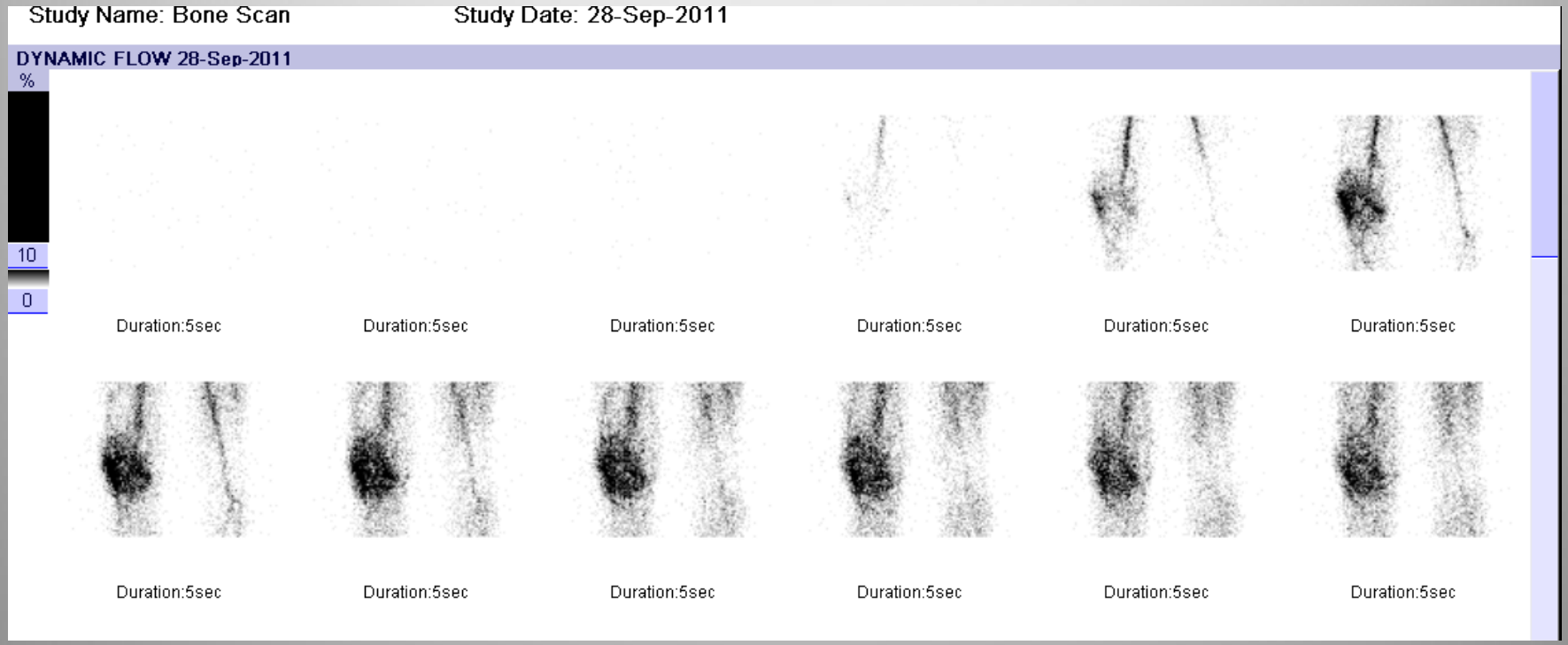
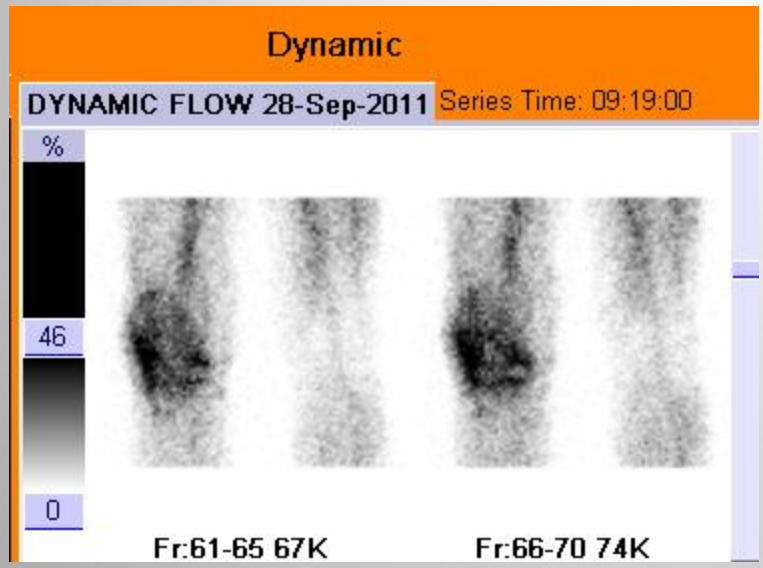
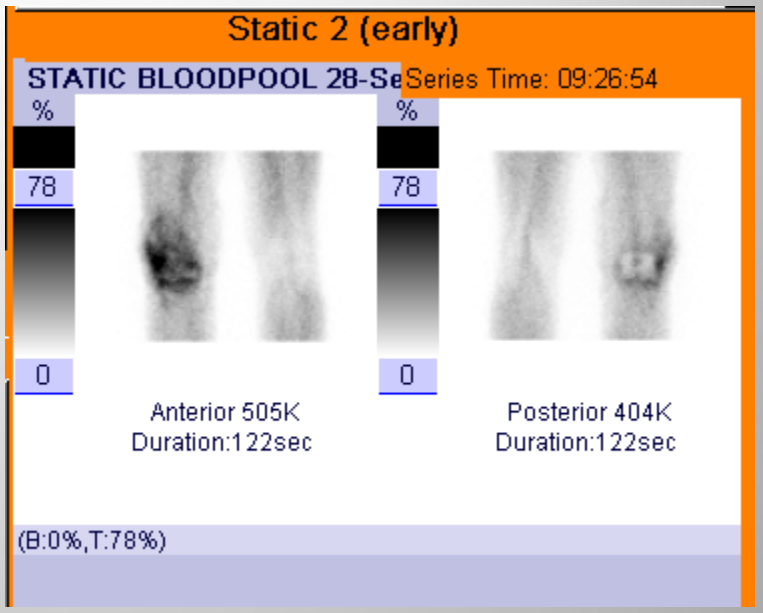


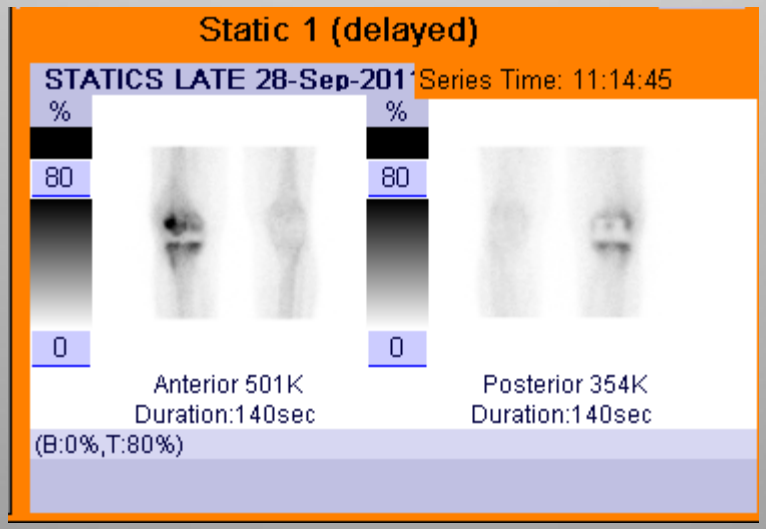
FIGURE 9–39. Loose hip prosthesis. This patient had bilateral cemented hip replacements 3 years ago. The prostheses account for the cold defects seen in the proximal femurs. The left prosthesis is loose, causing increased activity near the lesser trochanter and the distal tip of the prosthesis (*arrows*). The activity at the lesser trochanter is the fulcrum site, and the tip is the portion of the prosthesis with the greatest movement.



Right knee prosthesis-flow phase: increased perfusion (marked hyperemia)







Right knee prosthesis-positive all three phases of the three-phase scintigraphy: inflammation

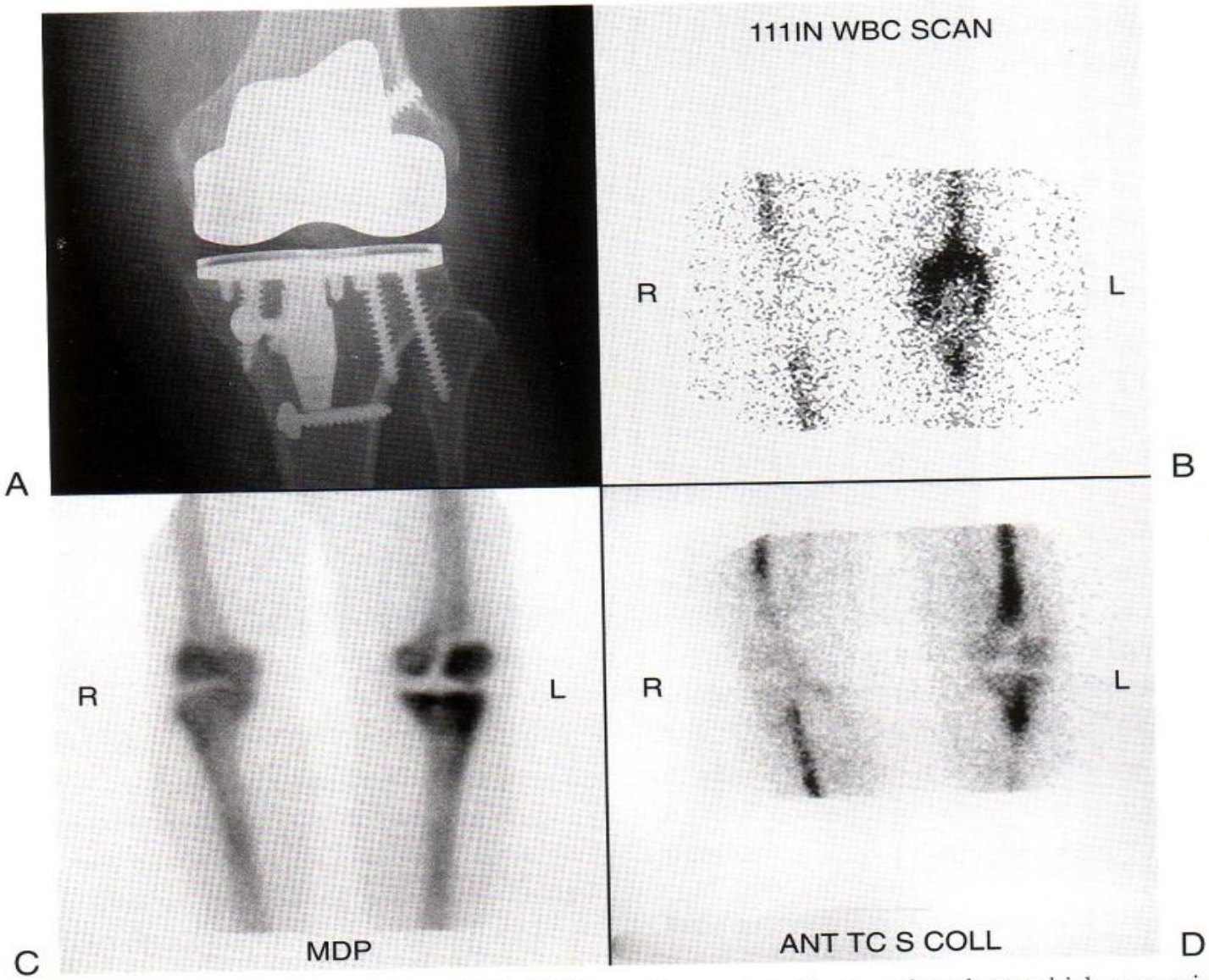
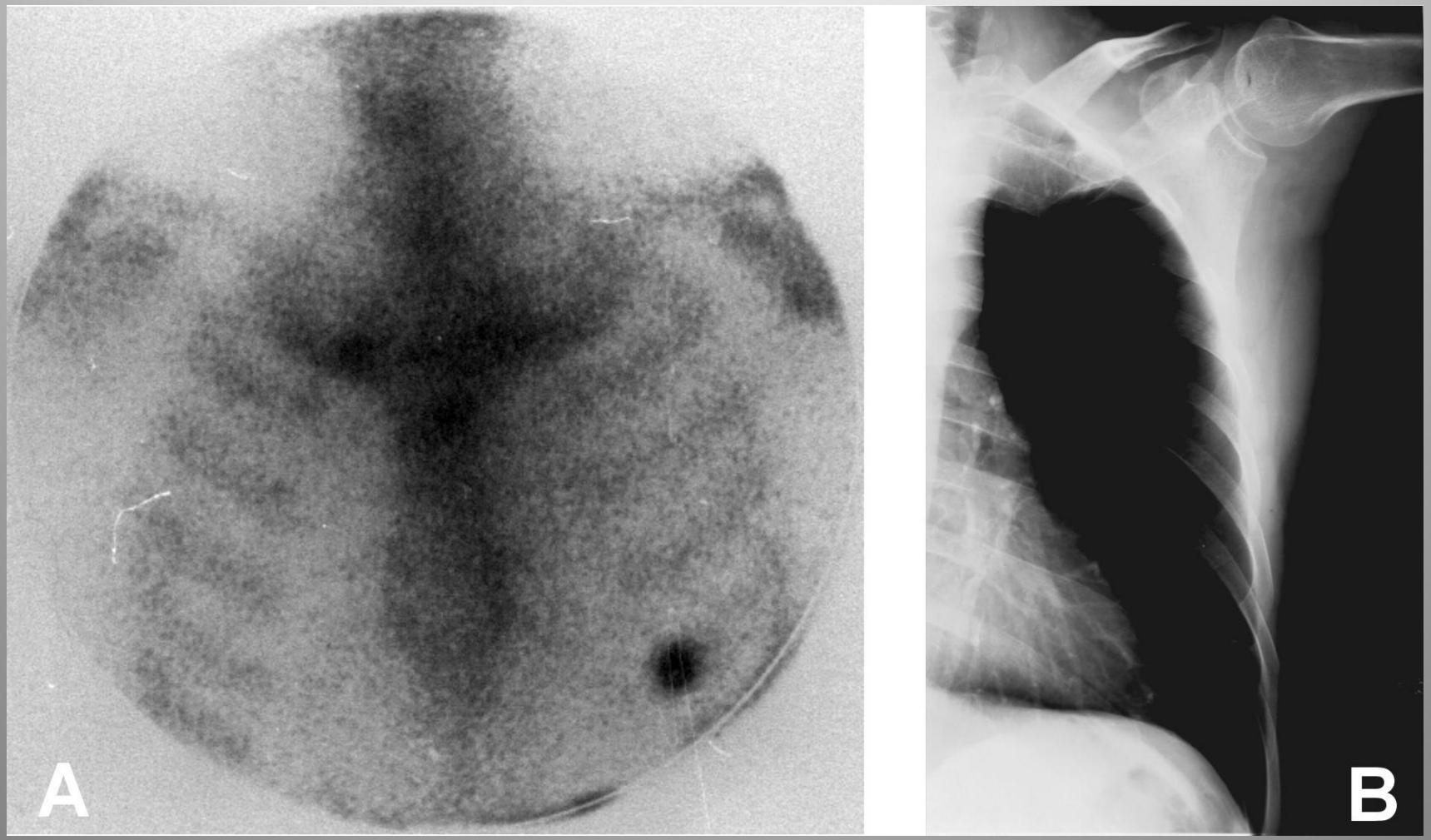


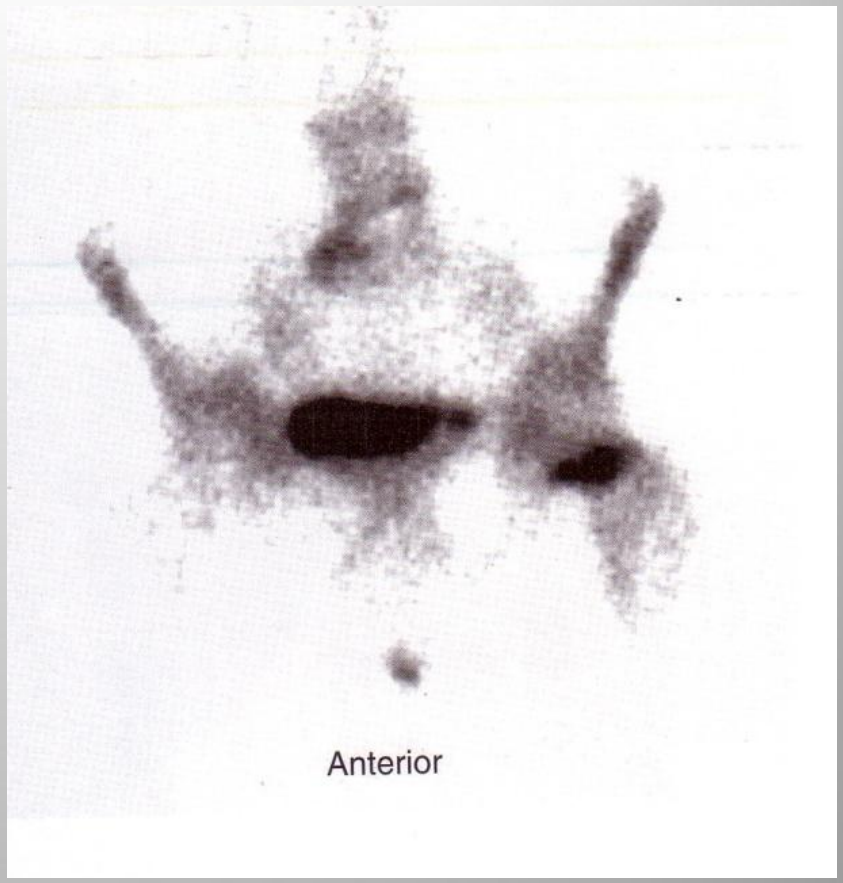
FIGURE 9–40. Infected prosthesis. *A*, An x-ray of the left knee shows a total knee arthroplasty which was painful. *B*, An indium 111 white cell scan shows activity about the proximal portion of the prosthesis and spatial nonconformity with the bone scan (*C*) activity. A bone marrow scan (*D*) done with technetium-99m sulfur colloid shows that the indium activity in not related t localized marrow hyperplasia.

Clinical aplication of skeletal scintigraphy

- **Detection of fractures:**
  - Clinically suspected and rdiographic negative
  - Only 72 hours after fracture.
  - Stress fractures in athletes which are generally diffcult to detect radiologically

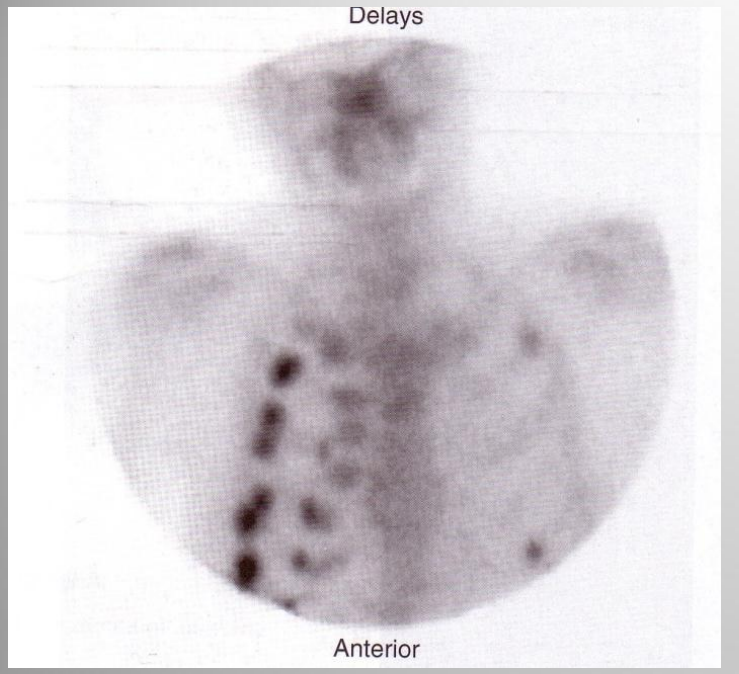
Fracture-positive on bone scan; negative on X-ray



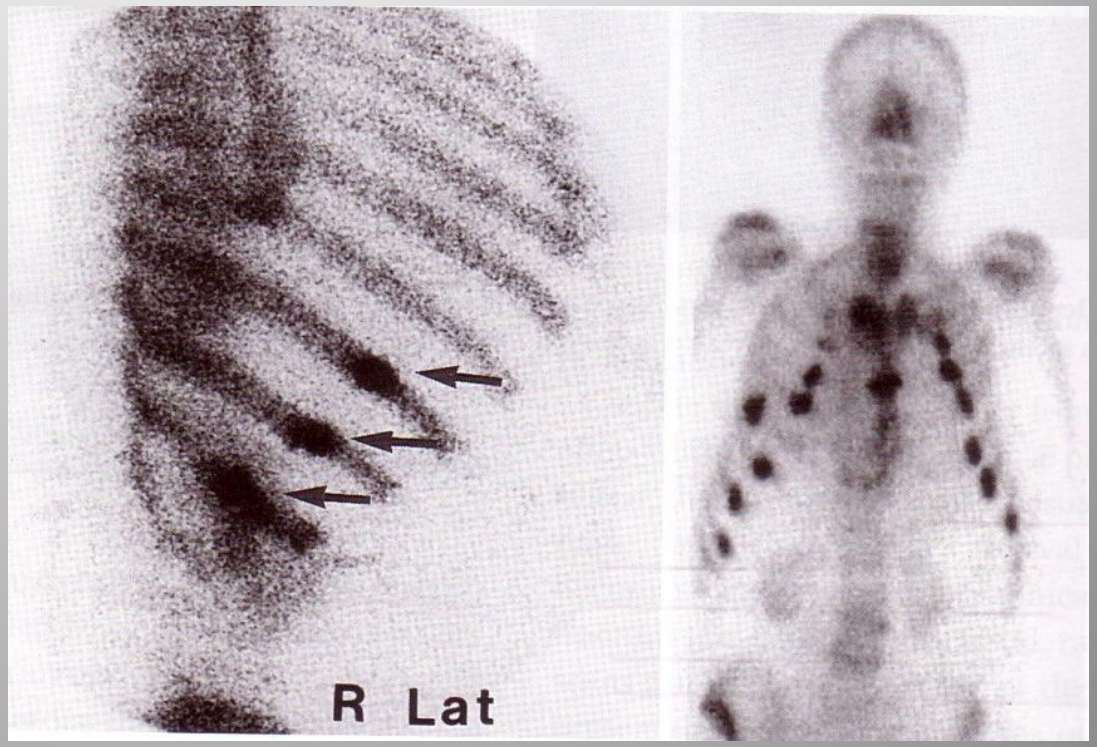


Occult fracture of the left hip:

- X-ray negative
- Scintigraphy: increased activity in the left femoral neck in the area of the fracture



