The Beauty of
basic knowledge
MSK radiology
ECR 2014

Metabolic, endocrine, marrow diseases

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Objectives

1. To understand the pathological processes involved in the respective imaging abnormalities.

2. To appreciate the musculoskeletal manifestations of systemic disorders and their underlying pathomechanisms.

3. To appreciate strengths and weaknesses of the imaging modalities in assessing these disorders.

We will focus on

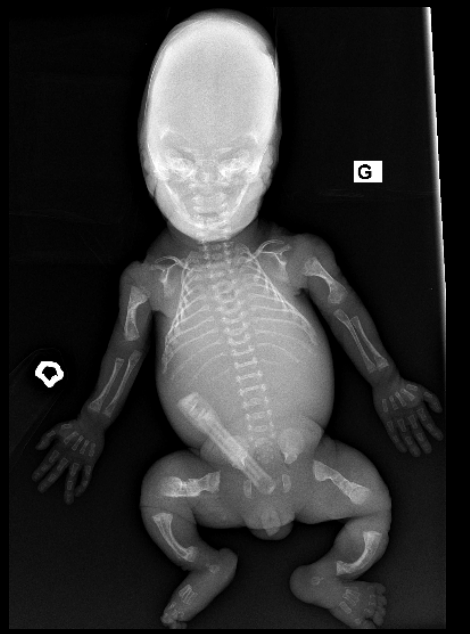
- Bone
- Marrow

Will be mentioned

- Extra-osseous changes
- Growing skeleton

We will skip

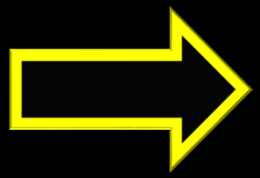
- Diabetus mellitus
  - soft tissue, osseous and joint infection
  - bone fractures
  - neuropathy
  - calcifications
- Crystal deposition diseases
- Inherited conditions, rare diseases



By the end of this lecture, you should

- Remember imaging features observed in bone and marrow associated with metabolic disorders
- Be aware of limitations of medical imaging
- Recognize conditions in which you can modify patient care

Metabolic, endocrine , marrow disorders



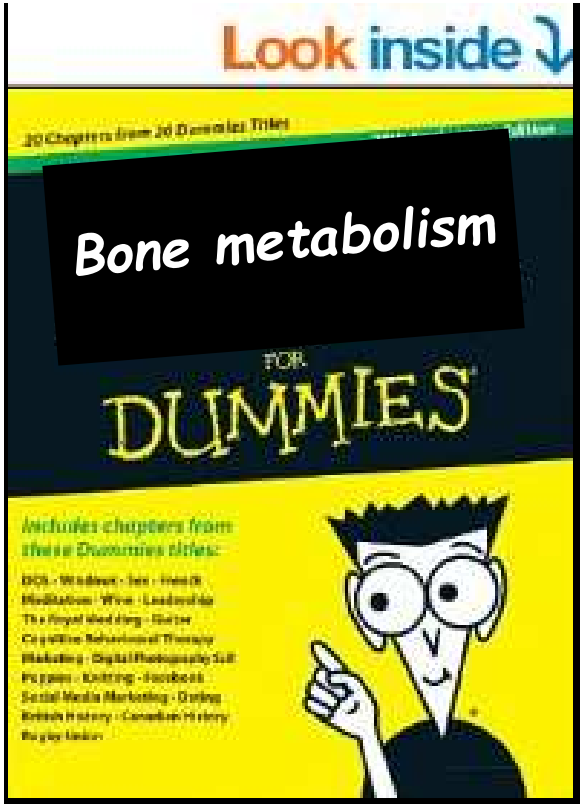
A. Normal bone and marrow metabolism

B. Overview on metabolic disorders

C. Imaging bone or marrow ?

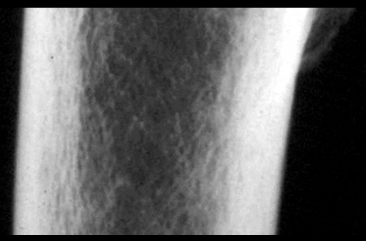
D. Metabolic bone disorders

E. Metabolic marrow disorders

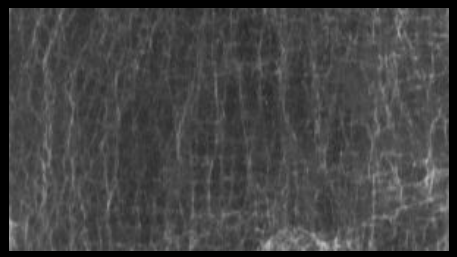


bone metabolism

* Cortical bone



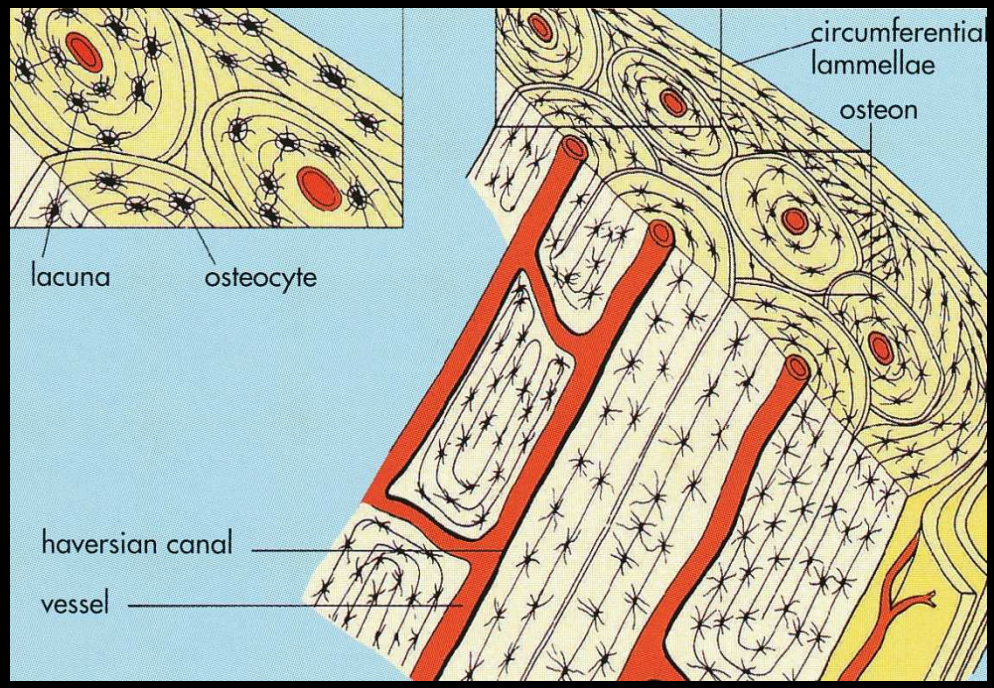
* Trabecular bone

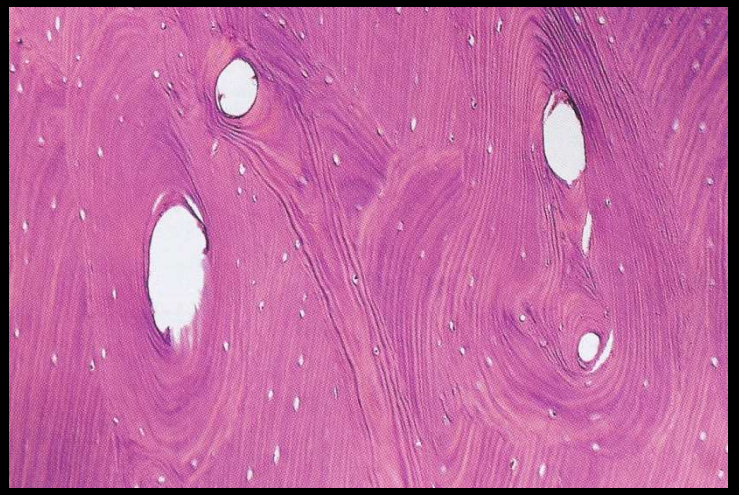


Bone architecture

Cortical or compact bone

- 80% of skeleton volume
- Low (10%) porosity (low surf.-to-vol.ratio)
- Protective and biomechanical role
- No role in P/Ca metabolism





In « orthopaedic pathology » by P Bullough Normal bone structure and develoment P 17

Bone architecture

Trabecular or cancellous bone :

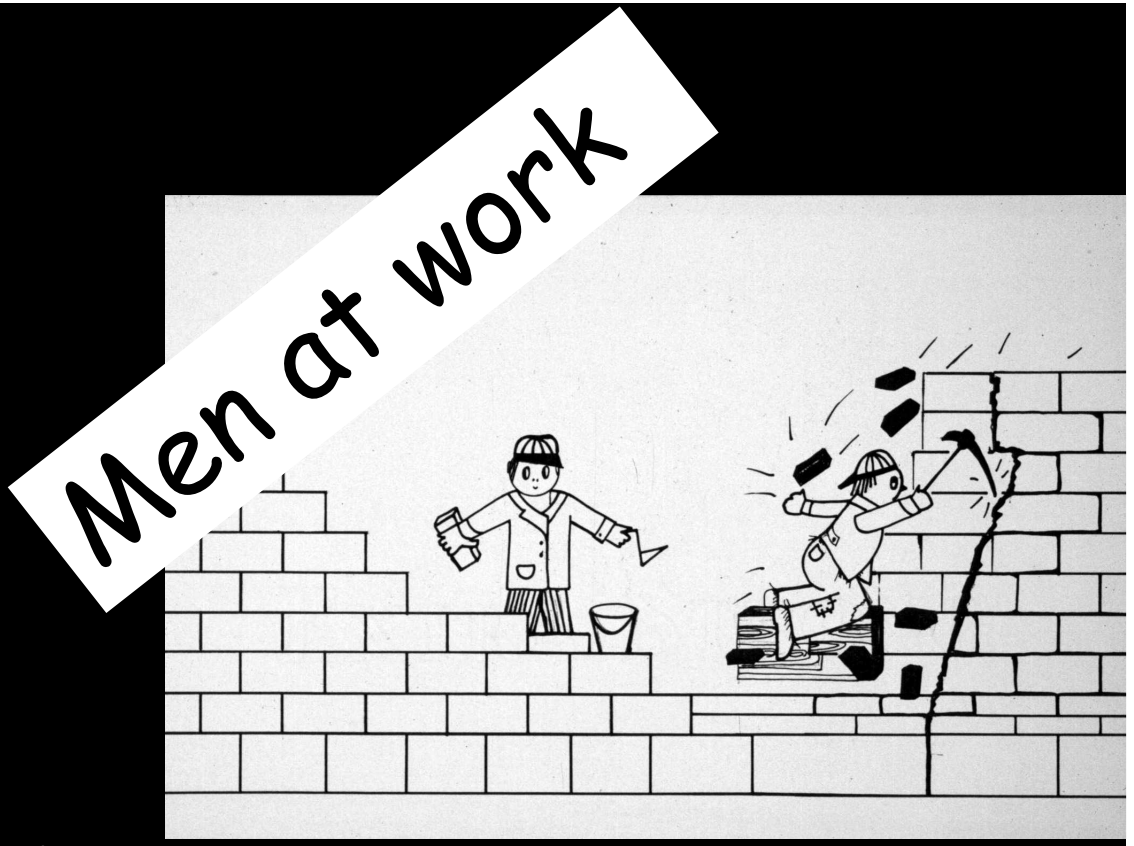
- 20% of skeleton volume
- High (75%) porosity (high surf.-to-vol. ratio)
- Metabolic role (P/Ca homeostasis)

Bone microstructure

Cells :
- osteocytes
- osteoblasts
- osteoclasts

Organic matrix :
- Type I collagen (90%)
- Proteoglycans and glycoproteins

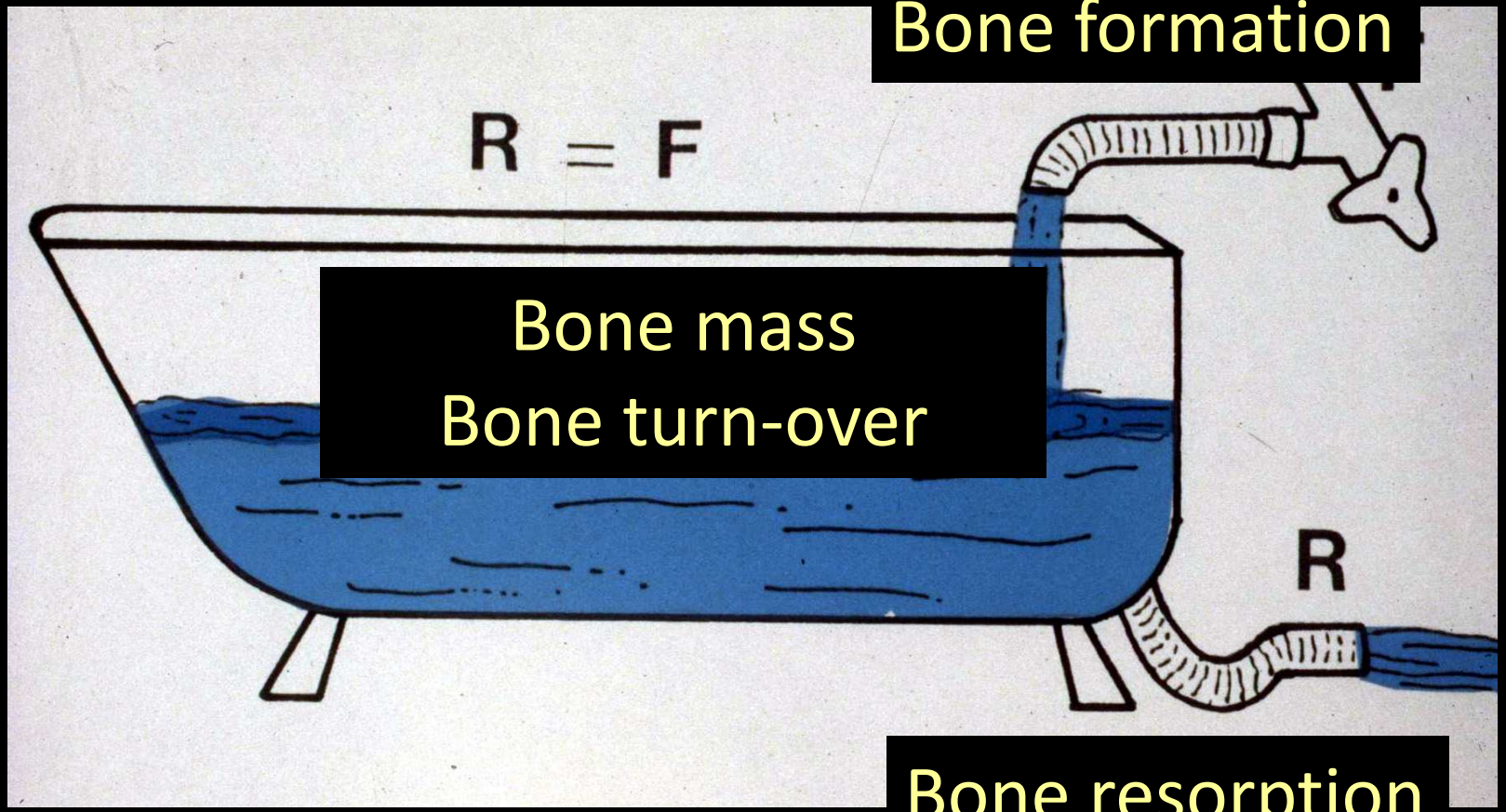
Crystalline inorganic matrix



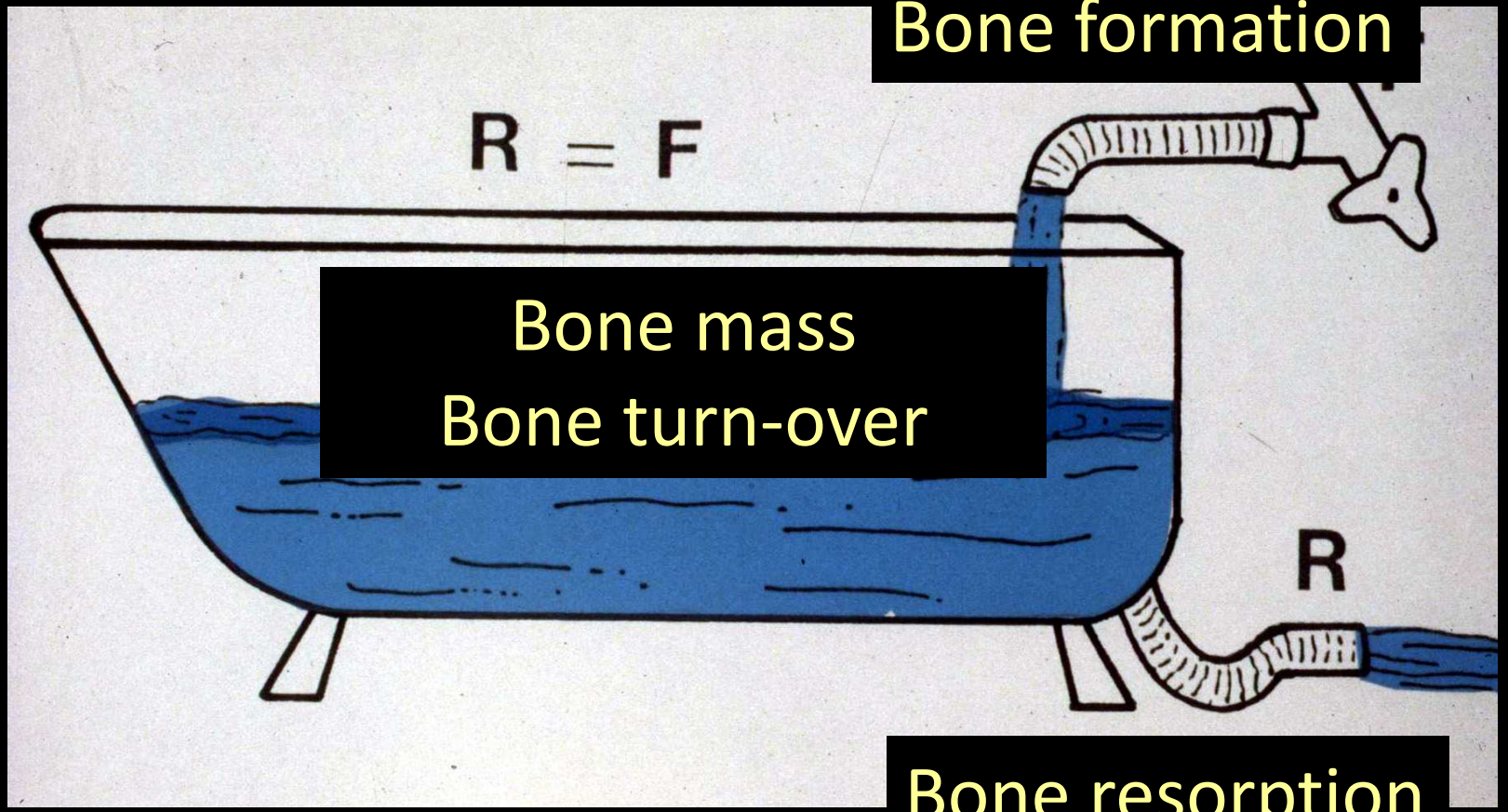
Basic multicellular unit

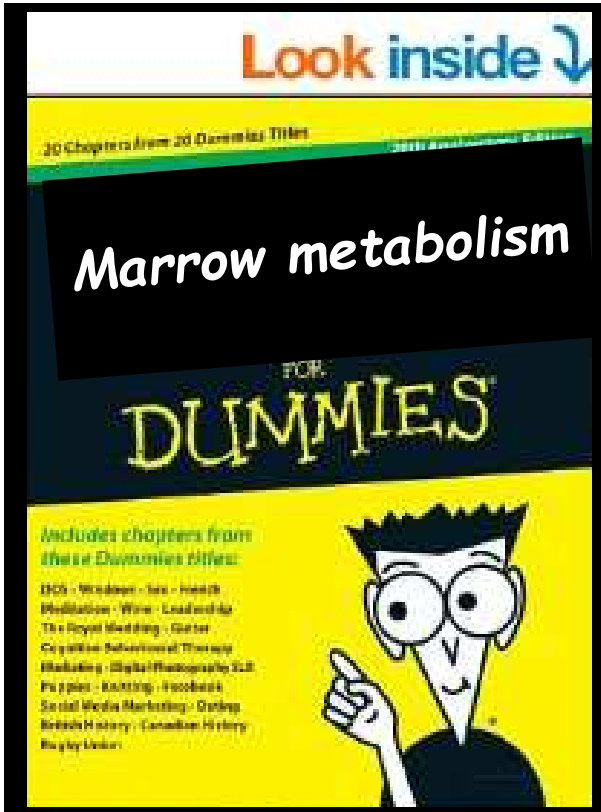
Estimated rate of bone remodeling:
5% of bone volume per year in adults
50% of bone volume per year in children

Bone mass and bone turn-over



1. During growth, bone mass increases / bone turn-over is high
2. Peak bone mass is reached by 25 and is higher in males.
3. After 40, total bone mass decreases, earlier and faster in females than in males.



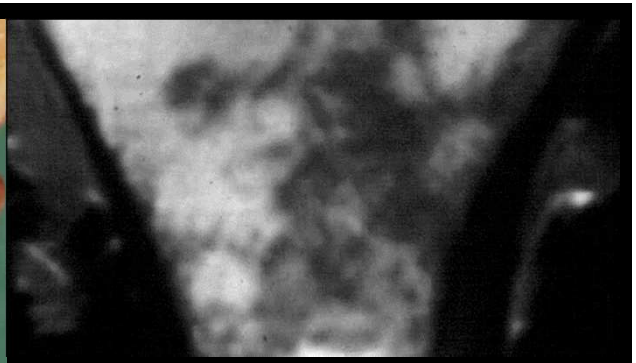


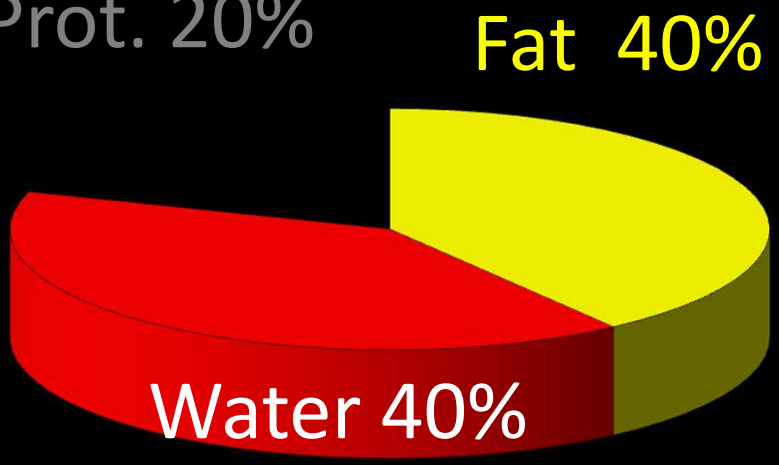
Marrow metabolism

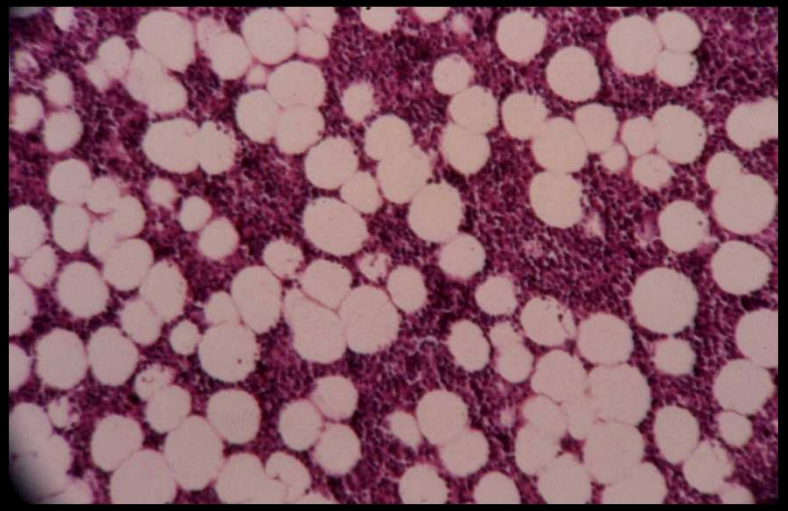
* Red marrow

* Yellow marrow

Red or hematopoietic marrow

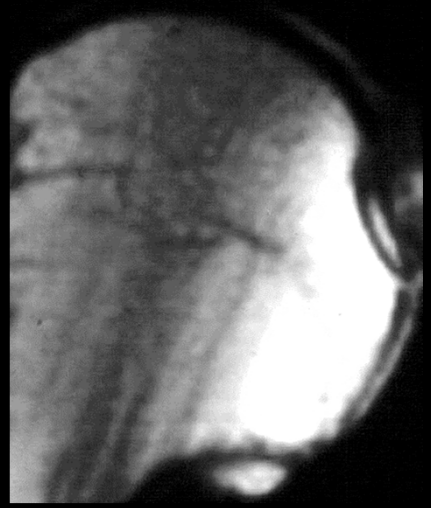




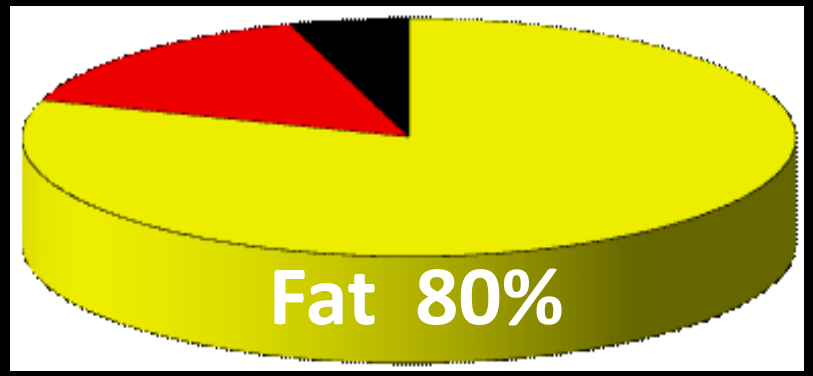


Rich network of highly permeable capillaries (sinusoids)

