PATHOLOGICAL FRACTURES

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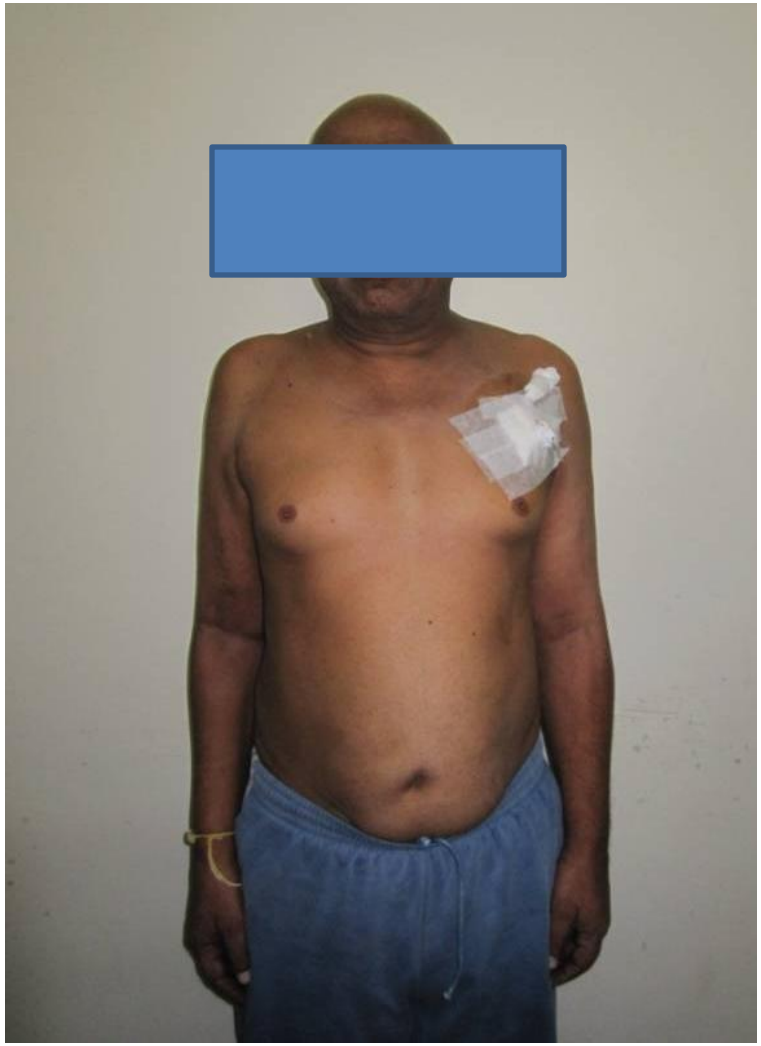
Bone School @ Bangalore

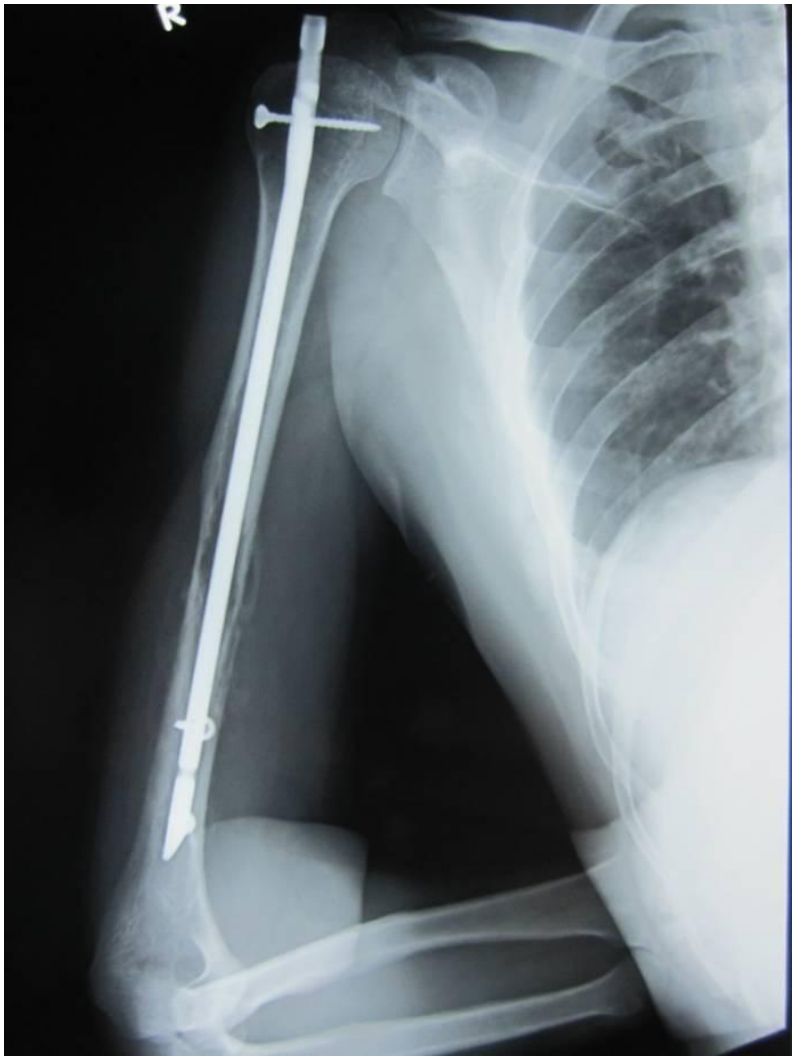
Overview of today's talk

- Introduction
- Incidence
- Mechanism of Metastasis
- Clinical Features
- Investigations / Radiology: salient features
- Evaluation
- Management – Principals
- Prognosis

50 yrs, Male

??? Diagnosis





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Definition :

A pathological facture is one in which a bone is broken, through an area, weakened by pre-existing disease, by a degree of stress, that would have left the normal bone intact.

In other words, a fracture involving "abnormal bone" is a pathological fracture.