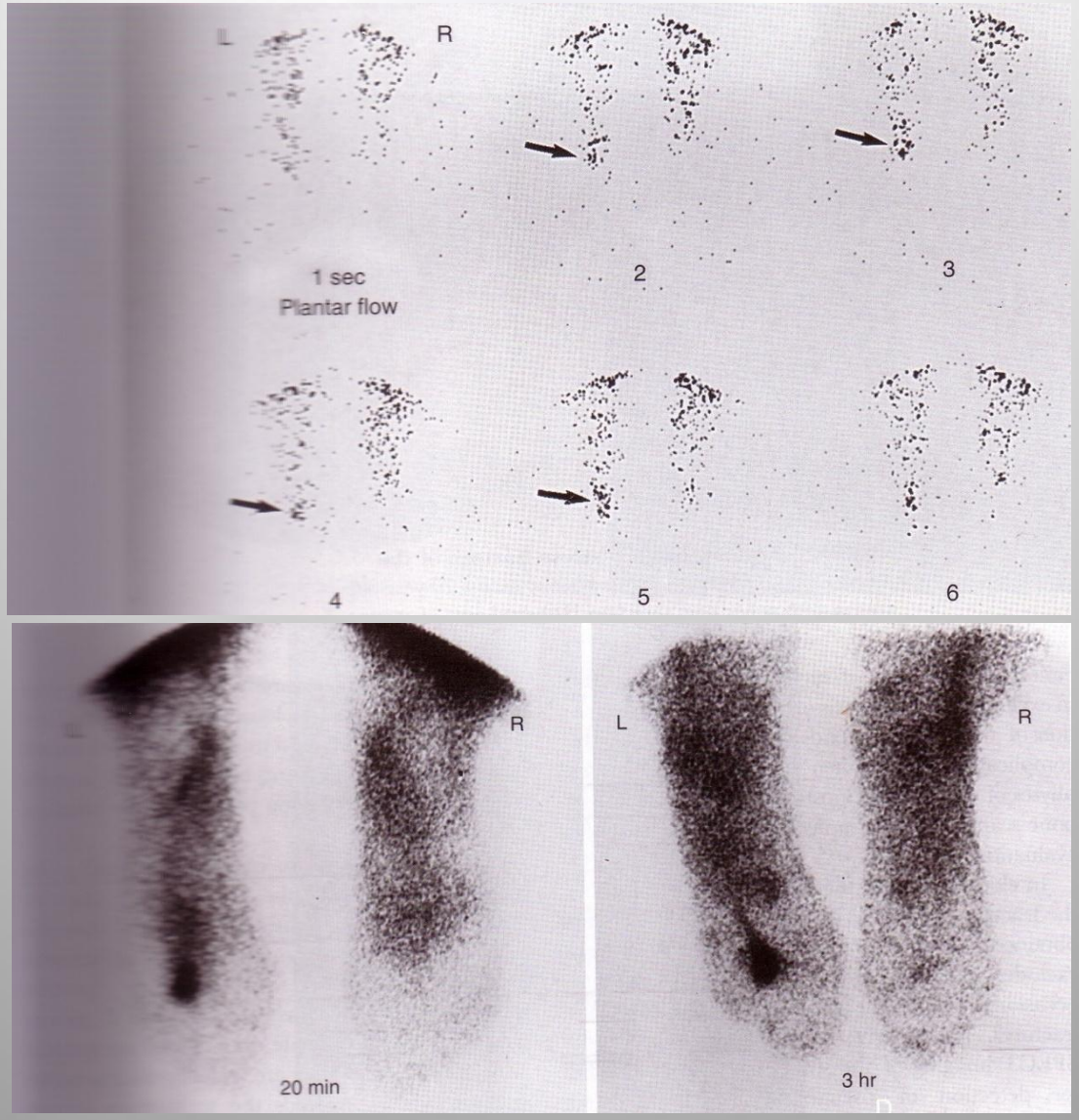
Serial fractures of the ribs after traffic accident



Serial fractures of the ribs and fracture of the middle part of the sternum after cardiopulmonary resuscitation

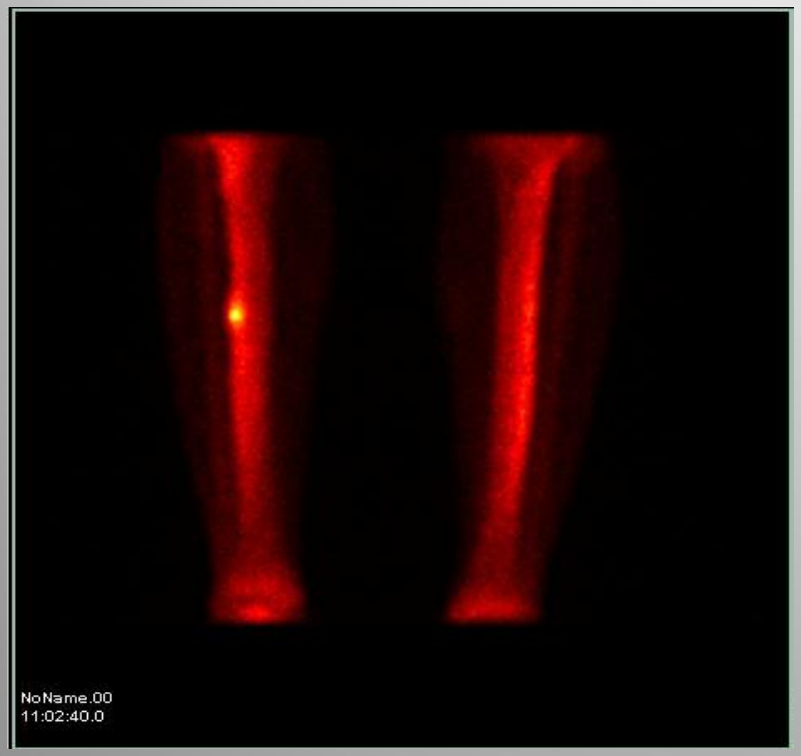
Stress fracture

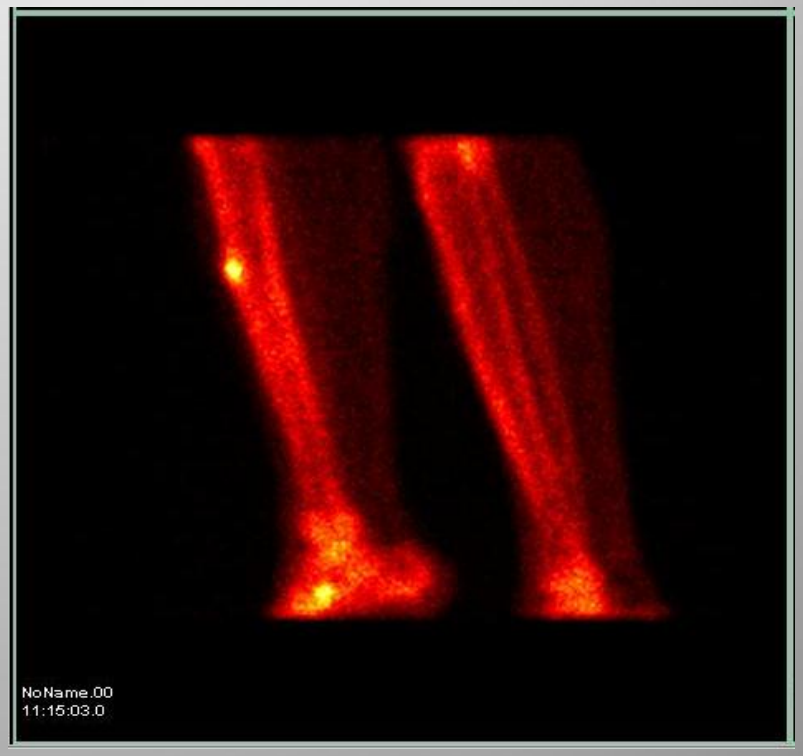
Stress fractures: fractures due to fatigue, overuse. Bone defects that occur due to repeated trauma, overcome ability of bone regeneration (volleyball, basketball, marathon runners)



Stress fracture of the third metatarsal bone of the foot of overuse with the soccer players: positive all three phases of the three-phase scintigraphy

Stress fracture





AP

Lateral

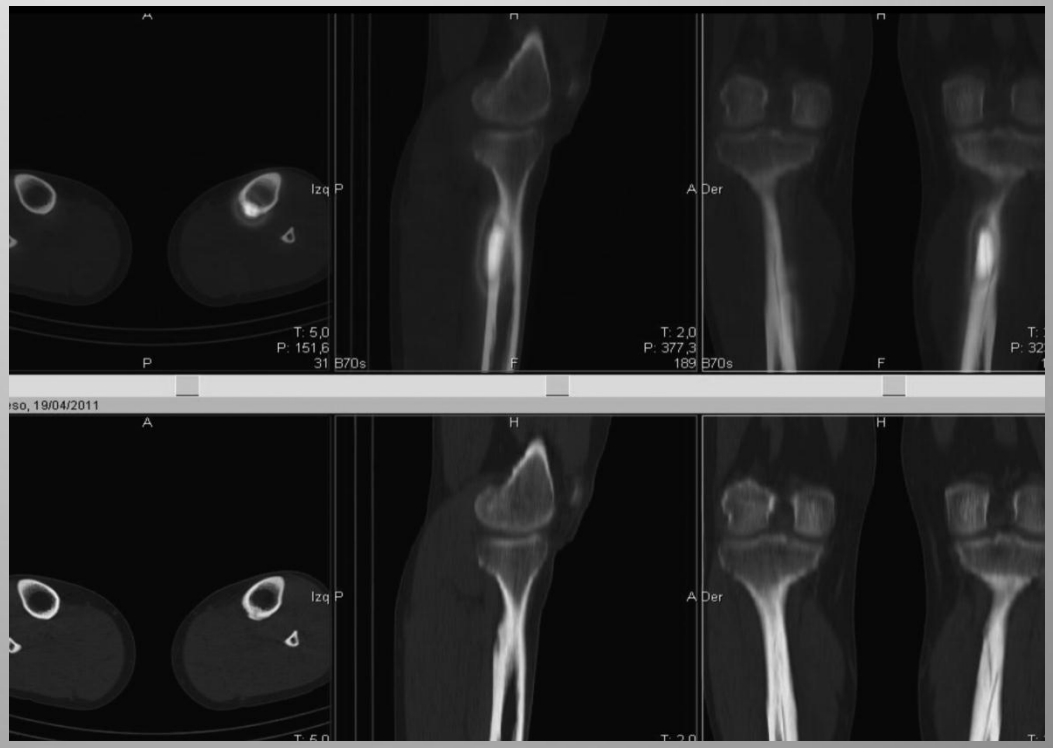
Stress fracture

Shin splints-enthesopathy

Enthesopathies: periosteal lesions (inflammatory changes in the area of insertion of tendons, ligaments and joint capsules)
cover a number of entities: the medial epicondylitis of elbow, Achilles tendinitis,.)

Shin splints: Pain along the insertion of the flexor muscles of the foot to the tibia or fibula.
Scintigraphy: superficial, linear lesions along the insertions of muscles, often the posteromedial and anterolateral due to overuse of the flexor muscles of the foot.

Stress fracture of the left tibia and shin splints of both tibias



Metabolic and degenerative diseases of bones and joints

Metabolic skeletal diseases

Because of the diffuse increased uptake in the bones (80%), activity do not appear in the kidneys (or very little), and is very small accumulation of activity in the bladder.

Secondary hyperparathyroidism.

Clinical use of skeletal scintigraphy

Diffuse metabolic diseases of the skeleton:
diffusely increased uptake in the skeleton, the most intense in the skull

- "super scan" (80%, normally about 60% of the administered dose),
faint uptake in kidney,
sometimes focal accumulation as a result of local disturbances of bone metabolism

Secondary hyperparathyroidism

PAGET'S DISEASE-OSTEITIS DEFORMANS

The acquired disorder of unknown etiology that is characterized with hyperactive destruction and new bone formation were the normal bone is replaced with the plenty, soft, poorly mineralized osteoid that accompanies significant fibrosis. Initialy increased bone resorption with strong osteoblastic response and collagen deposition.

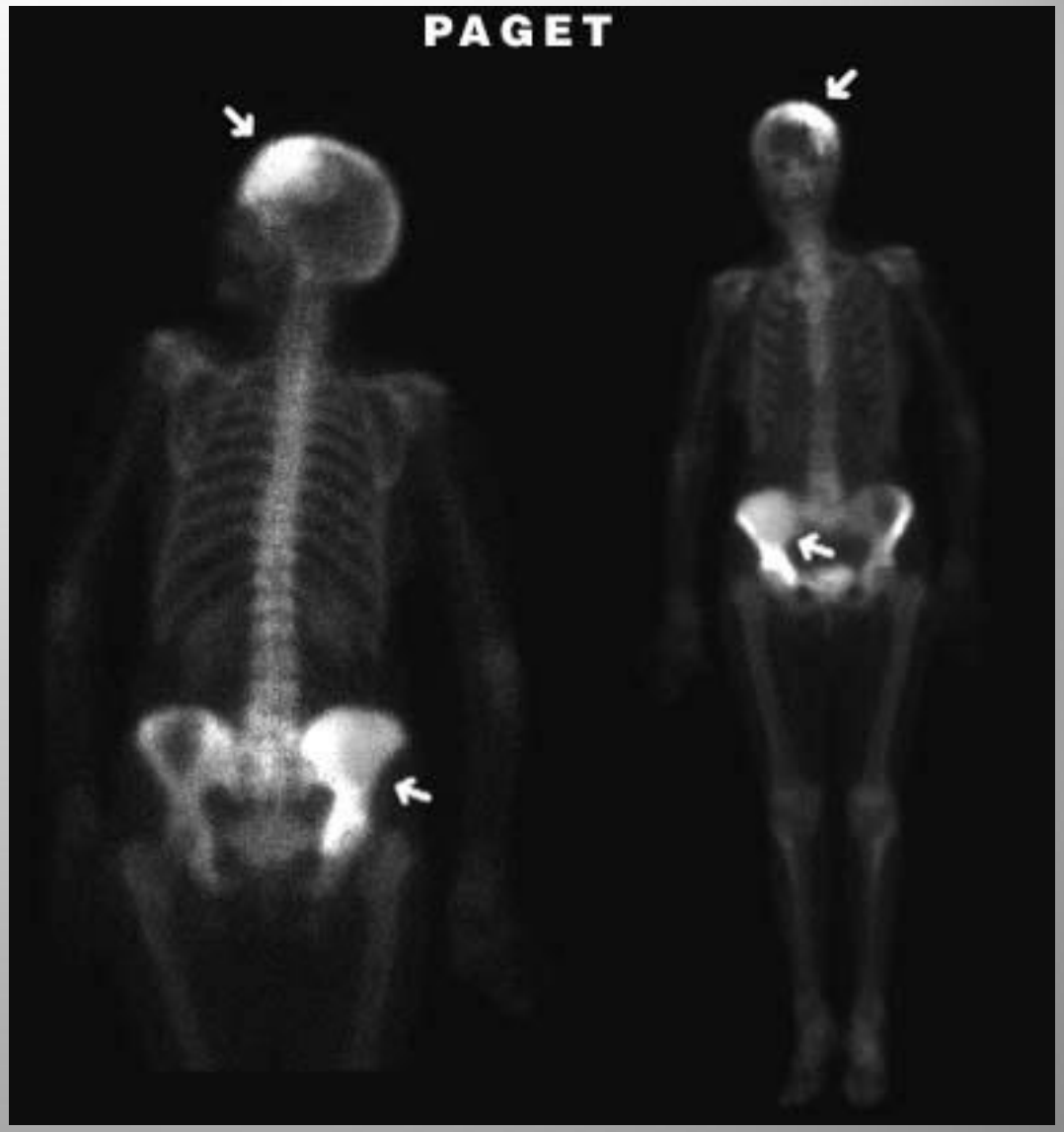
It rarely occurs in the age under 40 g., and is more common in men (2: 1).

Frequently affects more bones (80%): pelvic bones, skull, femur, spine but it can affect only one bone (then usually tibia).

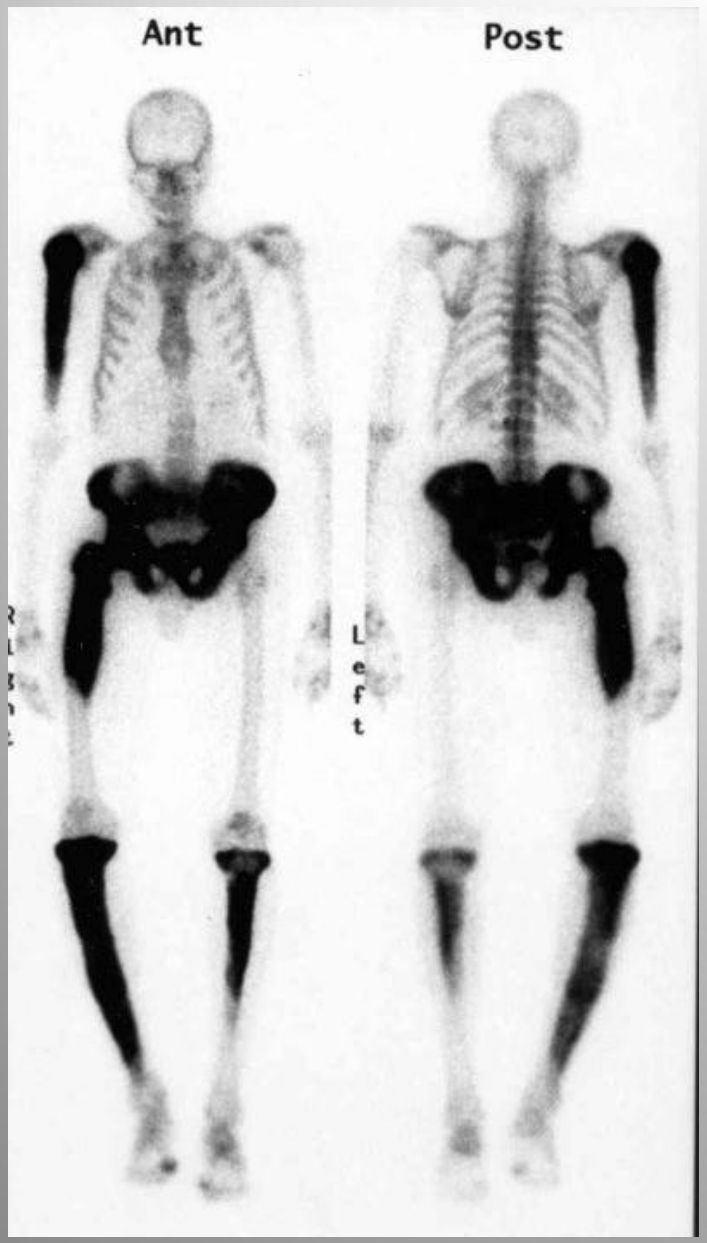
The bones are soft, deformed, thickened.

Paget's disease

- Initially increased bone resorption and than excessive osteoblastic response.
- It affects one or more bones.
- Very intensive radiotracer uptake.



Paget's disease



Paget’s disease

Rtg.- in the initial phase low density areas („increased airy"), at a later stage areas of sclerosis.

Sci.- very high local accumulation of activity,
on a three-phase sci. slightly increased perfusion in the initial stage and markedly intensive later

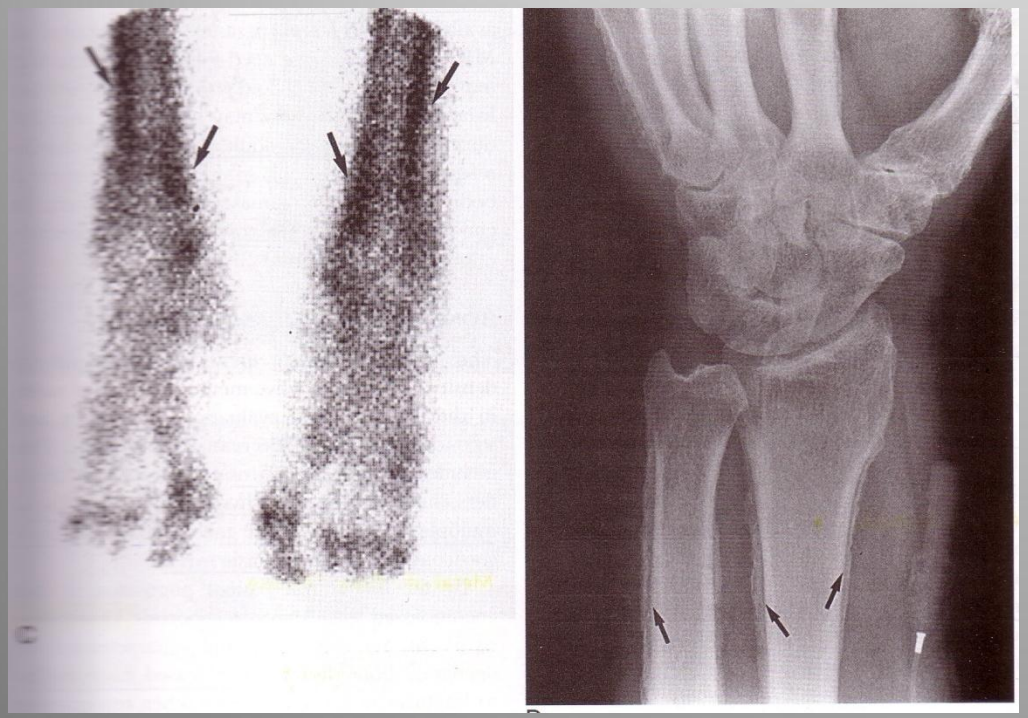
HYPERTROPHIC OSTEOARTHROPATHY

Associated with malignant or inflammatory intrathoracic disease or ulcerative colitis.

CLINICALLY: painful swelling of fingers, arthralgia, arthritis, redness and peeling of the skin.

It affects the **radius, ulna, tibia and fibula-scan shows symmetric increased uptake along the edges of the diaphysis of long bones.**

It differs from skeletal metastasis as they primarily affects the central part of the skeleton and has asymmetric focal lesions.



Hypertrophic pulmonary arthropathy

Increased accumulation of activity in cortical regions of radius and both tibia on bone scan after 3 hours

X-ray of the wrist shows periosteal reaction

ASEPTIC NECROSIS

The most common- femoral head.

In the initial stage of the disease there is reduced accumulation of activity, on perfusion scintigraphy (flow phase) there is cold zone, as a result of inability to attend rf. in the area, which supplies affected blood vessel.

At an advanced stage of the disease when occurs bone destruction, in late delayed scintigraphy we can see „cold” zone.

It is often used SPECT.