Yellow marrow



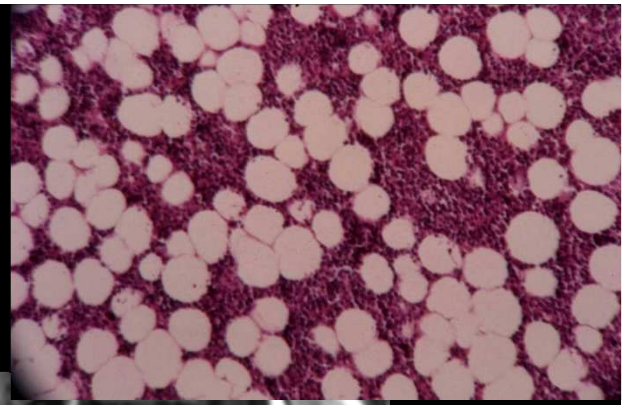
Water 15% **Prot. 5%**

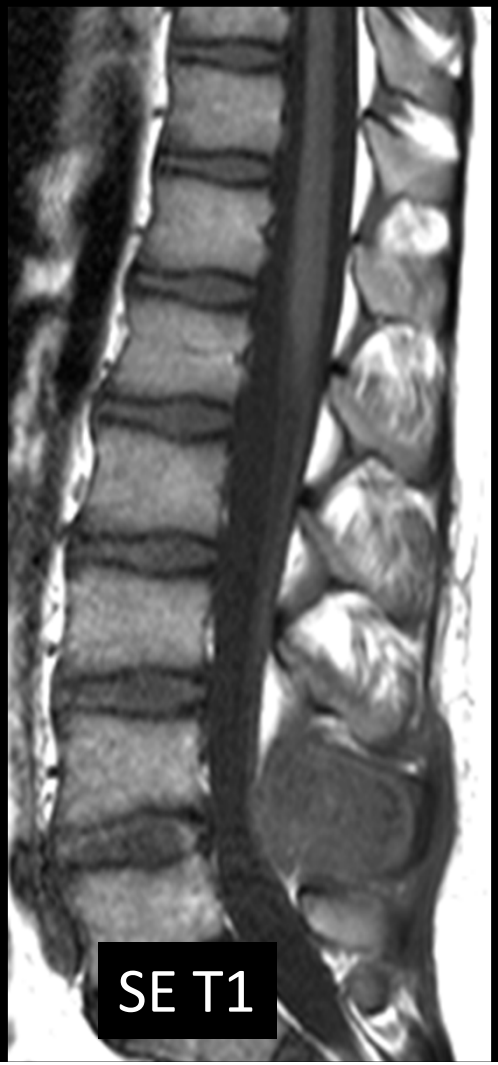


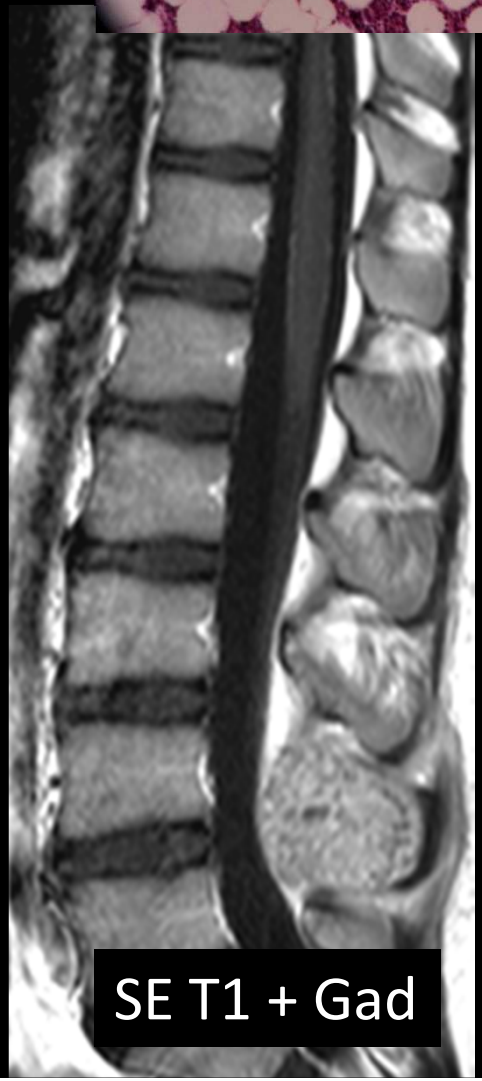
Poor network of capillaries

Red marrow of a 13-year-old boy

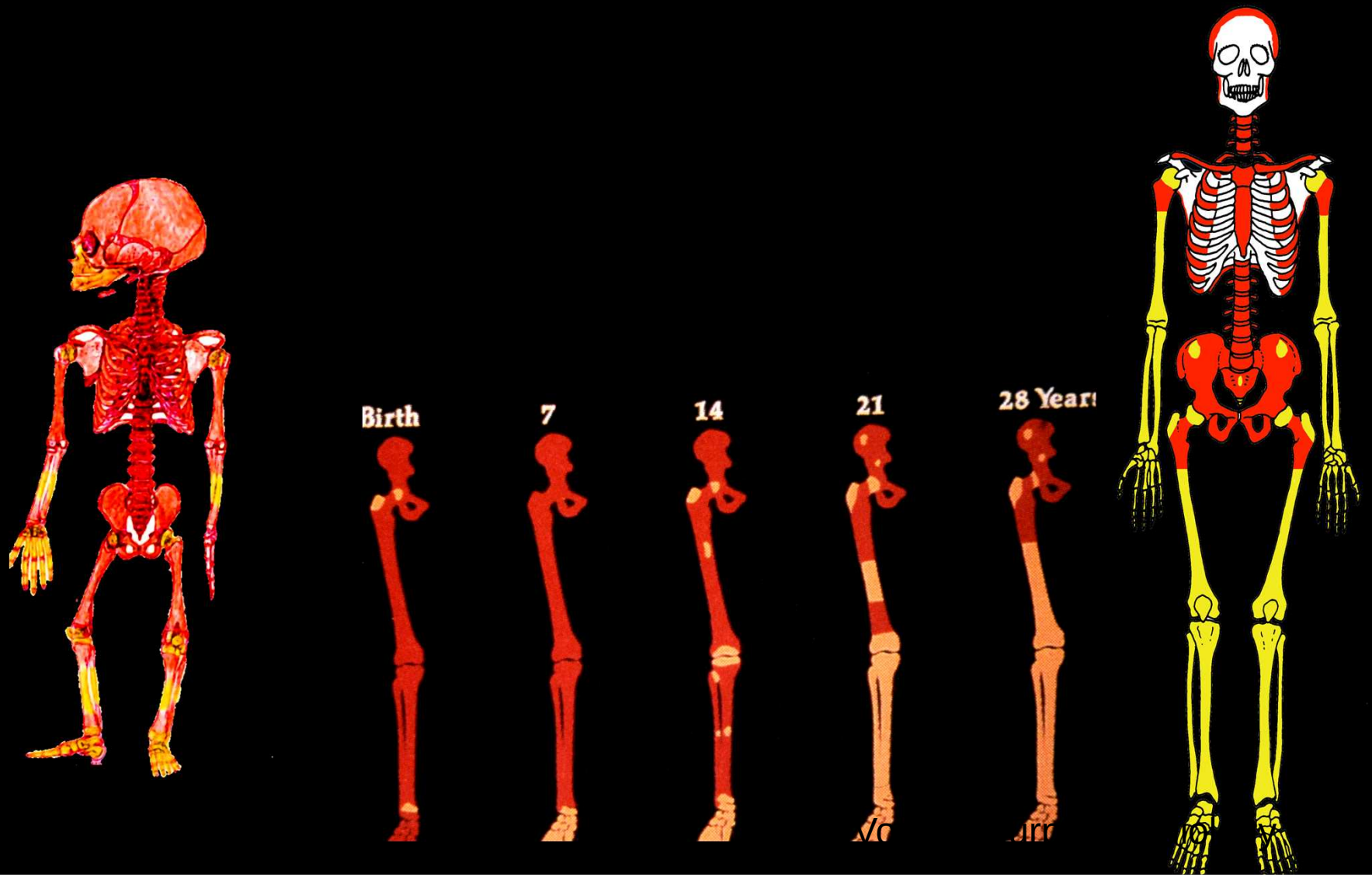
- Homogeneous signal
- Intermediate intensity on all sequences
- No or limited enhancement





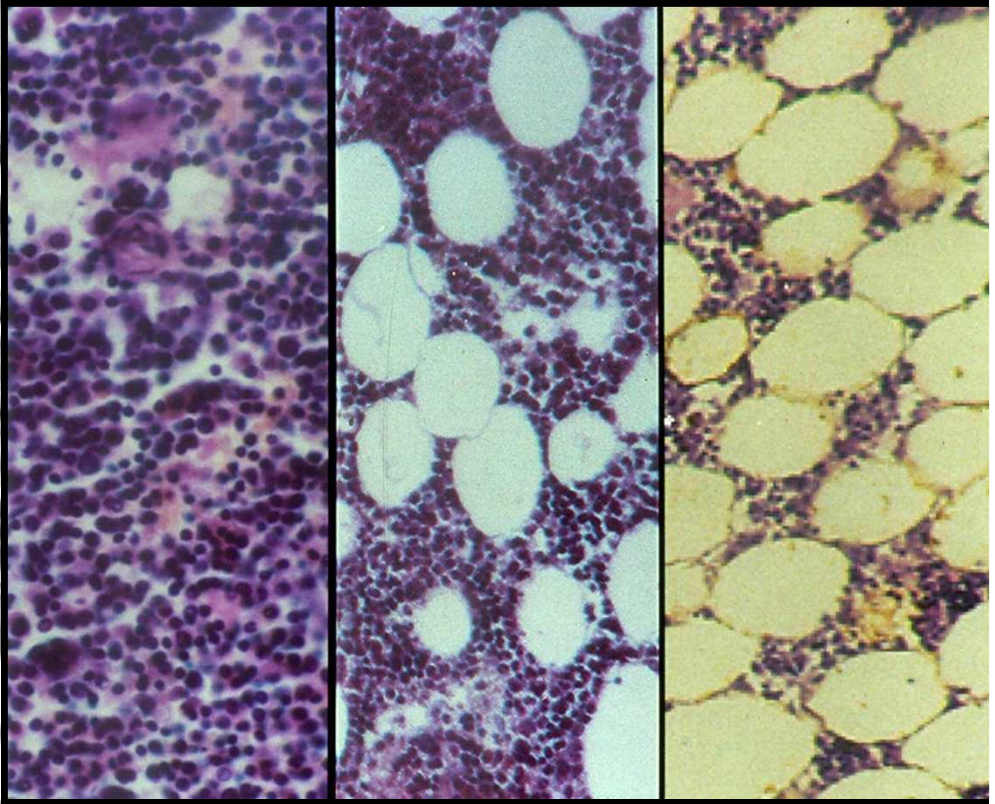


1. During growth, red marrow retracts and become less cellular.
2. Peak marrow mass is reached by 30 and is higher in females than in males.
3. After 30, marrow becomes less cellular and more heterogeneous at MRI.



Variations in marrow composition with age

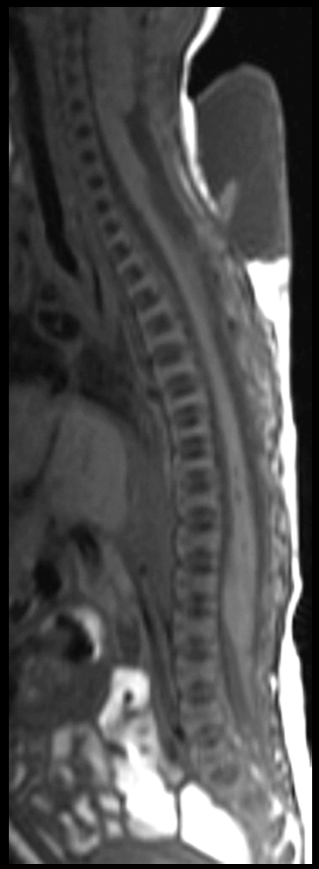
Birth 2 years 35 years

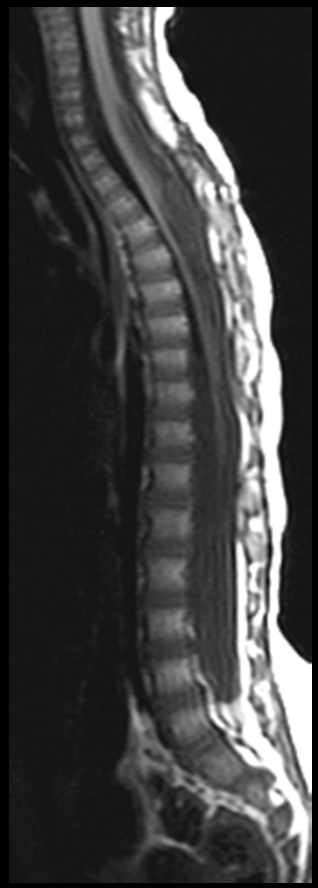


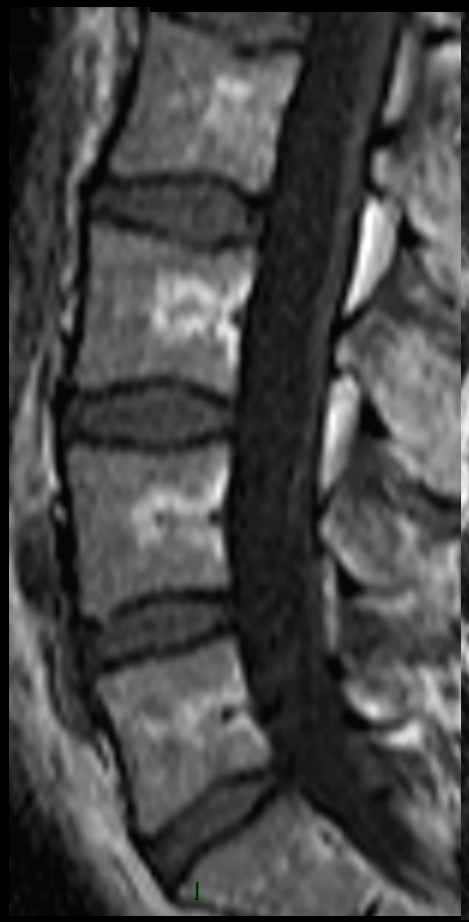
Birth 2 years 41 years

Important changes
in early life
Same patient

Limited changes
during adulthood
Same patient





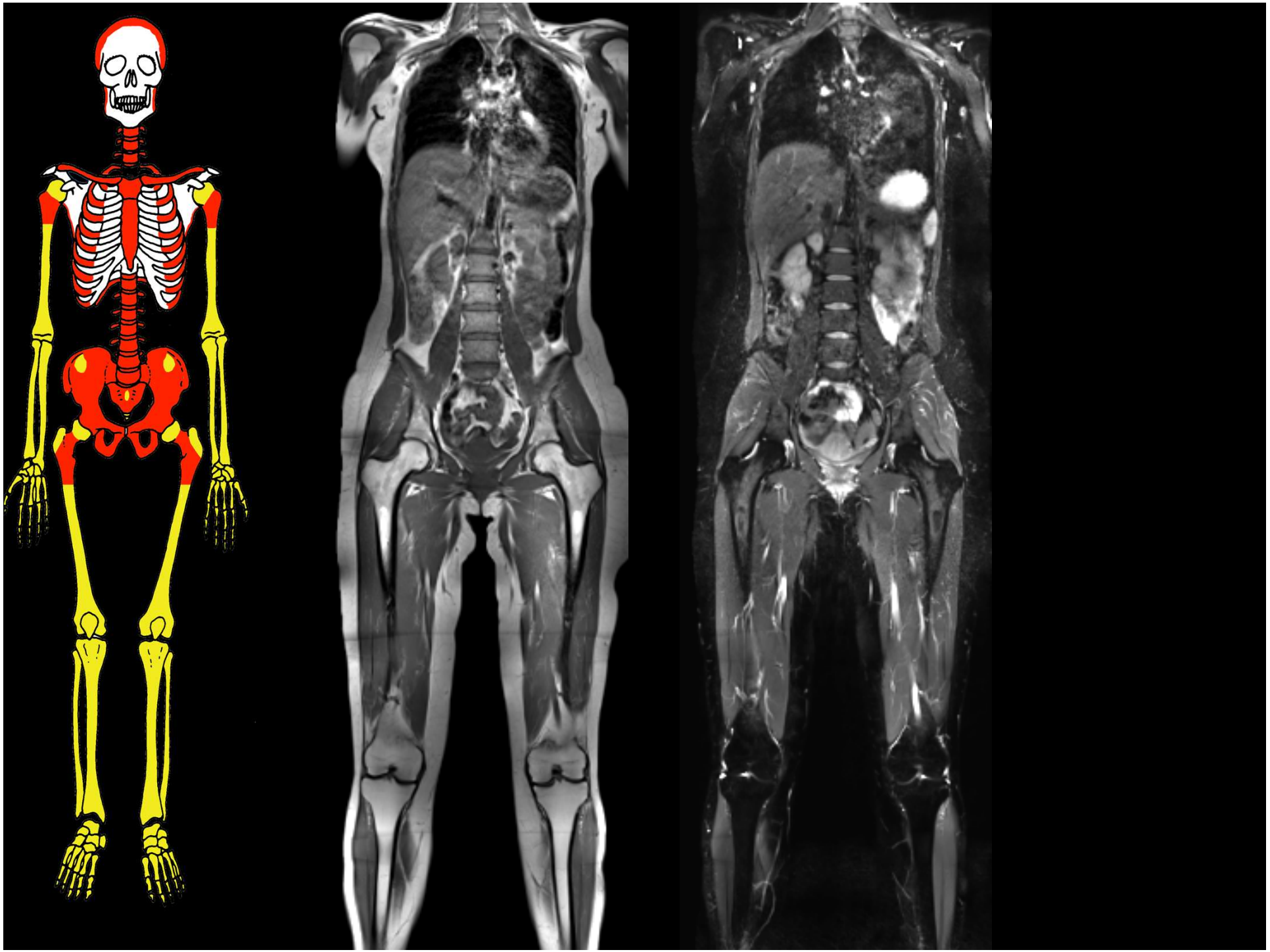


10 days

3 years of age

37 years

47 years of age



Red marrow hyperplasia

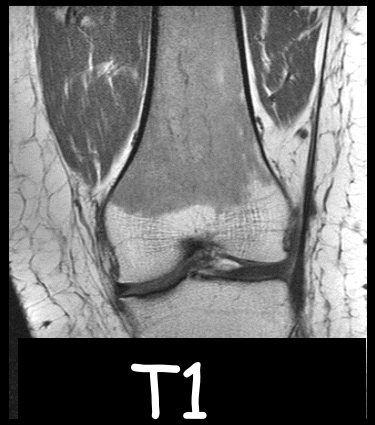
1. Borderline condition (between normal and abnormal)
2. in women between 35 and 60 years of age
3. red marrow in distal femoral metaphysis (not in epiphyses)
4. in response to mild chronic anemia (menstruations)

Normal adult marrow

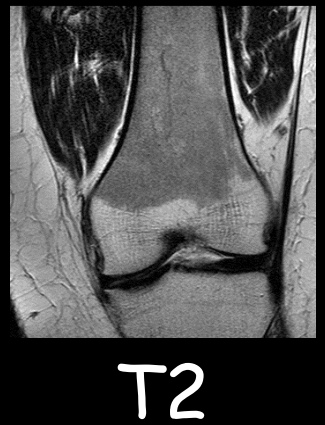
Red marrow hyperplasia

Red marrow hyperplasia

Interm. SI on on SE T1/ T2



T1



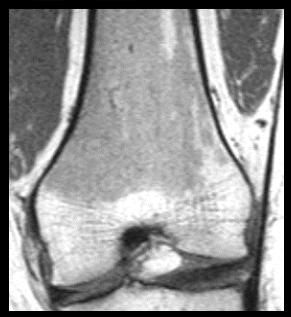
T2

Bilateral and symetrical

right

left

No change at follow-up

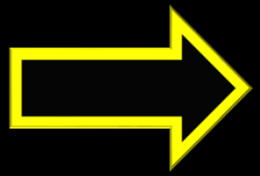


1999

2004

Metabolic, endocrine , marrow disorders

A. Normal bone and marrow metabolism



B. Overview on metabolic disorders

C. Imaging bone or marrow ?

D. Metabolic bone disorders

E. Metabolic marrow disorders

Metabolic disorders - Overview

Muscle
Sarcopenia
Drug-induced myopathies (Statins)
Necrosis (diabetus mellitus)
Fat atrophy (steroids)
…

Tendon
Hyperuricemia, Hypercholesterolemia
Calcifications
Hypervitaminosis A, Fluorosis
Quinolones and other drug-induced tendinopathies
….

Cartilage
Chondrocalcinosis
Hyperuricemia
Recurrent hemorrhage
Hemochromatosis, Ochronosis

Synovium
Amyloidosis
Hyperuricemia
Recurrent hemorrhage
….

Metabolic disorders- Overview

Bone	Marrow
Osteopenia/Osteoporosis	Hyperplasia
Rickets/Osteomalacia	Aplasia
Chr. Renal insufficiency	Hemosiderosis
Hyperparathyroidism	lipomatosis
Fluorosis, aluminium	Serous atrophy
……	…..

Metabolic disorders - Overview

Metabolic disorders
* Systemic disorders with multi-organ involvement
* Important geographical differences
* Treatable disorders / importance of prevention
* Long clinically silent phase (years)
* Diagnosis at the time of complications (except marrow)

Metabolic disorders- Overview

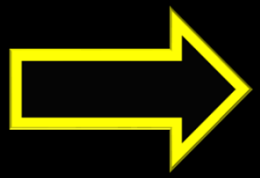
Metabolic bone disorders
Uneven involvement of trabecular or cortical bone
Fractures in bones with high cortical bone content (distal radius, fémur)
Fractures in bones with high trabecular content (vertebral body , metaphyses)

Metabolic marrow disorders
Uneven involvement of red and yellow marrow
Different complications will develop either in red (infection, necrosis) or in yellow marrow

Metabolic, endocrine , marrow disorders

A. Normal bone and marrow metabolism

B. Overview on metabolic disorders



C. Imaging bone or marrow ?

D. Metabolic bone disorders

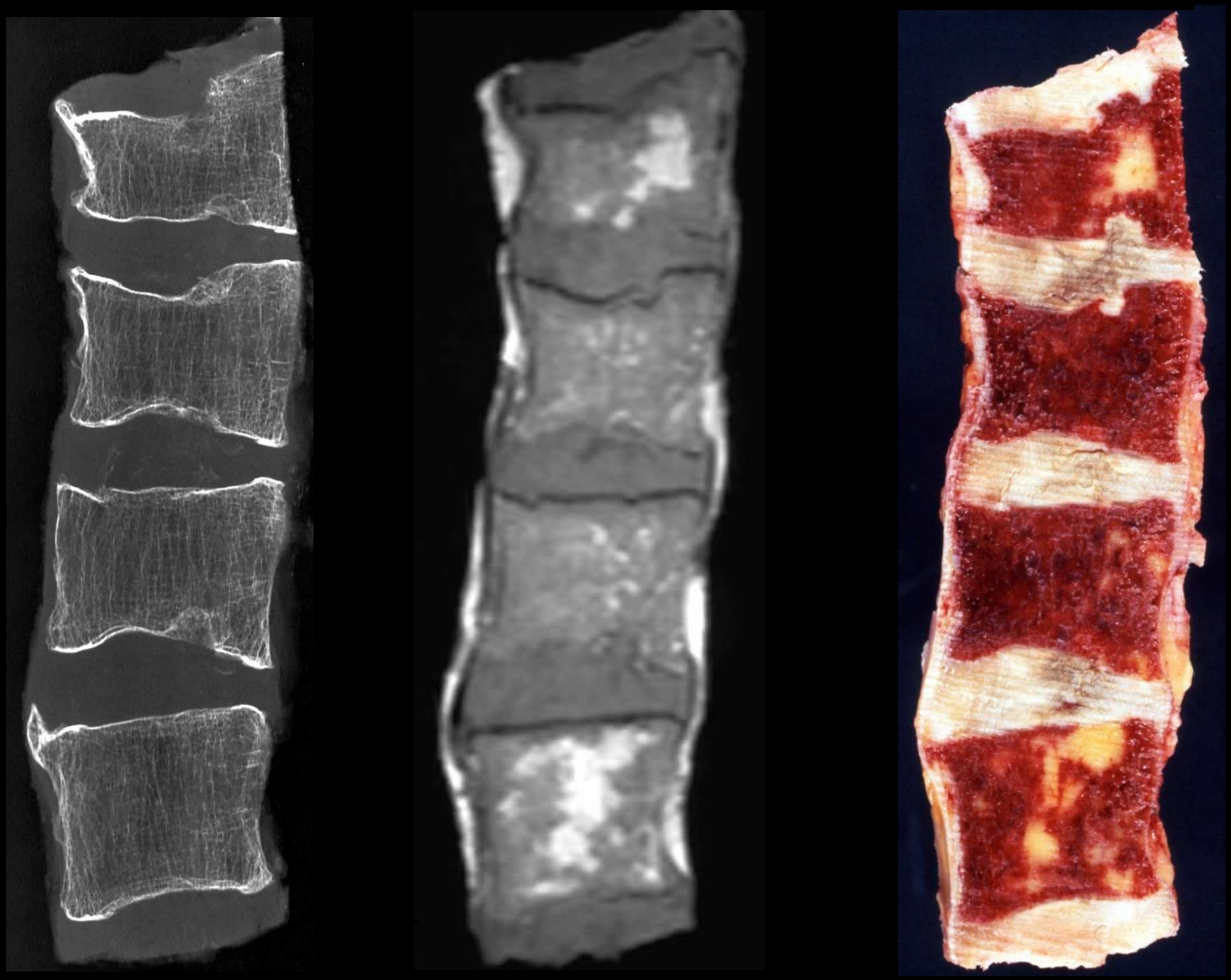
E. Metabolic marrow disorders

Imaging bone or marrow ?