Etiology :

Development disorders of bone :

a) Congenital defects of bone tissue :
   - Osteogenesis imperfecta
   - Osteopetrosis

b) Disorder of cartilage growth :
   - Achondroplasia
   - Diaphysealaclasis (multiple exostosis)
   - Dyschondroplasia (Ollier's disease)

Nutritional and vitamin deficiencies :

- Scurvy
- Rickets
- Osteomalacia

- **Hormonal imbalance :**
  - Hyperparathyroidism
  - Cushing's syndrome
  - Pathological fracture from cortisone treatment
  - Frohlich's syndrome (hypopituitarism)
- **Atrophic conditions of bone :**
  - Disuse osteoporosis
  - Senile osteoporosis
- **Pathological fracture through infected bone :**
  - Osteomyelitis
- **Cystic disorders and fibrous dysplasia of bone :**
  - Unicameral bone cyst
  - Aneurysmal bone cyst
  - Non – osteogenic fibroma of bone
  - Monostotic and polyostotic fibrous dysplasia

Paget's disease of bone

Primary and secondary tumors of bone :

a) **Primary benign tumours :**

- Chondroma
- Benign chondroblastoma
- Chondromyxoid fibroma
- Haemangioma of bone
- Giant cell tumour of bone
- Disappearing bone disease.

b**) Malignant tumours :**

- Osteosarcoma
- Chondrosarcoma
- Fibrosarcoma
- Malignant – fibrous histiocytoma
- Malignant round cell tumour
- Multiple myelomatosis

c) **Metastatic tumours of bone** – lungs, thyroid, kidney, GI tract, prostrate and breast

Marrow cell disorder:

Histiocytos

Gaucher's disease

Parasitic disease of the bone :

Hydatid disease

Neurotrophic dystrophies of the bone :

Tabes dorsalis

Syringomyelia

Diabetic neuropathy

Iatrogenic pathological fracture :

Through screw hole stress protection phenomenon

Through biopsy

After removal of infected bone

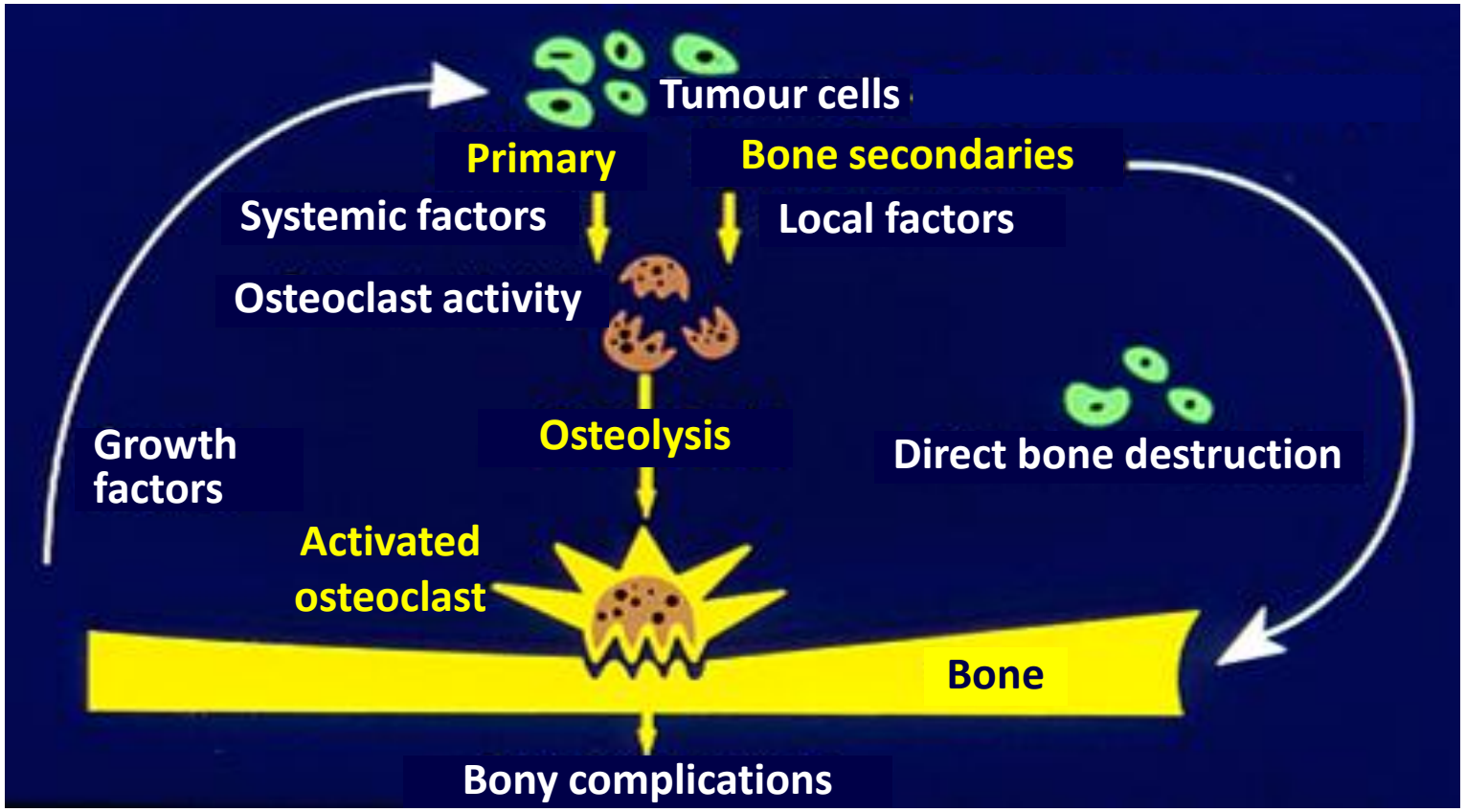
Through a donor site for a bone graft

Clinical Importance and Prognosis of Bone Metastases

	Disease prevalence, U.S. (in thousands)	Bone mets. incidence (%)	Median survival (mo)
Myeloma	**75 - 100**	**70 - 95**	**24**
Renal	**198**	**20 - 25**	**12**
Melanoma	**467**	**14 - 45**	**6**
Bladder	**582**	**40**	**6 - 9**
Thyroid	**207**	**60**	**48**
Lung	**386**	**30 - 40**	**7**
Breast	**1,993**	**65 - 75**	**24**
Prostate	**984**	**65 - 75**	**36**