JOINT DISEASES

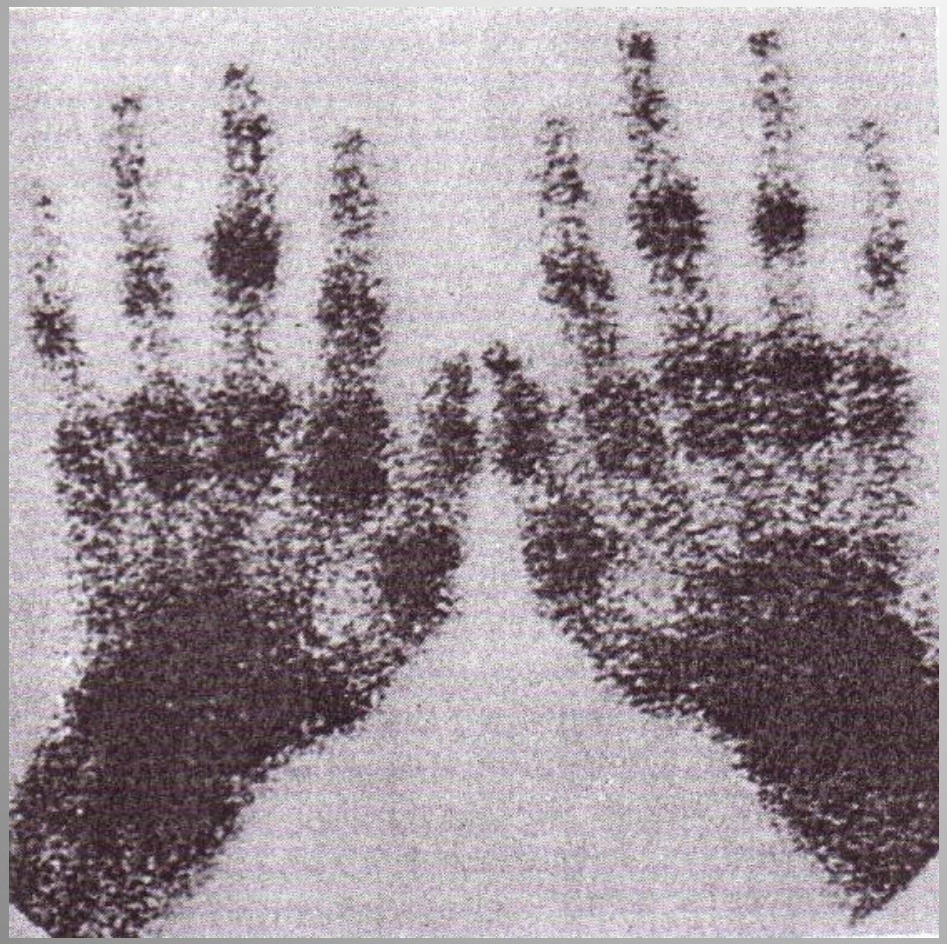
In normal joints there are symmetrical activities.

INFLAMMATORY: rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and Reiter's syndrome.

NONINFLAMMATORY: osteoarthritis, neuroartropathy, reflex sympathetic dystrophy.

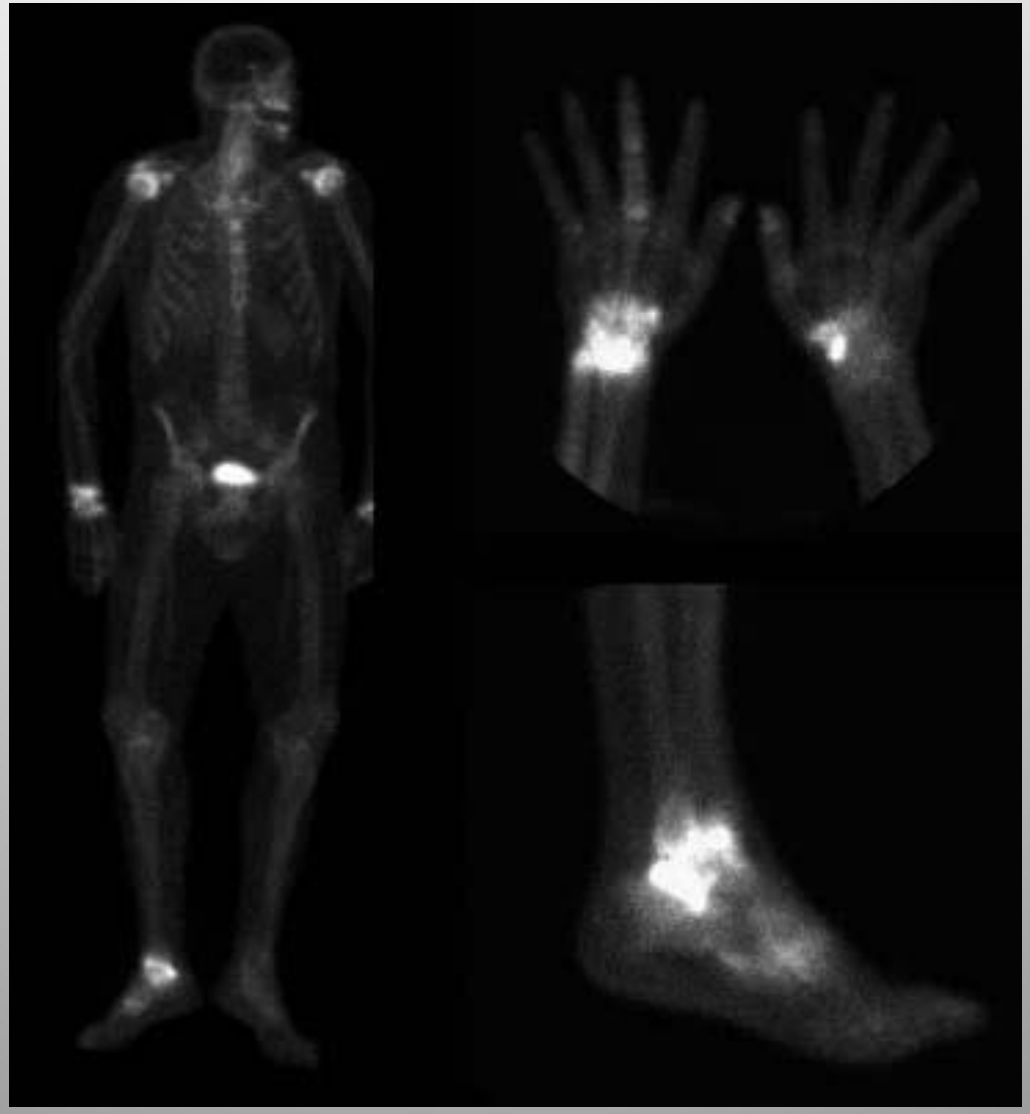
SACROILIITIS: ROI of the SI joints on the sacrum

Using radionuclides we can differentiate synovitis (1st) from destruction of bone parts of the joint (3rd)
We use a three-phase bone scen, ROI (increased perfusion in case of synovitis).



Rheumatoid arthritis

The early phase of RA: increased uptake in the carpal joints, metacarpophalangeal joints and proximal interphalangeal joints



Arthritis

Degenerative changes

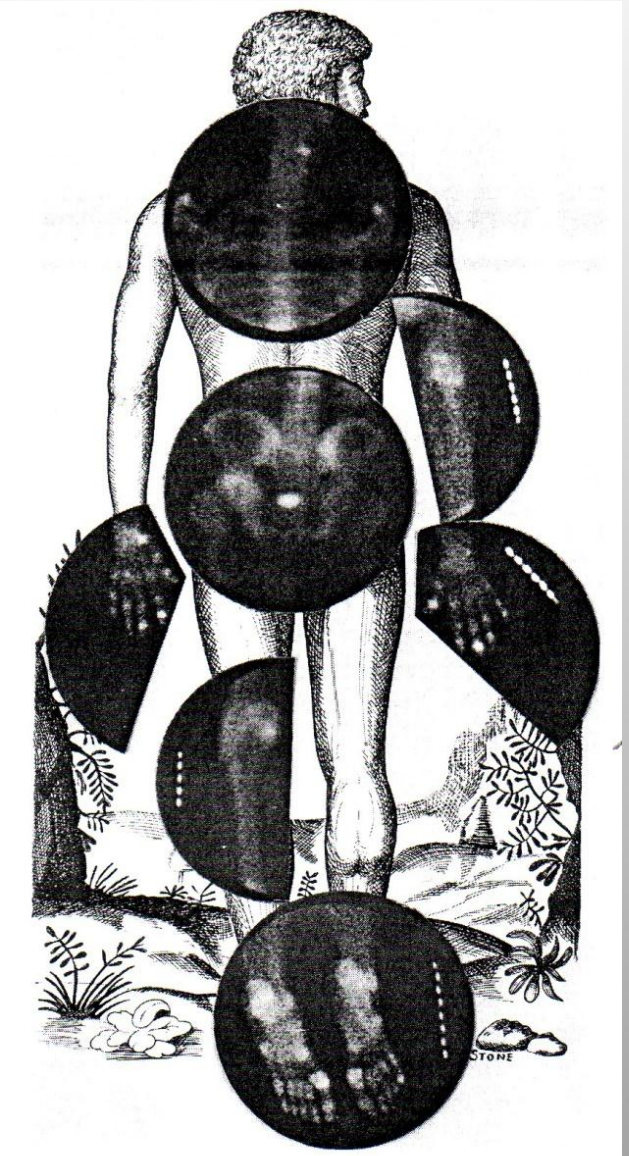


Fig. 8–34. Composite showing degenerative changes in cervical spine, right elbow, left hip, left knee, and both feet and hands.

RF uptake in soft tissues: calcification of soft tissue and heterotopic ossification

- **NEOPLASMS** of soft tissue can calcify, (some of cells producing mucin) as npl. of breast, gastrointestinal tract, ovary, lung, lymphoma, neuroblastoma.
- Diffuse increased activity can be seen in malignant pleural effusion and malignant ascites.
- After postop. scars, heart attack, brain, spleen, dermatomyositis, calcifying tendinitis, inflammation, in paraplegics - heterotopic ossification, muscle trauma, ossifying myositis, calcifying hematoma ...
- Sec. hyperparathyroidism due to renal impairment causes the accumulation of activity in gastric mucosa, in the lung, in the kidneys.

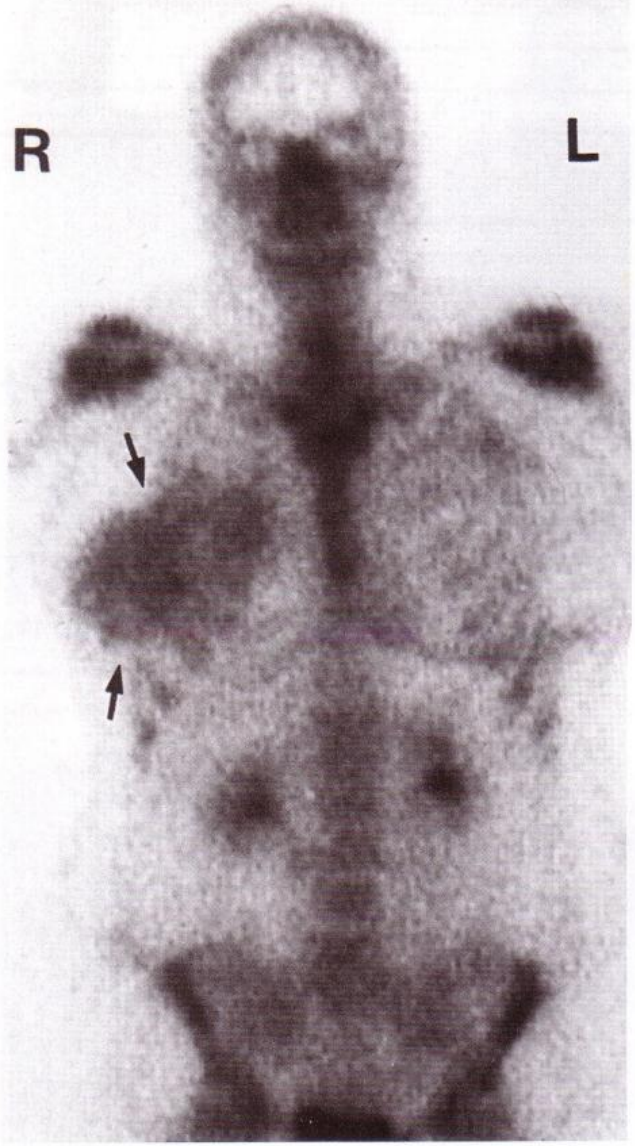
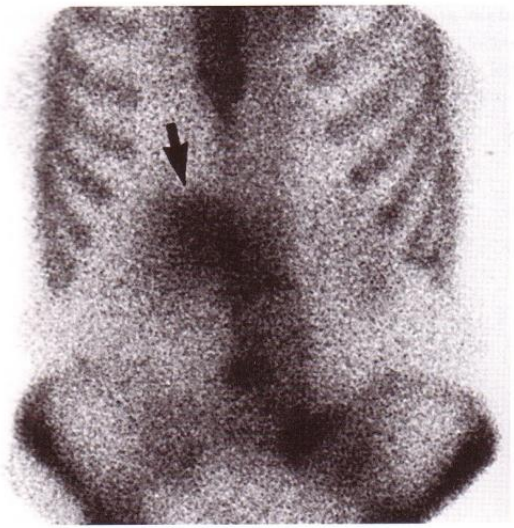


FIGURE 9–18. Activity in breast cancer. A bone scan in this patient with a right breast tumor shows marked asymmetric increased activity in the tumor (*arrows*).



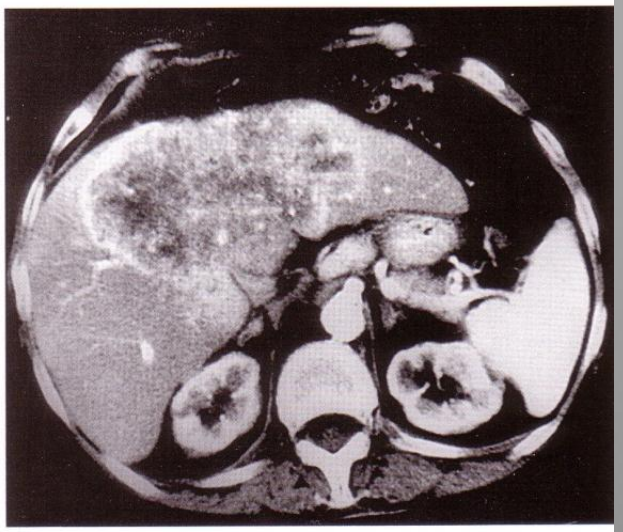


FIGURE 9–19. Liver metastases. This patient with a known mucinous colon carcinoma was thought to have hepatomegaly. *Left*, A bone scan done as part of the workup shows soft-tissue activity in the right upper quadrant (*arrow*). *Right*, A subsequent computed tomography scan clearly demonstrates a large hypervascular metastasis in the left lobe of the liver.

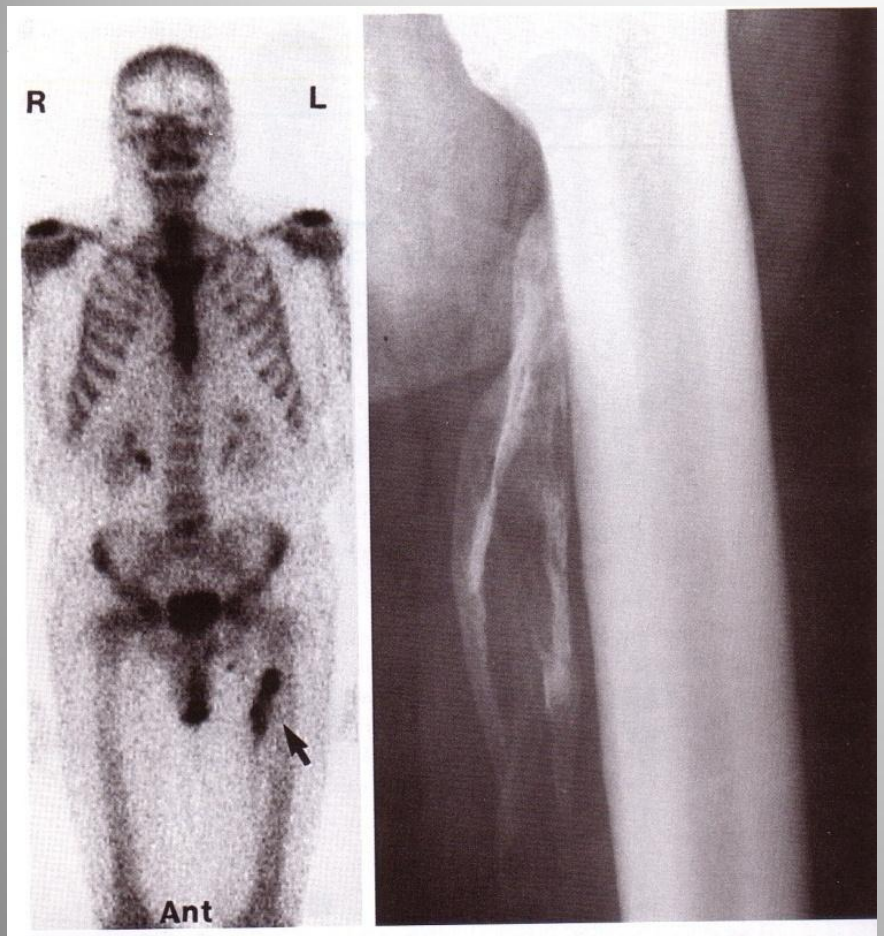


FIGURE 9–29. Myositis ossificans. This college football player had a history of trauma to the inner left thigh with residual firm swelling and limitation of motion. *Left,* The bone scan shows soft-tissue activity that is greater than the nearby bone, indicating that the process is not mature and should not yet be removed. *Right,* A radiograph shows the well-defined soft-tissue calcification.

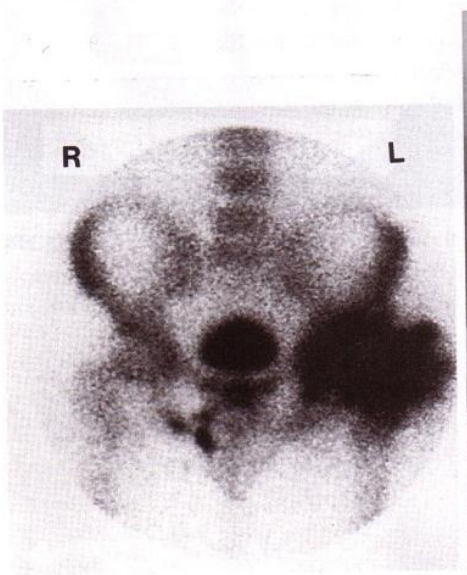


FIGURE 9–30. Heterotopic calcification. This patient was involved in a motor vehicle accident 6 months earlier and had a posterior dislocation of the left hip without fracture. *Left,* An anterior image of the pelvis from a bone scan now reveals increased activity in a periarticular soft-tissue pattern. *Right,* The radiograph shows extensive soft-tissue dystrophic calcification.

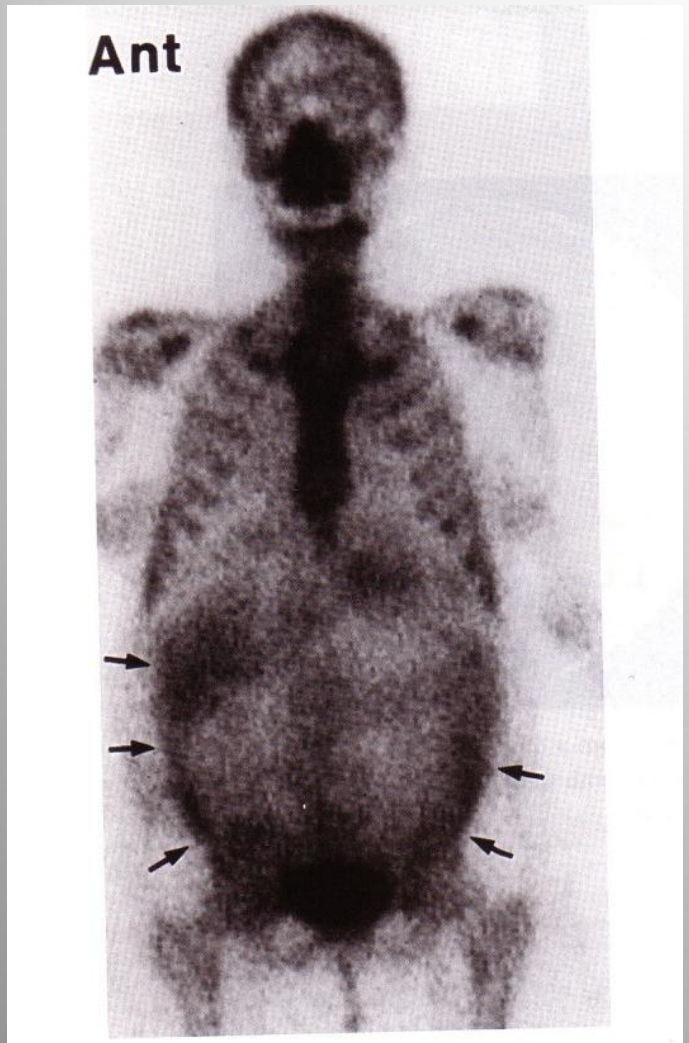


FIGURE 9–24. Malignant ascites. This 45-year-old woman has known ovarian carcinoma. Three-hour images from the bone scan show diffusely increased activity (*arrows*) over the entire peritoneal cavity.

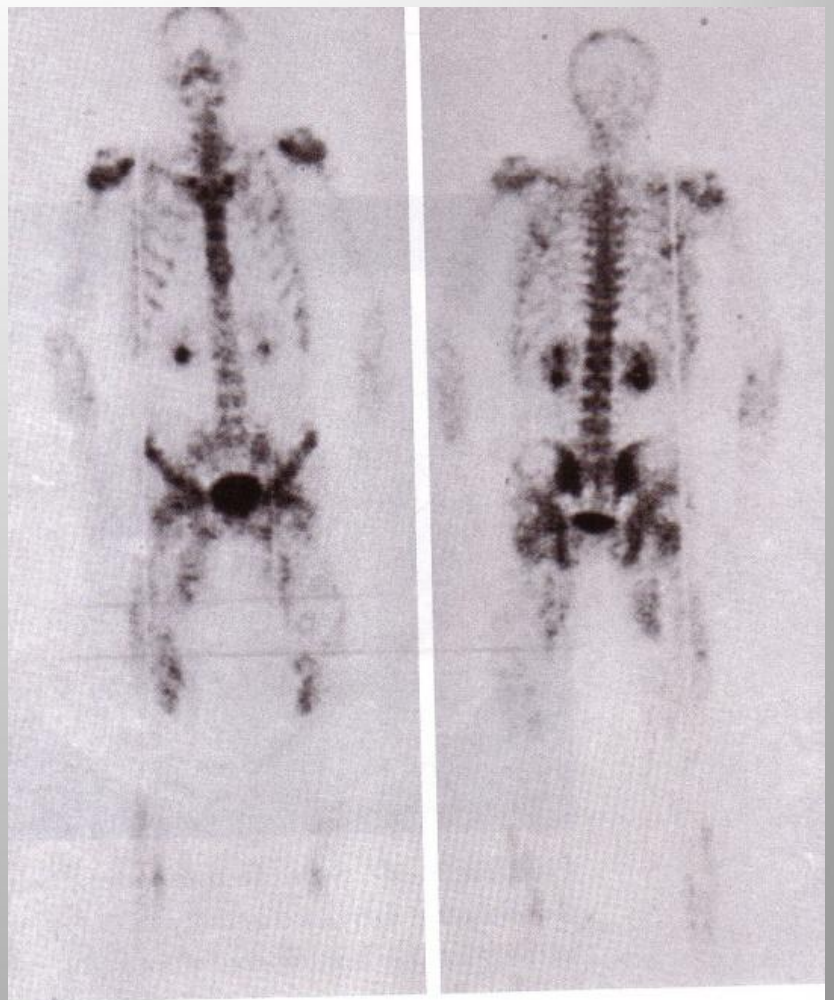


FIGURE 9–25. Dermatomyositis. Soft-tissue activity is seen on the bone scan in the large muscle groups of both lower extremities of a patient with dermatomyositis. *Left*, Anterior. *Right*, Posterior.