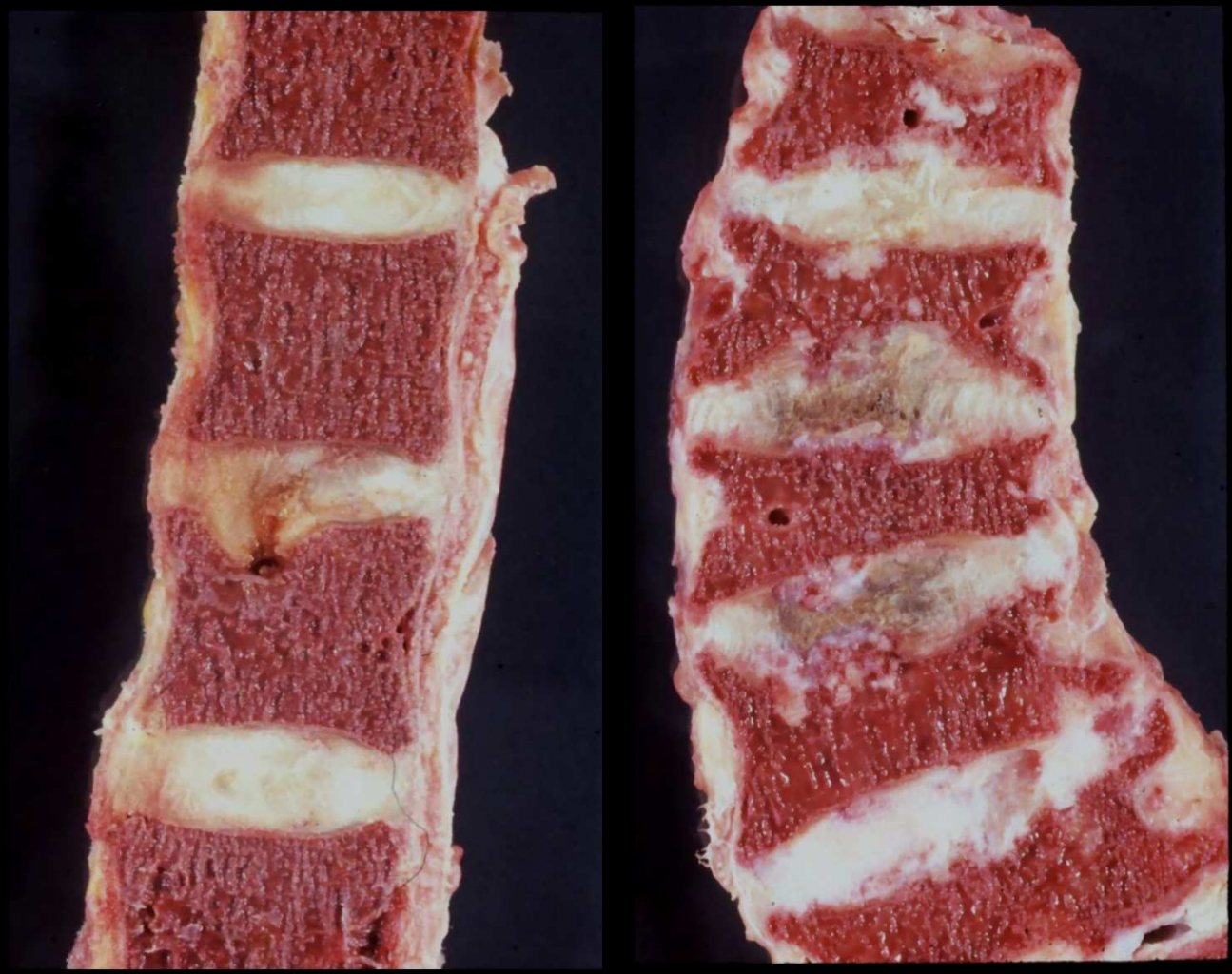
Imaging bone or marrow ?

Imaging bone or marrow ?

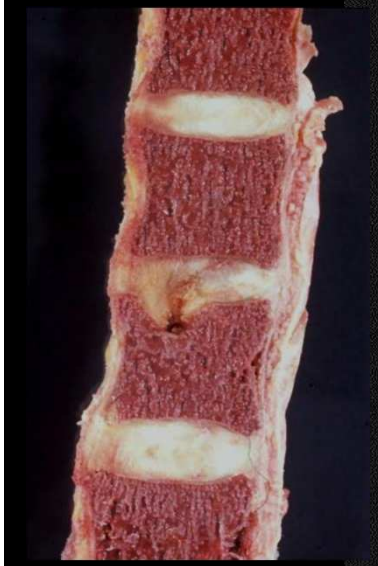
Dissociation between Bone and Marrow picture

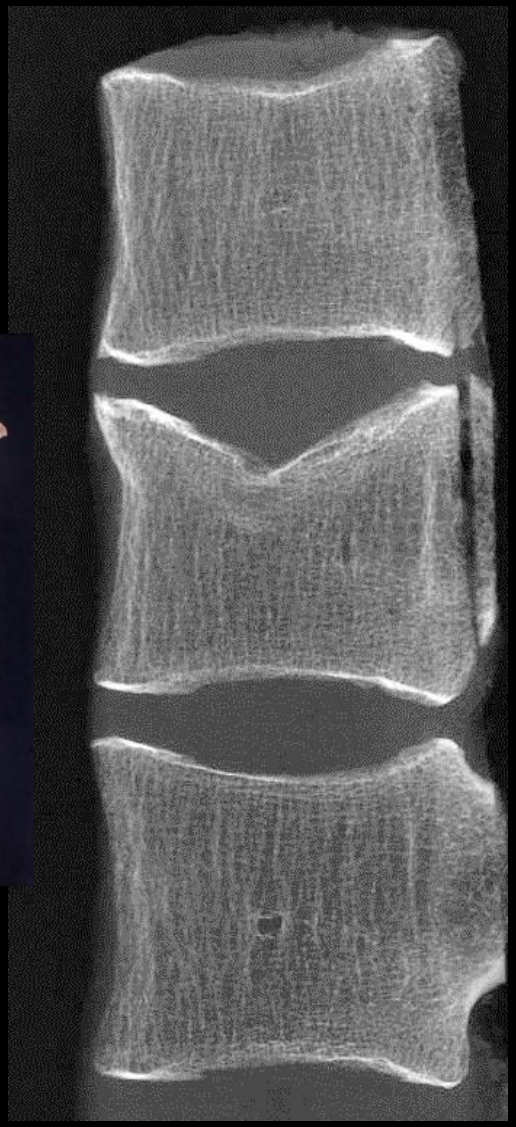


Two different patients : Marrow or bone diseases ?

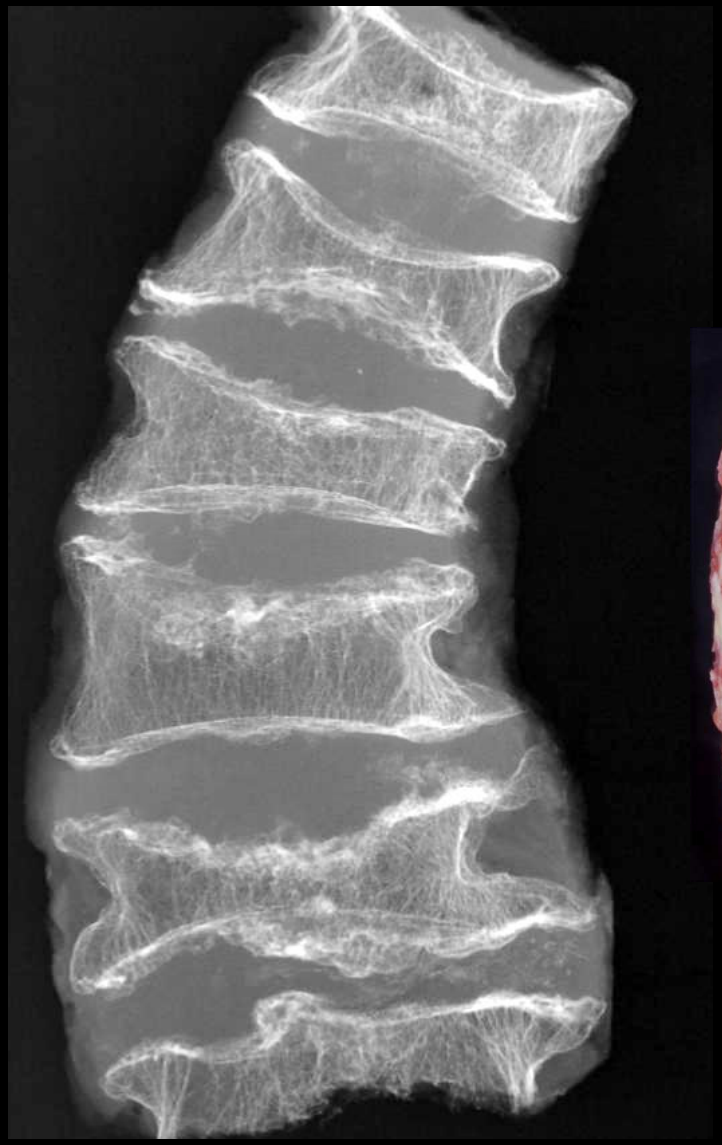


Two different patients: Marrow or Bone disease ?



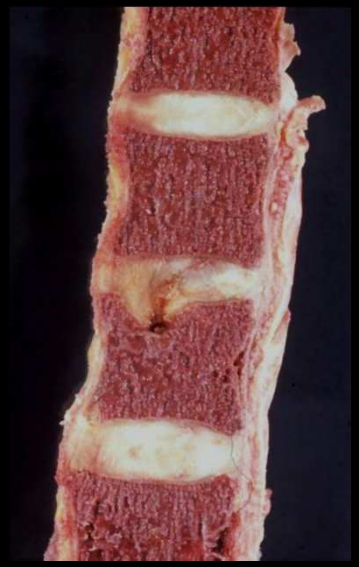


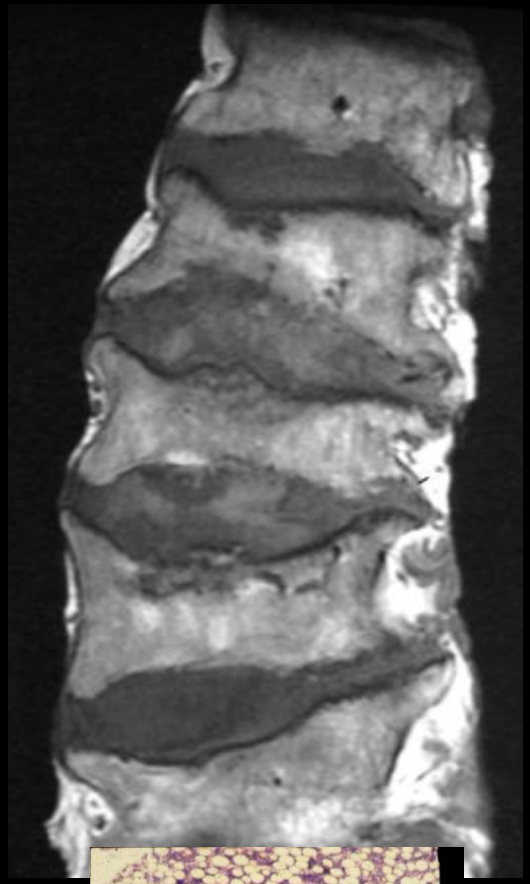
Normal bone

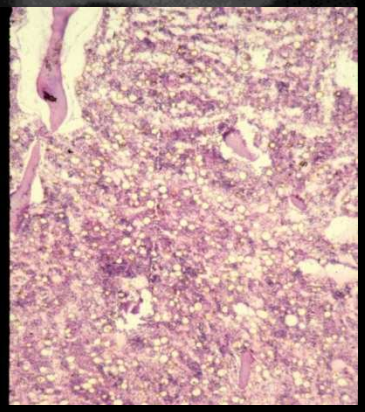


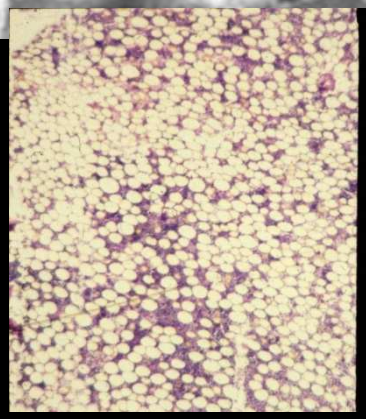
Osteoporosis

Two different patients: Marrow or Bone disease ?









Abnormal marrow Normal marrow

MR imaging
of marrow diseases

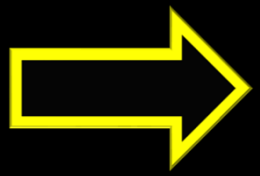
X-ray / CT imaging
of bone diseases

Metabolic, endocrine , marrow disorders

A. Normal bone and marrow metabolism

B. Overview on metabolic disorders

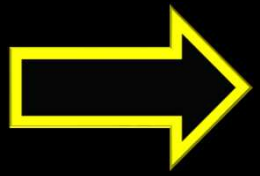
C. Imaging bone or marrow ?



D. Metabolic bone disorders

E. Metabolic marrow disorders

Metabolic bone disorders



Bone
Osteopenia/Osteoporosis
Rickets/Osteomalacia
Chr. Renal insufficiency
Hyperparathyroidism
Fluorosis, aluminium
……

Cortical thinning
Bone structure normal

Osteopenia

Mainly a quantitative bone disorder

Osteoporosis

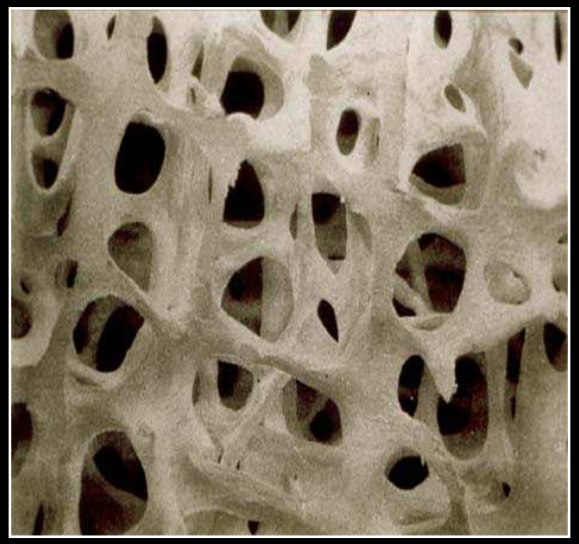
A disease characterized by

low bone mass

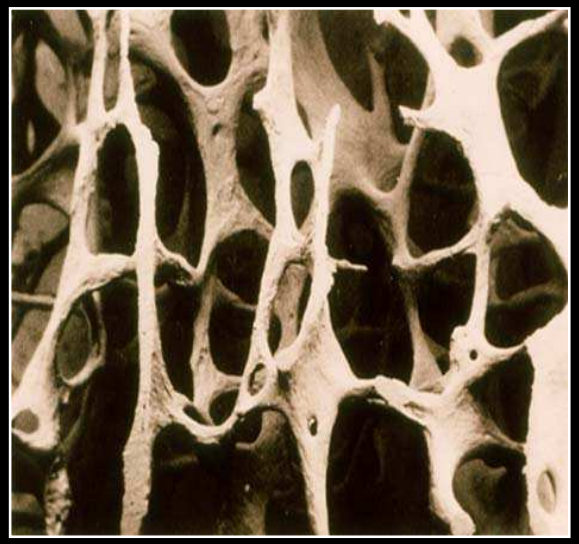
microarchitectural deterioration of bone tissue

leading to enhanced bone fragility and a consequent increase in fracture risk.

World Health Organization (WHO), 1994



Normal bone



Osteoporosis

Osteoporosis

Diagnosis is based on mineral bone density measured
by Dual Energy X-ray Absorptiometry (DXA – spine, fem.neck)

Osteopenia : T score –1 and –2.5
Osteoporosis: T score < -2.5
Established osteoporosis if fracture

Clinical tool for
evaluation of fracture risk
« FRAX » (combines MBD and risk factors)

Disorders associated with osteoporosis

I Primary osteoporosis
- Involutional osteoporosis
  - Postmenopausal
  - Senile
- Juvenile osteoporosis

II Secondary osteoporosis
- Endocrine (hypogonadism, cushing's disease..)
- Marrow disease (multiple myeloma, thalassemia…)
- Iatrogenic (steroids, heparin..)
- Chronic disease (renal or hepatic insufficiency..)
- Deficiency states (vit D, malnutrition,..)
- Inborn erros of bone metabolism (osteogenesis imperf.,…)
- ……..

	1ary osteoporosis*		
	Post-menop. Type I	Senile Type II	2ary osteop.
Age	55-70	75- 90	any
Sex ratio (F:M)	8:1	2:1	1:1
Fracture site	spine wrist	spine hip long b.	spine hip long b.
Bone loss			
Trabecular	+++	++	+++
Cortical	+	+++	+++

* Juvenile or adult-onset osteoporosis excluded

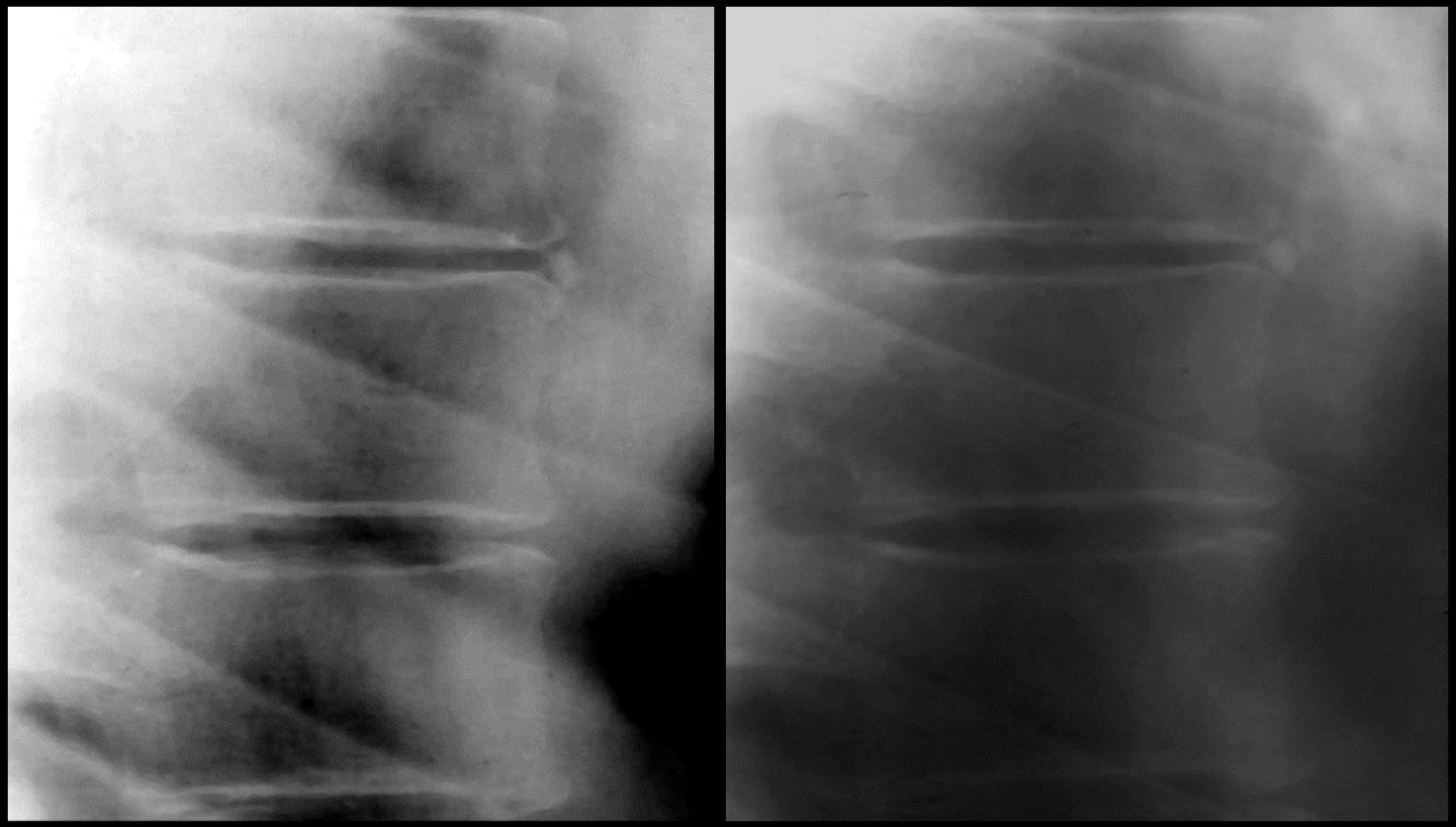
Primary osteoporosis (metabolic bone disorder)

Axial and peripheral skeleton
variable involvement of cortical and trabecular bone
normal bone marrow

How to measure OP ?

- increased radiolucency
- cortical thinning
- trabecular bone resorption
- fracture - deformation

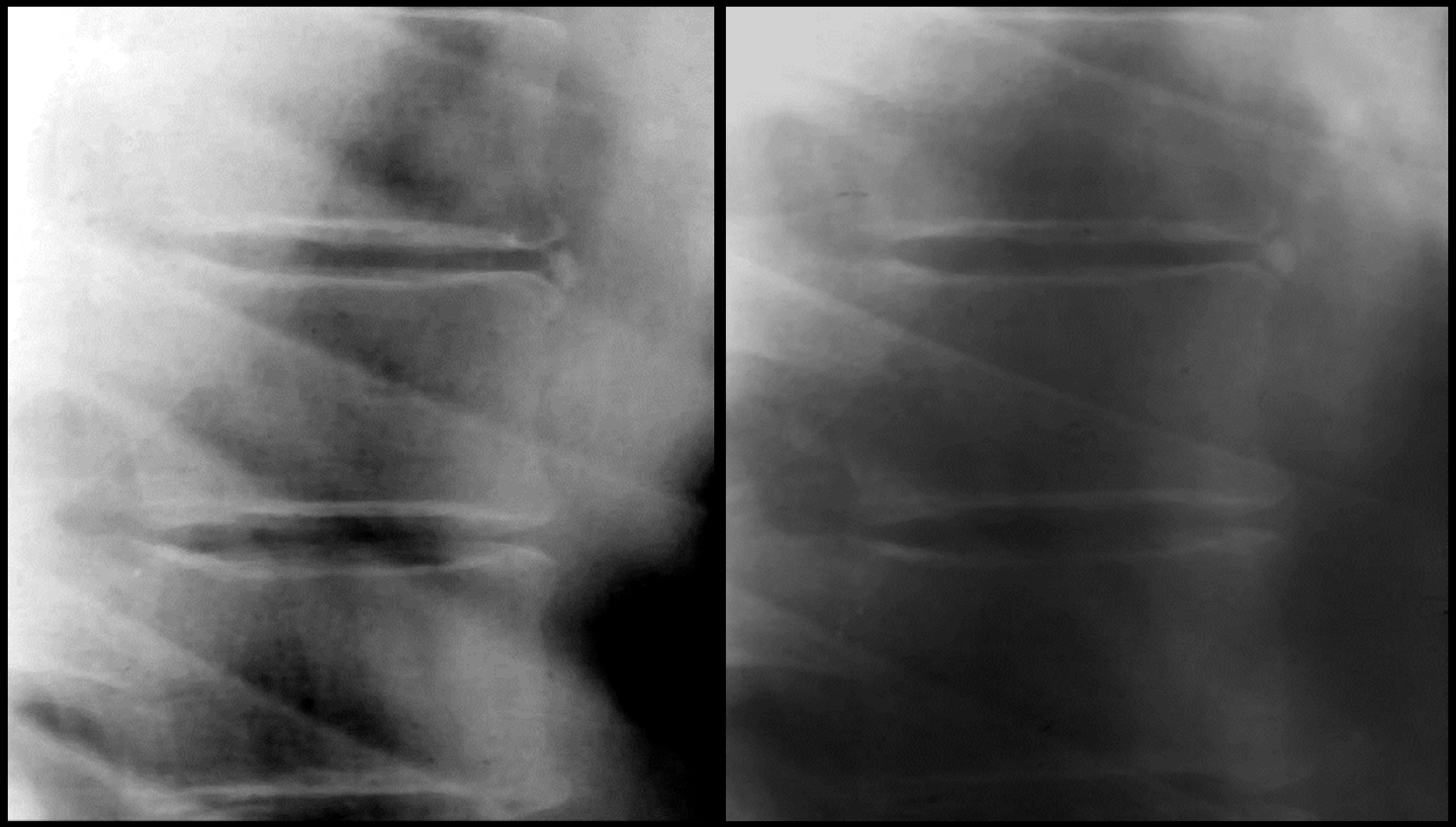
?Increased radiolucency ?