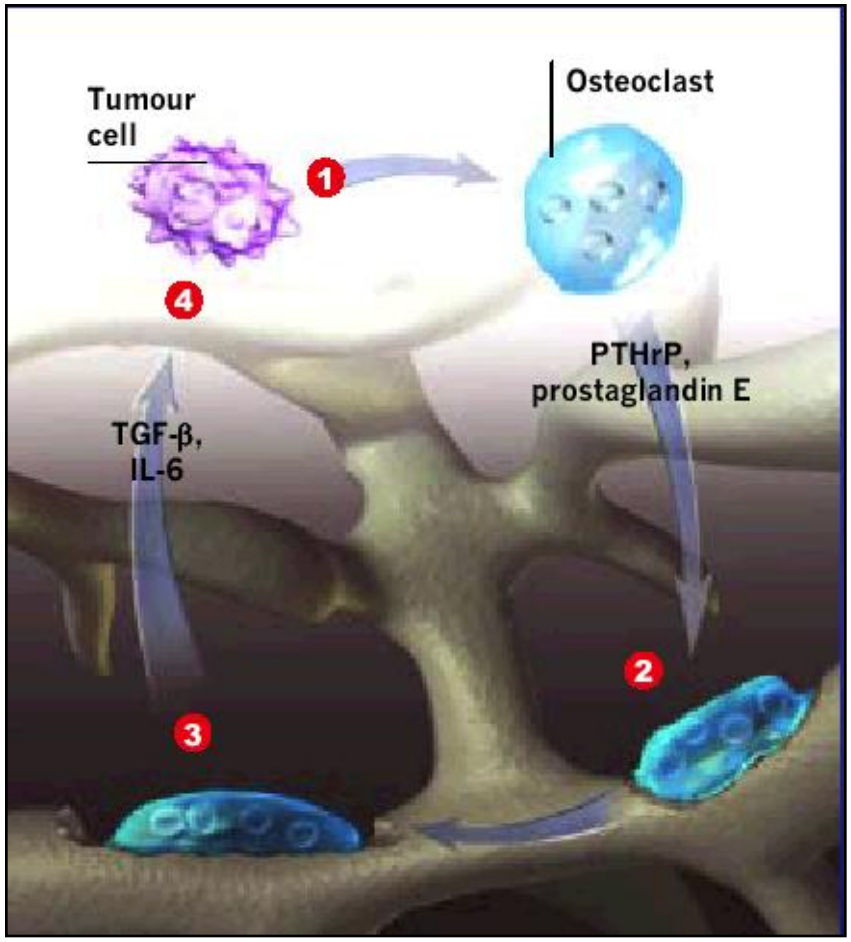
NCI, 1997; International Myeloma Foundation, 2001.