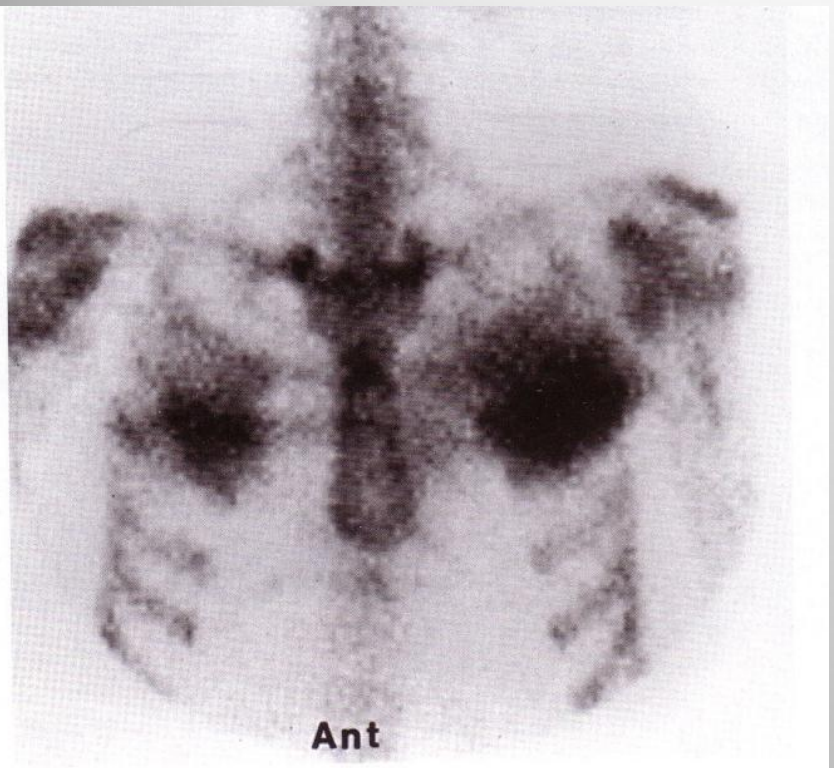
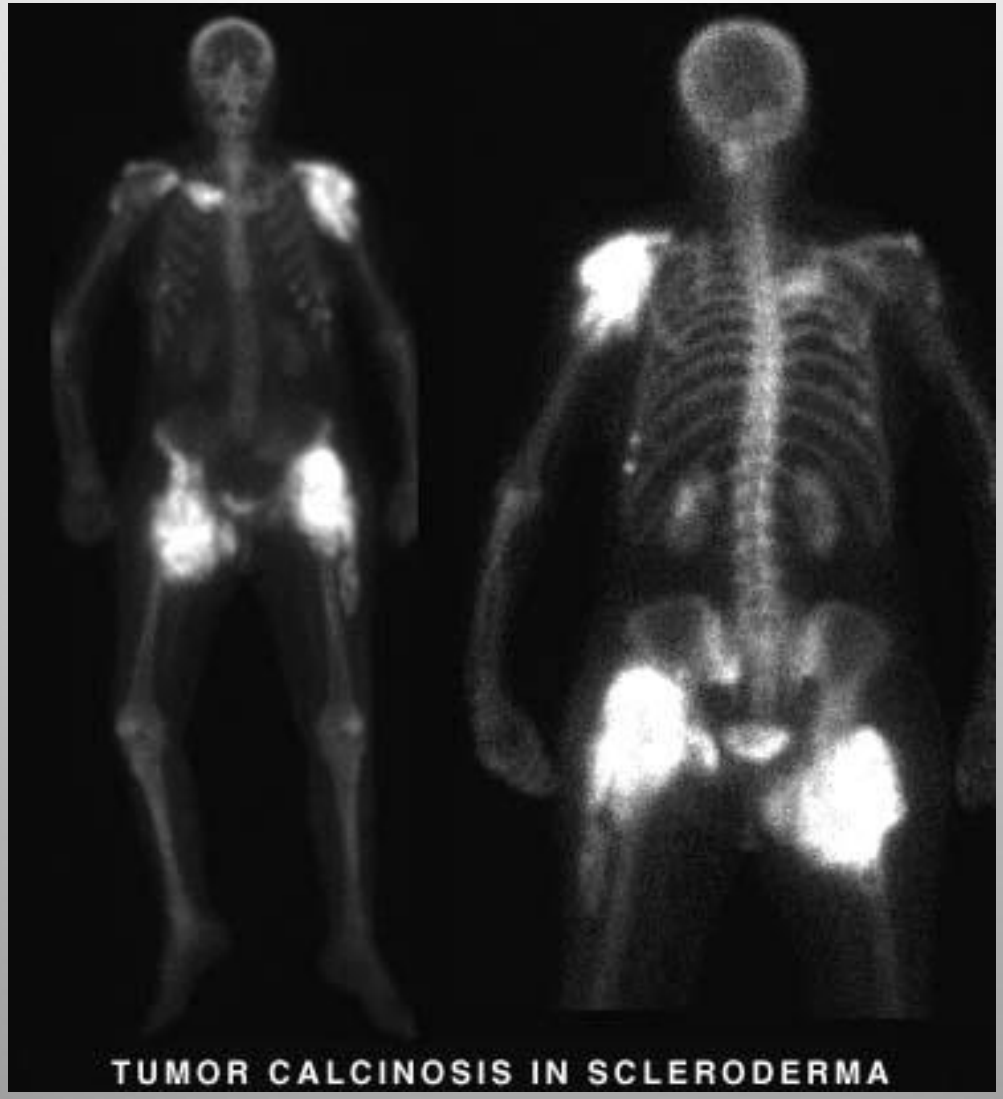


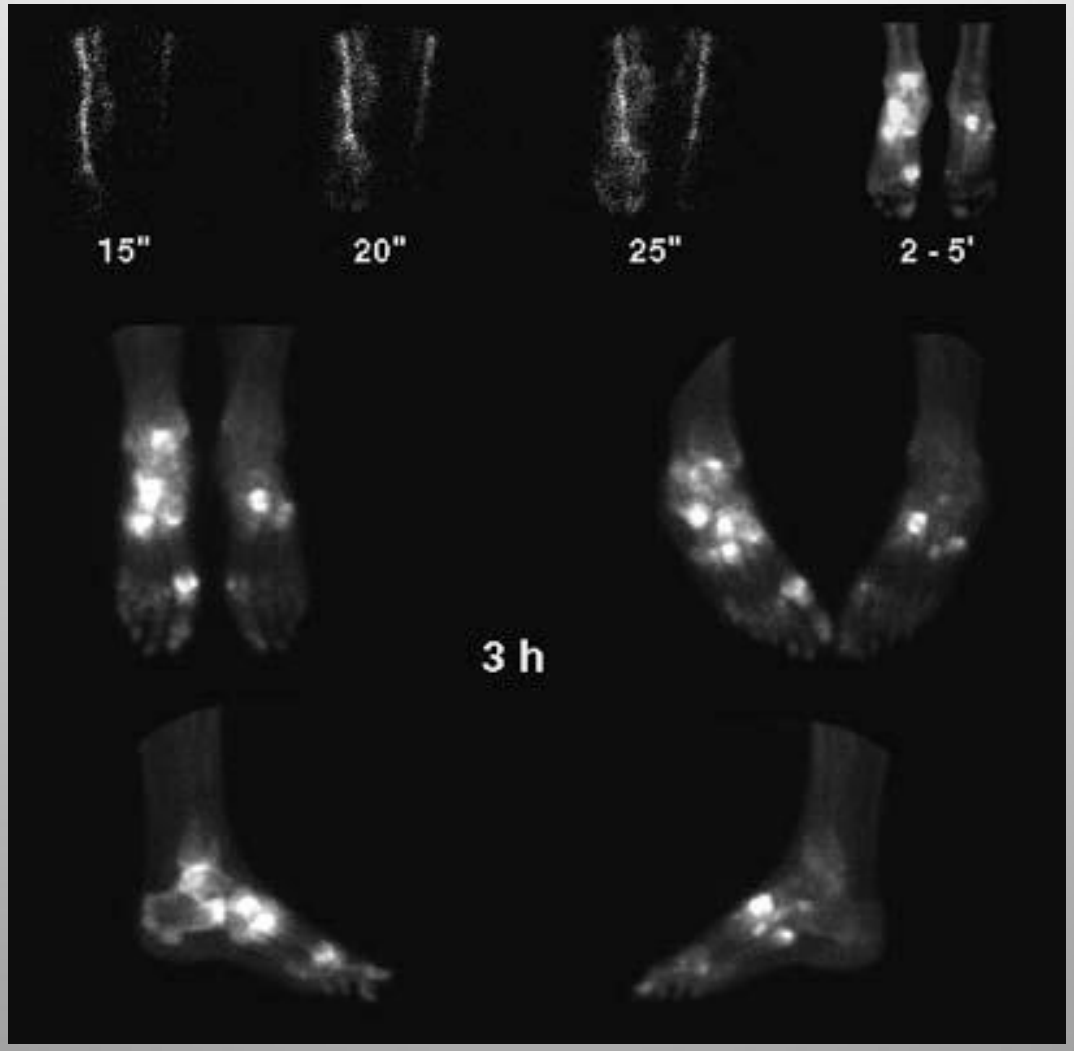
FIGURE 9–26. Muscle trauma. This young air force recruit experienced anterior chest wall pain after weight-lifting. The bone scan demonstrates increased activity in both pectoral muscles as a result of the trauma (rhabdomyolysis). Increased activity is also commonly seen for several weeks in various muscle groups after marathons or ironman competitions.

FIGURE 9–27. Splenic infarction. Selected images from a diphosphonate bone scan demonstrate increased activity in the spleen in a patient with sickle cell disease. This activity has been attributed to ongoing splenic infarction.

FIGURE 9–28. Hyperparathyroidism. Anterior bone scans in two different patients with hyperparathyroidism. *Left,* The first case demonstrates a typical superscan with lack of significant renal or bladder activity and with increased activity diffusely throughout the skeleton. Of note is the particularly increased activity in the calvarium, facial bones, mandible, and large joints that has been described in patients with hyperparathyroidism. *Right,* Bone scan of a second patient with hyperparathyroidism demonstrates increased activity around the major joints and significantly increased activity in the lungs, stomach, renal parenchyma, and thyroid, compatible with so-called metastatic calcification, which may be found in certain soft-tissue organs in severe cases of this disease.



Scleroderma

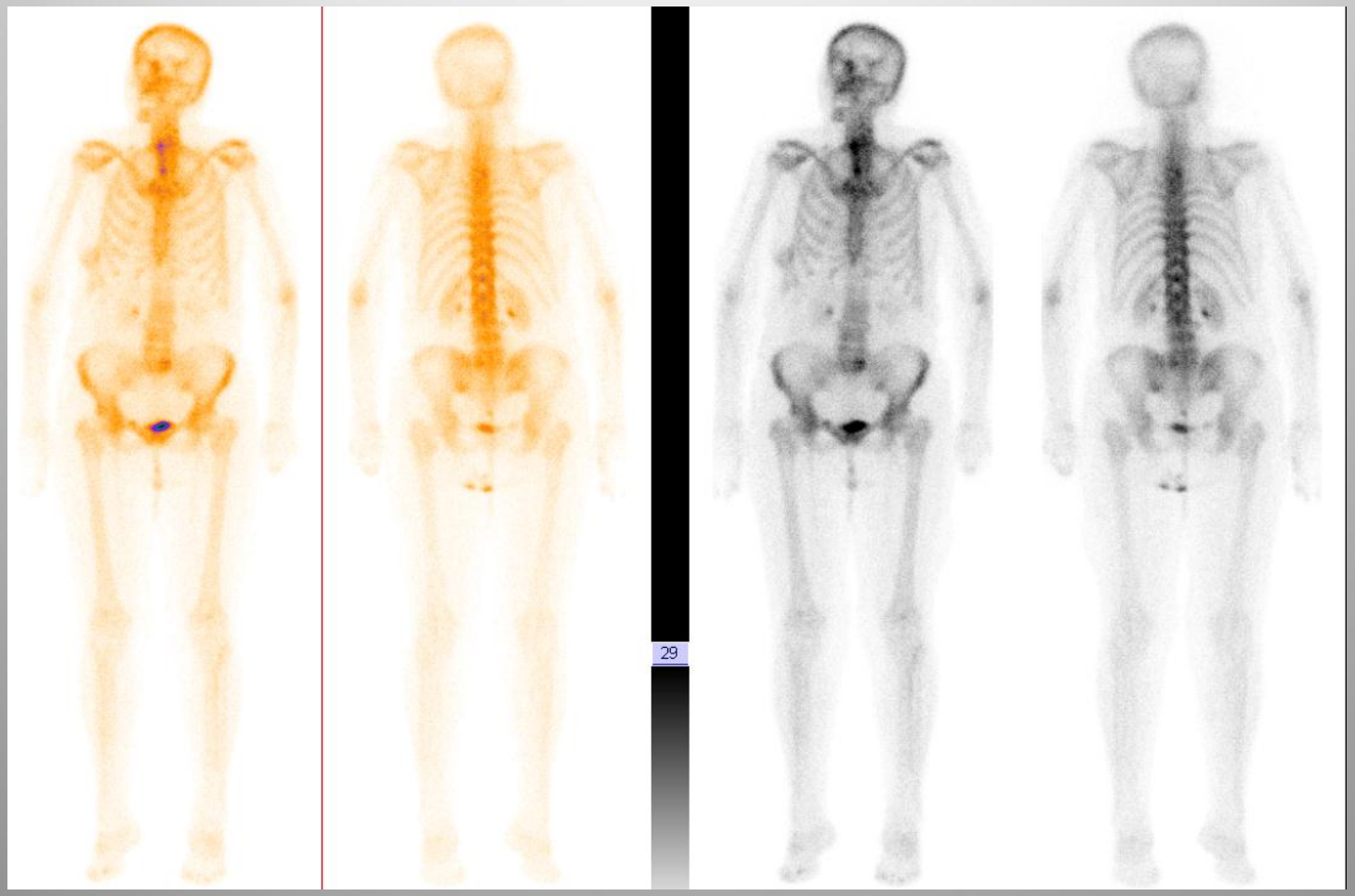


Sudeck atrophy

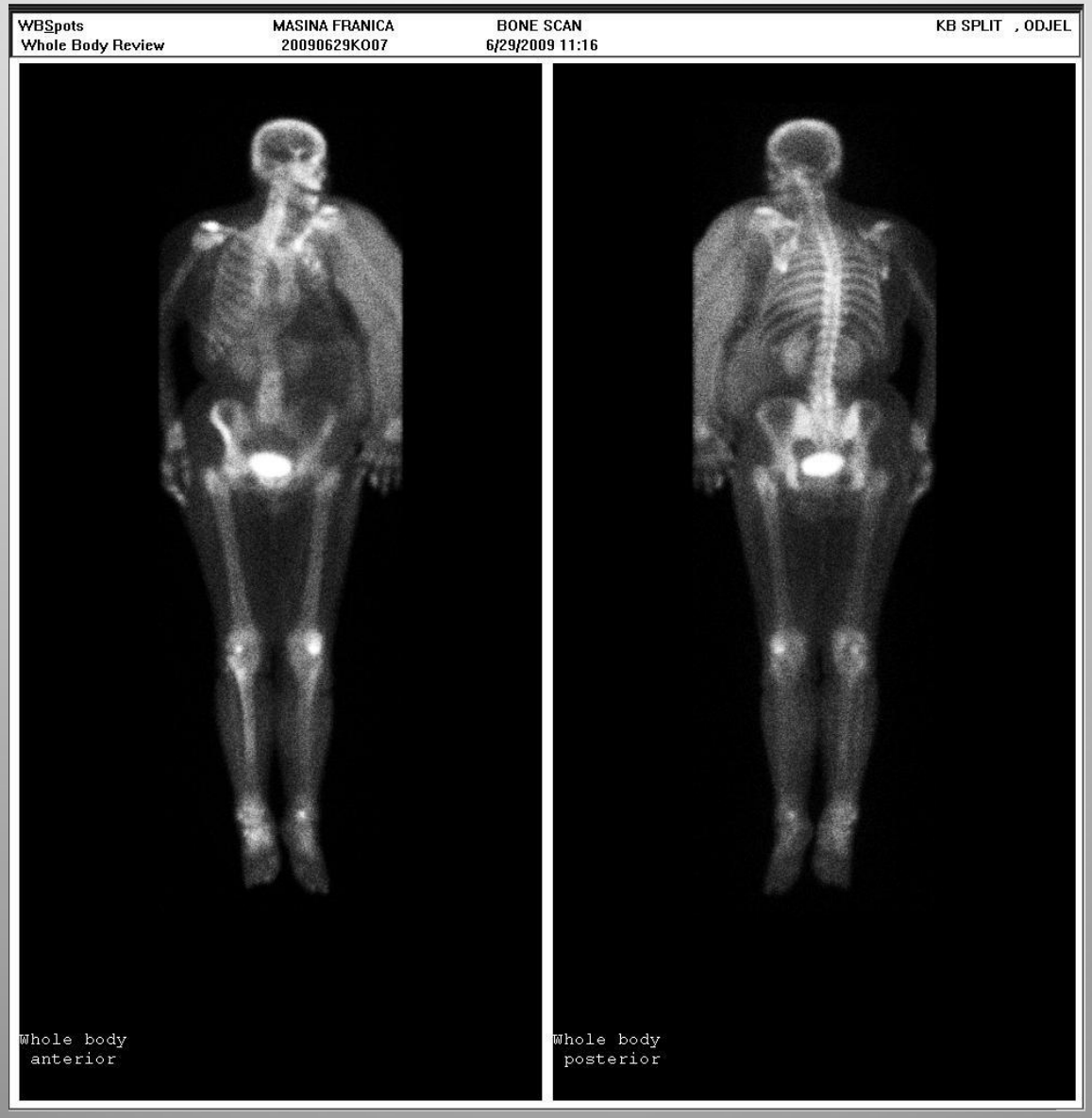
Possible accumulation on bone scan

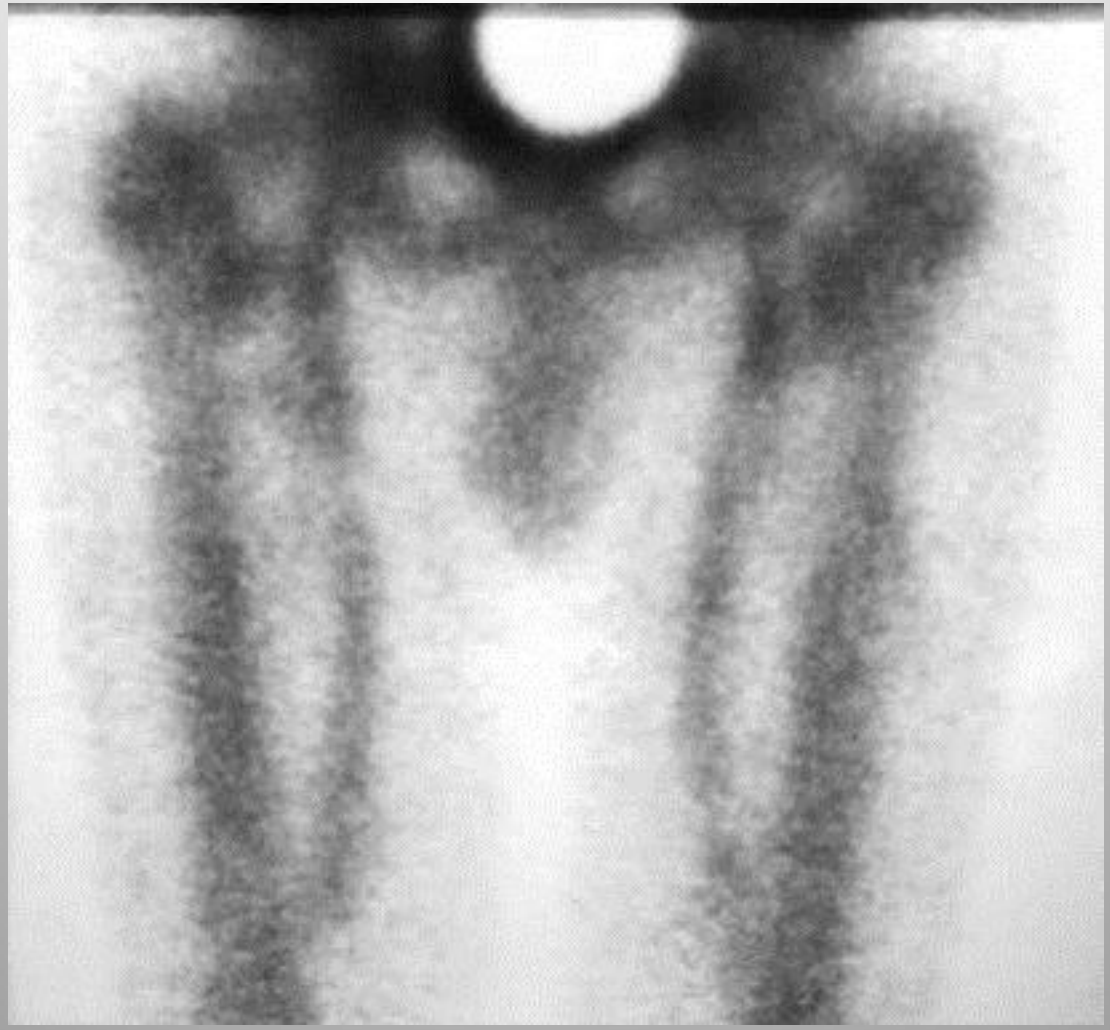
- Bilateral increased activity **along the tibia cortex** due to hypertrophic osteoarthropathy, periosteal reaction, tibial splint.
- Diffuse activity in the **liver**: hepatic necrosis, the problem with radiopharmaceutical.
- Focal activity in the **liver**: metastasis of colon cancer or breast, ovary, or lung.
- Diffuse activity in the **spleen** because of splenic infarction or sickle cell anemia.
- Diffuse activity in the **kidney** due to chemotherapy.
- **DISCITIS:** in children increased activity in two adjacent vertebrae, without compression fractures.