« International osteoporosis foundation »; slide kit

! Increased radiolucency is not a reliable sign !

Two different expositions

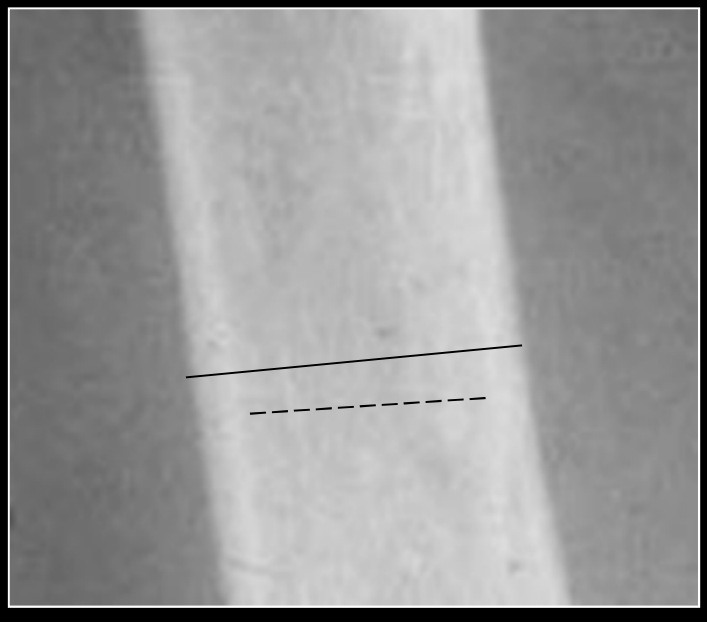


« International osteoporosis foundation »; slide kit

Radiogrammetry – combined cortical thickness

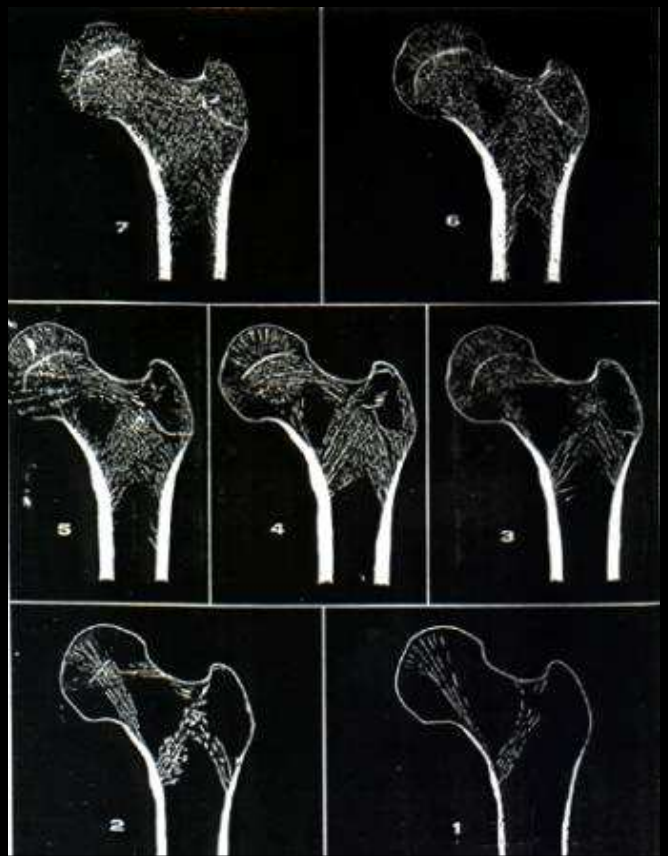
- ~~increased radiolucency~~
- cortical thinning
- trabecular bone resorption
- fracture - deformation

Male: > or = 5 mm
Female: > or = 4 mm

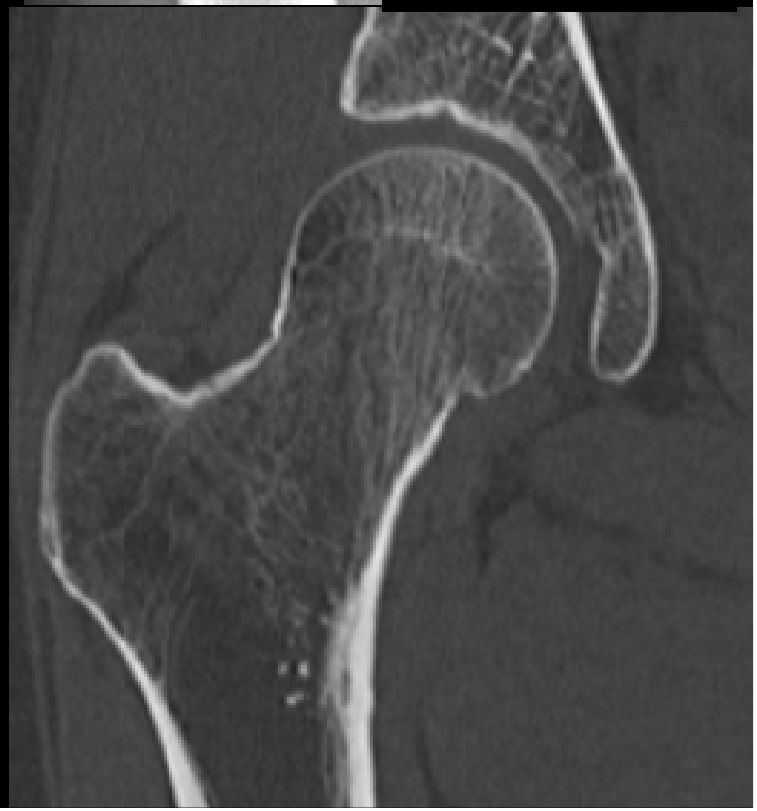


Singh index

- trabecular bone resorption

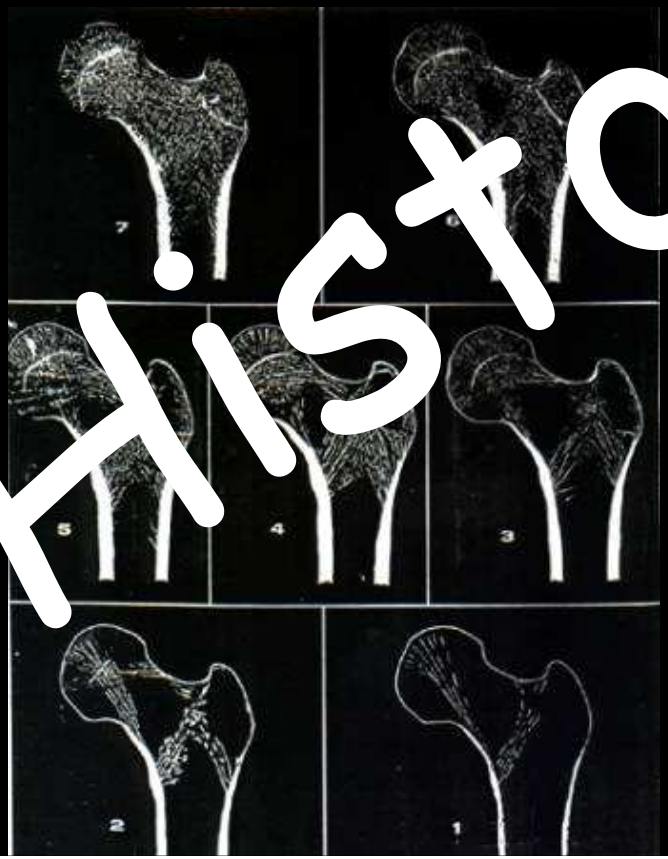


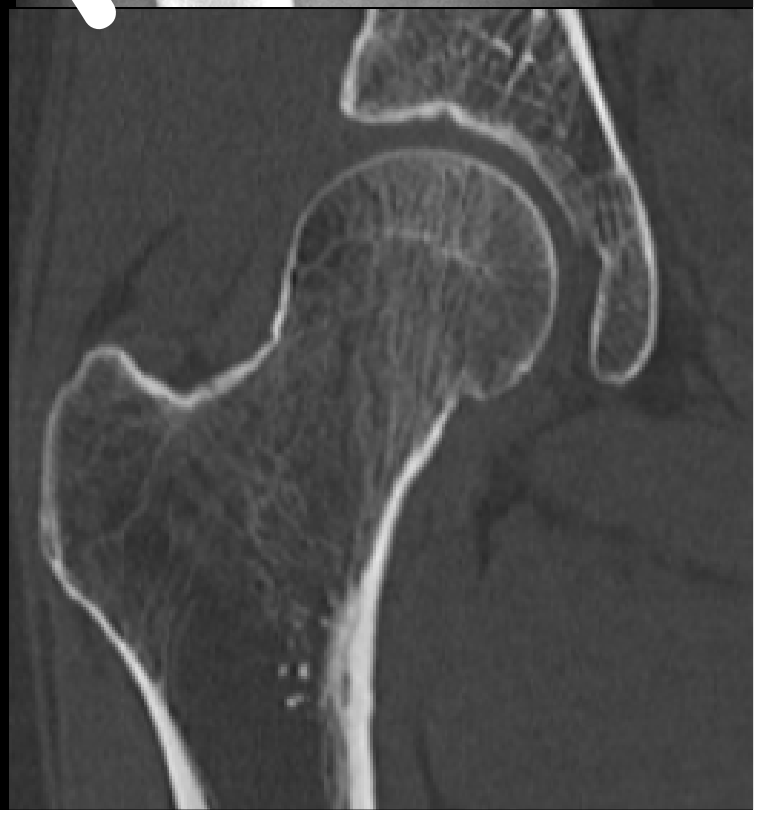
35-yo woman
Osteopenia ??



Singh index

- ~~trabecular bone resorpti~~on





Historical

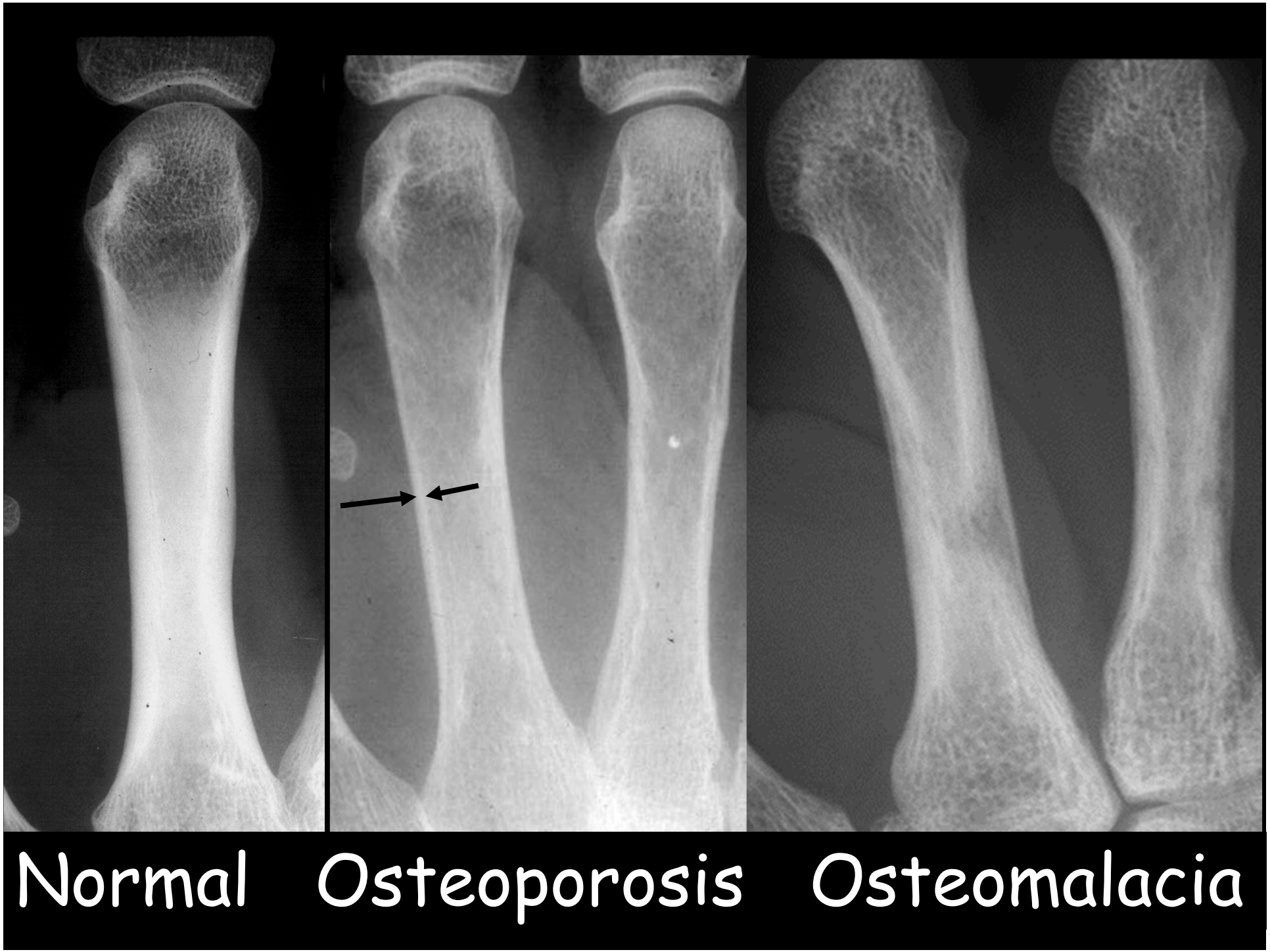
Radiology. 2014 Jul;272(1):184-91. doi: 10.1148/radiol.14131390. Epub 2014 Mar 9.

Assessment of risk of femoral neck fracture with radiographic texture parameters: a retrospective study.

Thevenot J(1), Hirvasniemi J, Pulkkinen P, Määttä M, Korpelainen R, Saarakkala S, Jämsä T.

Author information:
(1)From the Department of Medical Technology (J.T., J.H., P.P., M.M., R.K., S.S., T.J.) and Institute of Health Sciences (R.K.), University of Oulu, PO Box 5000, Oulu 90014, Finland; Department of Sports and Exercise Medicine, Oulu Deaconess
Institute, Oulu, Finland (R.K.); Institute of Health Sciences (R.K.) and Department of Diagnostic Radiology (S.S., T.J.), Medical Research Center Oulu, Oulu University Hospital and University of Oulu (J.T., J.H., P.P., M.M., R.K., S.S., T.J.).

PURPOSE: To investigate whether femoral neck fracture can be predicted retrospectively on the basis of clinical radiographs by using the combined analysis of bone geometry, textural analysis of trabecular bone, and bone mineral


Normal
Osteoporosis
Osteomalacia

Osteomalacia

A qualitative disorder of bone

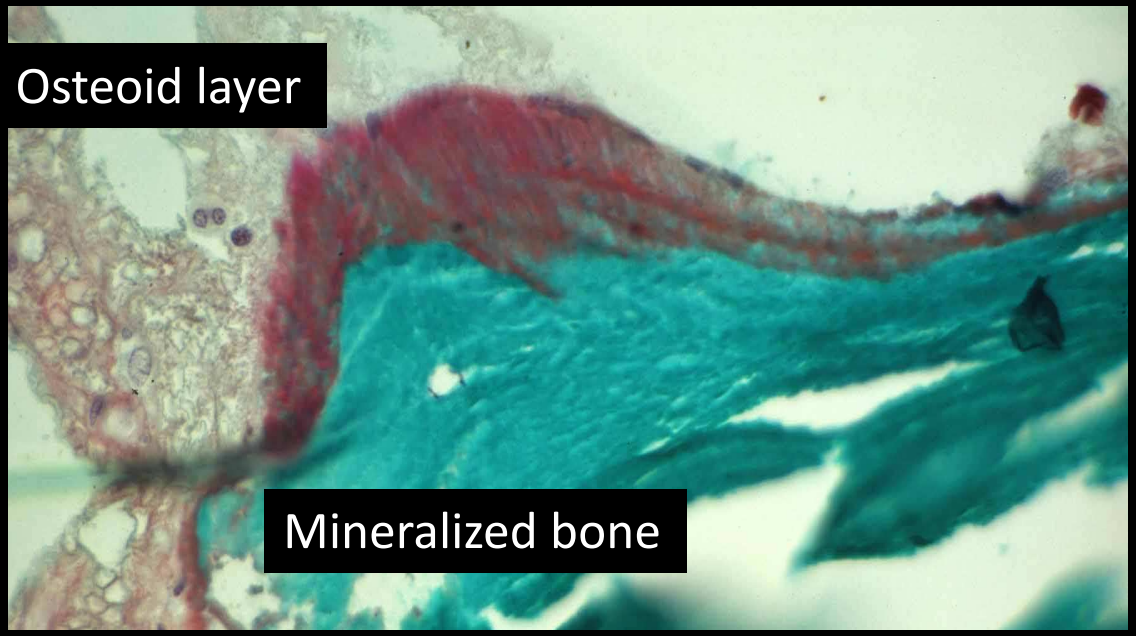
characterized by deficient

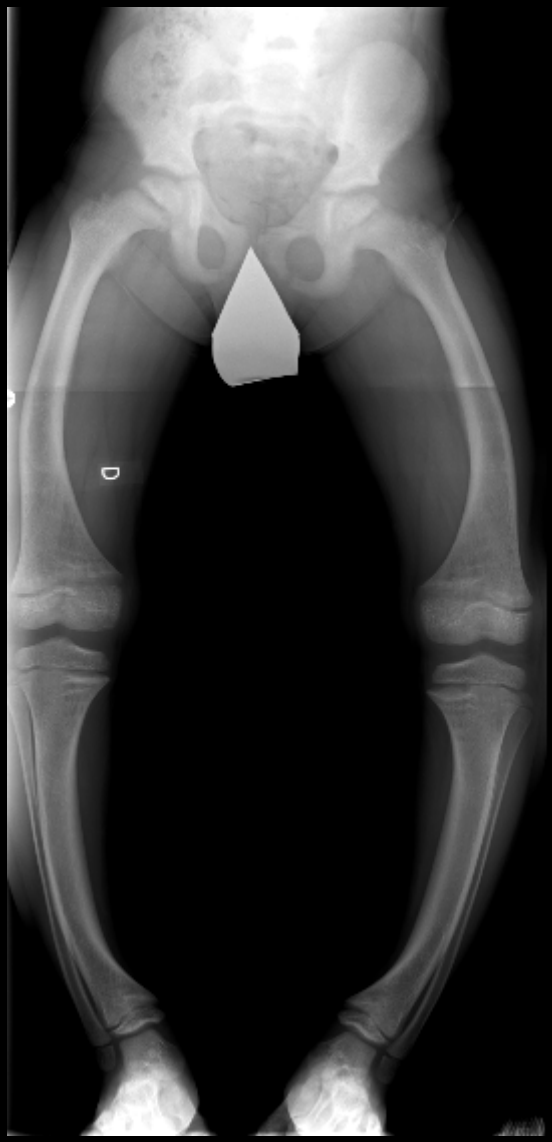
(absent or delayed)

mineralization of the bone matrix.

Osteomalacia - Softened bone

Histology
Increased thickness
of non mineralized
osteoid substance

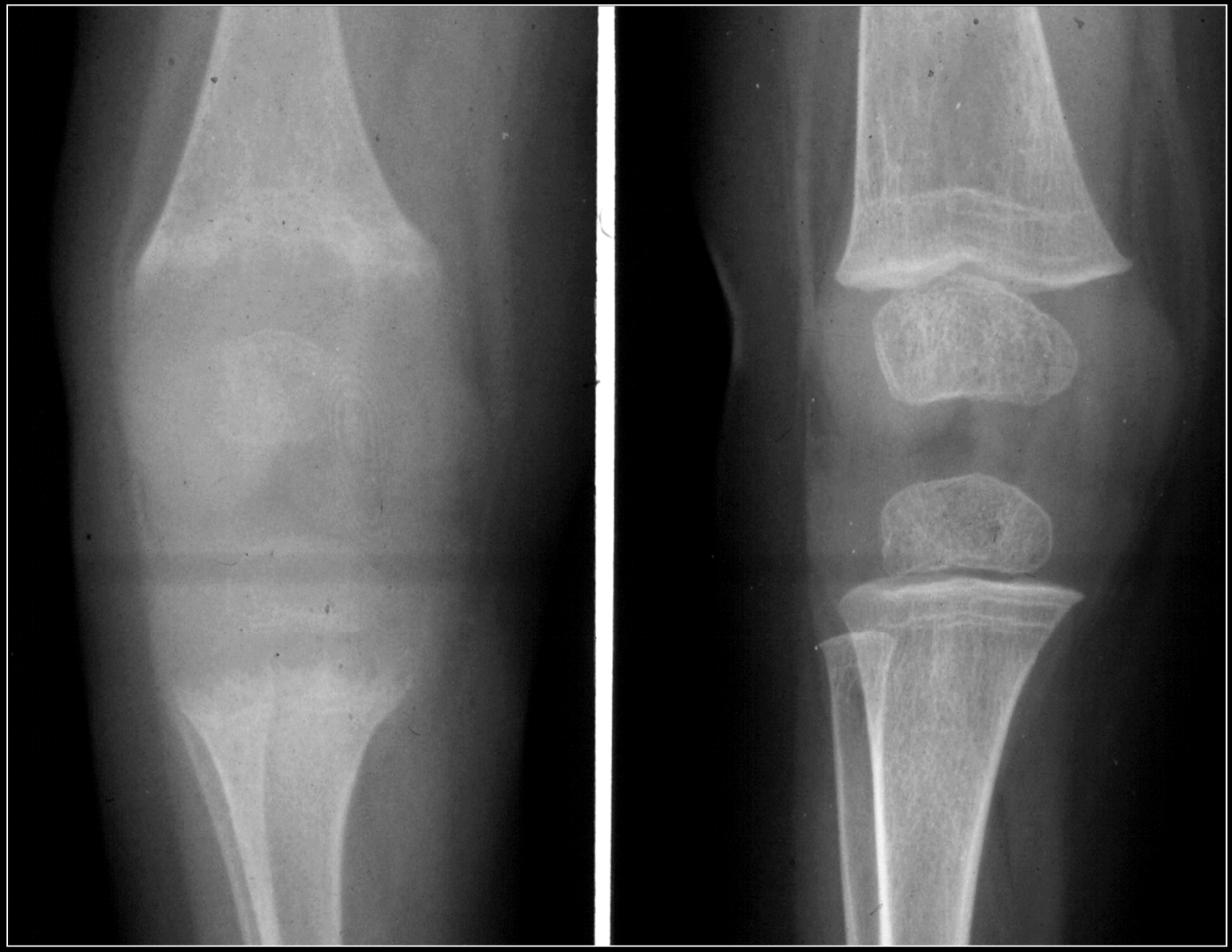




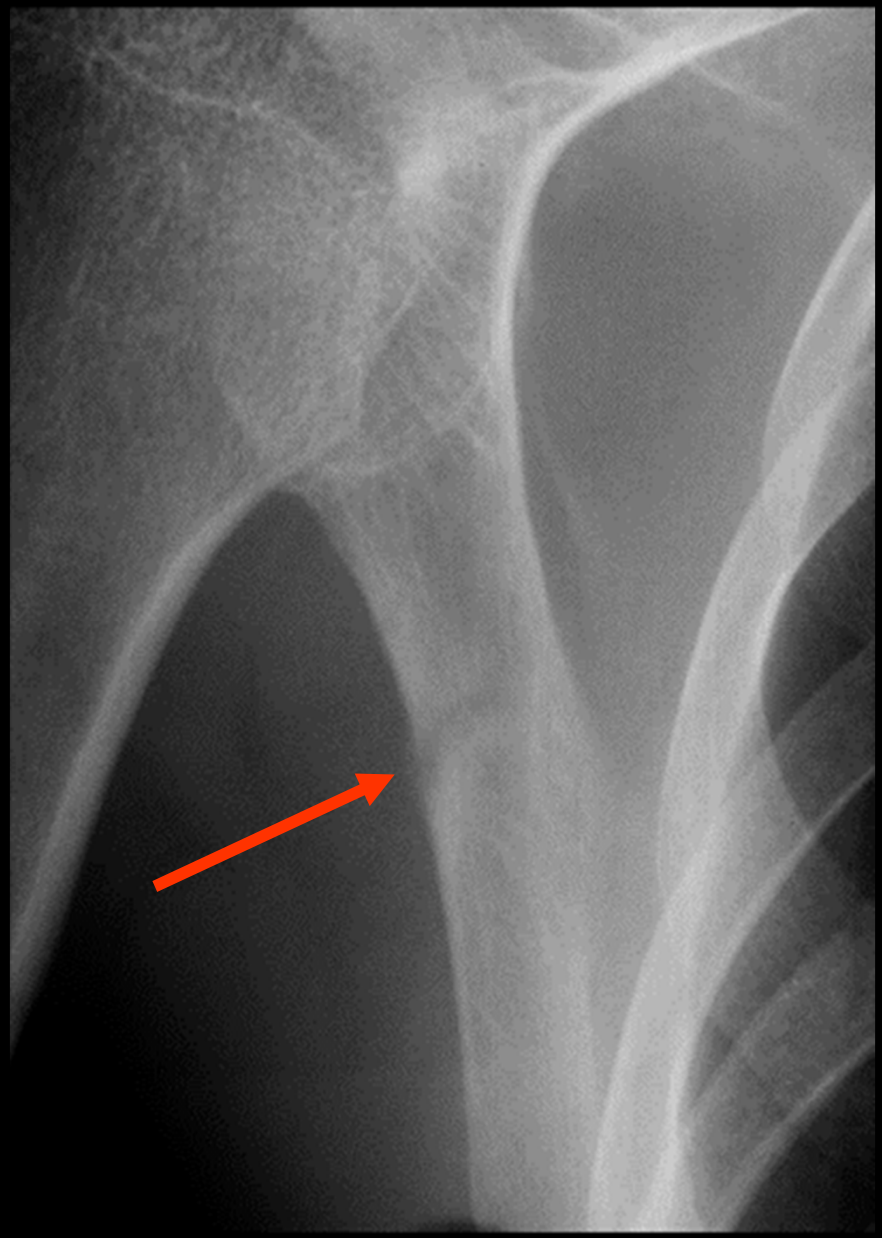
Rickets

Disease characterized by impaired bone mineralization with accumulation of uncalcified bone matrix (osteoid).