Pathophysiology of Bone Metastases

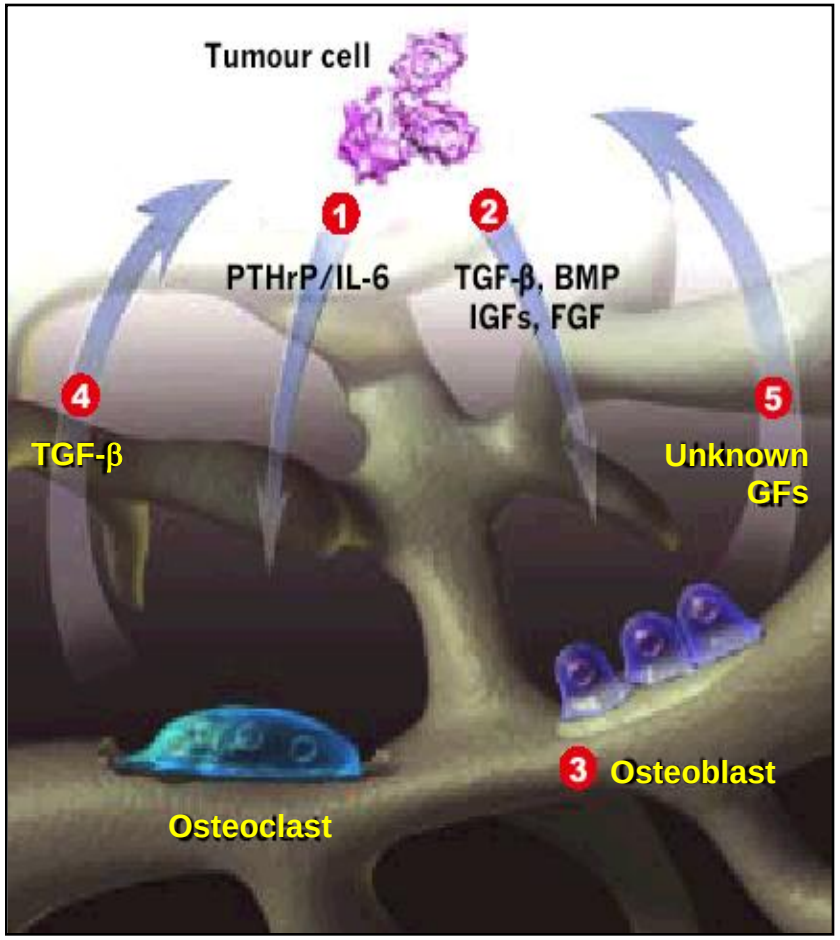


Cancer and Bone Cell Interactions

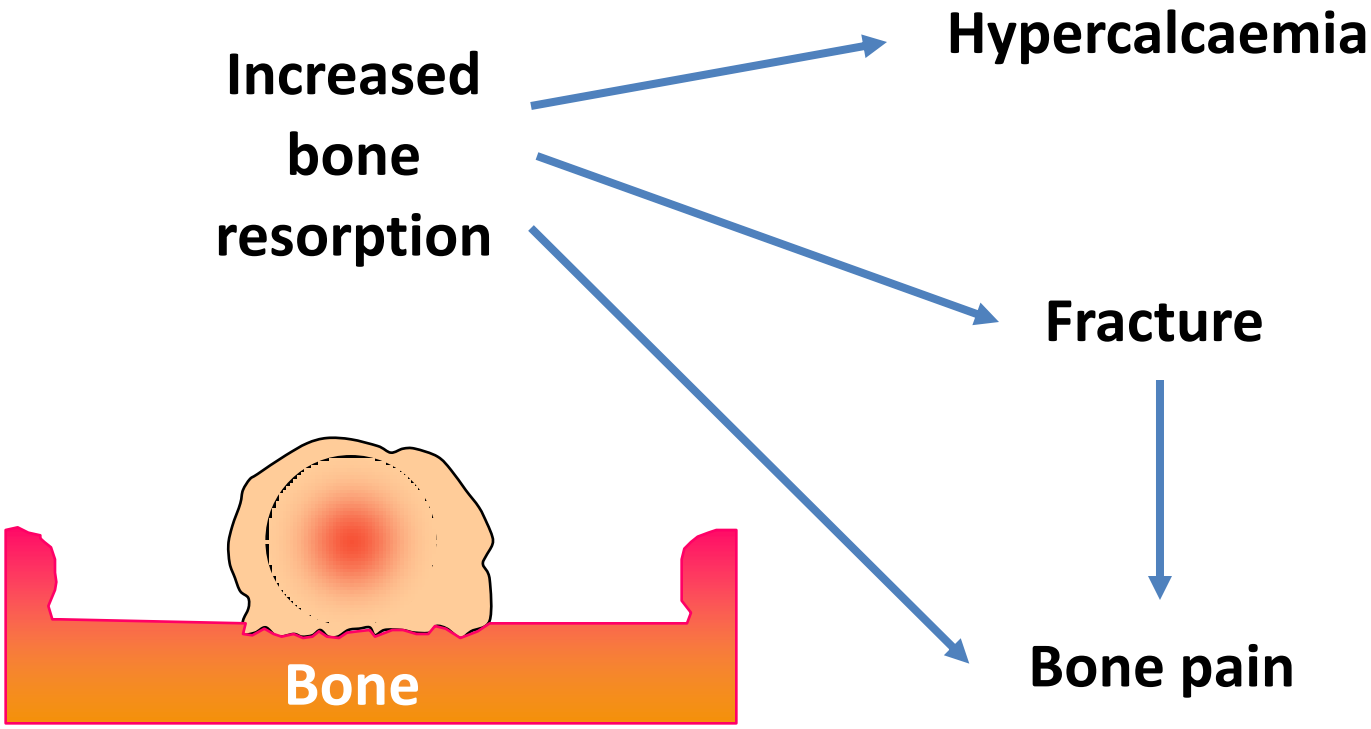
Osteolytic bone disease



Osteoblastic bone disease



Consequences of Increased Bone Resorption



Common cancers which metastatise to bone

Osteoblastic

- Breast
- Prostate

Endothelin – 1

ILGF

Osteolytic

- RCC
- Thyroid
- Lung

Interleukin - 6

PTHrp

Mixed

- Breast

85 % of metastases from Breast, Lung, Prostate

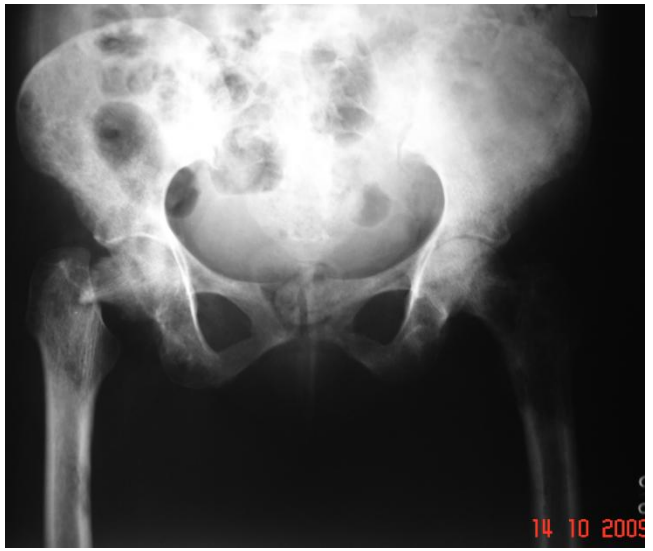
12 % From RCC , Thyroid

3 % GIT

Pathological fracture is suspected when fracture occurs:

- Spontaneously
- After minor trauma
- Unusual fracture pattern
- History of recent several fractures
- Older patient
- History of primary malignancy

➢ Risk factors



INVESTIGATIONS :

RADIOGRAPHY :

PLAIN –X-RAY :

- Study the Fracture
- Don’t ignore the perifracture changes
  - Other lesions
  - Alteration in density and architecture
  - Extra osseous masses or abnormalities

- **Lesion location:**
  - Usually eccentric
  - Cortical involvement
  - Diaphyseometaphyseal junction

- **Densities within the lesion**:
  - Bone formation suggests – Osteosarcoma
  - Calcification suggests – Chondrosarcoma

- **Reaction (periosteal / endosteal)** should be examined.
- Zone of transition
- Moth eaten or permeative pattern of bone reaction

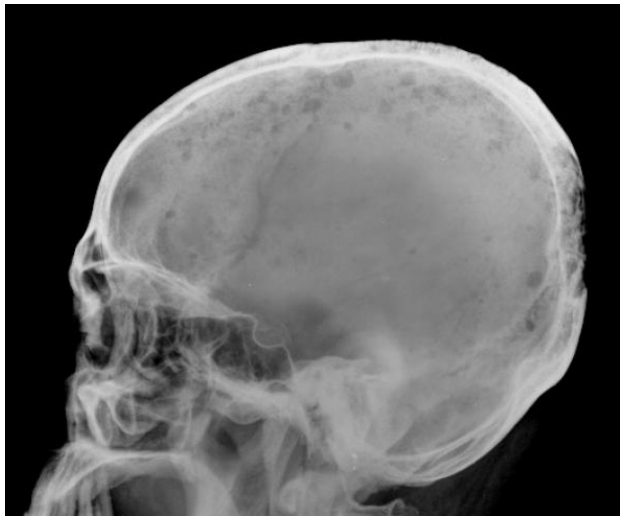
LABORATORY STUDIES :

- ✓ Complete haemogram
- ✓ Peripheral smear
- ✓ Serum glucose
- ✓ Serum albumin
- ✓ Serum calcium, Phosphate
- ✓ Alkaline phosphatase
- ✓ LFT
- ✓ Urine sugar and albumin
- ✓ Bence-Jones proteins
- ✓ Serum electrophoresis