Right breast carcinoma

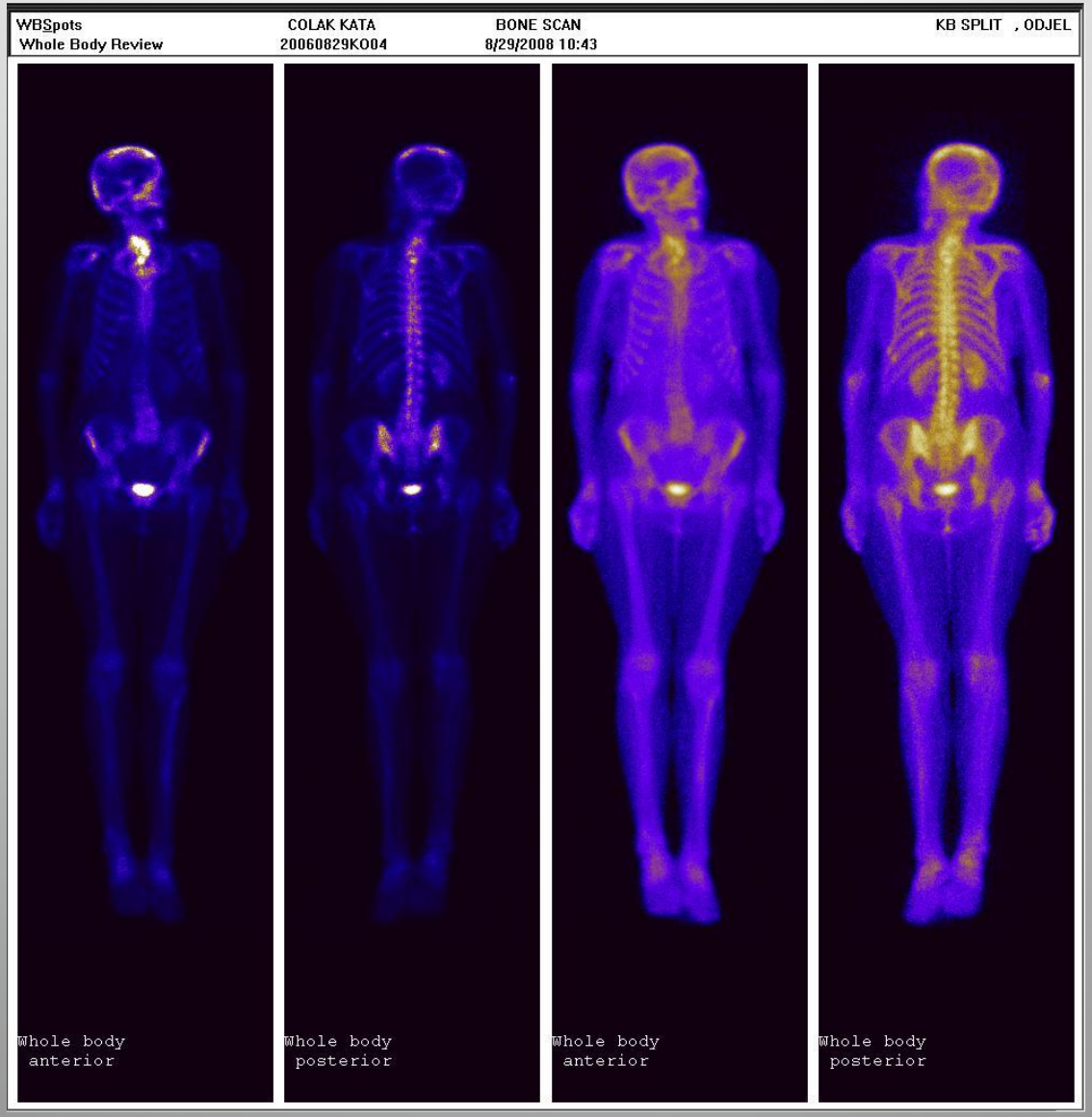


Lymphoedema of the left arm





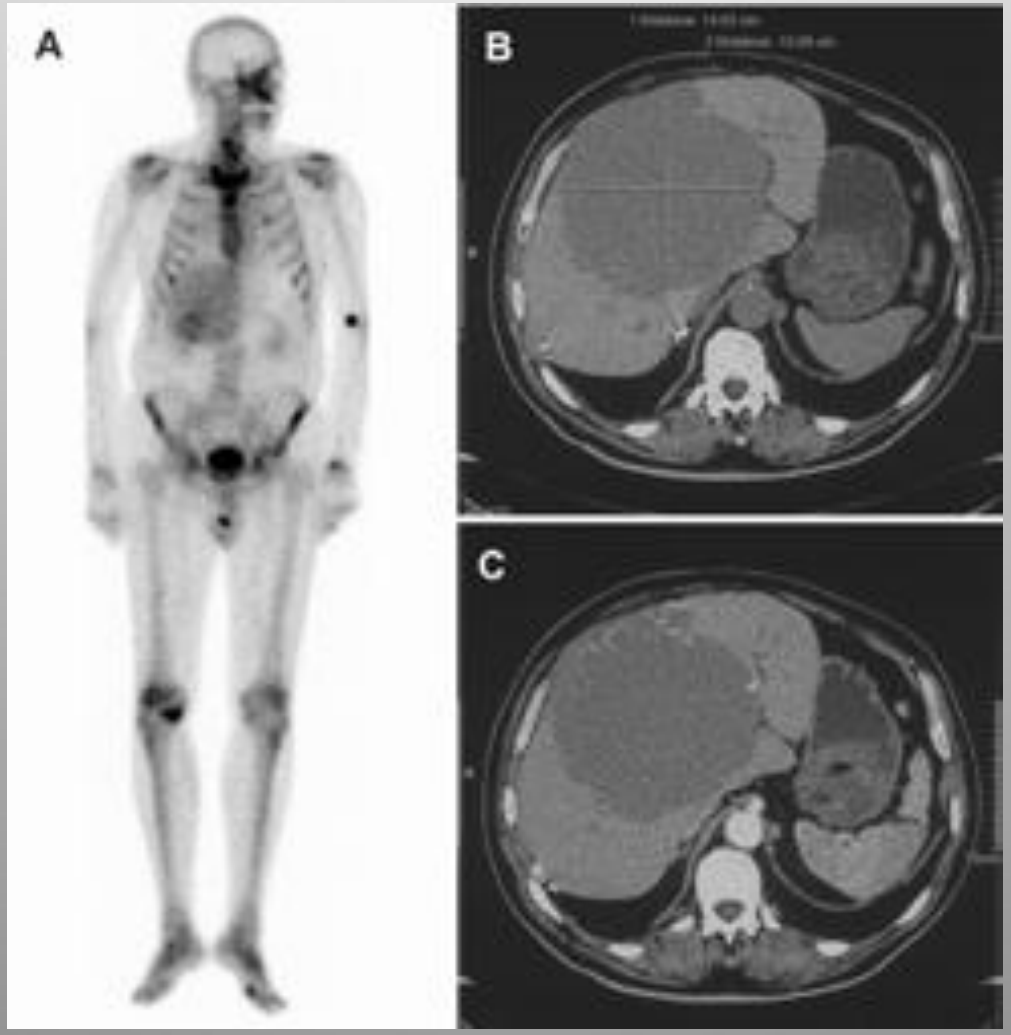
Calcified a. femoralis



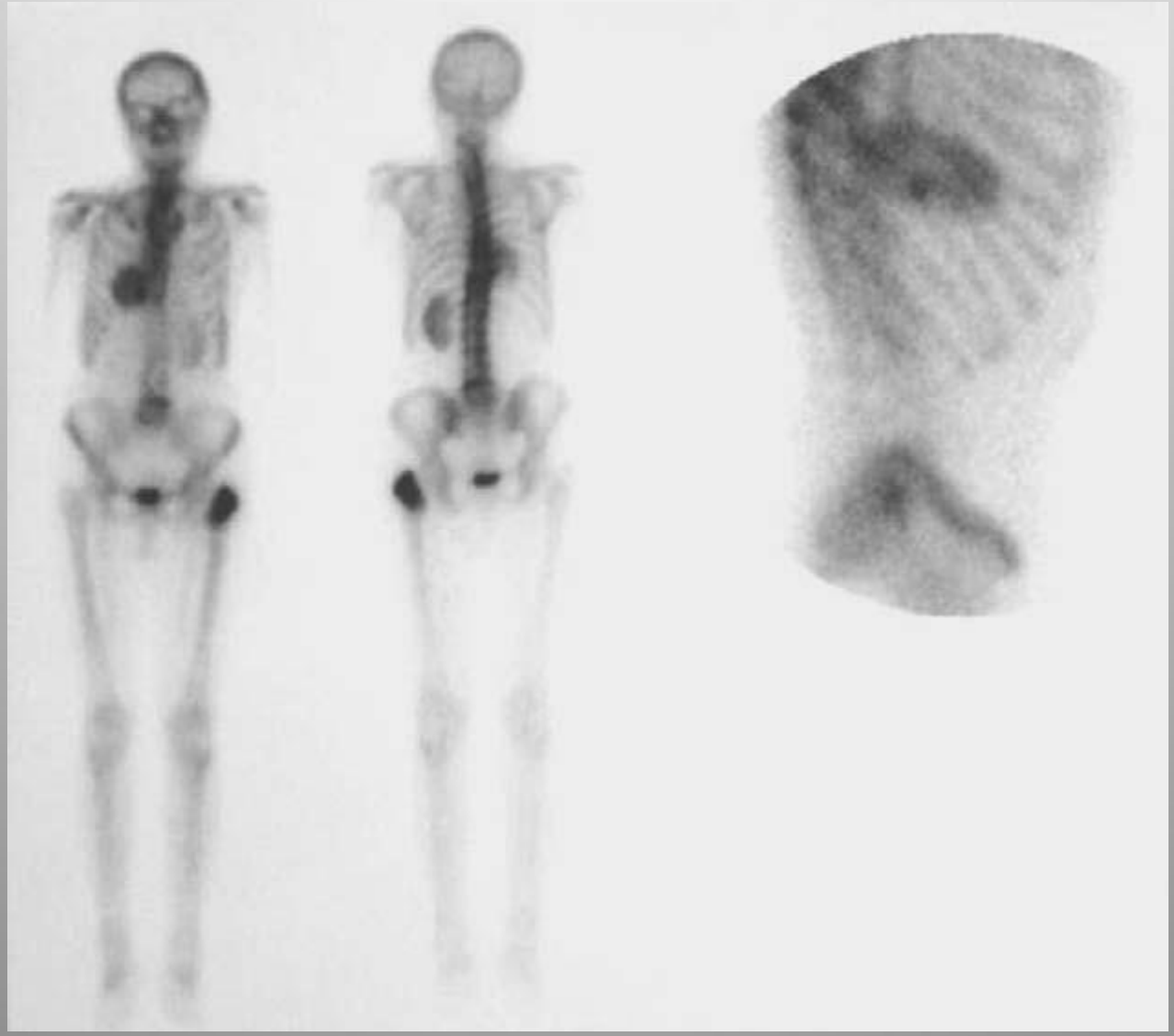
Calcifications in the thyroid gland

Marković V, Eterović D, Punda A, Brdar D, Tadić T, Grandić L.

Unusual bone scan finding: gigantic hepatic hemangioma visualized on bone scintigraphy. Hell J Nucl Med. 2012;15(3):260.



Ectopic kidney



Skeletal scintigraphy is highly sensitive method but not specific.

It is complementary to radiological testing, CT and MRI

The intensity of accumulation of the rf. does not depend of the size of lesions, than on its metabolic activity, while in radiological testing bone density must be reduced by 30-50% compared to healthy bone so the lesion could be detected.

Because of its high sensitivity it has the advantage in early detection of the lesions, while other methods has advantage in the localization of the lesion.

- Bone metastases can be detected up to a year earlier before it becomes visible on X-ray.

Bone marrow scintigraphy

Bone marrow scintigraphy is a diagnostic method for visualization of the bone marrow with radiopharmaceuticals that accumulate in erythrocyte precursors or in the cells of the bone marrow RES

- **Radiopharmaceuticals:**

  - **Fe-59**, $T_{1/2f}$=45 d, gama photons of 1 MeV - unfavorable
  - **Fe-52**, positron emitter, cyclotron production - hardly avaible
  - **In-111-chloride**, as an analog of Fe, dose 74-148 MBq (2-4 mCi)
  - Tc-99m-sulfur kolloid, 444 MBq (12 mCi)
  - Tc-99m marked monoclonal antigranulocyte antibodies

Functional bone marrow

- IN THE AXIAL SKELETON BONES:
- In the corpus vertebrae
- Pelvis
- Sternum
- Ribs
- Scapula
- Skull
- The proximal parts of long bones

Erythrocyte precursors sci. of bone marow

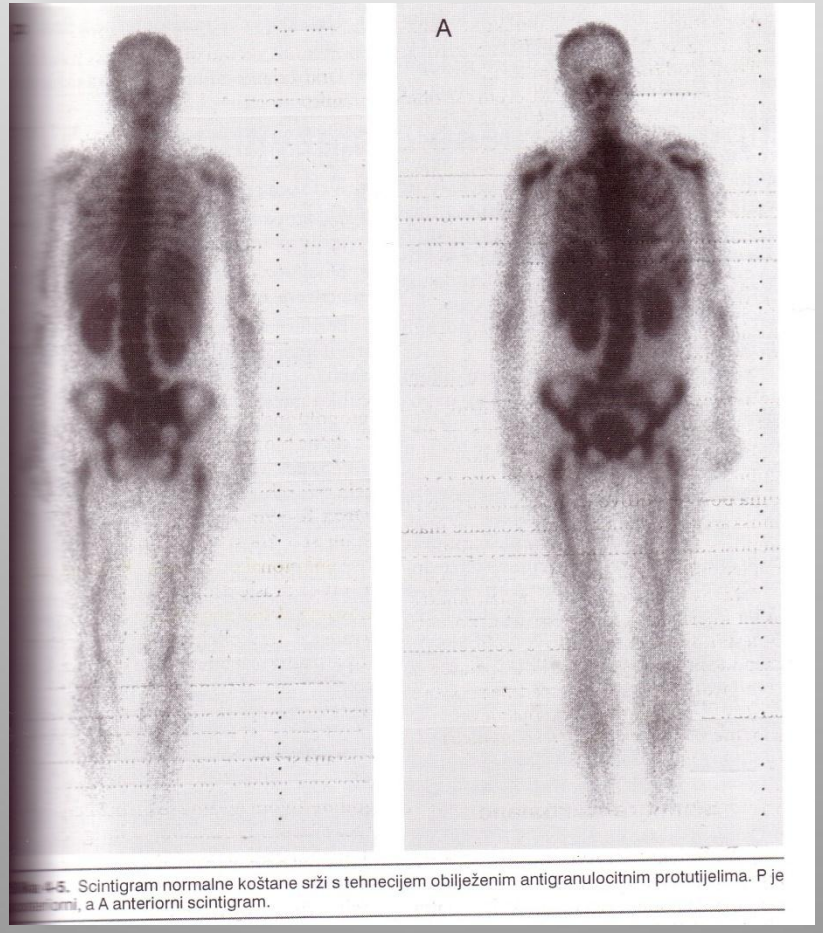
- INCORPORATION OF RADIOACTIVE IRON AND ANALOGUES IN ERYTHROCYTE PRECURSORS
- The radioactive isotopes of iron **Fe-59**: a long half-life of 45 days, gamma photons with energy greater than 1 MeV which requires heavy collimators of small efficiency. Dose is 10-40 μCi.

- The radioactive isotopes of iron **Fe-52**: positron emitter, expensive and less available as a cyclotron product, dose is 100-200 μCi.
- From a physiologic standpoint optimal, but have adverse physical features.

- It is used **In-111-chloride** as analog of iron, dose is 2-4 mCi.

- **Tc -labeled monoclonal antigranulocyte antibodies**.

Sc. of bone marrow with Tc-marked antigranulocyte antibodies



4-5. Scintigram normalne koštane srži s tehnecijem obilježenim antigranulocitnim protutijelima. P je ...ni, a A anteriorni scintigram.

Scintigraphy of the reticuloendothelial elements of bone marow

The principle is the phagocytosis of radioactive colloids in the reticuloendothelial cells of bone marrow

It is used **Tc-99m-sulfur colloid.**

Dose is 444 MBq tj. 12 mCi.

- **Indications**

  - Evaluation of the amount of active bone marrow after chemotherapy and radiation therapy

  - Detection of extramedullary hematopoesis

  - Identification of the best places for a bone marrow biopsy

  - Diagnosis and staging of some hematologic disease

  - Multiple myeloma: a greater sensitivity of bone scan with Tc-99m-diphosphonate

INTERPRETATION OF IMAGES

- We analyze the **presence of activity** in the central bone marrow.
- We analyze the **absence of activity** in the central bone marrow.
- We analyze the **peripheral extension and focal defects.**
- On scintigraphy of the reticuloendothelial cells it is possible to analyze **liver and spleen.**

Bone densitometry (DXA)

- DXA (dual energy x-ray absorptiometry), the method is based on the difference in absorption of X-rays in bone and soft tissue for direct measurement of bone mineral mass (g) and for the indirect measurement of bonedensity (g / cm2).

- The most common places that are measured are lumbar spine, upper third of the femur (femoral neck) and forearm.

- There are also measuring of bone density of the whole body.

Clinical application

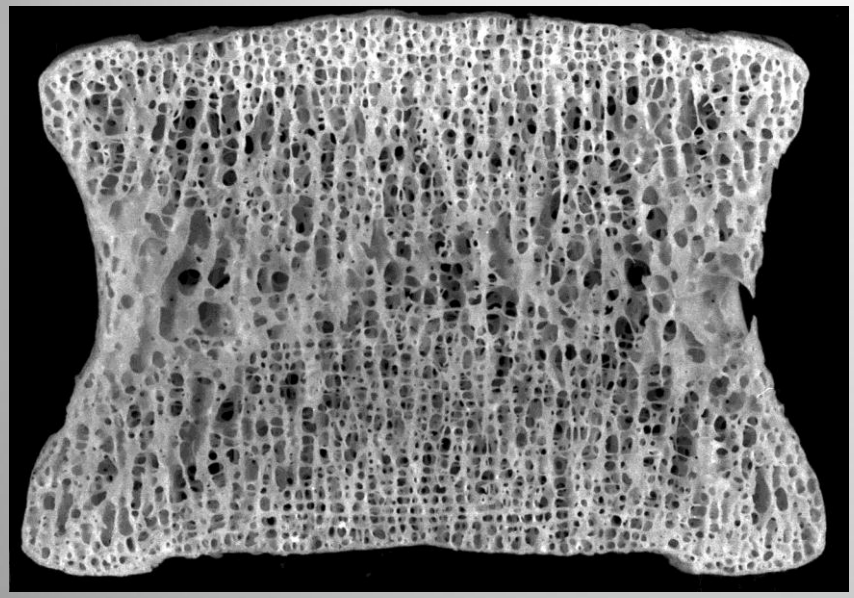
- In the diagnosis and monitoring of **osteoporosis** treatment, in assessing the risk for osteoporotic bone fractures.

- **Osteoporosis** is a progressive bone disease characterized with reduced bone mass and changes in microarchitecture of bone tissue. The consequences of these changes are increased bone fragility and increased bone fracture risk.

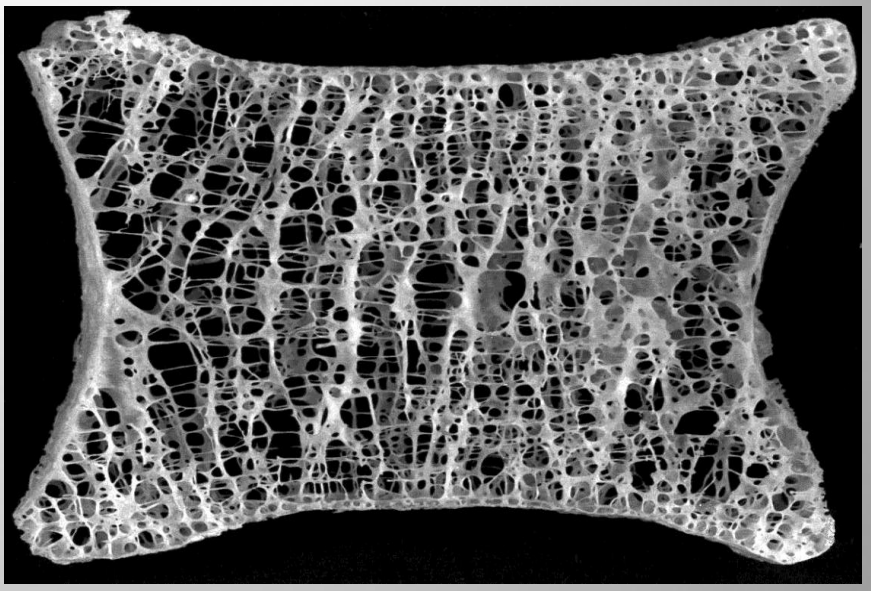
- We divide osteoporosis into the primary (postmenopausal and seni)l and secondary (PHPT, corticosteroid th., ..)

- We use **DXA** in the diagnosis and monitoring of oteomalacia, renal dystrophy, hyperparathyroidism, ..

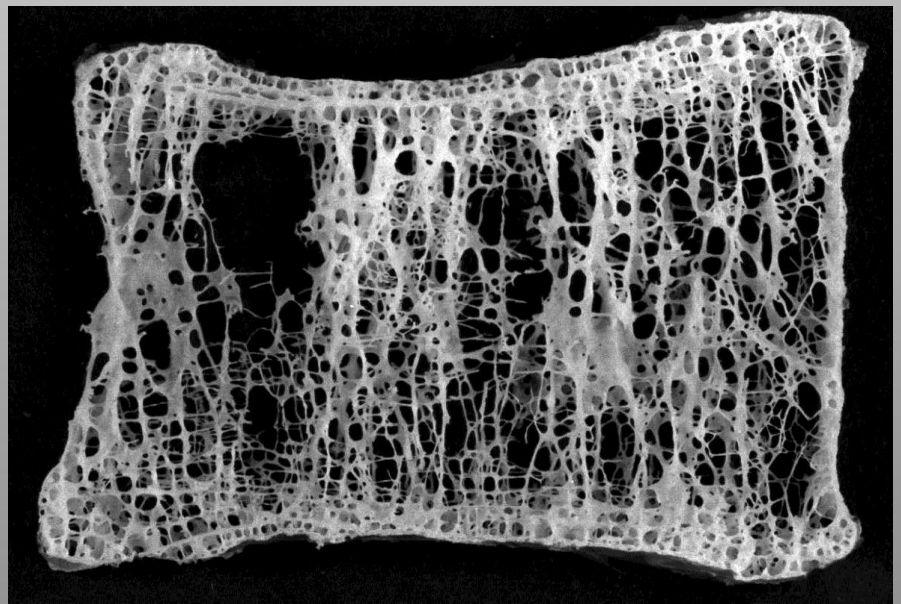
Normal



Osteoporosis



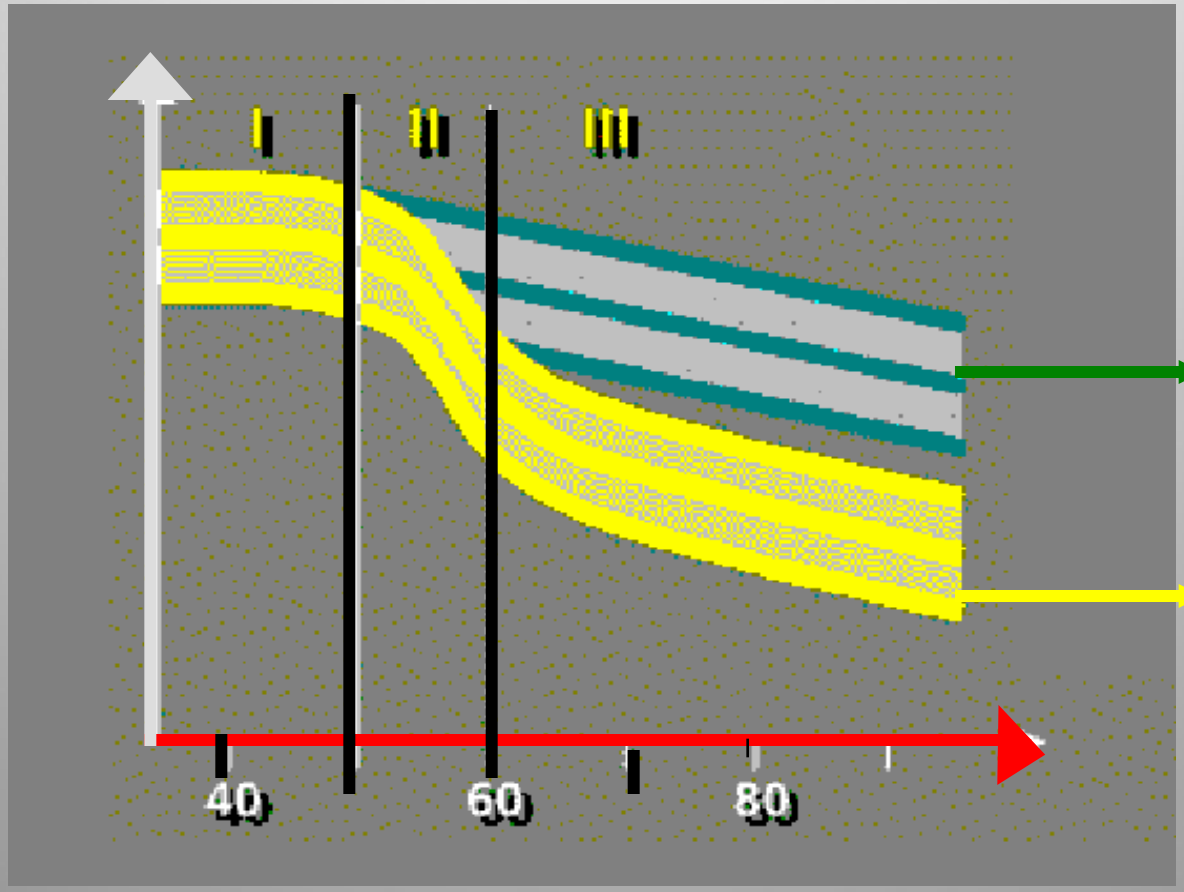
Severe Osteoporosis



Courtesy Dr. A. Boyde

BONE DENSITY LOSS THROUGHOUT LIFE

BONE DENSITY



men

20% to - 30%

women

-35% to -50%

age

OSTEOPOROSIS AND OSTEOPENIA

- the most common metabolic diseases of the developed world **(8-10% of the population, "silent epidemia", "tip of the iceberg", "unrecognized", ...)**
- leading socio-economic and public health problem (USA - 29 million patients; 1.3 million fractures annually; ½ spine, femoral neck ¼, and ¼ forearm)
- the risk of osteoporotic fracture has 40% women older than 50 years (Kanis, 2000);
- It is diagnosed only 30-50% of osteoporotic fractures of the spine

Prevalence 2000 : 2050 = double

due to the age increase of the population and way of life!