- Bone deformity
- Coarse trabecular pattern
- growth plate alteration



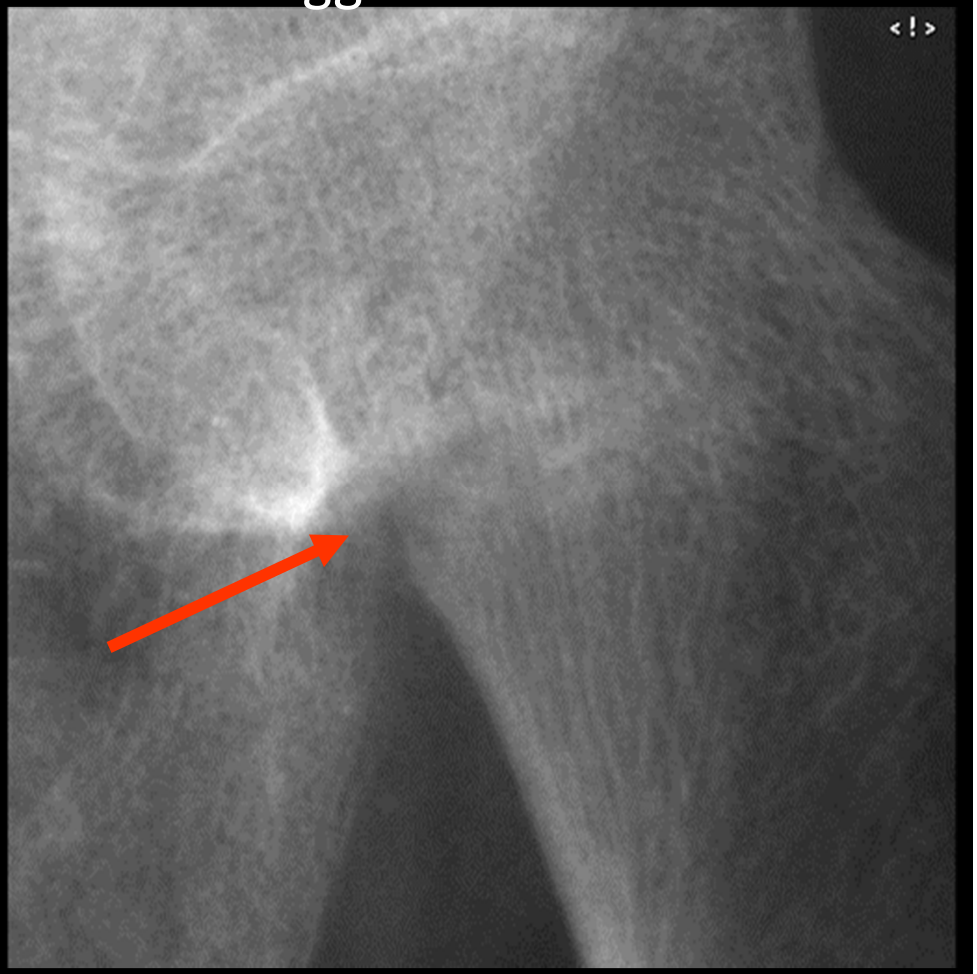
Before and after treatment of rickets



Loozer’s zone

Cortical fractures

Suggestive areas

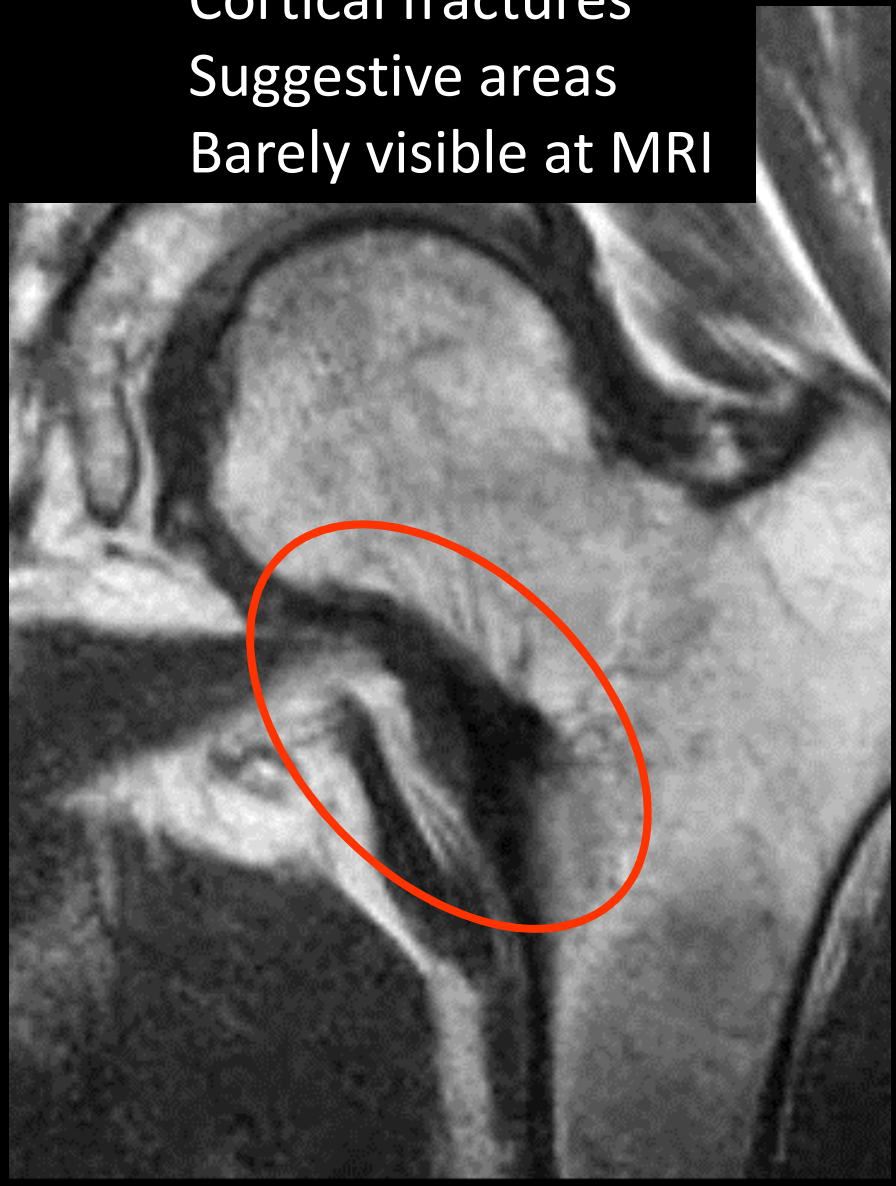


Loozer's zone

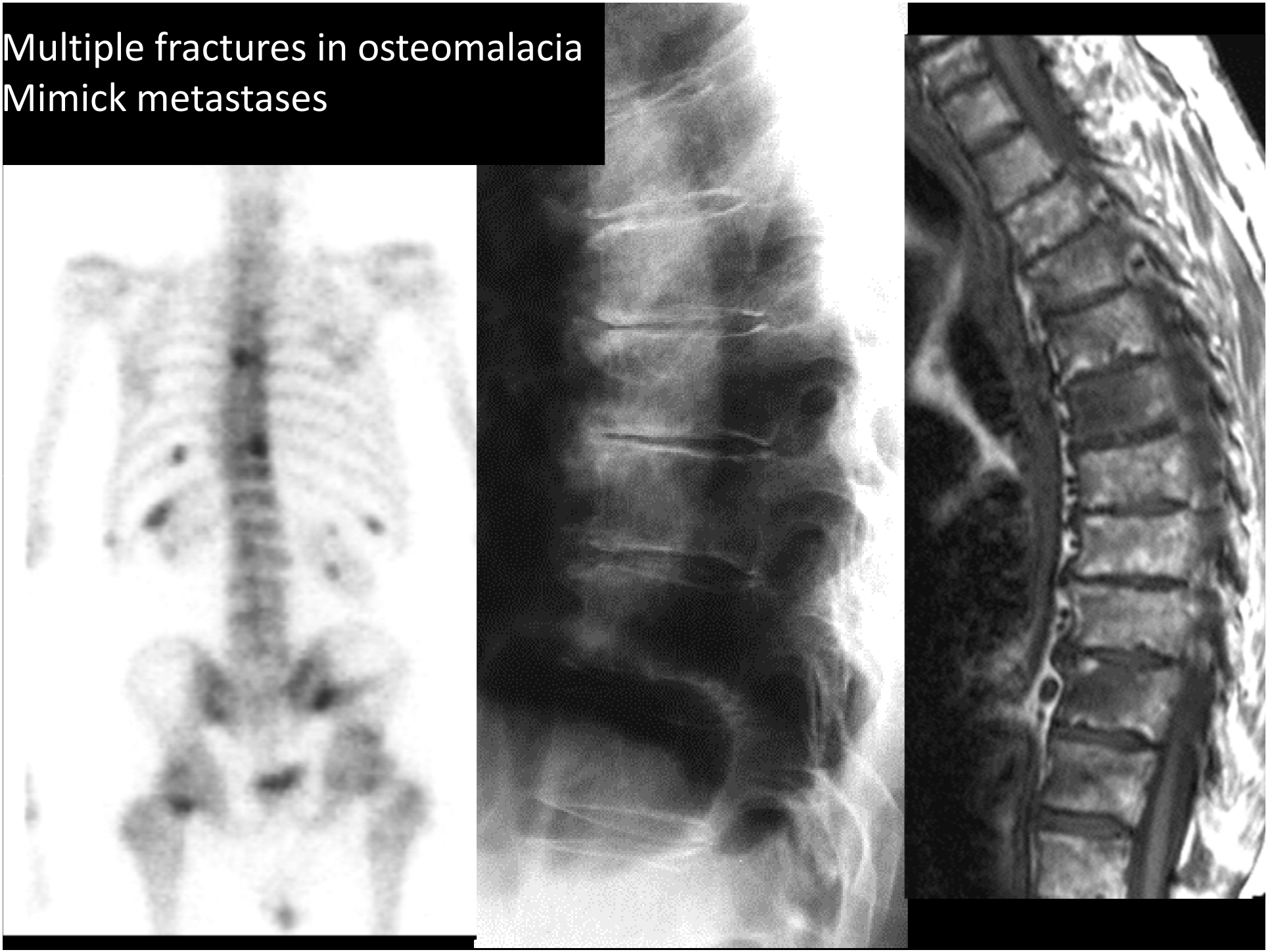
Cortical fractures

Suggestive areas

Barely visible at MRI

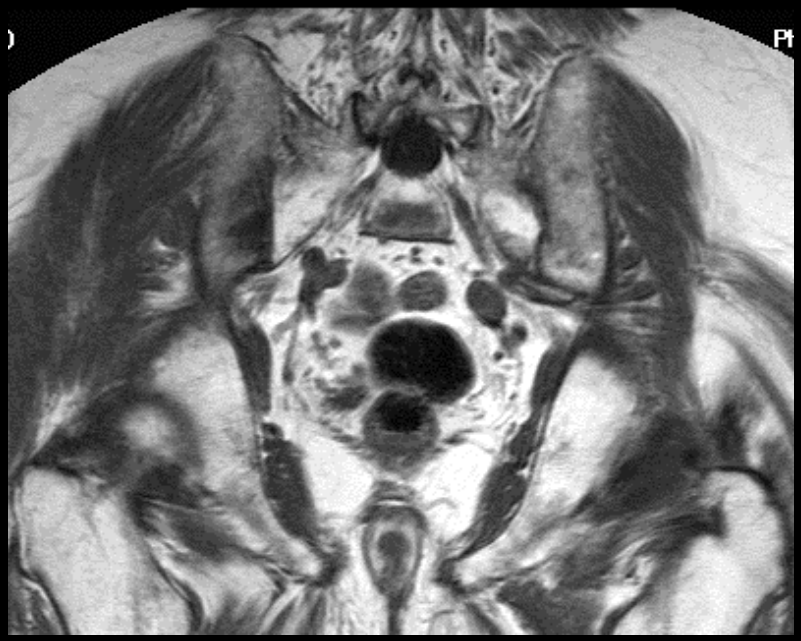


Multiple fractures in osteomalacia
Mimick metastases



MRI features suggestive of osteomalacia

1. Multiple cortical or marrow lesions
2. Imaging features suggestive of fractures
3. Fractures at variable stage of the healing process



Hyperparathyroidism

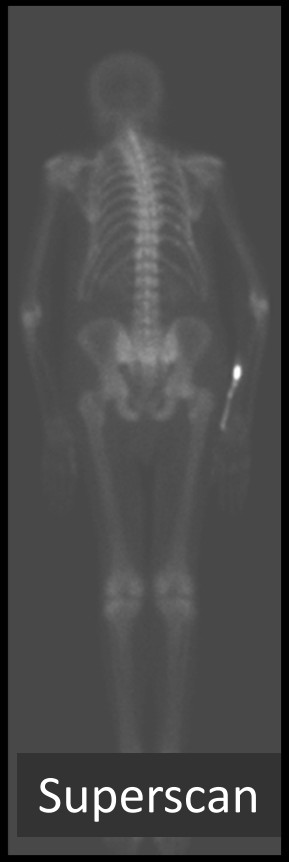
Disease characterized by increased level of bone resorption (osteoclast) due to overproduction of PTH.

Primary or secondary
Increased bone resorption

Different patients
Normal hyper PTH

Same patient
Before after treatment

Renal osteodystrophy



Superscan

Osteoporosis
High bone turn-over

Destructive
arthropathy

Bone deformity (osteomalacia)
Rugger jersey spine

Soft tissue
calcifications

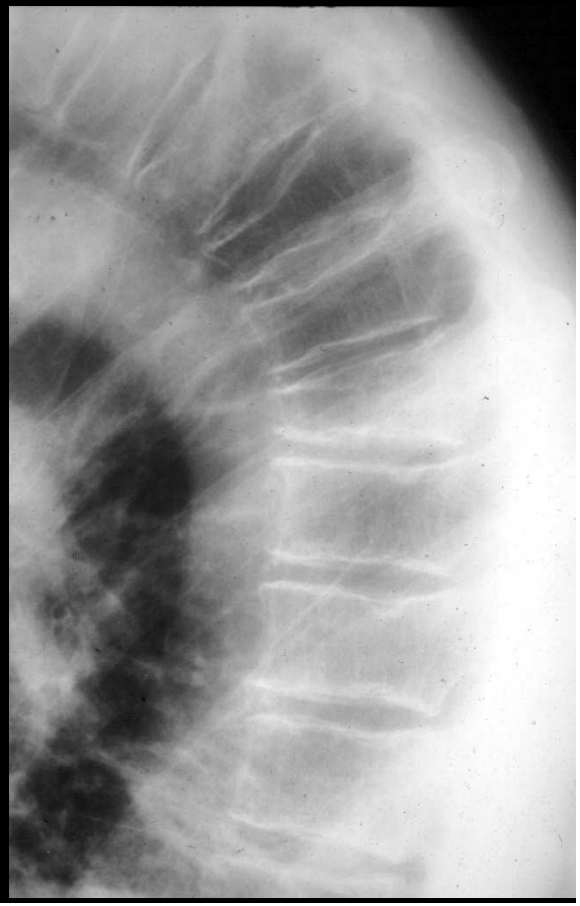
Key-message Metabolic bone disorders

* Medical imaging can neither detect nor quantify osteoporosis.

* If severe, we should be able to detect it.

* Our goals : detect and characterize complications
    - Fractures
    - Deficient healing process

- Fractures occasionnaly unidentified by patients (spontaneous resolution)



Insufficiency fracture
Normal stress
Decrease bone strength (diffuse)

Fatigue fracture
Repetitive increased stress
Normal bone

Fracture classification (mechanism)

Traumatic fracture
Acute increased stress
Normal bone

Pathological fracture
Normal stress
Decrease bone strength (focal)

Acute spontaneous vertebral body fracture

Abnormal shape

Osteoporosis ?

Acute spontaneous vertebral body fracture

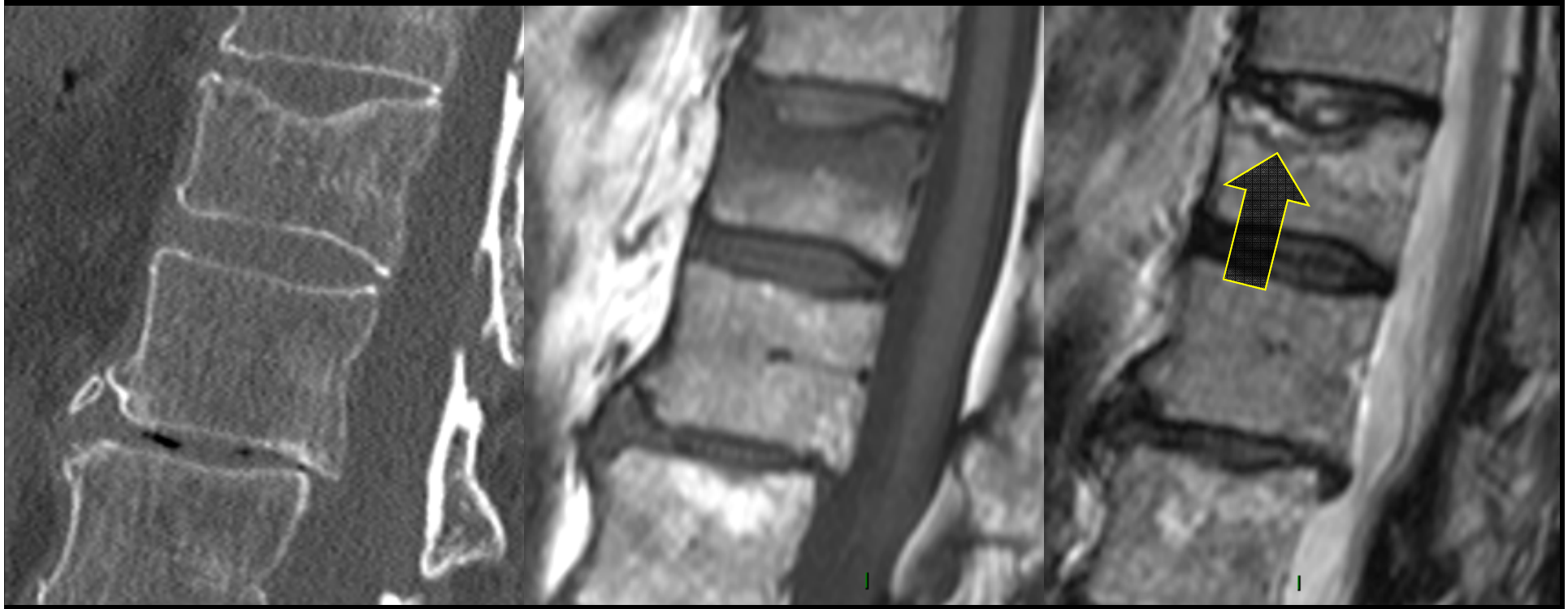
Abnormal shape

Osteoporosis ?

Marrow infiltration

Abnormal shape

Acute spontaneous vertebral body fracture



Abnormal shape

Osteoporosis ?

Marrow infiltration

Abnormal shape

Marrow edema

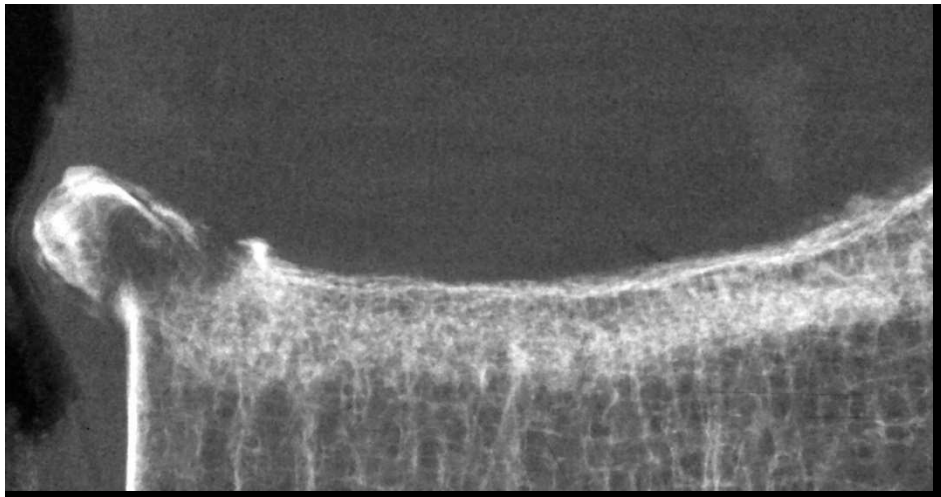
Trabecular bone fracture

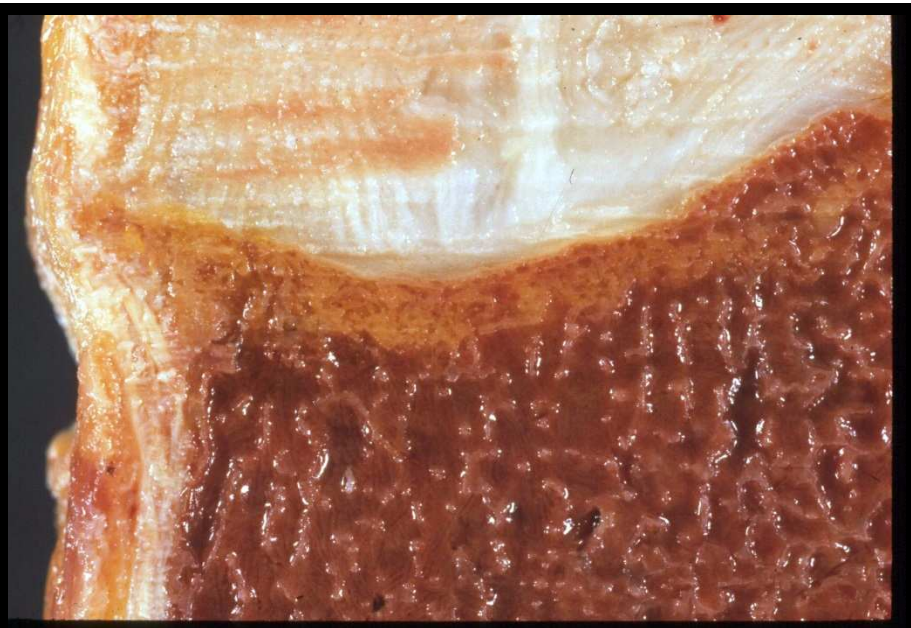
Spontaneous vertebral body fracture

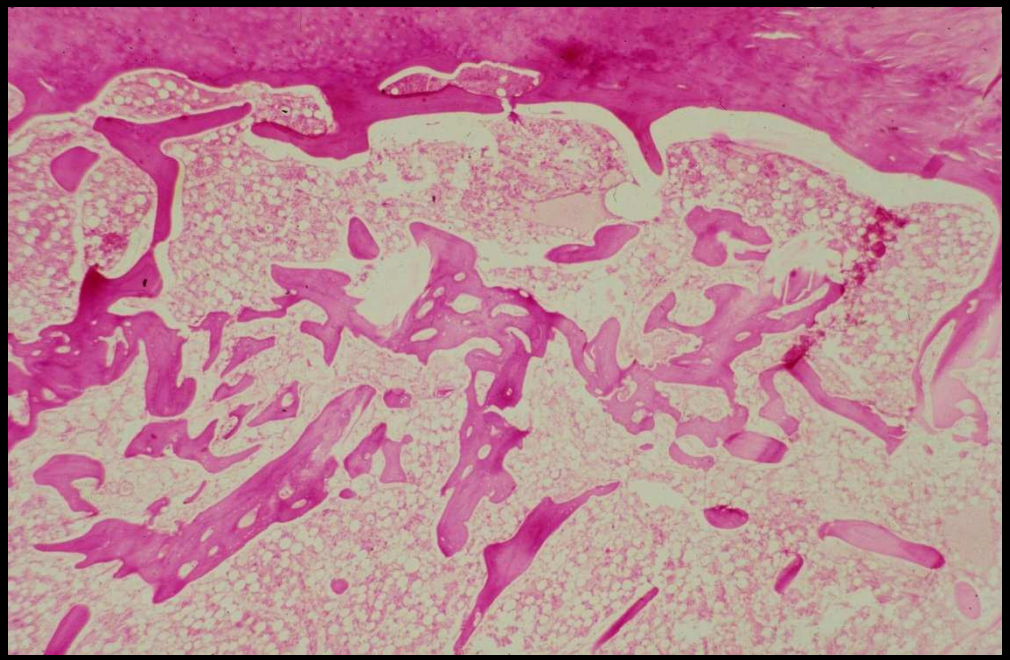
Acute fracture

Healing fracture
(+ 2.5 months)

Vertebral fracture (subacute ?)