Tumor markers: Ca 125, Ca 19.9, CEA

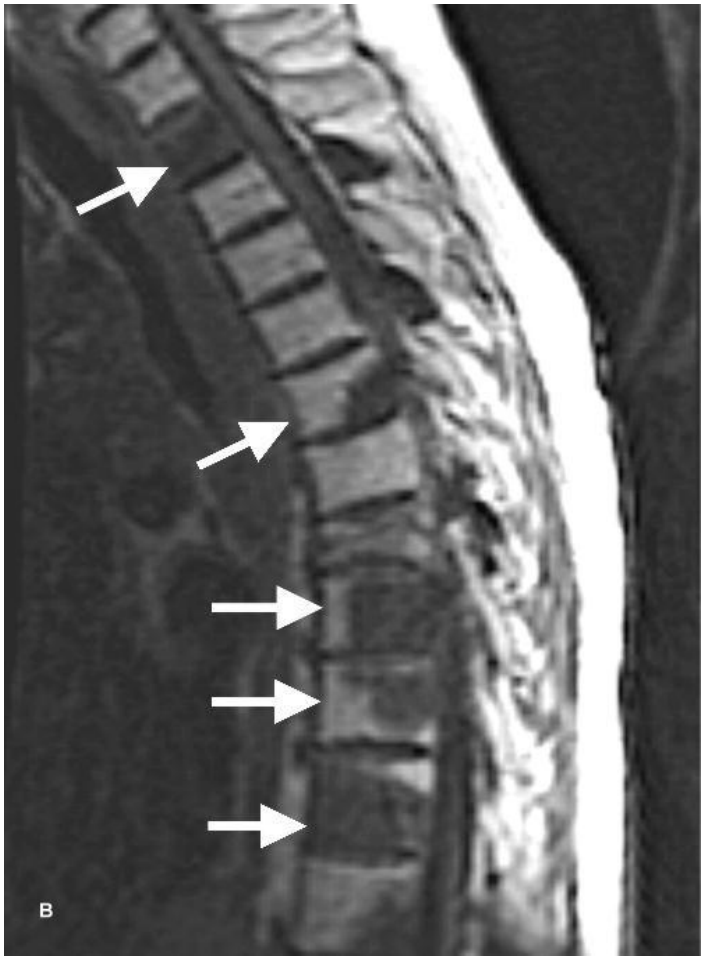
Search for occult primary carcinoma :

- ✓ Breast -
  - Examination
  - Mammography
- ✓ Lung – Chest X-ray
- ✓ Kidney – Ultrasonography
- ✓ Thyroid – Digital palpation
- ✓ Prostate – Serum PSA
  - Digital prostate examination
- ✓ Myeloma – Bone marrow examination
  - Bence-Jones proteins
  - Serum and urine electrophoresis
  - Skeletal Survey - X-ray skull, spine and pelvis.
- ✓ Other organs

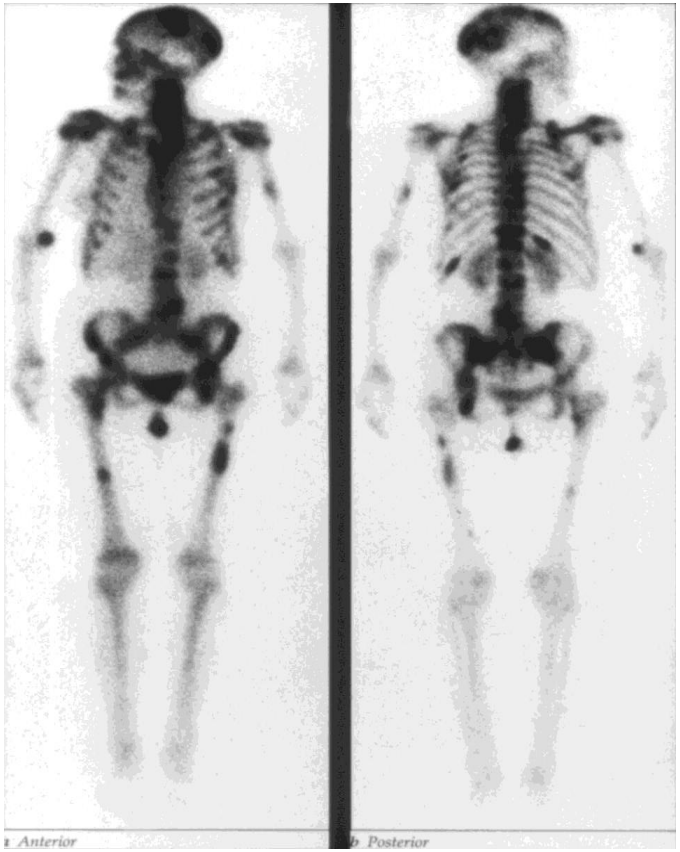


MRI

- Marrow disease
- Epidural and nerve root compression can be detected
- Localize the disease



Bone scan



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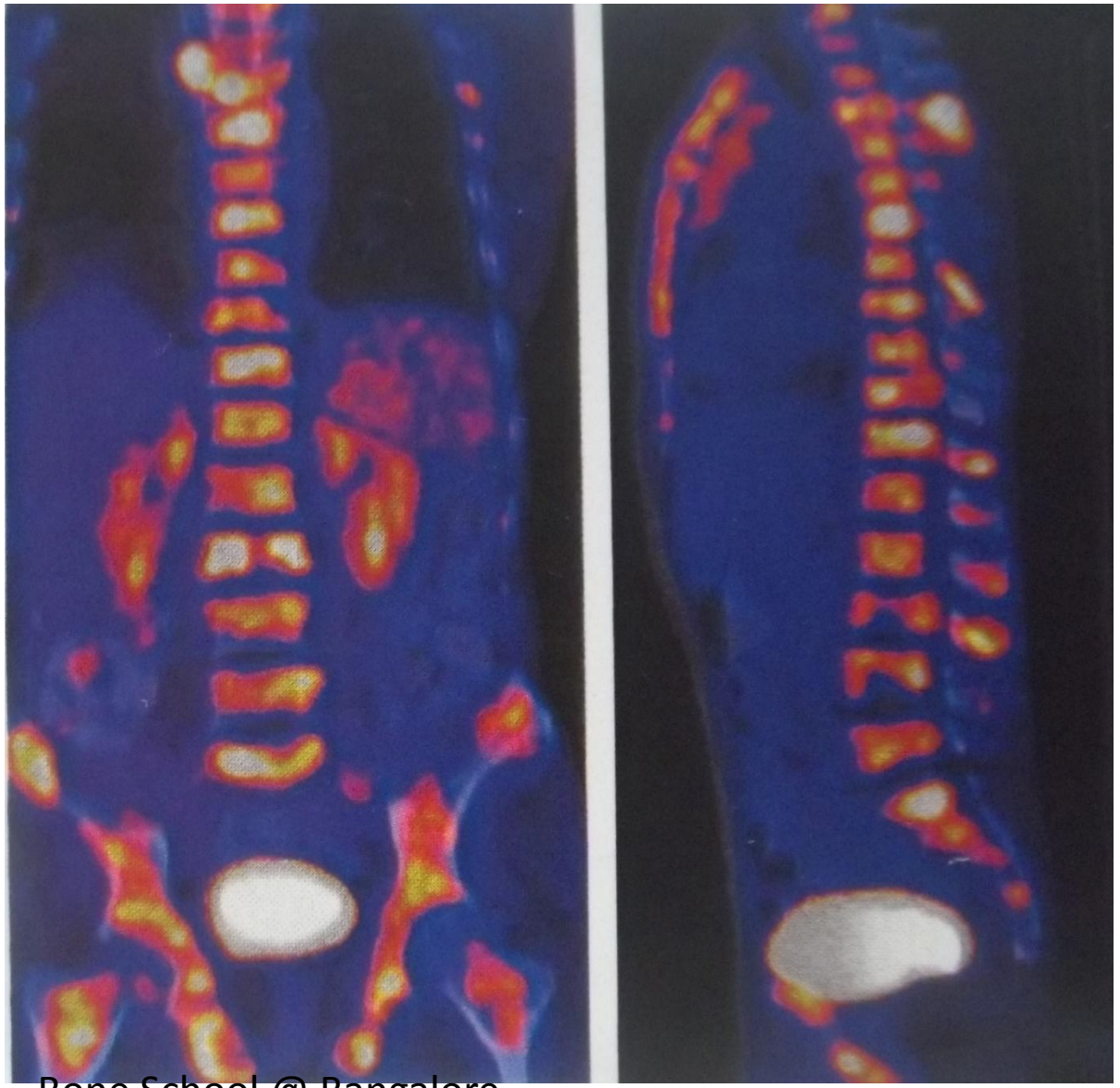
Scan pattern