EPIDEMIOLOGY

MANKIND IS BECOMING MORE NUMEROUS AND OLDER

– doubled the number of elderly (7 ⇨ 13 %)

– reduction in the proportion of young people *(27 ⇨ 17 %)*

- progressiv with age: 50 => **13%**; 60 => **27%**; 70 => **47%**; 80 > **67%**
- medicine is advancing
- the expected duration of life (69 i 77 god.)
- technique improvement (DXA, US)
- most often unrecognized, clinically underestimated
- level of understanding of the issues insufficient
- medical care in osteoporosis is limited

CROATIA

(2001 year)

	> 50 god.	> 60 god.	> 70 god.
Men	**643.000**	**386.000**	**155.000**
Women	**842.000**	**570.000**	**286.000**

osteopenia **260 000**

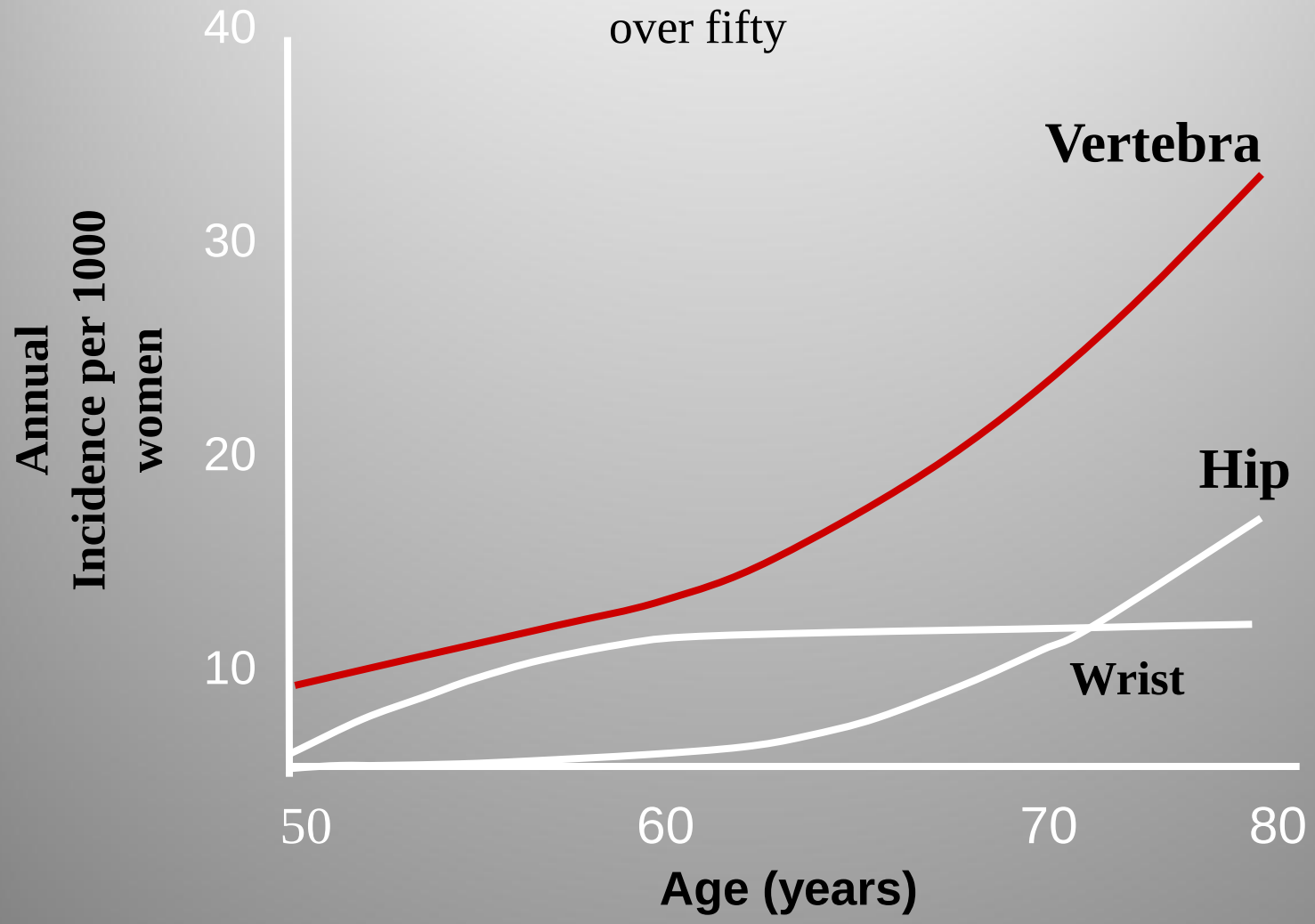
osteoporosis **130 000**

+ 50%

HDO, Zagreb, 21.10.2005.

Osteoporosis

The incidence of fractures of the spine, wrist and hip in women over fifty

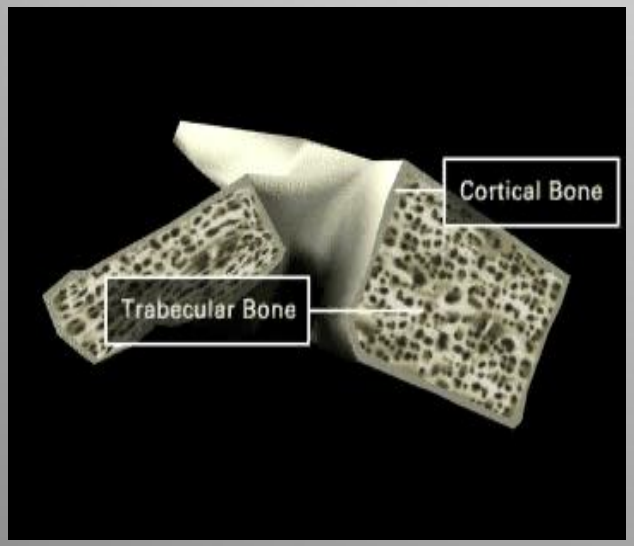


Osteoporosis

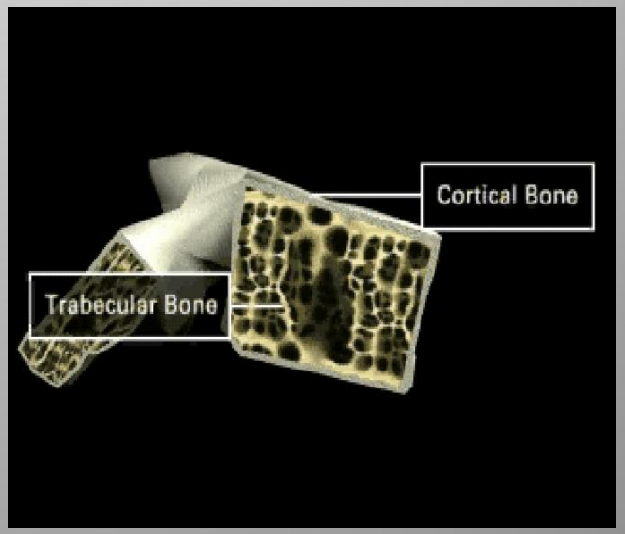
- In the first six years after the menopause women can lose up to one third of bone mass.

- 40% of women aged over 50 years experience osteoporotic fracture.

healthy vertebra



osteoporotic vertebra



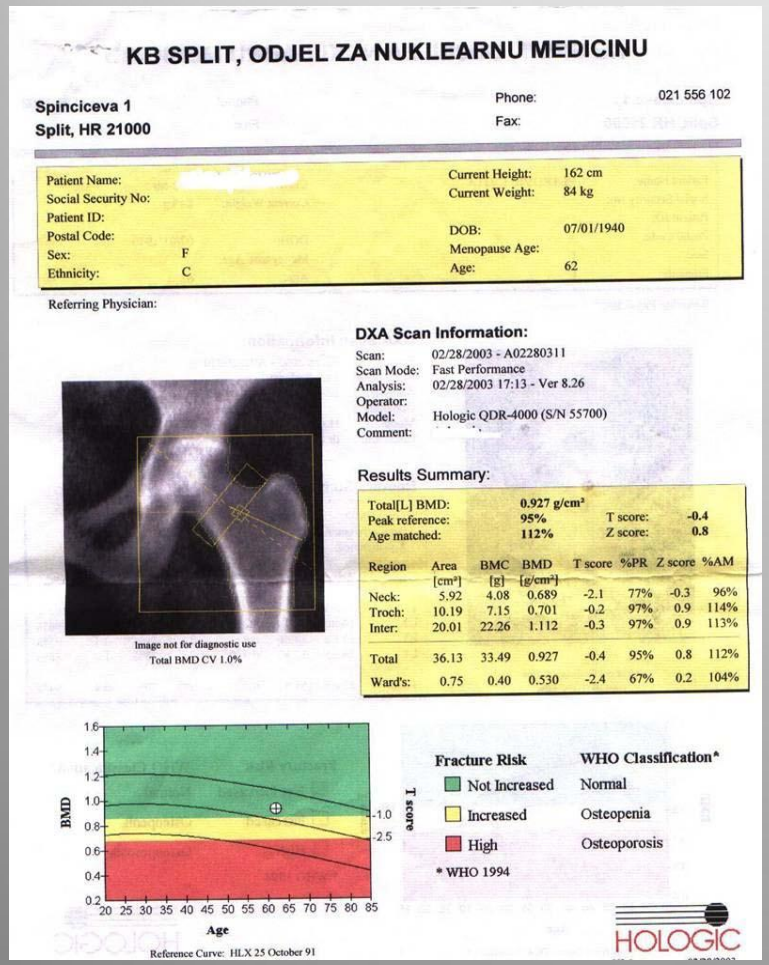
Bone densitometry (DXA-dual energy X-ray absorptiometry)

1. bone density measurement for the diagnosis of osteoporosis
2. assessment of fracture risk
3. monitoring of treatment effect

Imaging is easy, fast and completely painless, radiation minimum, the patient don’t take his clothes off

The report consists of three parts:

- bone picture
- tables with quantitative parameters
- graphical representation



KB SPLIT, ODJEL ZA NUKLEARNU MEDICINU

Spinciceva 1
Split, HR 21000

Phone: 021 556 102
Fax:

Patient Name:
Social Security No:
Patient ID:
Postal Code:
Sex: F
Ethnicity: C

Current Height: 162 cm
Current Weight: 84 kg
DOB: 07/01/1940
Menopause Age:
Age: 62

Referring Physician:

DXA Scan Information:

Scan: 02/28/2003 - A02280311
Scan Mode: Fast Performance
Analysis: 02/28/2003 17:13 - Ver 8.26
Operator:
Model: Hologic QDR-4000 (S/N 55700)
Comment:

Image not for diagnostic use
Total BMD CV 1.0%

Results Summary:

Total[L] BMD: 0.927 g/cm²
Peak reference: 95% T score: -0.4
Age matched: 112% Z score: 0.8

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
Neck:	5.92	4.08	0.689	-2.1	77%	-0.3	96%
Troch:	10.19	7.15	0.701	-0.2	97%	0.9	114%
Inter:	20.01	22.26	1.112	-0.3	97%	0.9	113%
Total	36.13	33.49	0.927	-0.4	95%	0.8	112%
Ward's:	0.75	0.40	0.530	-2.4	67%	0.2	104%

BMD / T score

Age

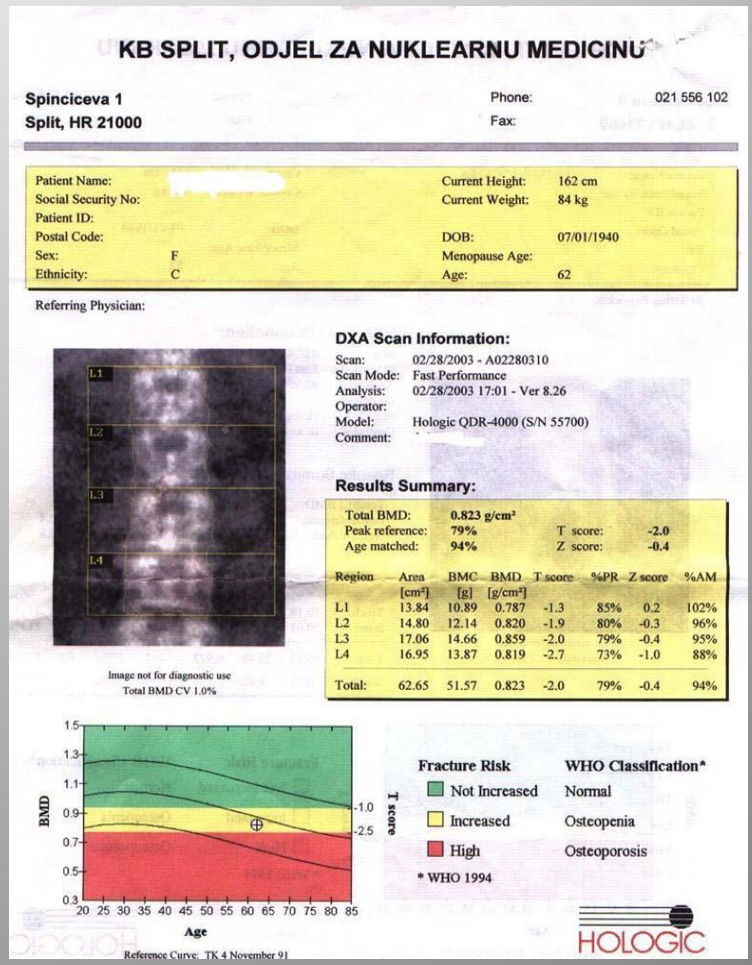
Reference Curve: HLX 25 October 91

Fracture Risk
Not Increased
Increased
High

WHO Classification*
Normal
Osteopenia
Osteoporosis

* WHO 1994

HOLOGIC



KB SPLIT, ODJEL ZA NUKLEARNU MEDICINU

Spinciceva 1
Split, HR 21000

Phone: 021 556 102
Fax:

Patient Name:
Social Security No:
Patient ID:
Postal Code:
Sex: F
Ethnicity: C

Current Height: 162 cm
Current Weight: 84 kg
DOB: 07/01/1940
Menopause Age:
Age: 62

Referring Physician:

DXA Scan Information:

Scan: 02/28/2003 - A02280310
Scan Mode: Fast Performance
Analysis: 02/28/2003 17:01 - Ver 8.26
Operator:
Model: Hologic QDR-4000 (S/N 55700)
Comment:

Image not for diagnostic use
Total BMD CV 1.0%

Results Summary:

Total BMD: 0.823 g/cm²
Peak reference: 79% T score: -2.0
Age matched: 94% Z score: -0.4

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	13.84	10.89	0.787	-1.3	85%	0.2	102%
L2	14.80	12.14	0.820	-1.9	80%	-0.3	96%
L3	17.06	14.66	0.859	-2.0	79%	-0.4	95%
L4	16.95	13.87	0.819	-2.7	73%	-1.0	88%
Total:	62.65	51.57	0.823	-2.0	79%	-0.4	94%

BMD / T score

Age

Reference Curve: TK 4 November 91

Fracture Risk
Not Increased
Increased
High

WHO Classification*
Normal
Osteopenia
Osteoporosis

* WHO 1994

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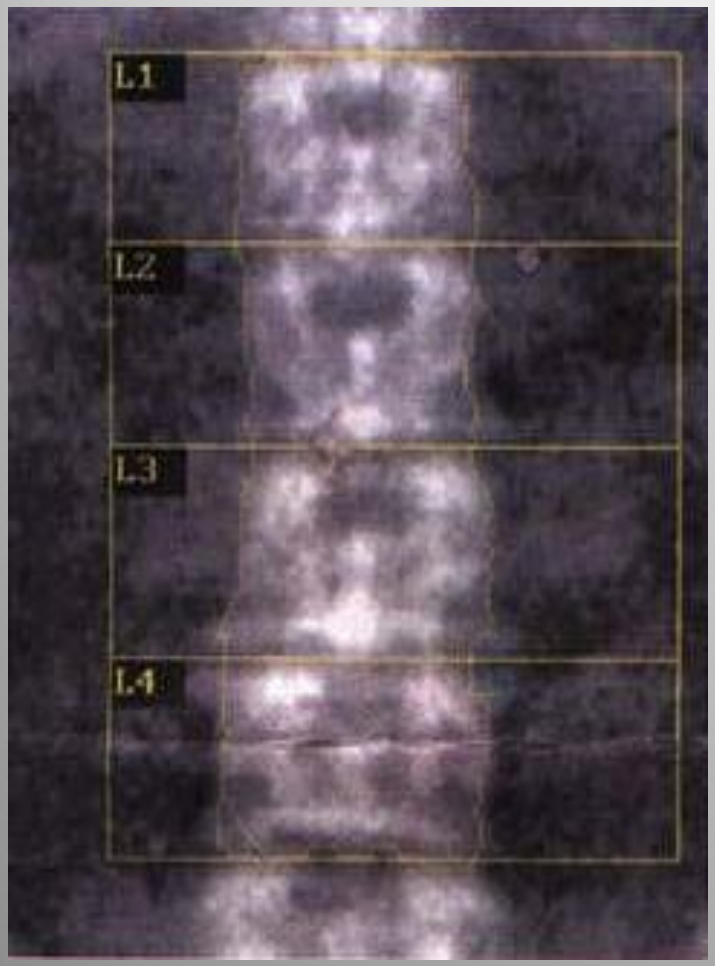
Picture of bones



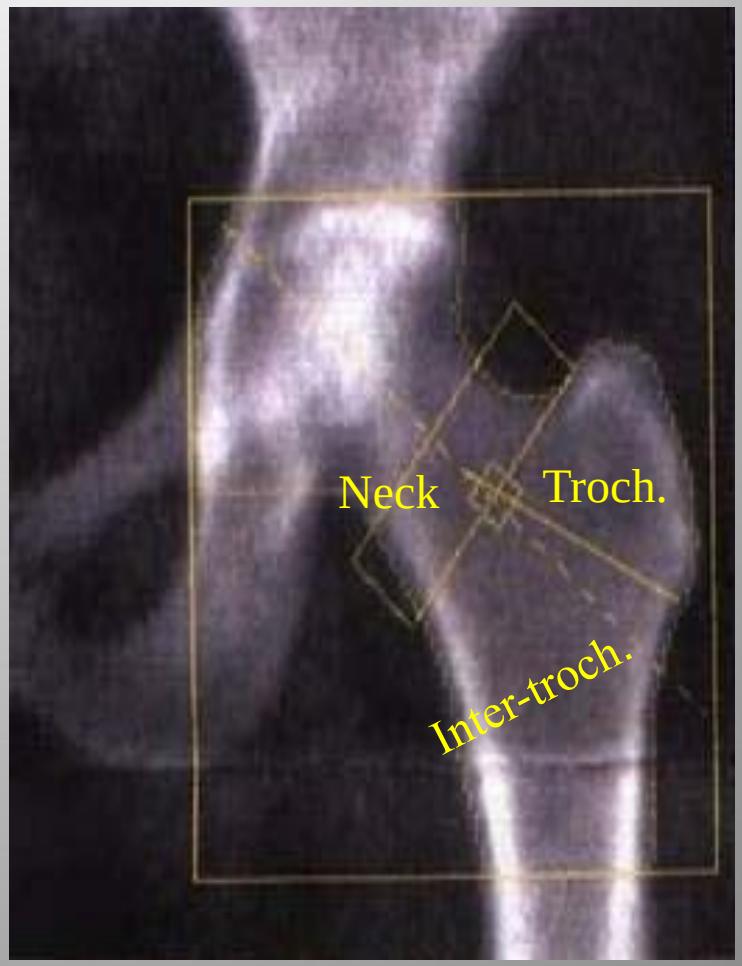
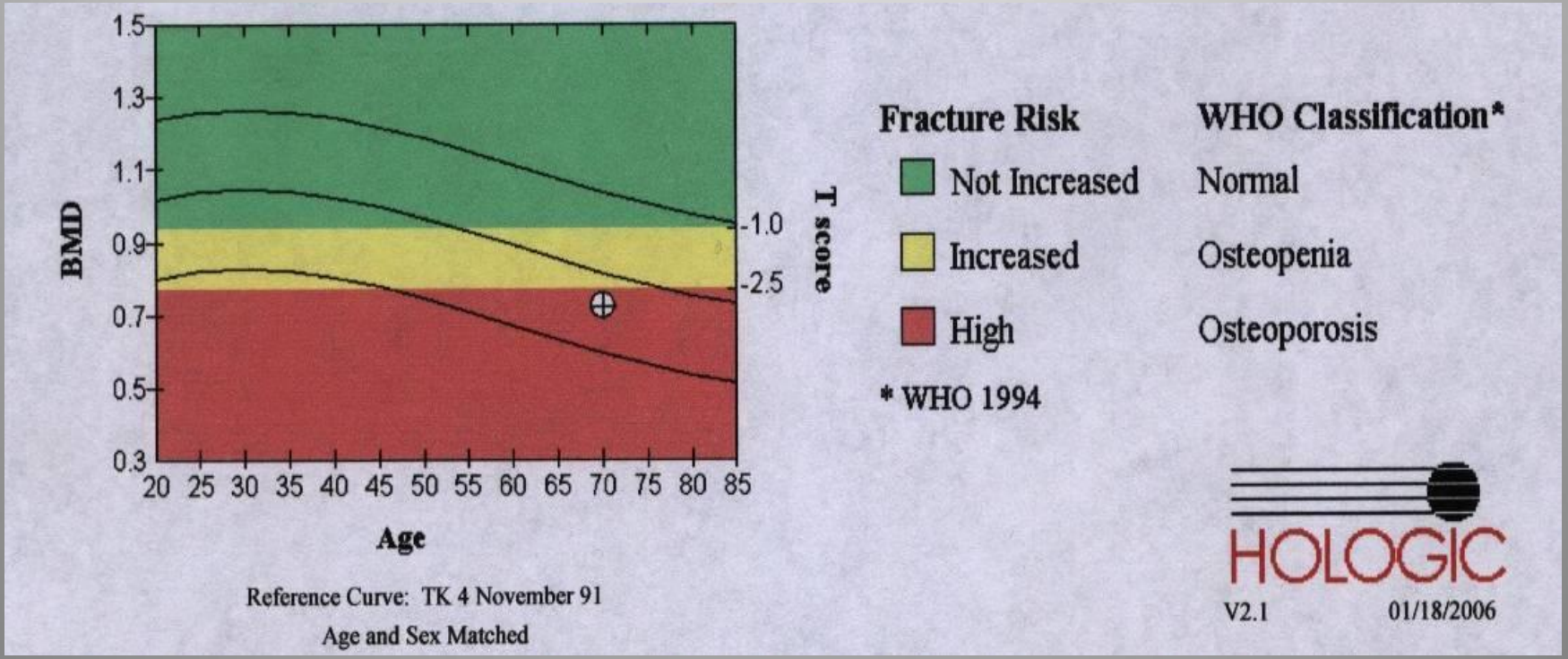


Table with quantitative parameters

Total BMD:	**0.724 g/cm²**						
Peak reference:	**69%**			T score:		**-2.9**	
Age matched:	**89%**			Z score:		**-0.8**	
Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	11.97	7.93	0.662	-2.4	72%	-0.5	92%
L2	13.10	8.47	0.646	-3.5	63%	-1.4	81%
L3	13.61	10.63	0.781	-2.8	72%	-0.6	93%
L4	13.38	10.68	0.799	-2.9	72%	-0.6	92%
Total:	52.06	37.70	0.724	-2.9	69%	-0.8	89%

Graphic representation:

- **lines show the mean BMD of normal population ± 2 SD**
- **cross indicates the measured BMD**



T score

- T score = deviation of the measured BMD from the mean BMD of young adults of the same sex, in standard deviations.