Elementary changes in vertebral fractures

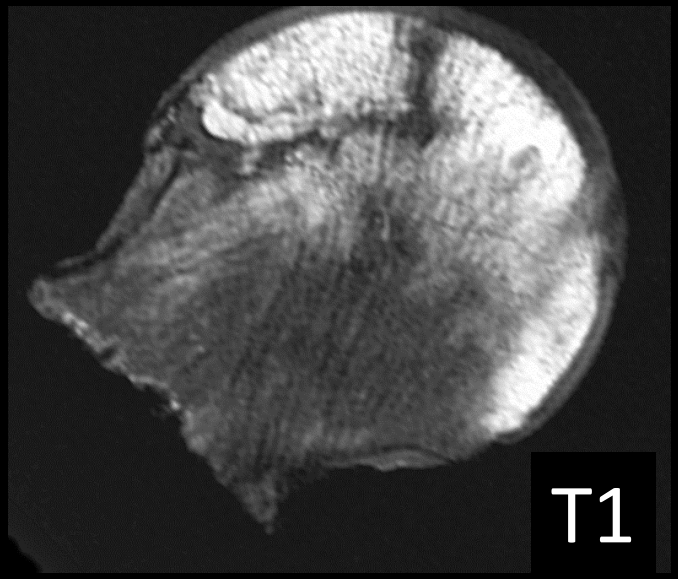
- vertebral body deformity
- marrow “oedema”
- trabecular band of low signal
- subtle soft tissue changes
- homogeneous enhancement after Gad on T1

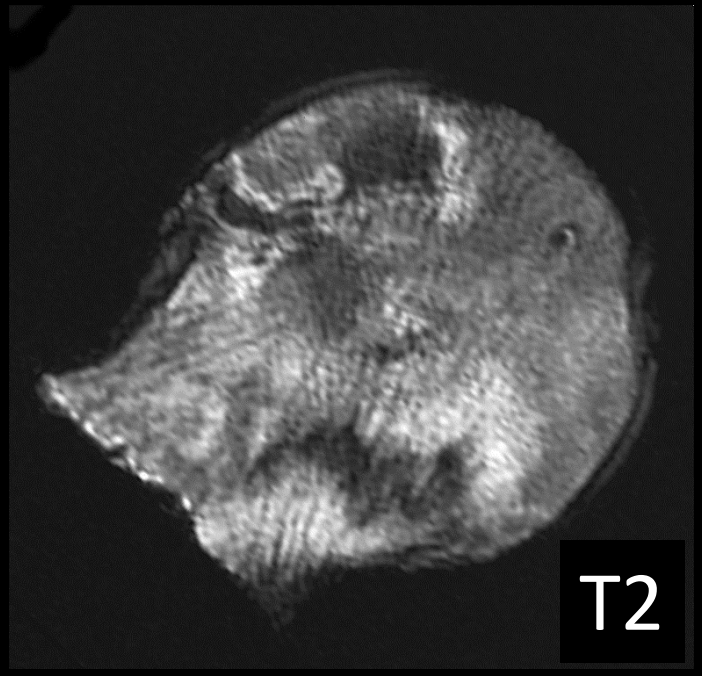
??????????????????????????????

??????????????????????????????

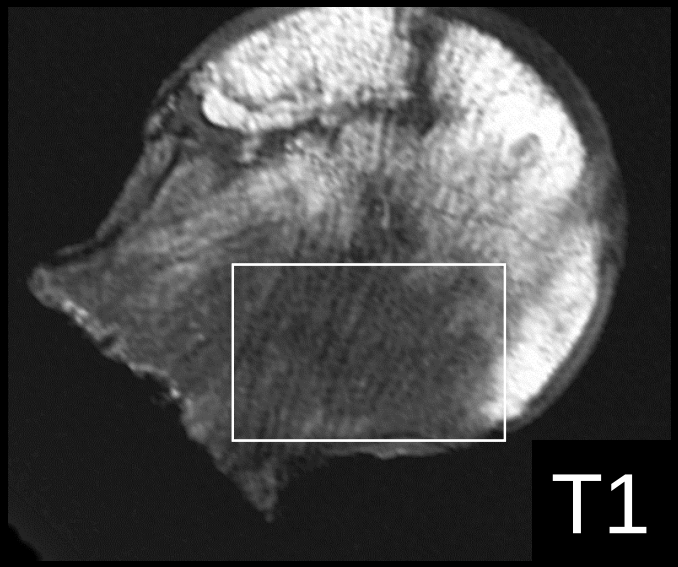
Acute insufficiency fracture

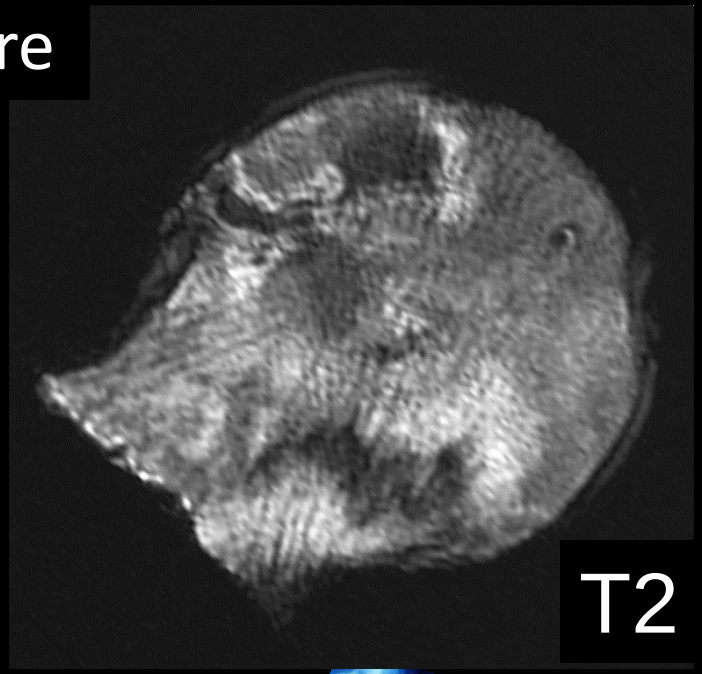
Subacute trabecular bone fracture

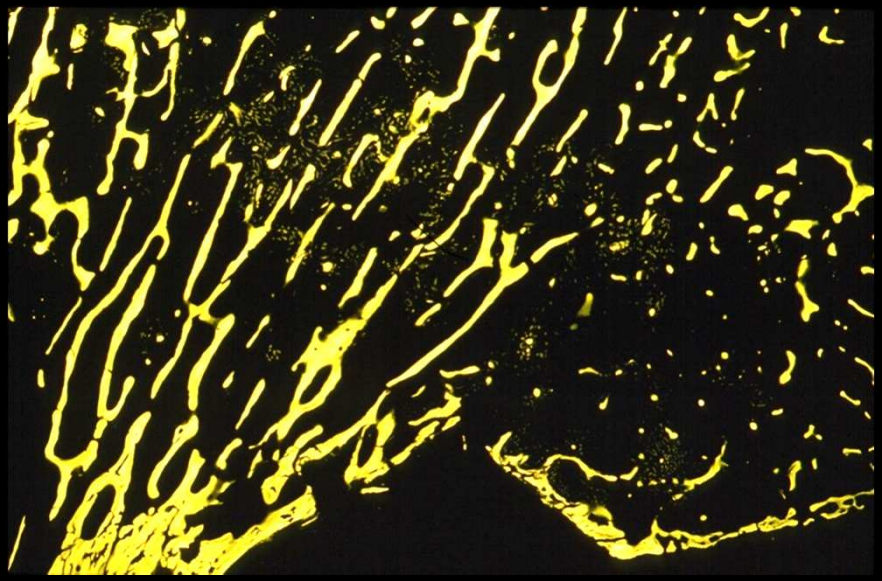




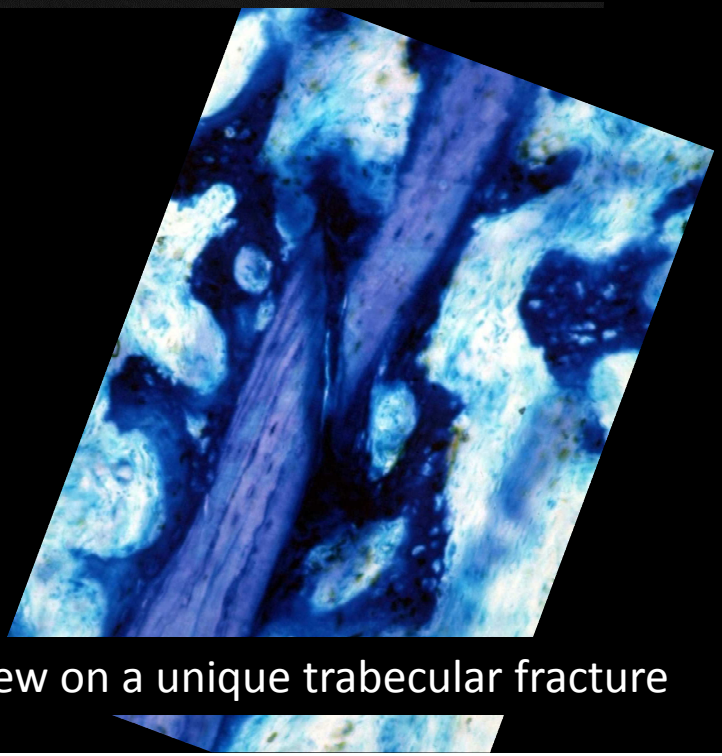
Subacute trabecular bone fracture







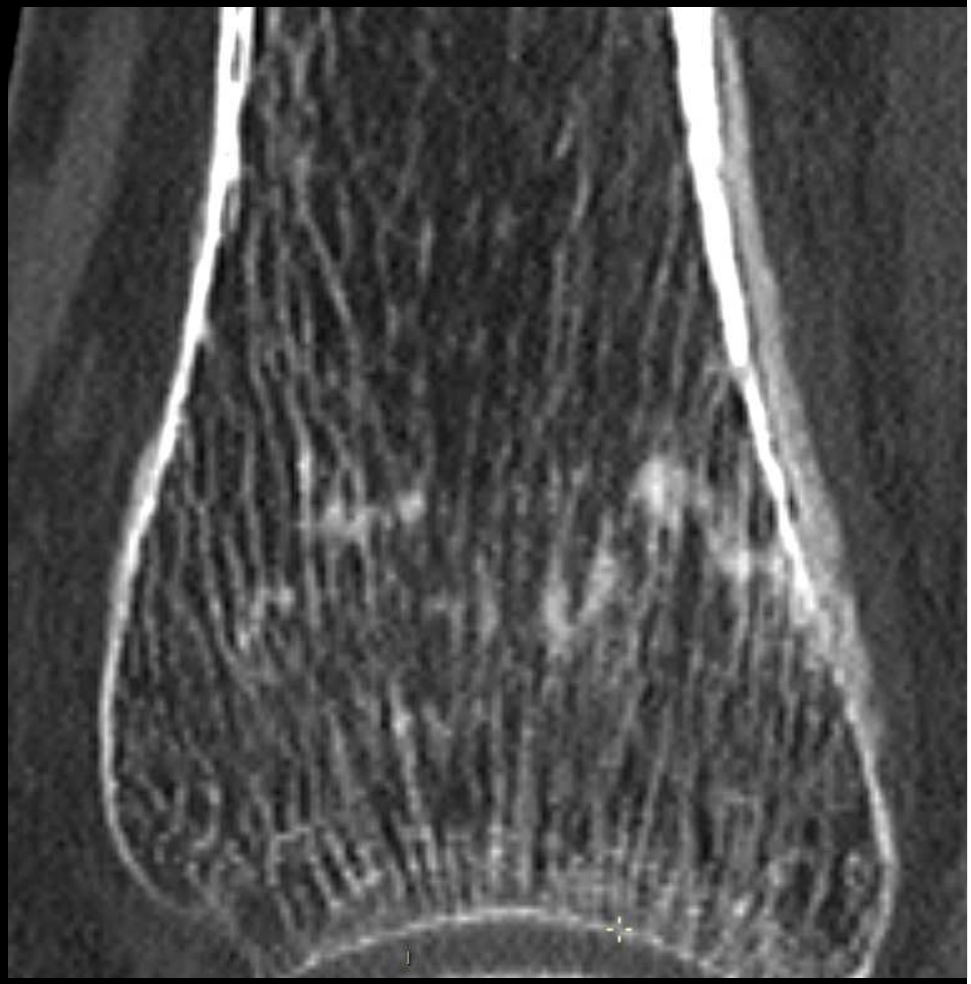
Multiple trabecular fracture



close-up view on a unique trabecular fracture

Early insufficiency fracture

3 months later



Delayed diagnosis on X-ray/CT

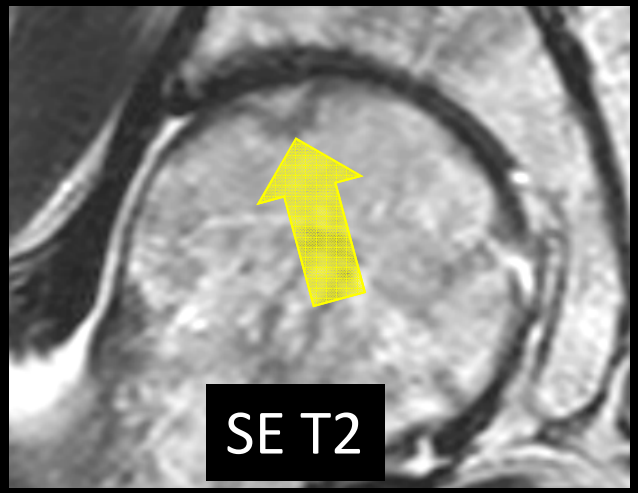
Uncommon insufficiency fractures

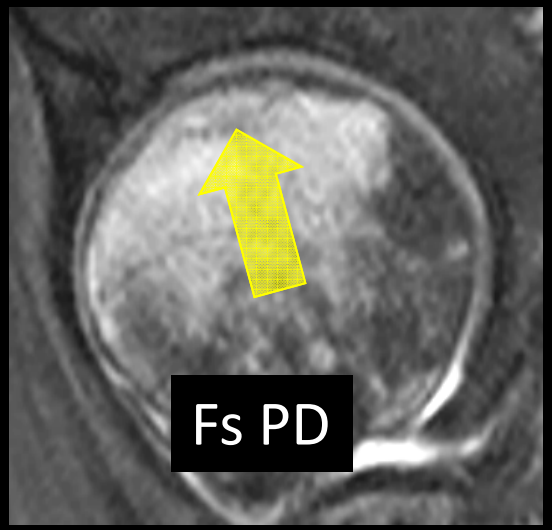
Loozer’s zones
Epiphyseal fractures
Longitudinal cortical fractures
Bisphosphonate-associated fractures
Steroid-associated fractures

Misleading lesions / controversial literature

47-year-old male; R hip pain after lifting an heavy chair
Normal spine CT !

Insufficiency fracture of the femoral head





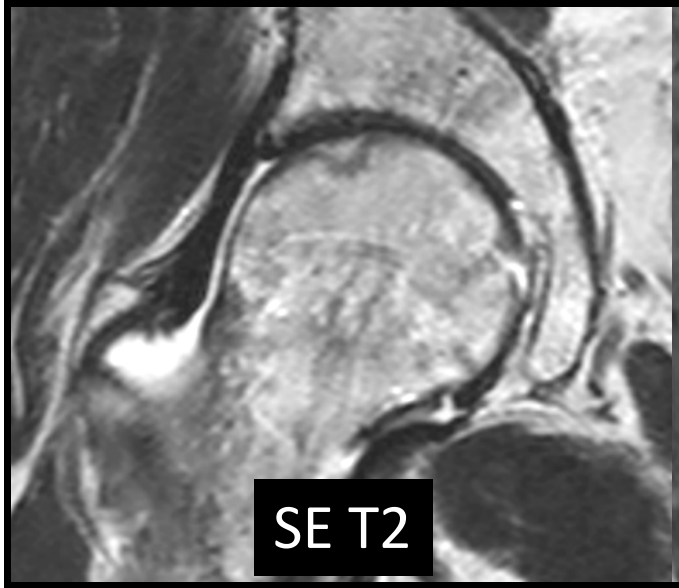
Biological work-up

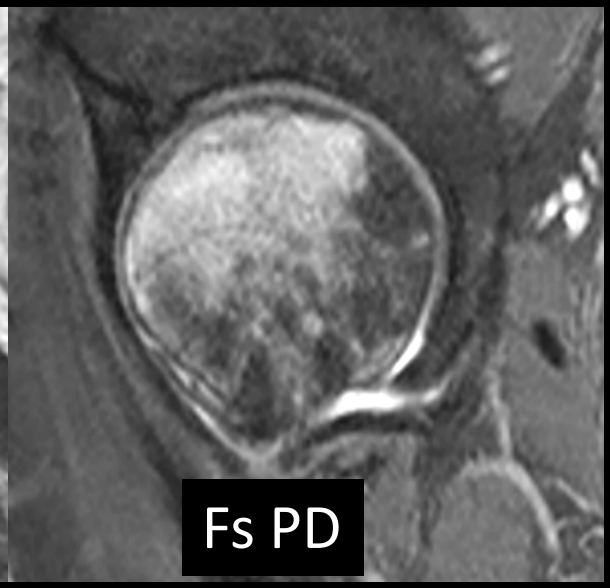
Blood Calcium: 9,81 mg/dL (8,8-10,4)
Blood Phospore: 2,1 mg/dL (2,4-4,7)
25(OH)Vit D: 8 ng/ml (30-100)

Left Hip BMD T-score: -1,4

Spine BMD T-score: -1,7

W-body BMD T-score : -2,1



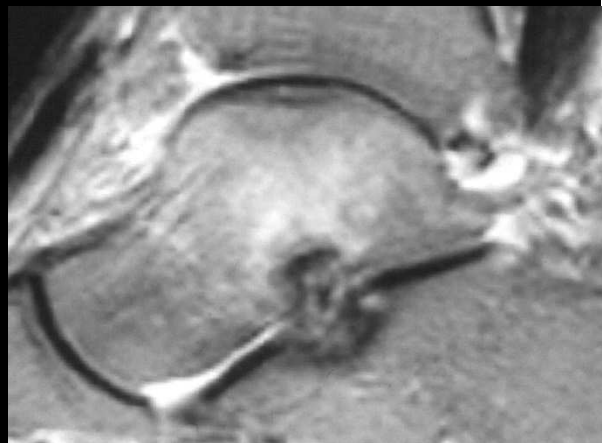


Epiphyseal insufficiency fractures

- involve lower limb epiphyses
- mainly convex articular surfaces
  (fem. head and condyles, talus, metatarsal head)
- Non contributive radiographic findings
  - normal
  - subtle deformity
  - subtle sclerosis

- MR
  - marrow “edema”
  - subchondral lines
  - subtle deformity of bone plate

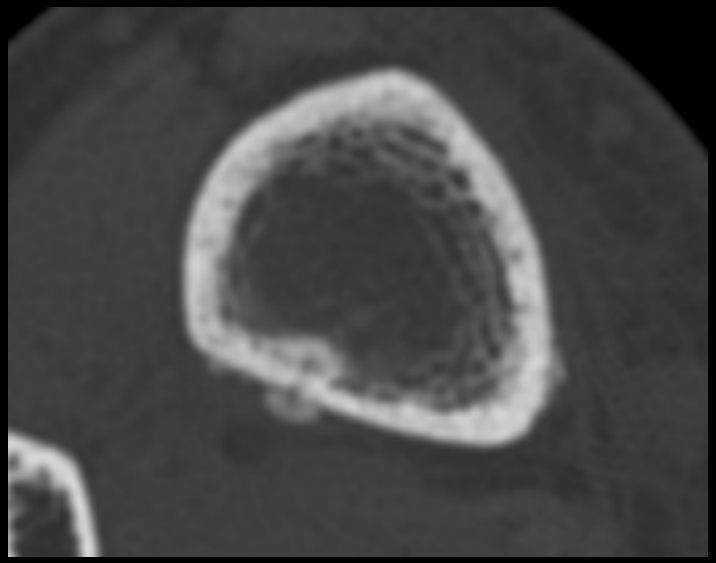
- DD: osteonecrosis, osteoarthritis

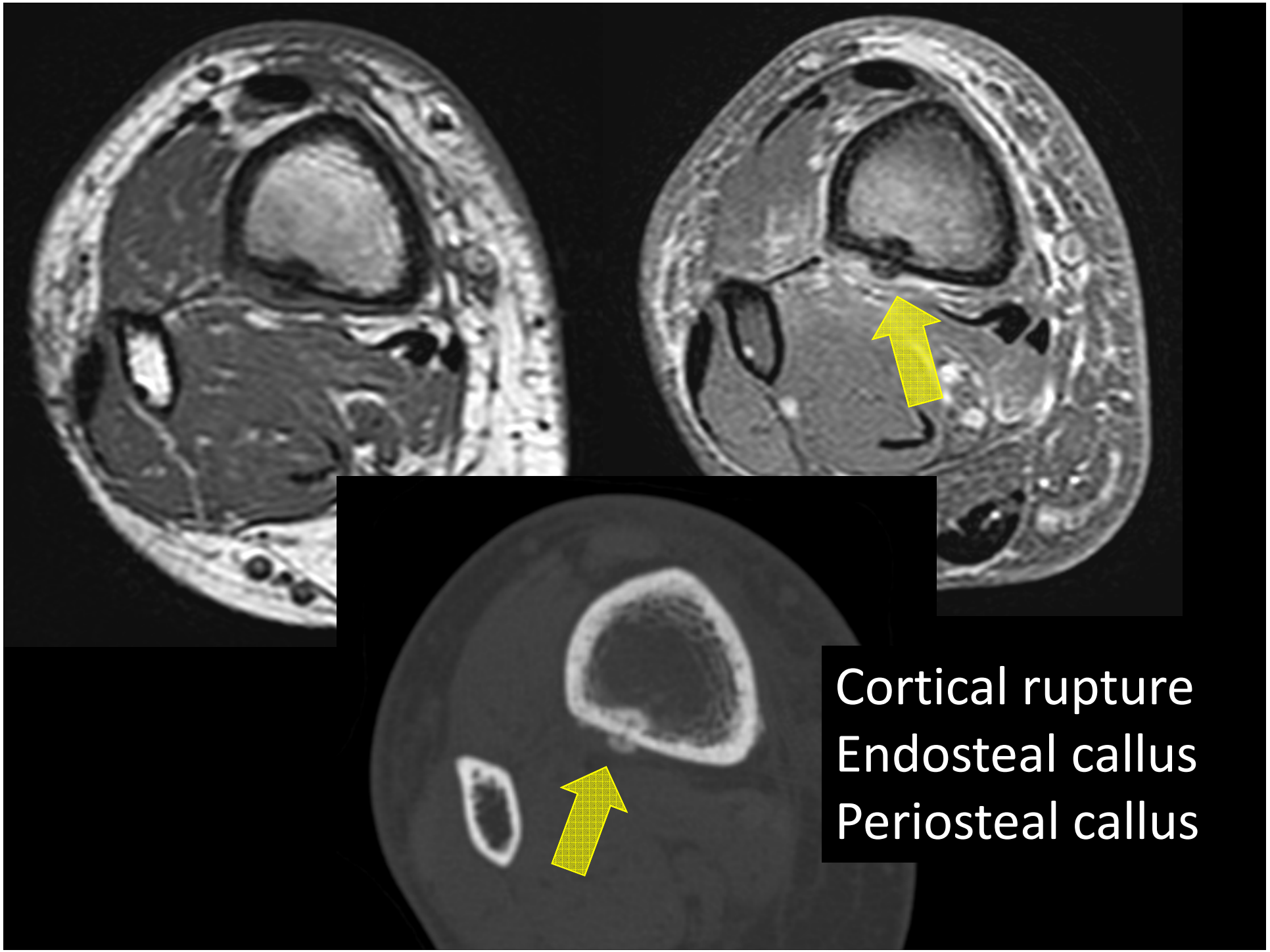


Longitudinal insufficiency fracture

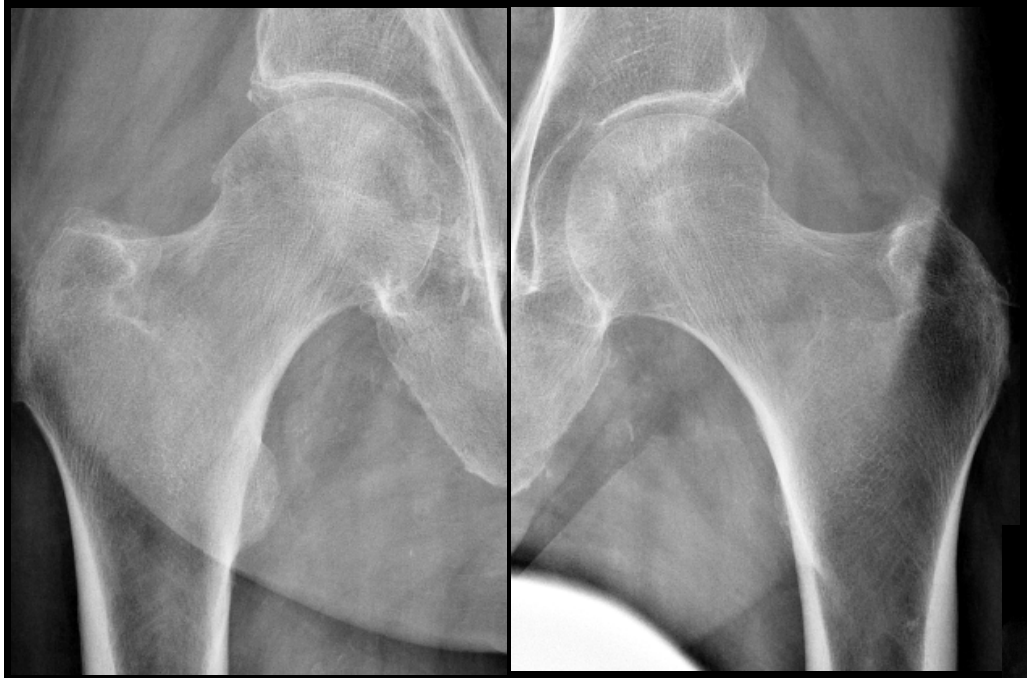
- Tibia (femur, metatarsal bones)
- Elderly females
- Chronic pain with swelling

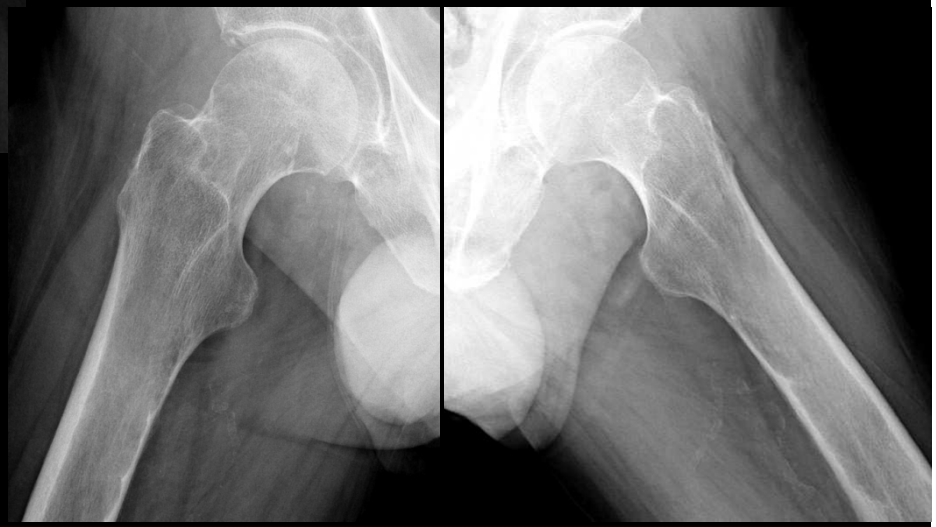
- Extensive edema in medullary cavity and soft tissues
- Clue : cortical interruption (axial CT images !)