1. Increased accumulation in the bone - hot lesion
2. Defect cold lesion (MULTIPLE MYELOMA some metastases –breast)
   - rare (very fast growing – no bone reaction)
3. Flare phenomenon – increased number of lesions in the case of effective therapy
4. Super-scan - diffusely increased uptake (spread malignancies)

PET Scan



GOALS OF TREATMENT Metastatic Bone tumors:

To provide pain-free maintenance of normal daily function

Management of Metastatic Bone Tumors

- Management of pain
- Avoiding the fracture
- Bone stabilization

- **Conservative measures**
- **Role of Irradiation**
- **Role of Surgery**

Pain management

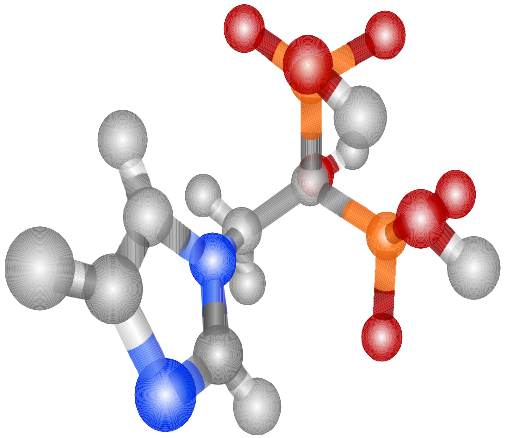
- Non-narcotic analgesics
- Nonsteroidal anti-inflammatory drugs
- Narcotic analgesics
- Interventional anesthetic techniques

Systemic Therapy

- Hormone therapy : Ca breast and prostate
- Chemotherapy
- Bisphosphonates : Zolindronic acid
- Targeted therapy : Denosumab

Mechanism of action – Zolindronic acid

They have affinity for hydroxyapapatite crystals in bone.



1. Inhibit osteoclastic activity.
2. Prevents bone resorbtion.
3. Induces osteoclastic apoptosis.
4. Increases osteoblastic activity
5. Antiangiogenic properties (animal studies)

Radiotherapy

- External-beam radiotherapy
- Stereotactic Body Radiotherapy(SBRT)
- Radiopharmaceuticals : Unsealed source therapy with bone-seeking radionueclides

Indication:

✓ Pain

✓ Impending Fracture/ Fracture (Bone healing)

External RT: Dose and fraction

- 800 cGy in single fraction
- 3000 cGy in 10 fractions
- 2000 cGy in 5 fraction

Multiple painful bony lesion:

- Hemibody irradiation 15-20 Gy given @ 2.5-4Gy/ Fraction
- Radioneuclide therapy

Radionueclides

- Strontium-89, Samarium-153, P-32, Rhenium – 186 are commonly used to treat bone mets
- They get concentrated in highly active site of the bone and emit beta - particles which intern destroy the tumor cells
- It takes 7-14 days to see clinical response and the procedure can be repeated once in 12 weeks

Surgical management

- Indication: Palliative
- Fracture: Ambulation / Pain relief
- Impending fracture

Impending fractures :

Mirel's criteria for risk of fracture :

Number assigned			
Variable	**1**	**2**	**3**
Site	**Upper arm**	**Lower extremities**	**Peritrochanteric**
Pain	**Mild**	**Moderate**	**Severe**
Lesion	**Blastic**	**Mixed**	**Lytic**
Size	**<1/3rd diameter of bone**	**1/3-2/3 diameter of bone**	**>2/3rd diameter of bone**

Mirel's criteria for risk of fracture :

- 7 or less – observation

  8 or more – prophylactic internal fixation

  Most commonly used indication for prophylactic internal fixation of impending fractures are presence of destructive painful lesion 2.5cm in diameter or loss of 50% or more of cortex of long bone.