- T score greater than -1 SD = normal results.

1. T score between -1 and -2.5 SD = osteopenia.

2. T score equal or less than -2.5 SD = osteoporosis.

3. severe osteoporosis = osteoporosis with one or more nontraumatic fractures.

Z score

- The deviation of the measured bone density from the average bone density of people of the same age and sex, expressed in standard deviations.
- Can reveal connections with other process, unrelated to aging or postmenopausal
- lower Z score = more likely to be a secondary osteoporosis.

Z-score

KB SPLIT, ODJEL ZA NUKLEARNU MEDICINU

Spinciceva 1
Split, HR 21000

Phone: 021 556 102
Fax:

Patient Name:	XXXXXXXXXX	Current Height:	164 cm
Social Security No:		Current Weight:	68 kg
Patient ID:	X		
Postal Code:		DOB:	09/28/1961
Sex:	F	Menopause Age:	
Ethnicity:	C	Age:	44

Referring Physician:

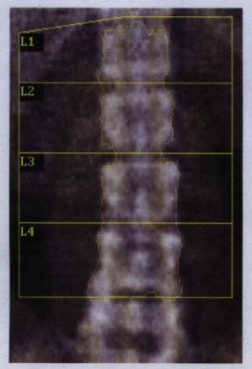


Image not for diagnostic use
Total BMD CV 1.0%

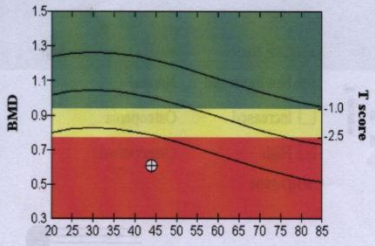
DXA Scan Information:

Scan:	03/08/2006 - A03080618
Scan Mode:	Fast Performance
Analysis:	03/08/2006 12:40 - Ver 8.26
Operator:	BK
Model:	Hologic QDR-4000 (S/N 55700)
Comment:	

Results Summary:

Total BMD:	**0.606 g/cm²**		
Peak reference:	**58%**	T score:	**-4.0**
Age matched:	**61%**	Z score:	**-3.6**

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	9.50	4.37	0.460	-4.2	50%	-3.9	52%
L2	12.54	7.03	0.561	-4.2	55%	-3.8	57%
L3	13.16	8.28	0.629	-4.1	58%	-3.7	61%
L4	16.85	11.86	0.704	-3.7	63%	-3.3	66%
Total:	52.05	31.55	0.606	-4.0	58%	-3.6	61%



Reference Curve: TK 4 November 91
Age and Sex Matched

Fracture Risk	WHO Classification*
Not Increased	Normal
Increased	Osteopenia
High	Osteoporosis

* WHO 1994

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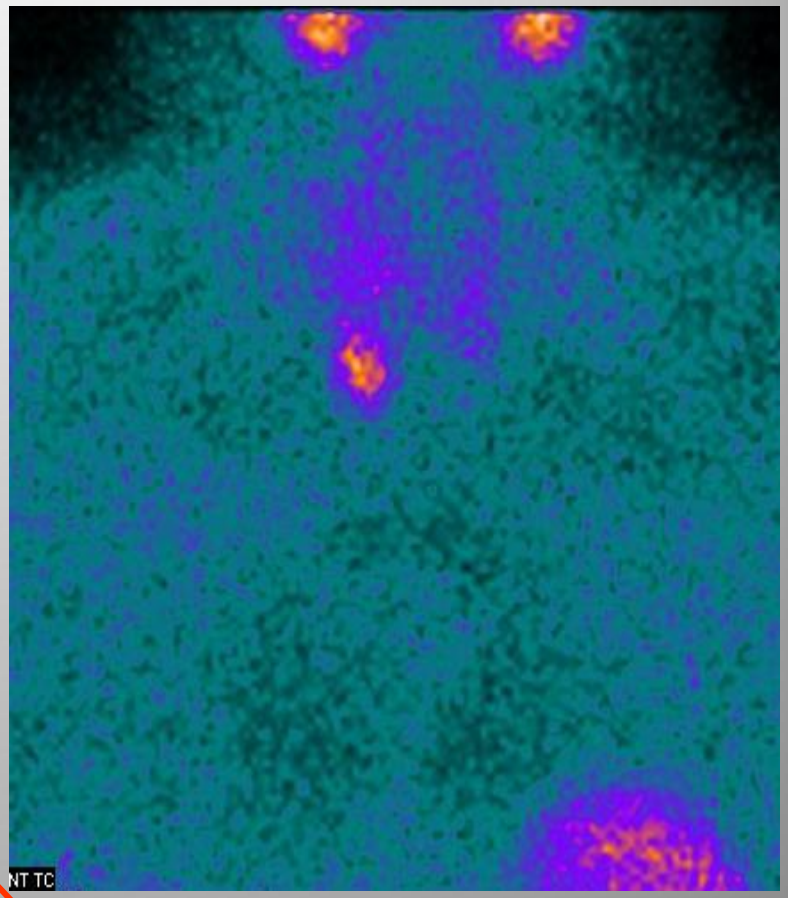
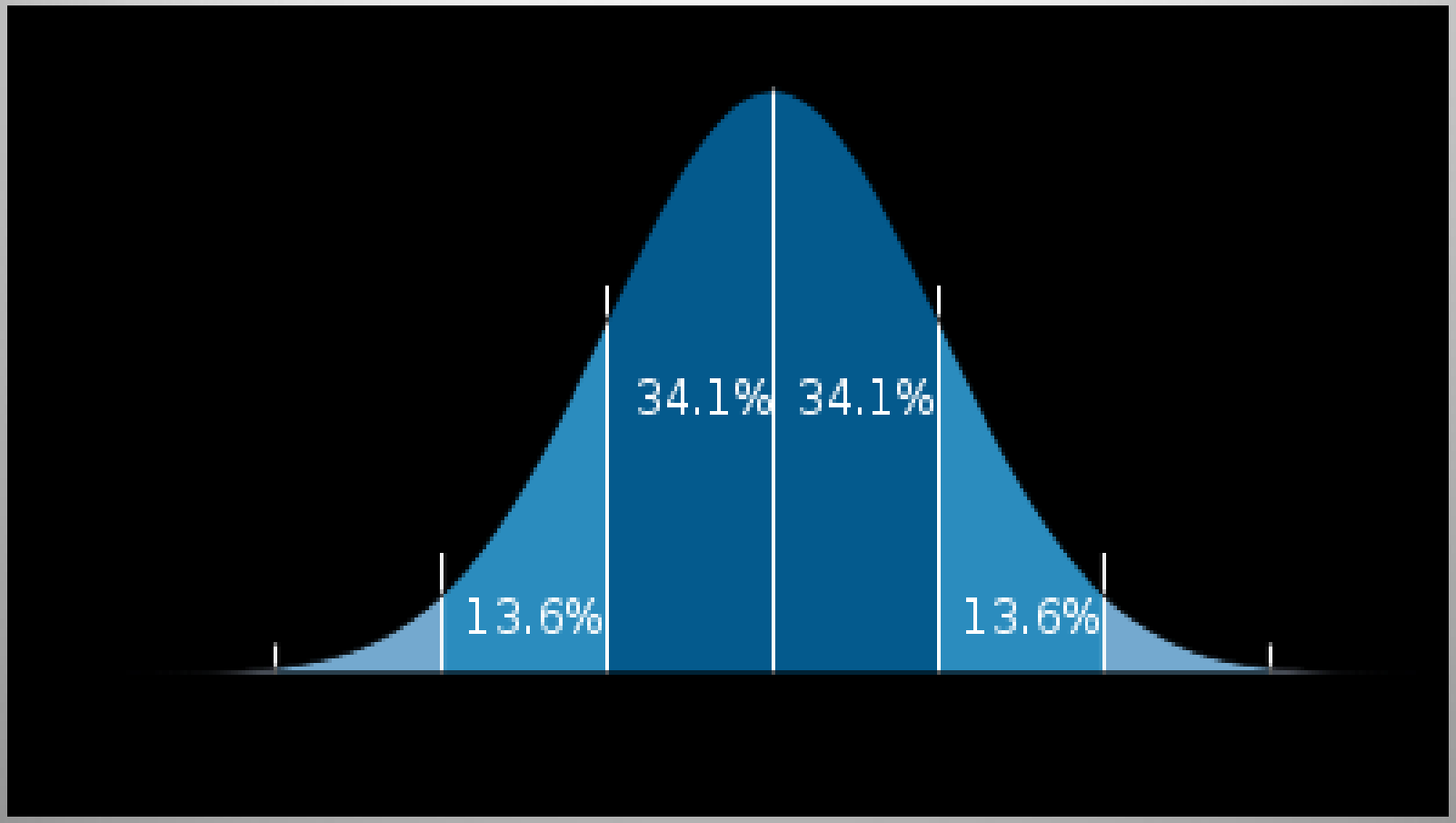
V2.1 03/29/2006



Normal or Gaussian distribution



X ± 1 SD= 68,2%

X ± 2 SD= 95,4%

X ± 3 SD= 99,7% (3 od 1000)

X ± 4 SD= 99,99% (1 od 10 000)

Radiation dose

For the patient	μGy	mrad
AP spine	9-44	1,9-4,4
Hip	28-66	2,8-6,6
For technologist on >1 m distance	2 μGy/h	0,2 mrad/h

Error (precision) of measurement

It depends on the precision of machine, software and technologists

Error of measurement		LSC
Spine	1-2%	> 3%
Hip	2-3%	> 6%

The minimum, statistically significant changes (<u>the least significant change, LSC</u>) is defined as the change that is 2.8 times greater than the measurement error, and it is best expressed in g/cm²

DXA

ADVANTAGES

- simplicity
- dg. before fracture

DISADVANTAGES

- dependence on the manufacturer
- errors in the analysis and interpretation of findings

Osteophytes

KB SPLIT, ODJEL ZA NUKLEARNU MEDICINU

Spinciceva 1
Split, HR 21000

Phone: 021 556 102
Fax:

Patient Name:		Current Height:	160 cm
Social Security No:		Current Weight:	61 kg
Patient ID:			
Postal Code:		DOB:	12/10/1930
Sex:	F	Menopause Age:	
Ethnicity:	C	Age:	75

Referring Physician:

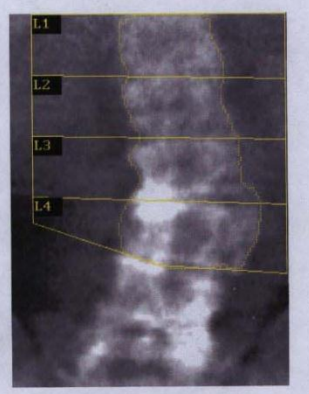


Image not for diagnostic use
Total BMD CV 1.0%

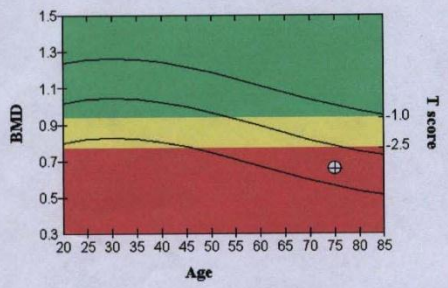
DXA Scan Information:

Scan:	01/20/2006 - A01200617
Scan Mode:	Fast Performance
Analysis:	01/25/2006 14:43 - Ver 8.26
Operator:	Z.K
Model:	Hologic QDR-4000 (S/N 55700)
Comment:	

Results Summary:

Total BMD:	**0.658 g/cm²**		
Peak reference:	**63%**	T score:	**-3.5**
Age matched:	**84%**	Z score:	**-1.1**

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	12.89	6.26	0.486	-4.0	53%	-1.8	70%
L2	12.62	6.11	0.485	-4.9	47%	-2.6	63%
L3	15.00	10.66	0.711	-3.4	66%	-0.9	88%
L4	17.73	15.27	0.862	-2.3	77%	0.3	104%
Total:	58.23	38.30	0.658	-3.5	63%	-1.1	84%



Reference Curve: TK 4 November 91
Age and Sex Matched

Fracture Risk	WHO Classification*
Not Increased	Normal
Increased	Osteopenia
High	Osteoporosis

* WHO 1994

HOLOGIC
V2.1 01/25/2006

KB SPLIT, ODJEL ZA NUKLEARNU MEDICINU

Spinciceva 1
Split, HR 21000

Phone: 021 556 102
Fax:

Patient Name:		Current Height:	160 cm
Social Security No:		Current Weight:	61 kg
Patient ID:			
Postal Code:		DOB:	12/10/1930
Sex:	F	Menopause Age:	
Ethnicity:	C	Age:	75

Referring Physician:

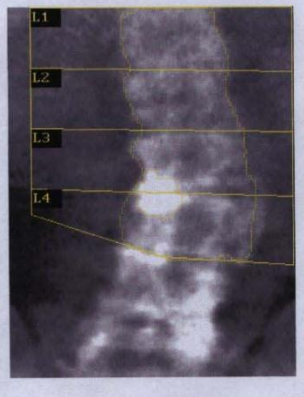


Image not for diagnostic use
Total BMD CV 1.0%

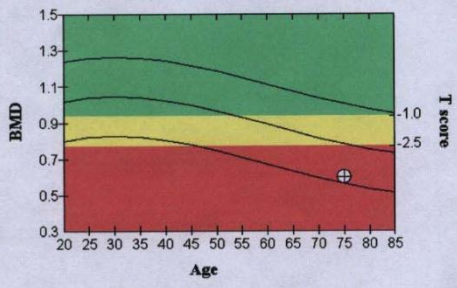
DXA Scan Information:

Scan:	01/20/2006 - A01200617
Scan Mode:	Fast Performance
Analysis:	01/20/2006 12:31 - Ver 8.26
Operator:	Z.K
Model:	Hologic QDR-4000 (S/N 55700)
Comment:	

Results Summary:

Total BMD:	**0.598 g/cm²**		
Peak reference:	**57%**	T score:	**-4.1**
Age matched:	**76%**	Z score:	**-1.7**

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	12.89	6.26	0.486	-4.0	53%	-1.8	70%
L2	12.62	6.11	0.485	-4.9	47%	-2.6	63%
L3	13.44	8.32	0.619	-4.2	57%	-1.7	77%
L4	15.09	11.63	0.770	-3.1	69%	-0.6	93%
Total:	54.03	32.32	0.598	-4.1	57%	-1.7	76%



Reference Curve: TK 4 November 91
Age and Sex Matched

Fracture Risk	WHO Classification*
Not Increased	Normal
Increased	Osteopenia
High	Osteoporosis

* WHO 1994

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V2.1 01/25/2006

Clinical application of DXA-e

1. diagnosis of osteoporosis
2. assessment of fracture risk
3. monitoring of treatment effect

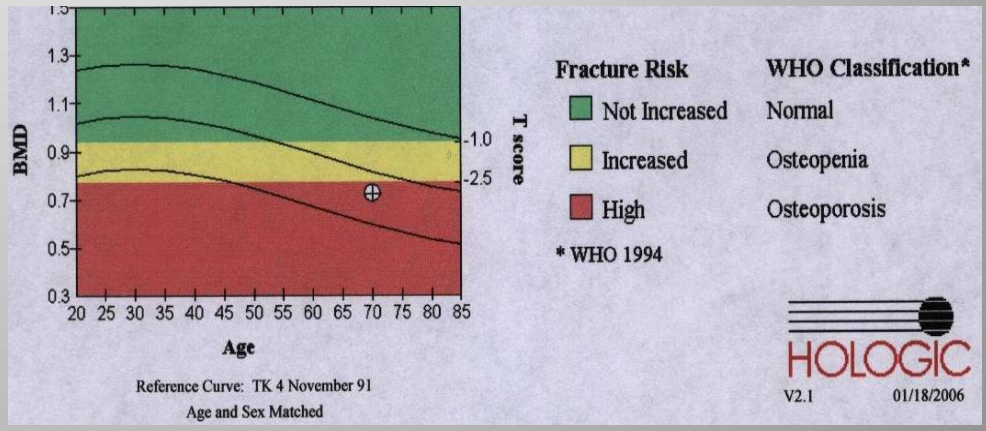
Diagnosis of OP

Clinical diagnosis of OP sets in the case of non-traumatic fractures

WHO Study Group on Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis

World Health Organization

Geneva 1994



- Postmenopausal women (T-score=≤2,5)
- Premenopausal women (Z-score)
- Men: T-score (>50 g.); Z-score (<50 g.)
- Children: Z-score

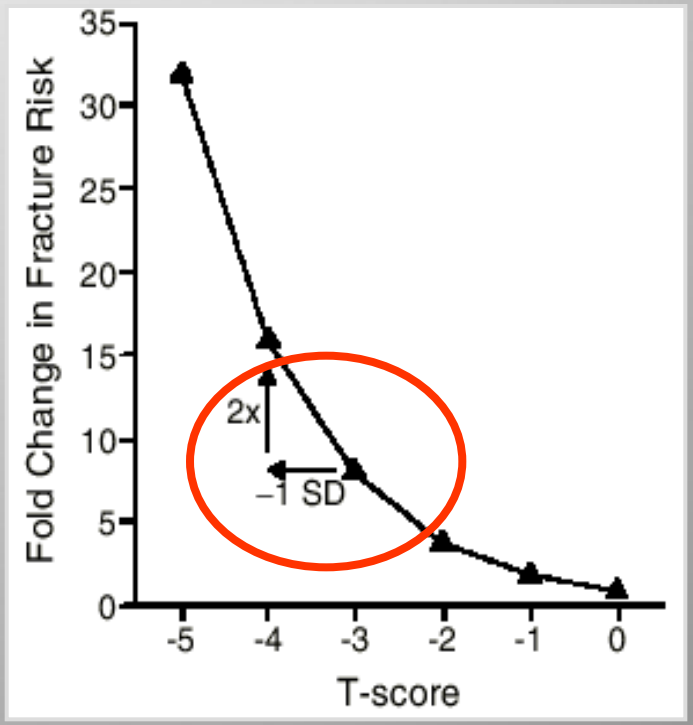
Clinical application of DXA-e

1. diagnosis of osteoporosis
2. assessment of fracture risk
3. monitoring of treatment effect

BMD and the risk of fractures

- The reduction of bone mineral density in untreated postmenopausal women is in closely correlation with the development of fractures.[1]

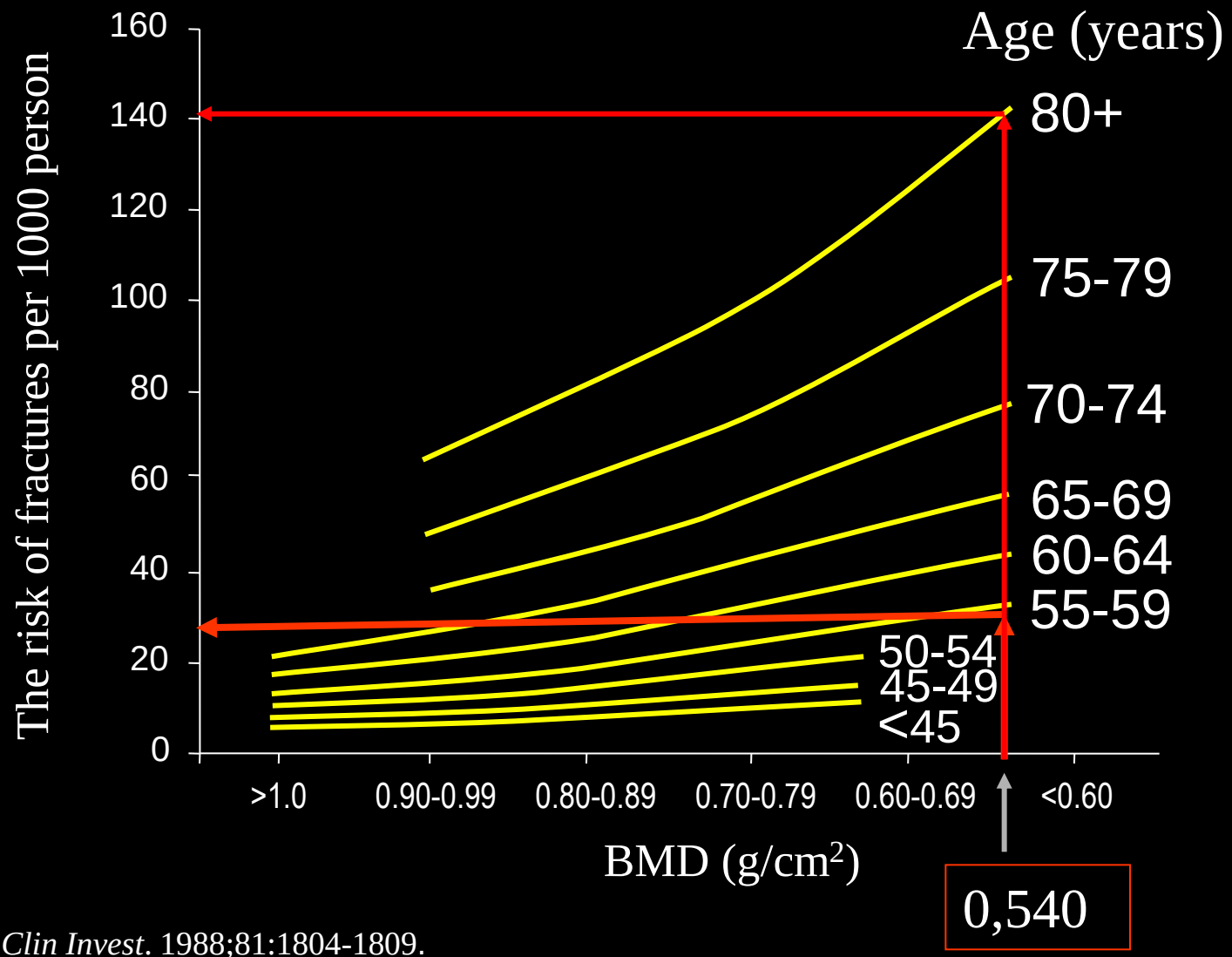
- Decrease in BMD for each standard deviation doubles the risk of fractures.[2]



[1] *Cummings SR i sur. NEJM 1993.*

[2] *Marshall D i sur. BMJ 1996*

Age and BMD as predictors of fracture



Hui SL, et al. *J Clin Invest*. 1988;81:1804-1809.