Cortical rupture
Endosteal callus
Periosteal callus

Case
77-yo man with diabetus mellitus, chronic renal insufficicency, on dialysis for 7 yrs
Spontaneous Lt hip pain 3 weeks





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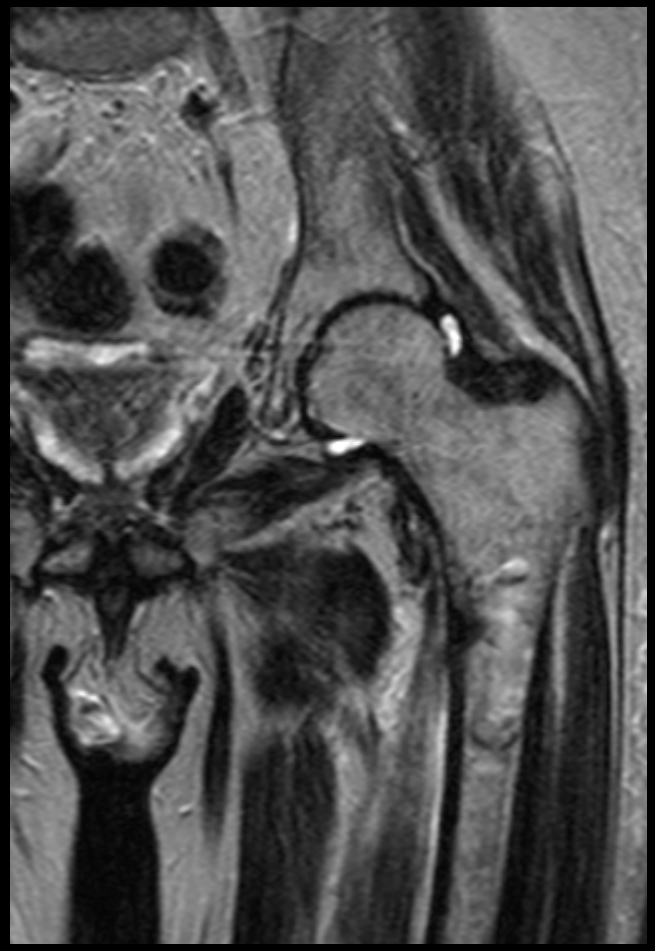

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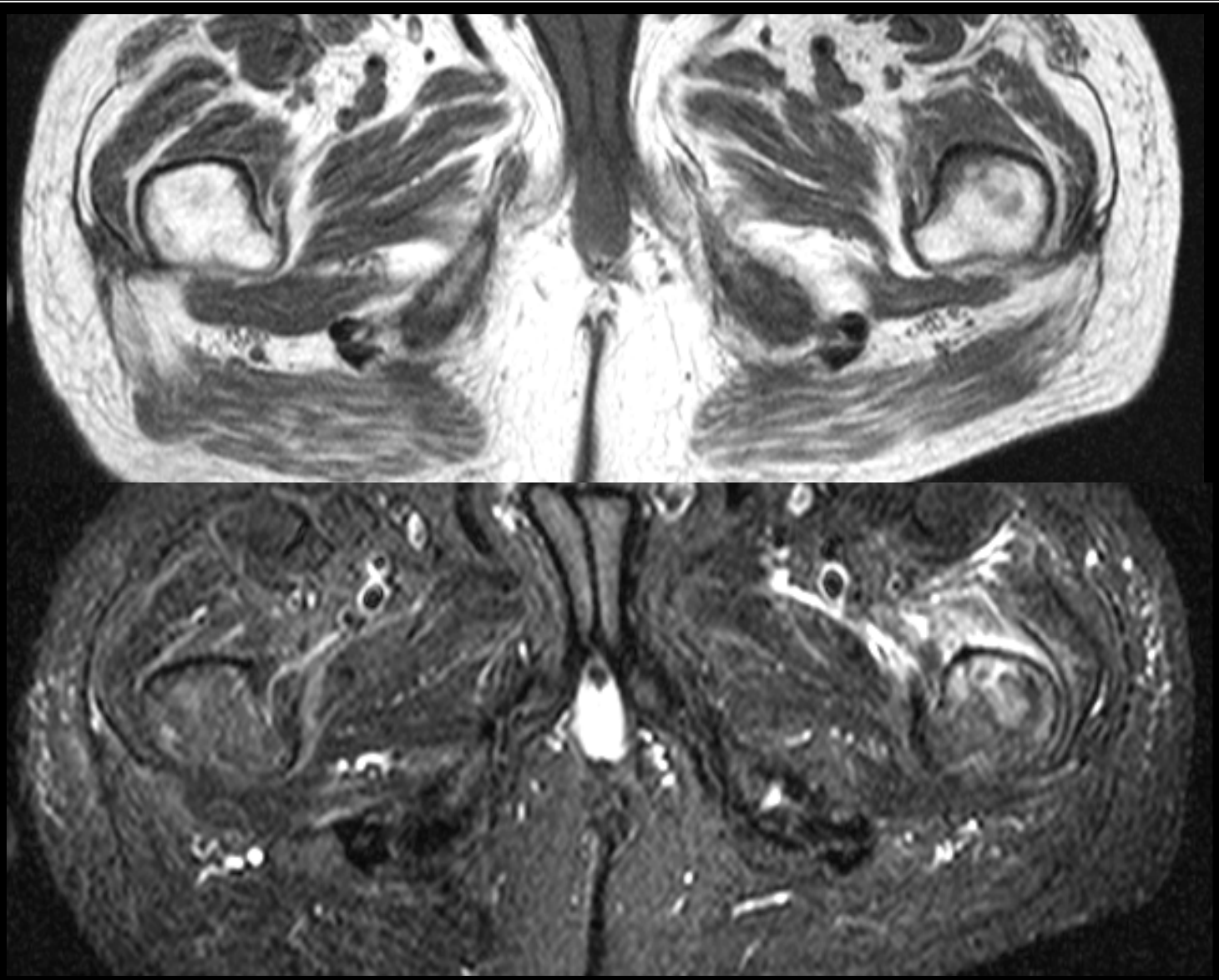
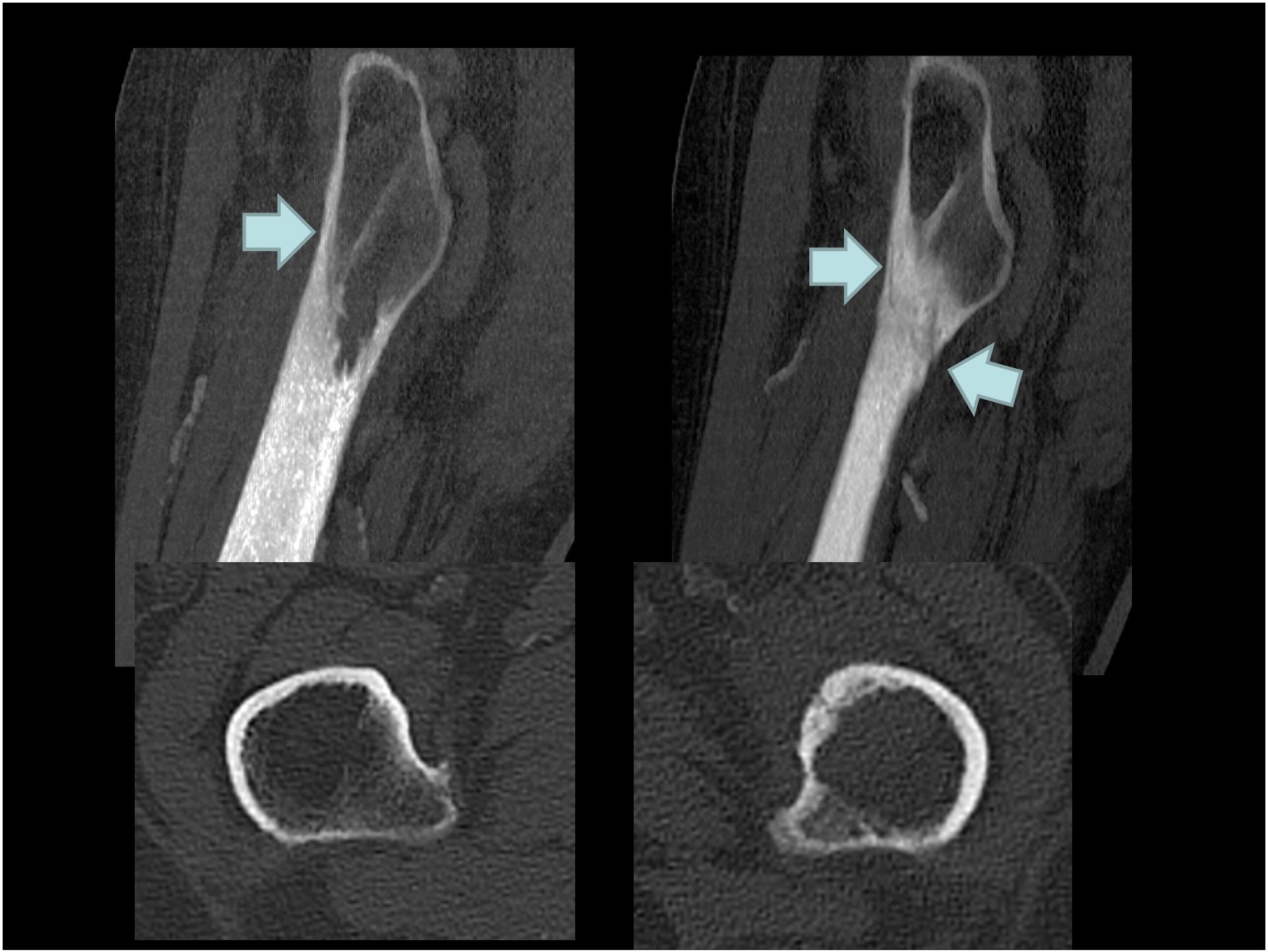
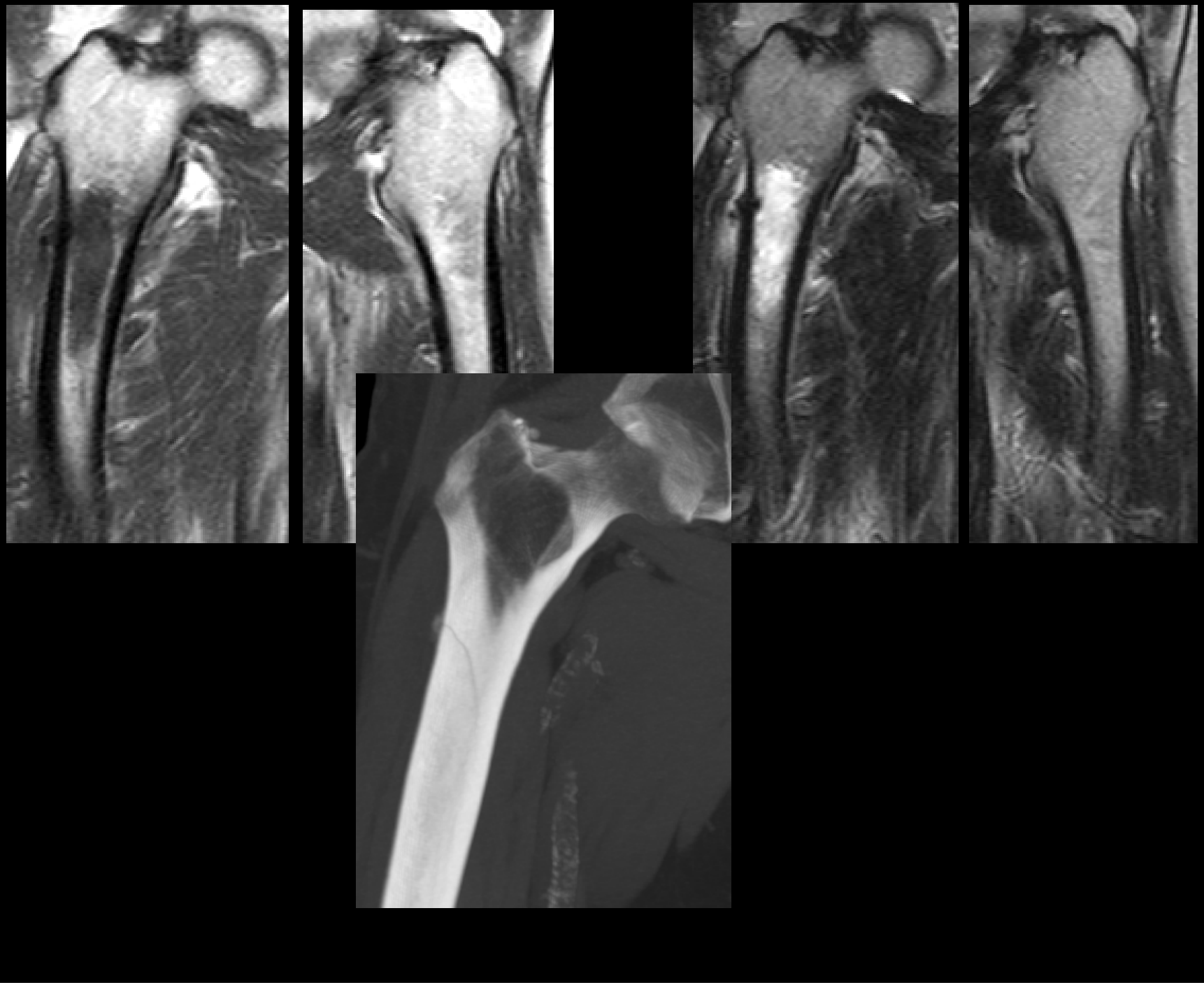






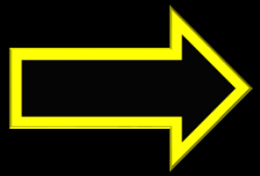
Metabolic, endocrine , marrow disorders

A. Normal bone and marrow metabolism

B. Overview on metabolic disorders

C. Imaging bone or marrow ?

D. Metabolic bone disorders

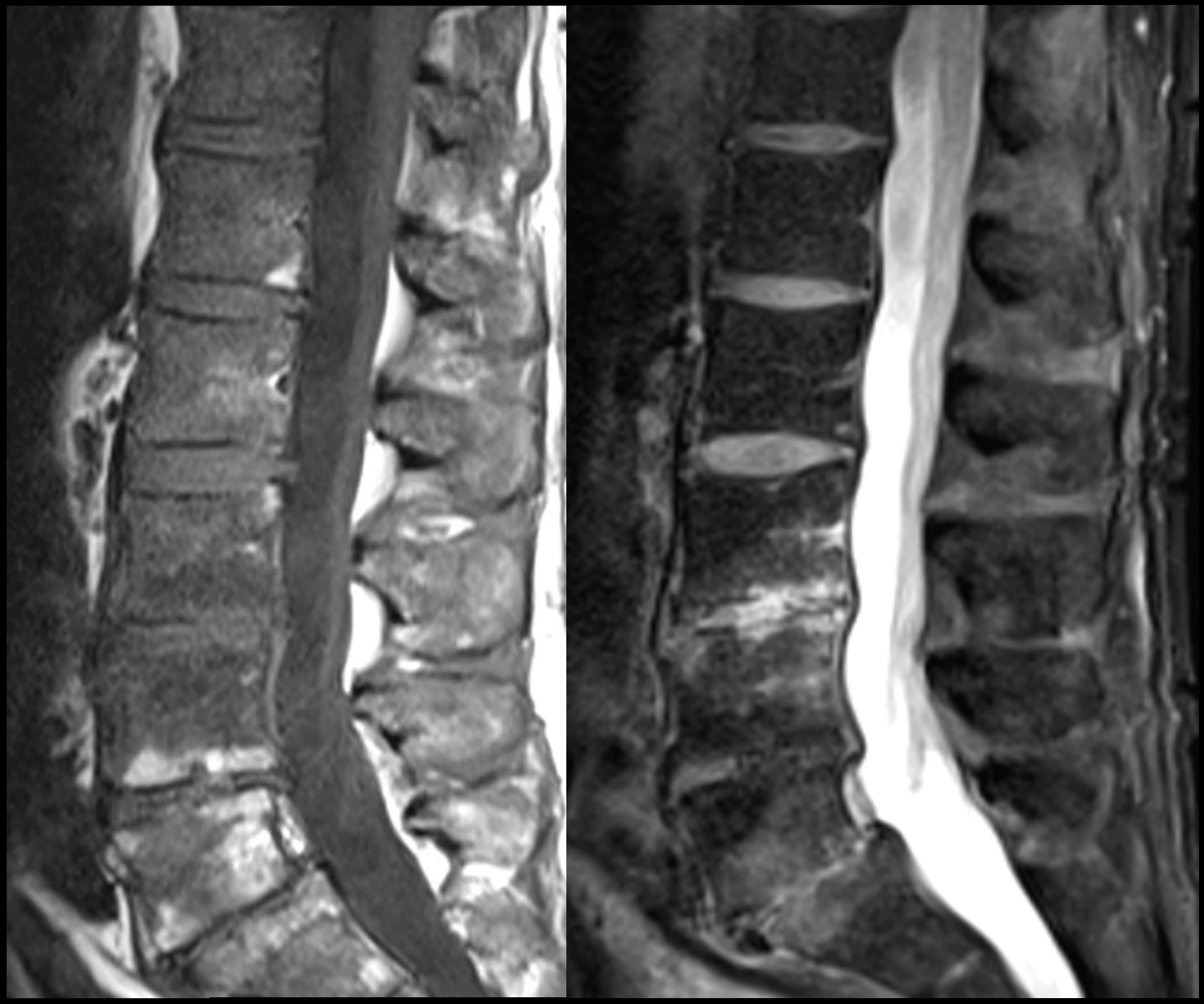


E. Metabolic marrow disorders

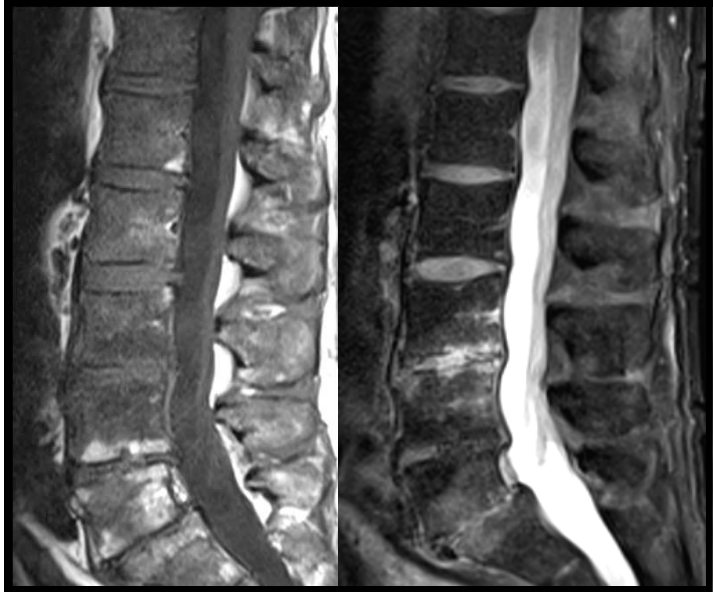
Metabolic disorders- Overview

Red marrow
Hyperplasia
Aplasia
Hemosiderosis
lipomatosis
…..

Yellow Marrow
Serous atrophy
…..



June 2013
Septicemia and L3-L4 spondylodiscitis

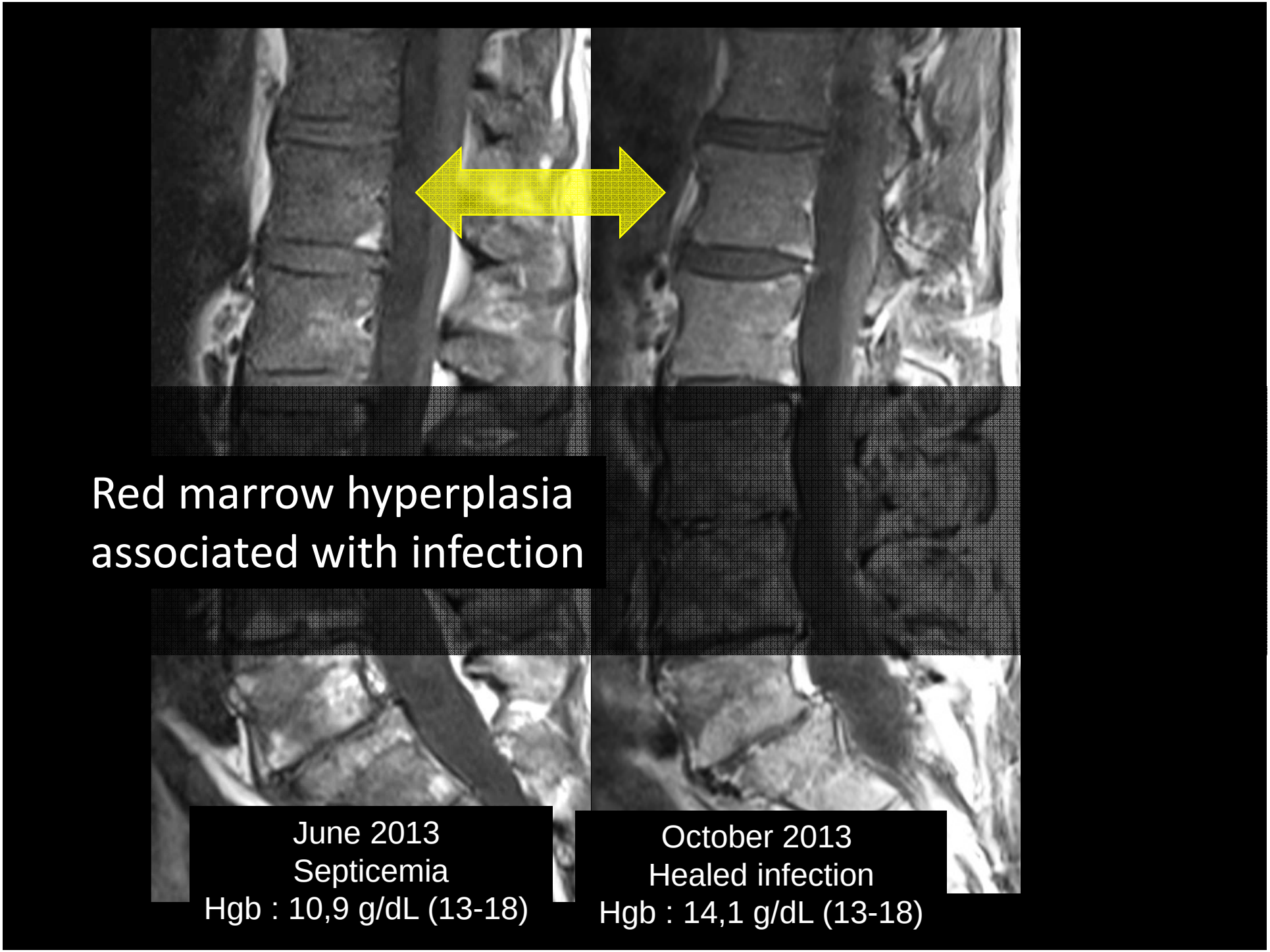


June 2013
Acute spondylodiscitis

October 2013
Healed spondylodiscitis

June 2013
Septicemia
Hgb : 10,9 g/dL (13-18)

Red marrow hyperplasia associated with infection ?