Prophylactic fixation :

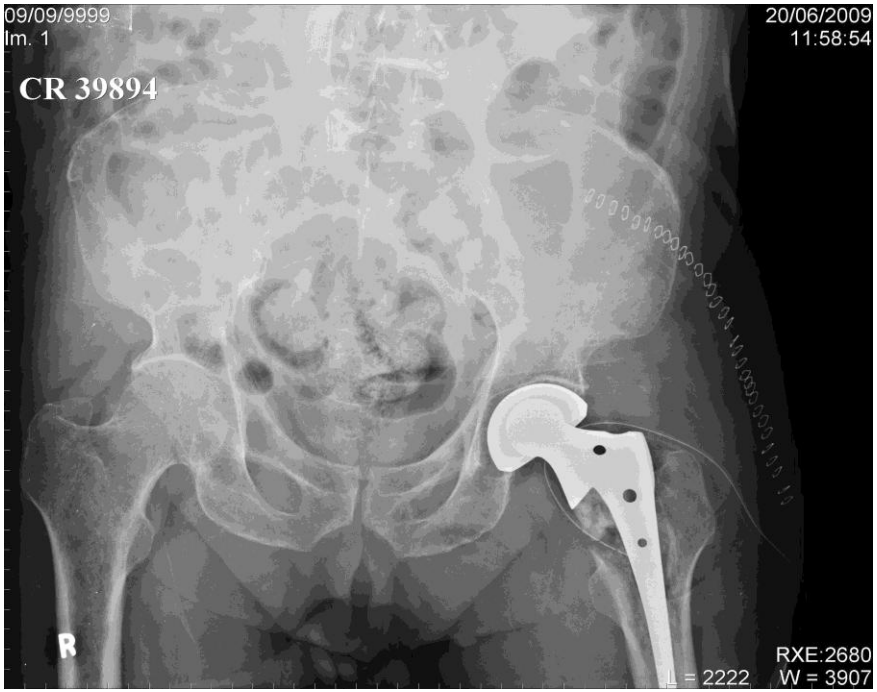
Advantages :

- Decreased morbidity
- Decreased hospital stay
- Easier rehabilitation
- More immediate pain relief
- Faster surgery and less complications
- Less blood loss during surgery

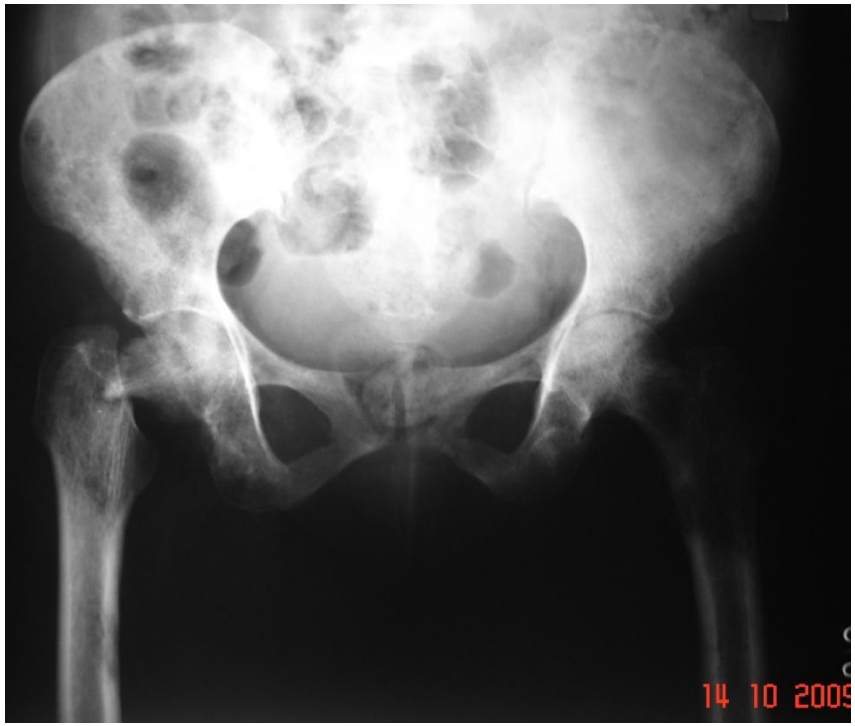
Risks :

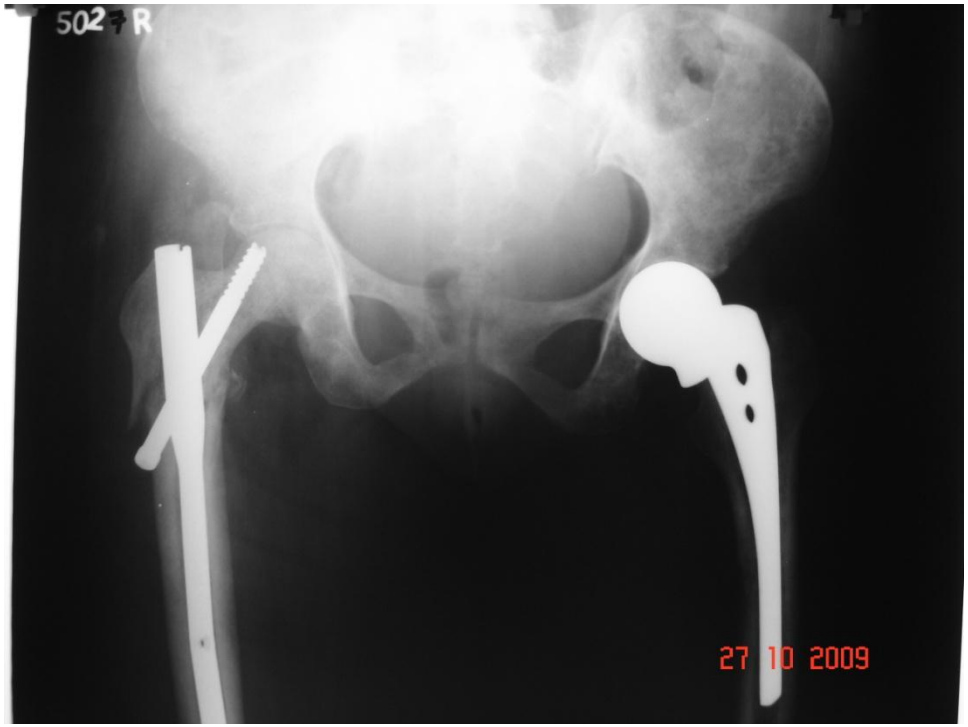
- Temporary
- Fixation device may eventually fail
- Loss of fixation is the most significant complication