Fractures of the vertebrae are the sign of new fractures

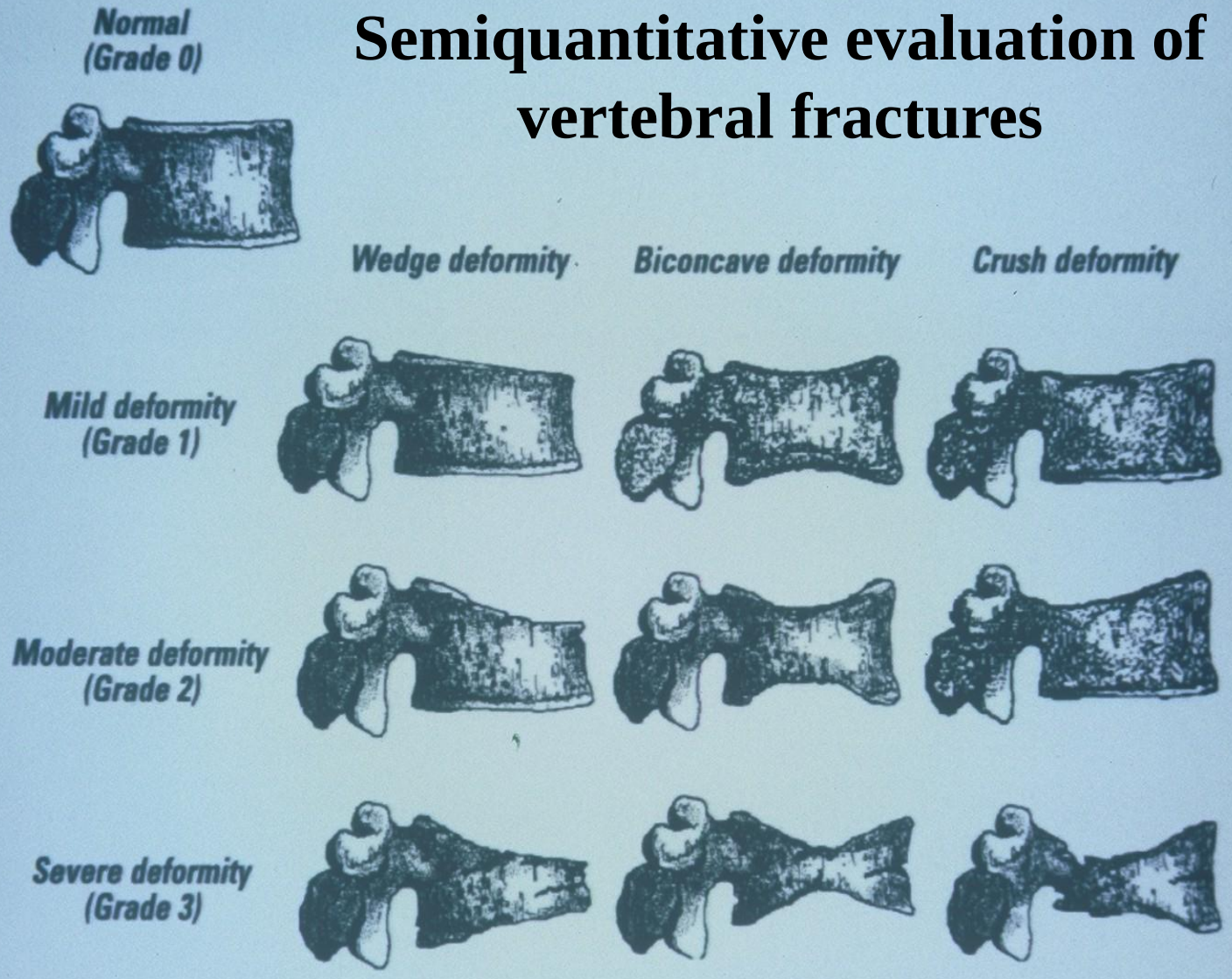
- **Women with fractured vertebrae have 5x higher risk of new vertebral fractures and 2x higher risk of hip fracture**

  Black i sur. J Bone Miner Res 1999
  Melton i sur. Osteoporos Int 1999

- **In 1 to 5 women with fractured vertebrae there will be a second fracture within a year**

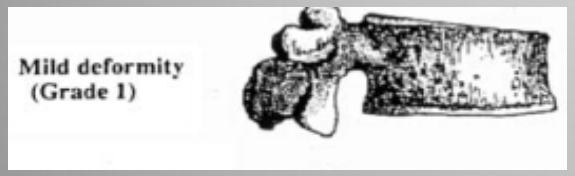
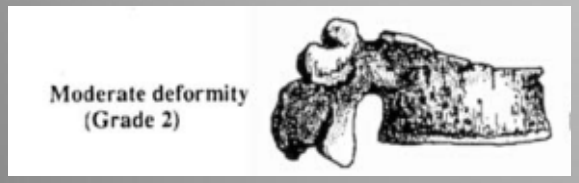
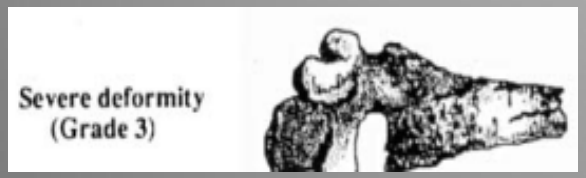
  Lindsay i sur. JAMA, 2001

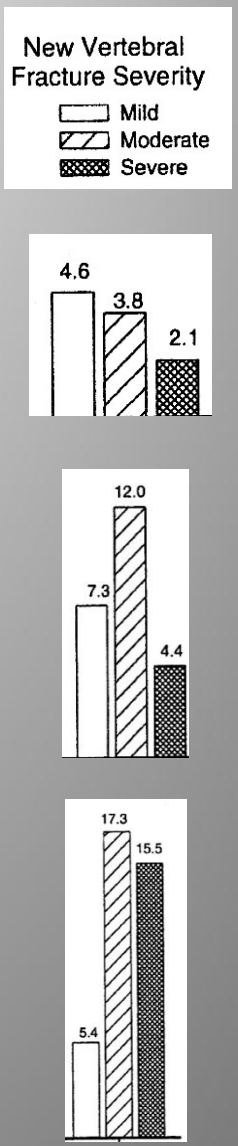
Semiquantitative evaluation of vertebral fractures



Genant HK, Wu CY, van Kujik C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res. 1993; 8(9):1137-1148.

The number and degree of existing VF symbolize general fragility of the skeleton

The degree of existing vert.fracture	The average number of existing fractures	The risk of new vertebral fracture in the next 3 years
	1,5	10,5 %
	2,1	23,6%
	3,5	38,1%



Assessment of vertebrae fracture from the lateral DXA images (VFA, Vertebral Fracture Assessment)

Detection of vertebral fractures using DXA will:

1. diagnose OP regardless of level of the measured T-score
2. it will change the diagnostic classification
3. provide a better assessment of the risk for further fractures
4. influence on the choice of therapy

The four main risk factors for fractures

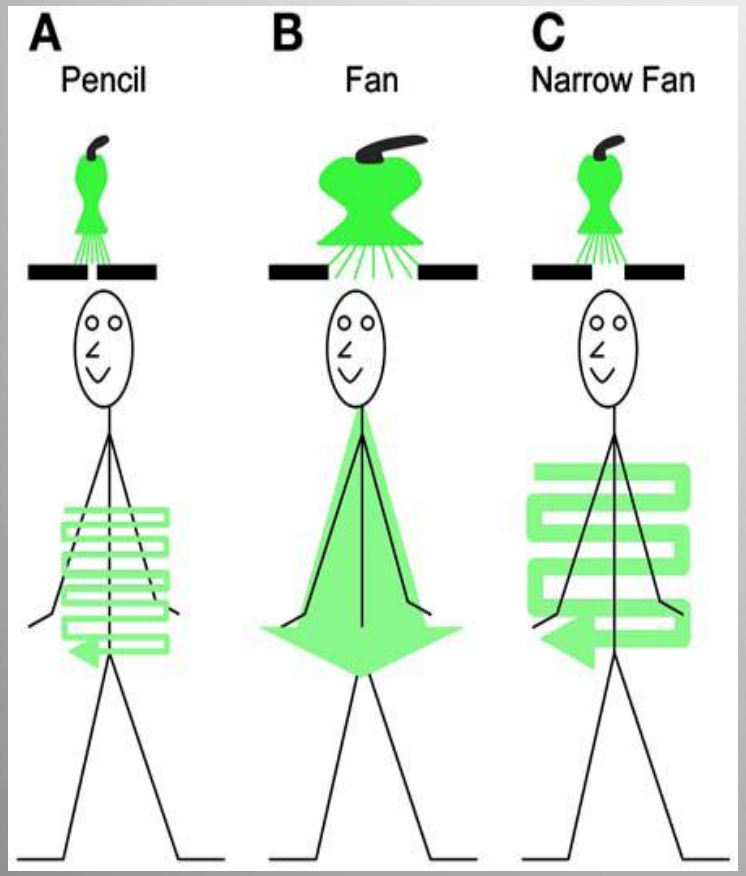
- Low BMD: the risk doubles for each SD
- Age: 10-year probability of OP fracture is 8x higher for women in the age of 85 years than for women in the age of 45 years and 5 times higher for men for the same BMD
- Previous OP fractures: risk greater 1,5-9,5x depending on the number and severity of previous fractures ----- average is 2.2 x greater than in those who did not have OP fracture
- OP fractures in the family: hip fracture in parents increases the risk for hip fracture 1,5-2x regardless of BMD
- Risk factors have a cumulative effect

Clinical application of DXA

1. diagnosis of osteoporosis
2. assessment of fracture risk
3. monitoring efficiency of treatment:
    a) control DXA
    b) comparison of findings
    c) reapiting interval
    d) interpretation of changes

- Control DXA: the same machine and the same technologist
- Comparison: BMD in g/cm^2, not with the T-score values
- Repeating interval of DXA-e: expected change > LSC
- The goal of treatment: stabilization or increase in BMD: Interpretation of changes

Control DXA: the same machine and the same technologist



Variations in technologies:

1. Various algorithms of detection bone edges
2. Different computer models of body size and composition of tissues
3. Different methods of calibration
4. Different methods of creating a two-photon beam and detector types
5. Different reference data
6. Different ROI

Do not compare results from different devices!

Comparision: g/cm² vs T-score

HIP

Before th.

Total[R] BMD:			0.466 g/cm²		T score:	-3.9	
Peak reference:			49%		Z score:	-2.1	
Age matched:			65%				
Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
Neck:	5.38	2.36	0.439	-3.7	52%	-1.6	72%
Troch:	10.84	3.41	0.314	-3.8	45%	-2.2	58%
Inter:	20.05	11.13	0.555	-3.5	50%	-1.9	65%
Total	36.27	16.90	0.466	-3.9	49%	-2.1	65%
Ward's:	1.14	0.33	0.291	-3.8	40%	-0.9	73%

After 12 month th.

Total[R] BMD:			0.502 g/cm²		T score:	-3.9	
Peak reference:			52%		Z score:	-1.8	
Age matched:			70%				
Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
Neck:	5.61	2.43	0.433	-4.6	48%	-1.9	70%
Troch:	12.03	4.26	0.354	-4.1	49%	-2.1	66%
Inter:	18.69	11.56	0.618	-3.8	54%	-1.7	73%
Total	36.33	18.24	0.502	-3.9	52%	-1.8	70%
Ward's:	1.03	0.24	0.231	-5.1	29%	-1.5	58%

Repeating interval?

Terapija	Studija	% Δ LS BMD
Raloksifen	MORE (3g)	2,9
	MORE (3g)	2,2
	MORE (1g)	
Kalcitonin	PROOF (5g)[3]	0,7
Alendronat	FIT I[1]	6,2
	FIT II (4g)[2]	6,8
	FIT (1g)	
Rizedronat	VERT-NA[5]	4,3
	VERT-MN[6]	5,9

1. Black DM i sur. Lancet 1996; 348:1535-41.
2. Cummings SR i sur. JAMA 1998; 280: 2077-82.
3. Chesnut CH 3rd i sur. Am J Med 2000; 109(4): 267-76.
4. Ettinger B i sur. JAMA 1999; 282: 637-45.
5. Harris ST i sur. JAMA 1999; 282: 1344-52.
6. Reginster J i sur. Osteoporosis Int. 2000; 11: 83-91.

* P < (
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When the expected change in BMD ≥ LSC

The purpose of osteoporosis treatment

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Reduction of fracture risk

Interpretation of changes

The goal of therapy: to reduce the risk of fractures

Checking the therapeutic effect: the stabilization or increase in BMD.

Improvement

Before th.

Total BMD:	**0.417 g/cm²**		
Peak reference:	**40%**	T score:	**-5.7**
Age matched:	**54%**	Z score:	**-3.3**

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	10.80	2.94	0.272	-5.9	29%	-3.8	40%
L2	12.58	4.47	0.356	-6.1	35%	-3.7	47%
L3	14.74	6.73	0.457	-5.7	42%	-3.1	57%
L4	15.05	8.00	0.532	-5.3	48%	-2.7	64%
Total:	53.18	22.15	0.417	-5.7	40%	-3.3	54%

After 12 month th.

Total BMD:	**0.514 g/cm²**		
Peak reference:	**49%**	T score:	**-4.8**
Age matched:	**67%**	Z score:	**-2.3**

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	10.74	4.79	0.446	-4.4	48%	-2.1	66%
L2	12.36	5.28	0.427	-5.5	42%	-3.0	57%
L3	14.86	7.63	0.514	-5.2	47%	-2.6	65%
L4	18.25	11.22	0.615	-4.6	55%	-1.9	75%
Total:	56.22	28.92	0.514	-4.8	49%	-2.3	67%

Why unchanged BMD is considered successful treatment?

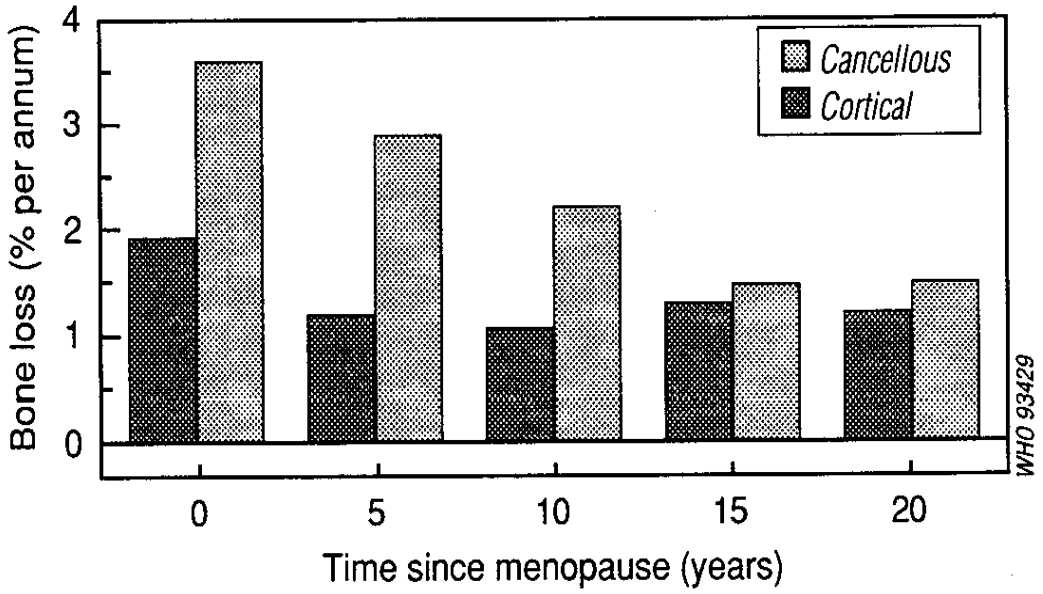
World Health Organization

Geneva 1994

WHO Study Group on Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis

Figure 15

Average rates of bone loss in postmenopausal women assessed at cortical sites (mid-radius, metacarpal) or predominantly cancellous sites (spine, distal radius), calculated from a literature survey



Reducing the risk of vertebrae fracture attributed to the increase in BMD with the use of antiresorptive and anabolic treatment

Alendronate[1]	16%
Risedronat[2]	28%
Raloxifene[3]	4%
Teriparatide[4]	40%

1. Cummings S, et al. *Am J Med* .2002;112:281-289.
2. Eastell R, et al.J Bone Miner Res. 2005;20:1261-1262.
3. Sarkar S. Et al.*J Bone Miner Res.2002*.17: 1-10.
4. Chen P, et al. J Bone Miner Res. 2006;21:1785-1790.

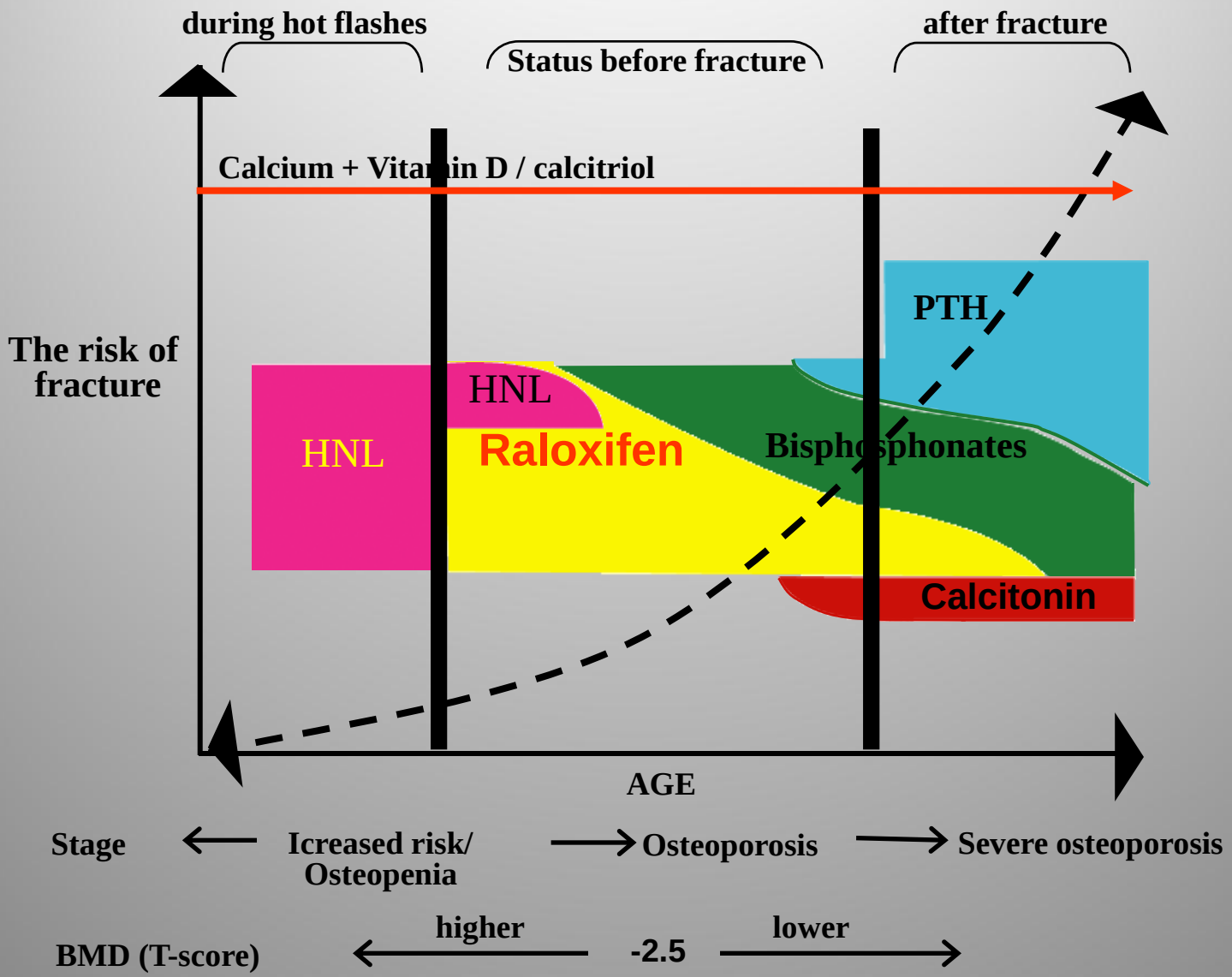
Possible factors that explain the effectiveness of anti-resorptive drugs in reducing the risk of fractures

- Increasing bone density (BMD): 4-40%
- Reducing excessive bone turnover
- Improving the quality of the bone
  - Reduced number of remodeling
  - Maintenance trabecular thickness and their conectivity
  - reducing the number of trabecular perforation
  - Reducing the microfracture
- Improving the quality of the matrix

Postmenopausal osteoporosis - Treatment options

- **Primary treatment: vit. D / calcitriol and calcium**
- **Hormone replacement therapy**
- **SERM: Selective estrogen receptor modulators- raloxifene**
- **Bisphosphonates: alendronate, ibandronate, risedronate ..**
- **strontium ranelate**
- **calcitonin**
- **PTH**
- **Denosumab: human monocl. antibody to RANKL** (RANKL induces osteclast differentiation, activation, and the prevention of osteoclast apoptosis, leading to enhanced bone resorption and bone loss).

The therapeutic algorithm for the treatment of osteoporosis in postmenopausal women



Densitometry should do:

- **All postmenopausal women <65 yr, which in addition have one or more risk factors**
- **All women> 65 g.**
- **Postmenopausal women with fractures to verify and assess the severity of the disease**
- **Adults with osteoporotic fractures**
- **Adults who have the disease, condition, or drugs which are associated with bone loss**
- **The people who have risk factors. and who are considering treatment of osteoporosis**
- **Control effect of treatment (2 g.), in the case of sec. osteoporosis often**
- **Men with clinically suspected osteoporosis, as well as all the older men of 70 yr.**
- **Women with long-term amenorrhea**

Hrvatski konsenzus o osteoporozi, Rovinj 2008.

THE END