Red marrow hyperplasia
associated with infection
June 2013
Septicemia
Hgb : 10,9 g/dL (13-18)
October 2013
Healed infection
Hgb : 14,1 g/dL (13-18)

Red marrow hyperplasia associated with infection

SE T1

SE T2

enh. SE T1

Red marrow hyperplasia may interfere with focal lesion detection
mimick marrow infiltration by abnormal cells

Transient drug-induced red marrow hyperplasia associated with haematopoietic stimulating factors

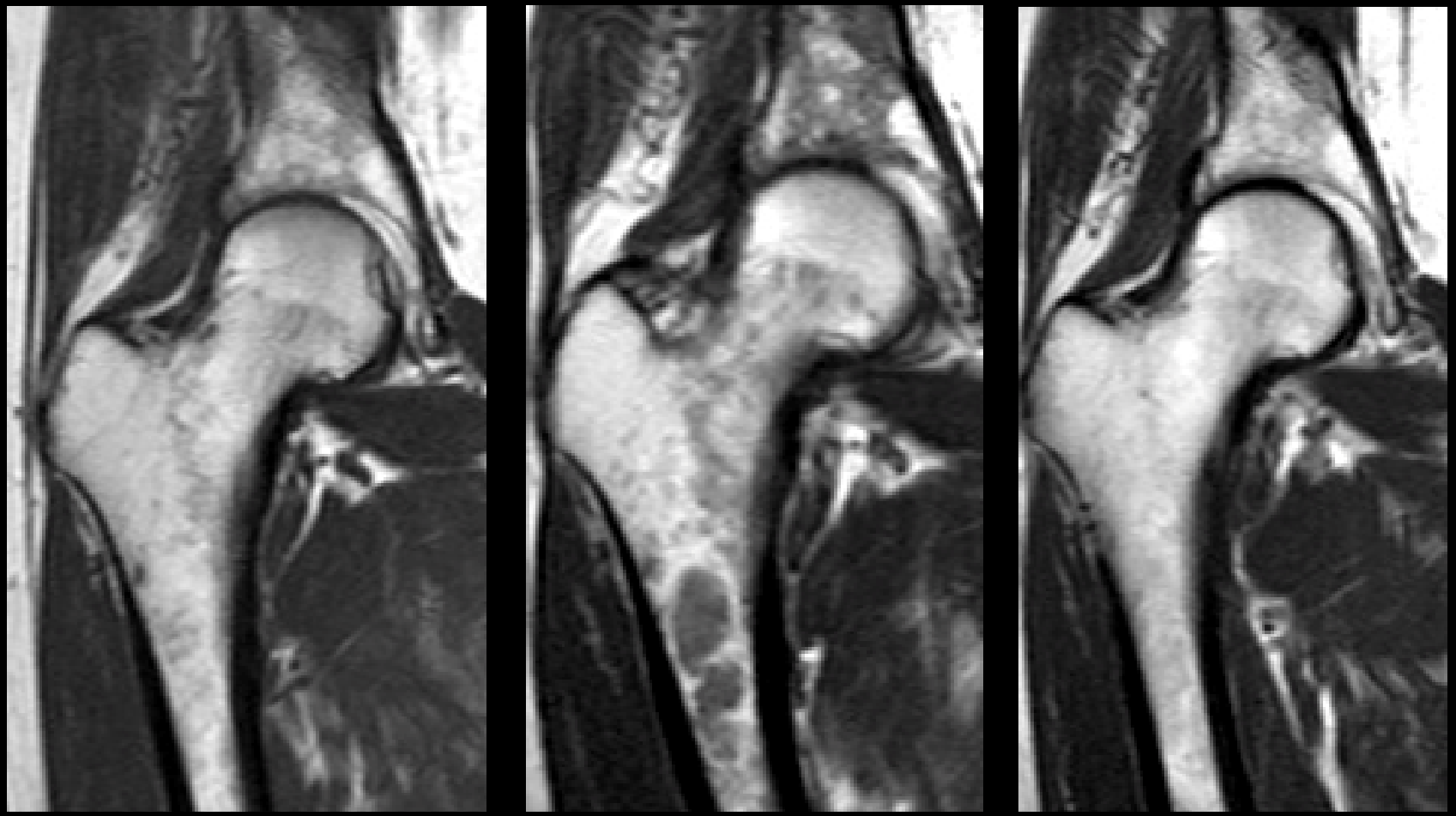
Before treatment during treatment after treatment

Red marrow hyperplasia may

interfere with focal lesion detection

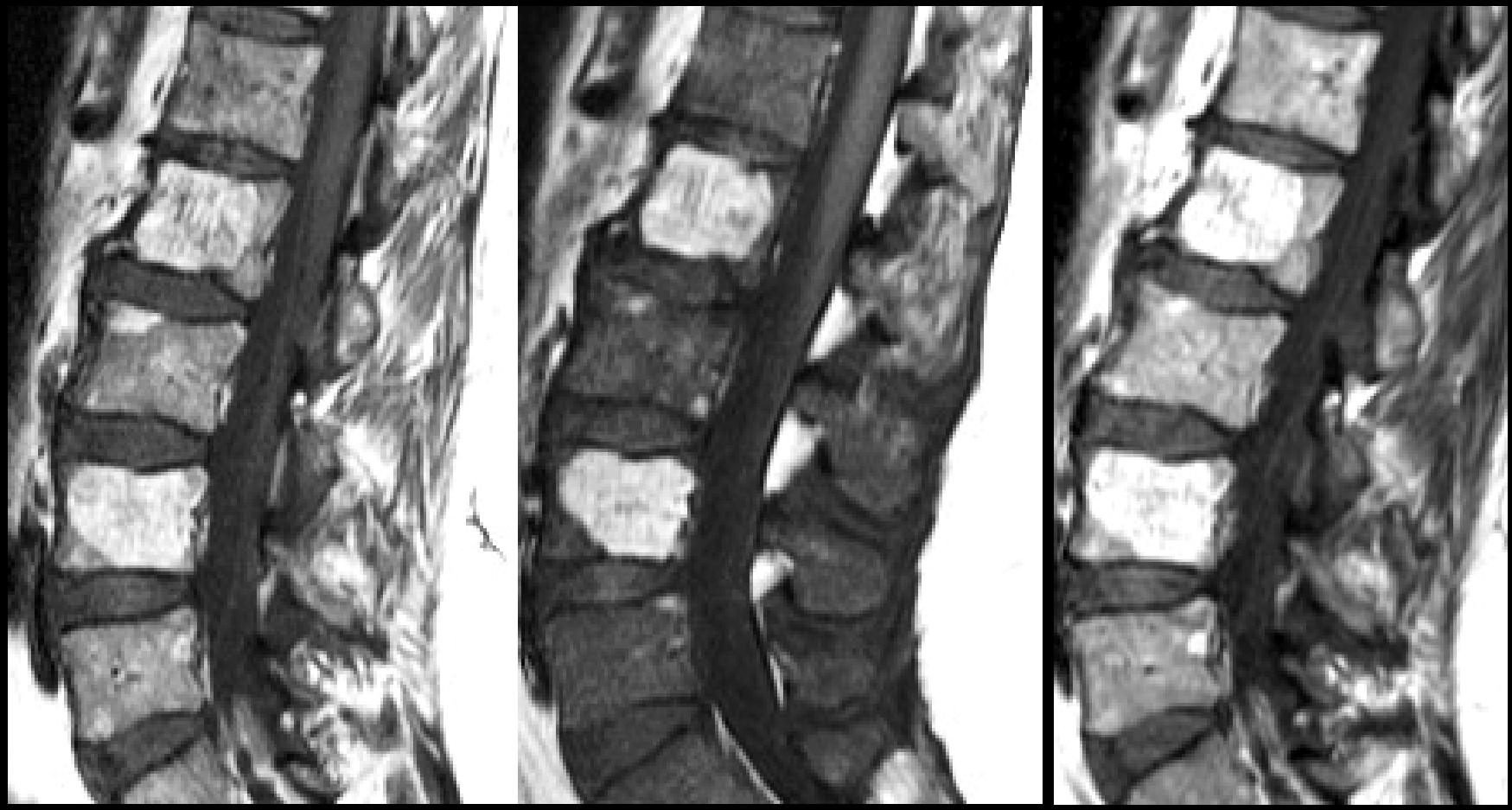
mimick diffuse marrow infiltration by abnormal cells

mimick focal marrow lesions in appendicular skeleton



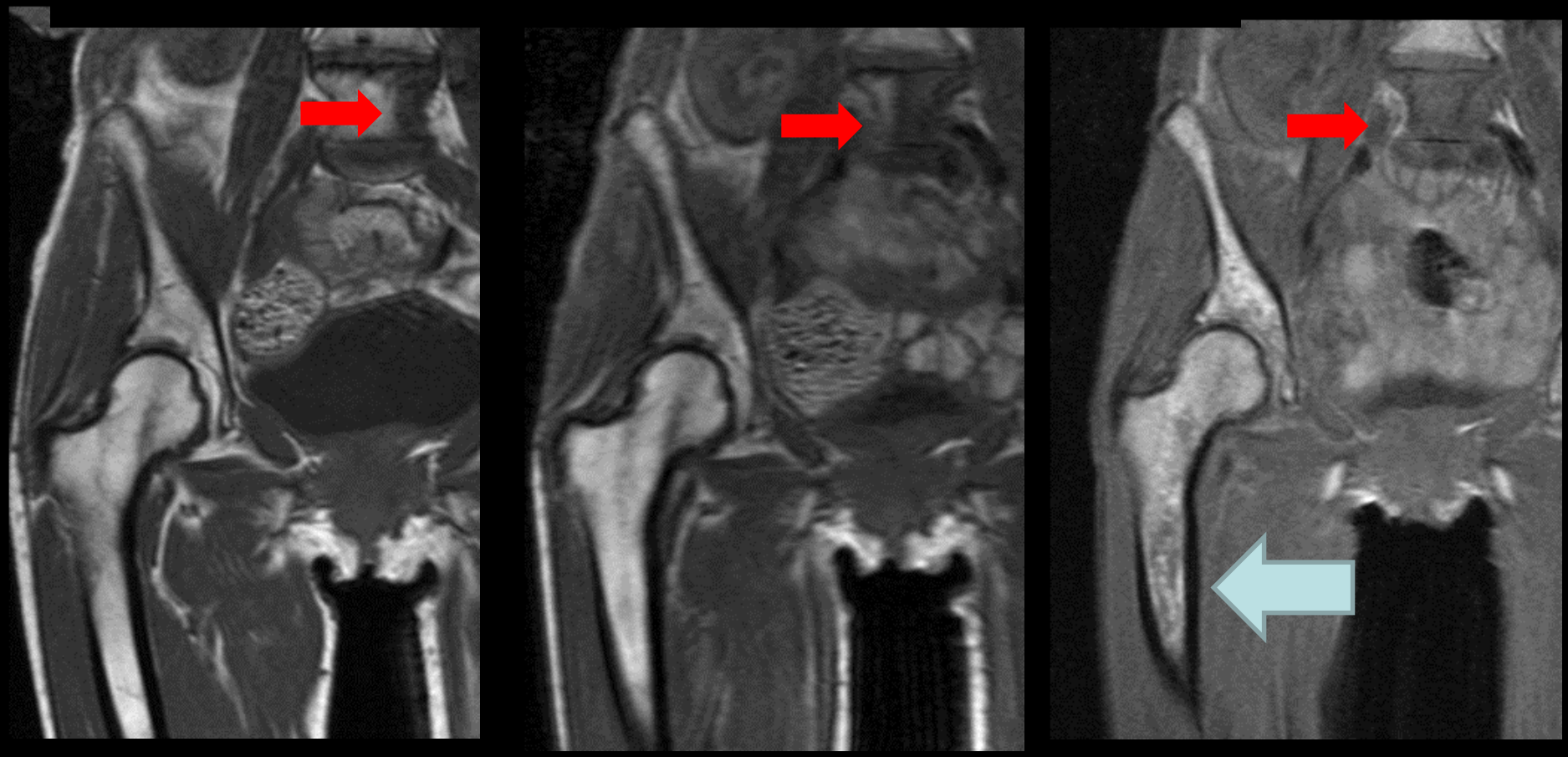
Before treatment after 2 months after 6 months

Not differenciable from any cause of marrow infiltration
High on perfusion, diffusion and Pet
Ask the clinician



Before during after

Cancer-related cachexia during chemotherapy
Serous atrophy of the marrow (disappearance of fat)



May July December

Metabolic disorder of fatty marrow

Serous atrophy of the marrow
Standard T1-w SE sequence
in a patient without fat.

Standard T1-w SE sequence
in a fat-sat patient

T1-w SE

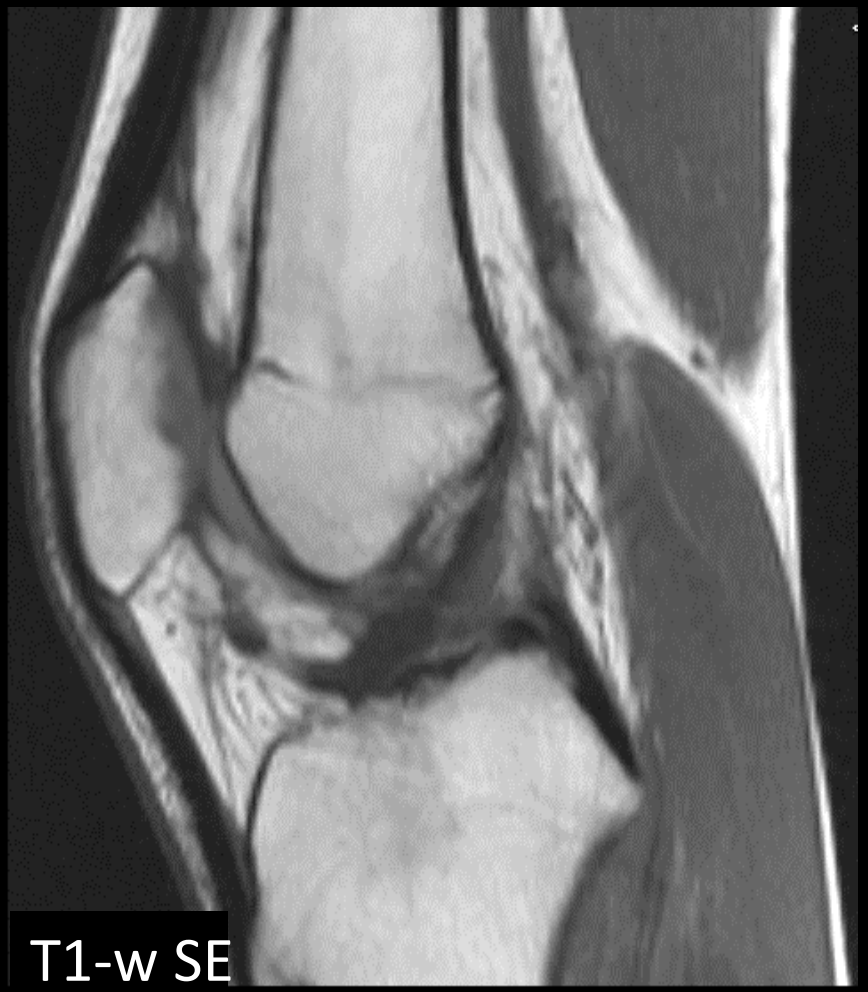
Standard patient
Fat-saturated T1-w SE sequence

Fat-sat T1-w SE

Standard SE T1 sequence
in a patient without fat

T1-w SE

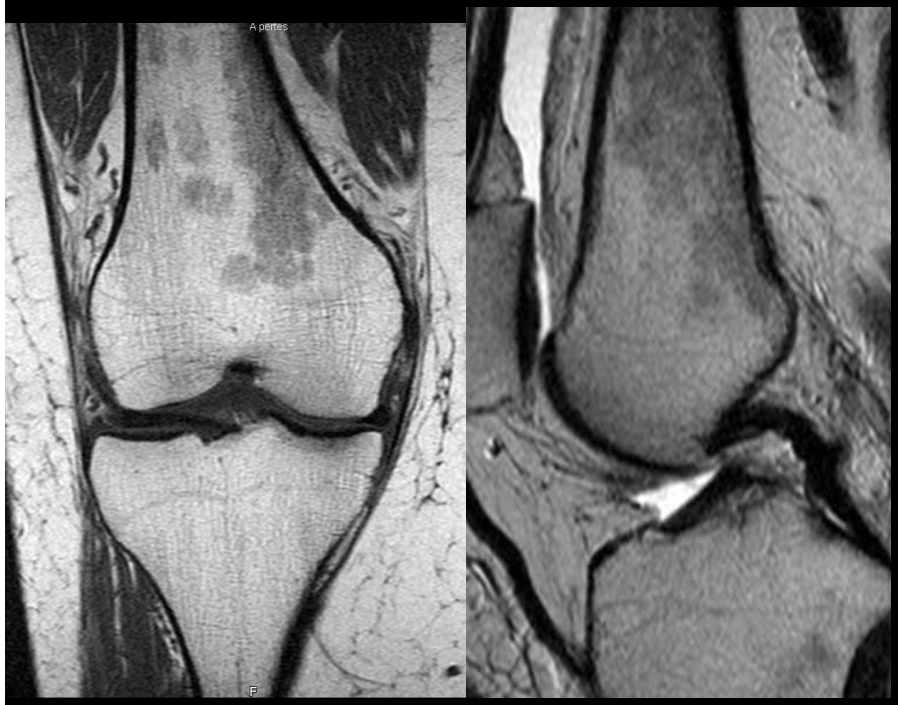
Same sequence (SE T1)
Same patient with more weight



T1-w SE

Serous atrophy of the marrow: a reversible process
Extracellular accumulation of hyaluronic acid / normal intracellular accumulation of lipids

64-yo woman
Moderate anemia



Moderate expansion of red marrow
Marrow signal within normal limits

34-yo man with minor thalassemia
Long-lasting anemia

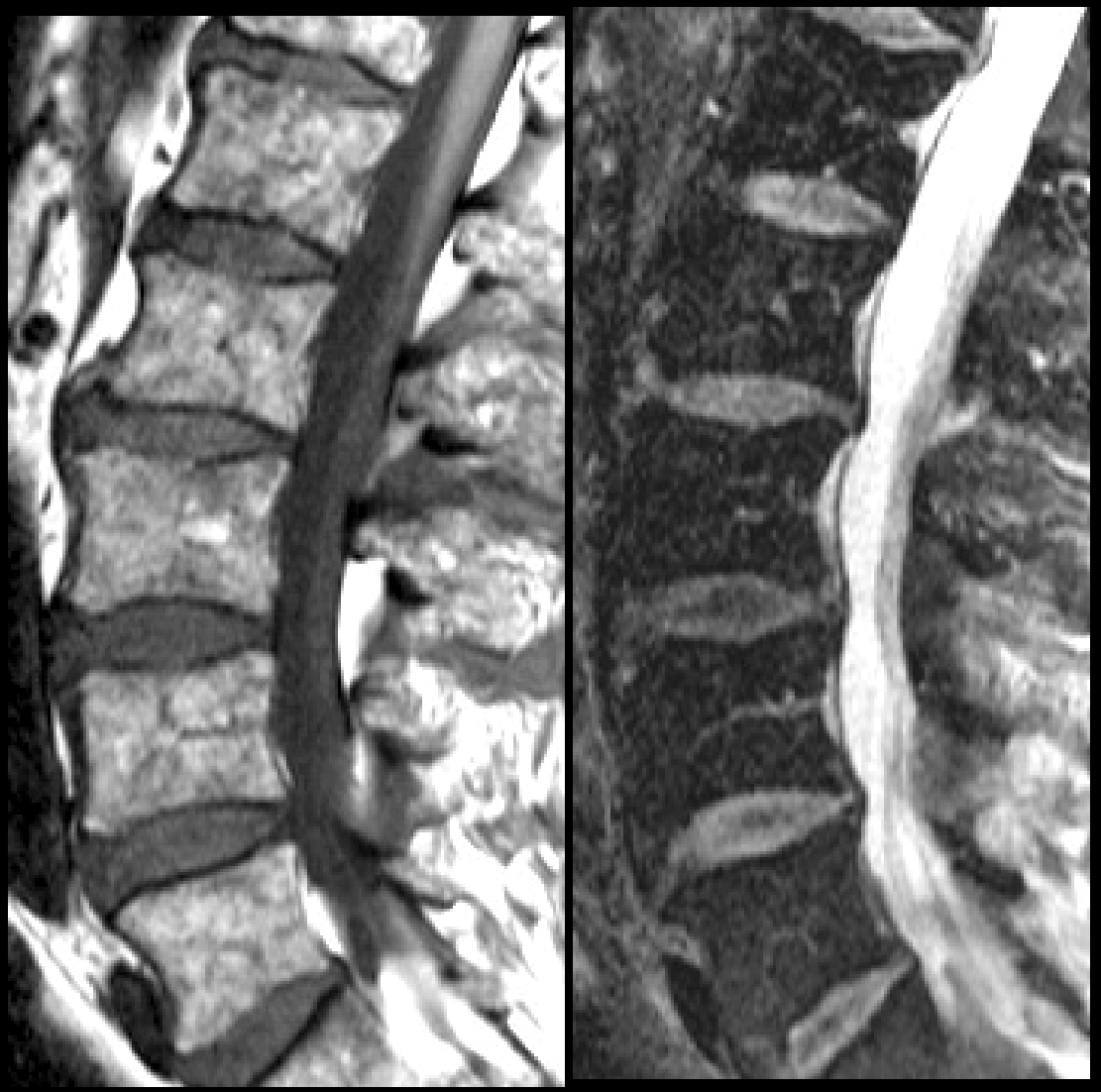
Marked expansion of red marrow
Very low signal of marrow

No more within normal limits

Hemosiderosis
Variable on SE T1
Very low on T2

Normal at birth
Until 6 months of age

Blood transfusion
Hemochromatosis



32-yo woman with scickle-cell anemia and Lt hip septic arthritis

Marrow expansion
Hemosiderosis

35-yo man with scickle-cell anemia

Marrow expansion
Hemosiderosis

Multiple infarcts

Value of Contrast material for the detection/characterization of complications

Sickle cell disease Haemolytic Anemia

Hemosiderosis Marrow infarction

SE T1

fs PD

SE T2

Enh. SE T1

Metabolic marrow disorders

Marrow changes are frequently unrecognized by radiologist.

This under-reporting has no impact on patient management.

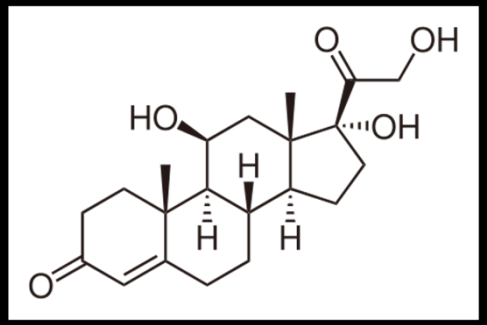
The abnormal background marrow can be misleading.

It may mimick diffuse marrow infiltration and it may reduce focal lesion conspicuity at MRI on SE T1 images.

Marrow aplasia
Idiopathic
Toxic
Iatrogenic

Systemic effects of corticosteroids on the skeleton

* Cortical and cancellous bone
* Red and yellow marrow
* Tendons
* Muscles
* fat



Effects on bone cells

Inhibition of bone formation

- Pluripotent cells
  - Facilitate osteoclast differenciation
  - Facilitate adipocyte differenciation
  - Decrease osteopblast differenciation
- Osteocytes
  - Increase apoptosis
- Osteoblasts
  - Decrease bone matrix formation
- Osteoclasts
  - Decrease apoptosis

on marrow cells

- Pre-adipocytes
  - Facilitate adipocyte differenciation
- Limb adipocytes
  - Stimulate lipolysis
  - Decrease number of cells
- Central adipocytes
  - Stimulate liposynthesis
  - Increase numpber of cells

Steroid-induced osteoporosis - Triad

1. Atrophic osteoporosis
2. Multiple fractures
3. Hypertrophic callus

Steroid-induced fractures

* Multiple fractures
* hypertrophic callus
* difficulties in healing
  - intravertebral vacuum

MR features in steroid treated patients

Less mineralized bone (not seen)
More medullary fat
More extraosseous fat
Muscle atrophy
Fractures

Multiple fractures / Limited edema / Slow changes over time

The Beauty of
basic knowledge
MSK radiology
ECR 2014

Metabolic, endocrine, marrow diseases

Take-home messages

Metabolic disorders – Take-home

Metabolic disorders
* Frequent and treatable systemic disorders (multi-organs)
* Bone, marrow, tendons, muscles, synovium, cartilage
* Long clinically silent phase (years)
* Medical imaging plays no role in detecting/quantifying/ monitoring the disease and its treatment.

Metabolic disorders – Take-home

Imaging in metabolic bone disorders
* Detection and characterization of fractures
* Accurate recognition of common and uncommon fractures

Metabolic disorders – Take-home

Imaging in metabolic marrow disorders
* Under-reporting at MRI (No clinical impact).
* May mimick severe conditions (focal or diffuse marrow infiltration by abnormal cells).
* May decrease potential of MRI (SE T1)
* MR imaging can be crucial for the appropriate management of complications.

The Beauty of
basic knowledge
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Metabolic, endocrine, marrow diseases

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