Prosthetic replacement



Fracture / Impending fracture





Spine

Solitary lesion

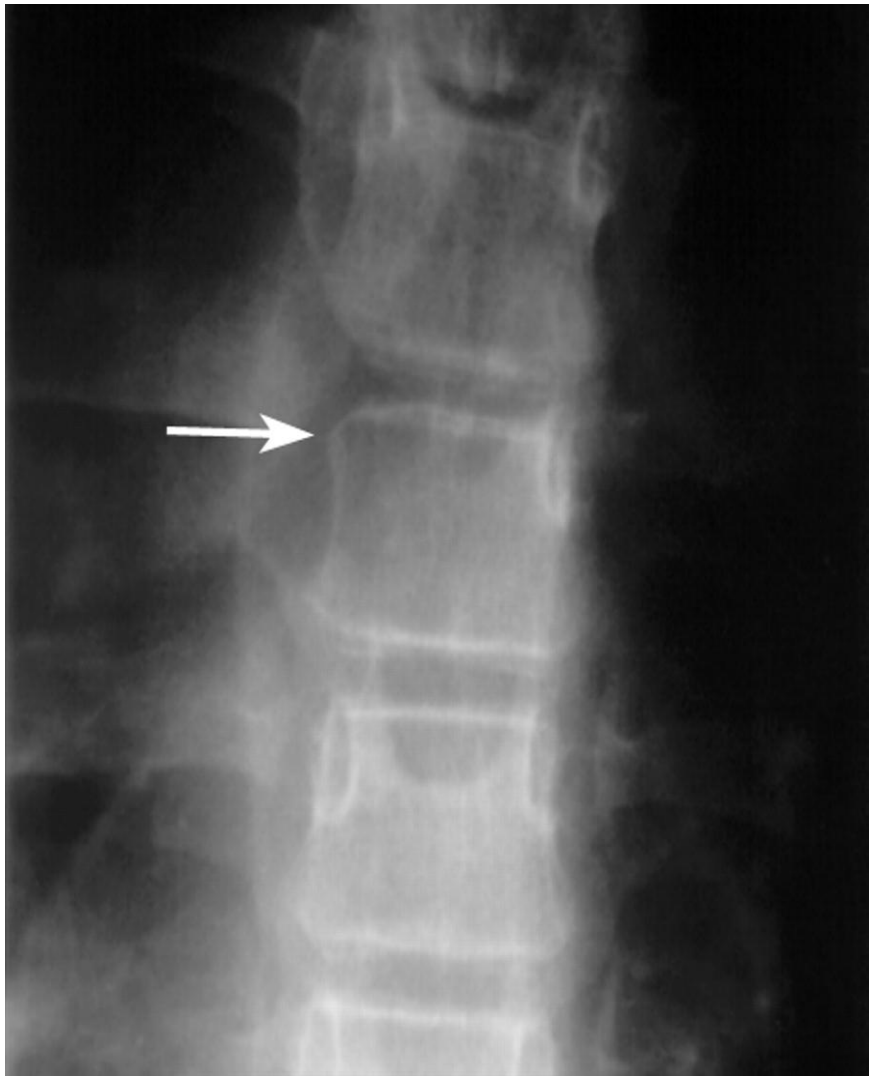
Multiple lesion

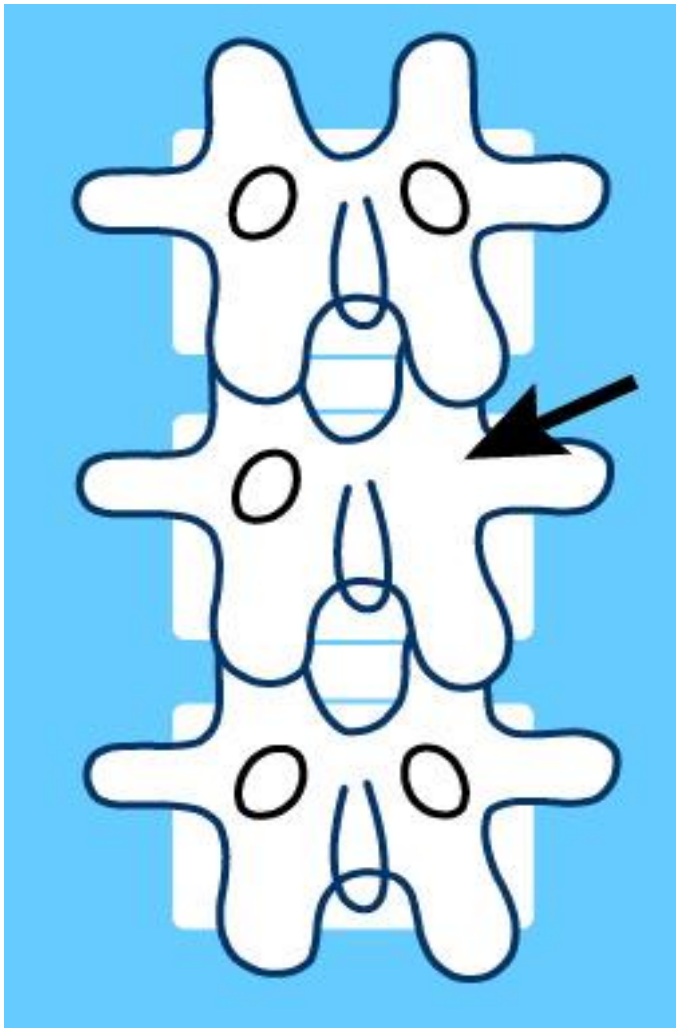
With / without neurological deficit

Management

- Diagnosis
- Prevention of neurological deficits

Winking Owl Sign





MRI Spine

	Score
General condition (Performance status)	
Poor (PS 10-40%) Moderate (PS 50-70%) Good (PS 80-100%)	0 1 2
No. of extraspinal bone metastases foci	
>/= 3 1-2 0	0 1 2
No. of metastases in the vertebral body	
>/= 3 2 1	0 1 2
Metastases to the major internal organs	
Unremovable Removable No metastases	0 1 2
Primary site of the cancer	
Lung, stomach, kidney, liver, uterus, thyroid, prostrate, breast, GI, others	0 1 2
Spinal cord palsy	
Complete Incomplete None	0 1 2

Assessment of Prognosis in Metastatic Spine tumors – Tokuhashi 1990

Treatment plan - Harrington

Class I: No significant neurological involvement

Class II: involvement of bone without collapse or instability and minimal neurological involvement

Recommended treatment for Class I & II:

Chemotherapy and hormonal manipulations. If no response, RT.

Class III: major neurological impairment without significant involvement of bone

Recommended treatment for Class III: usually only RT, if acute onset neurological deficit – add steroids.

Class IV: vertebral collapse with pain attributable to mechanical causes or instability but without significant neurological compromise

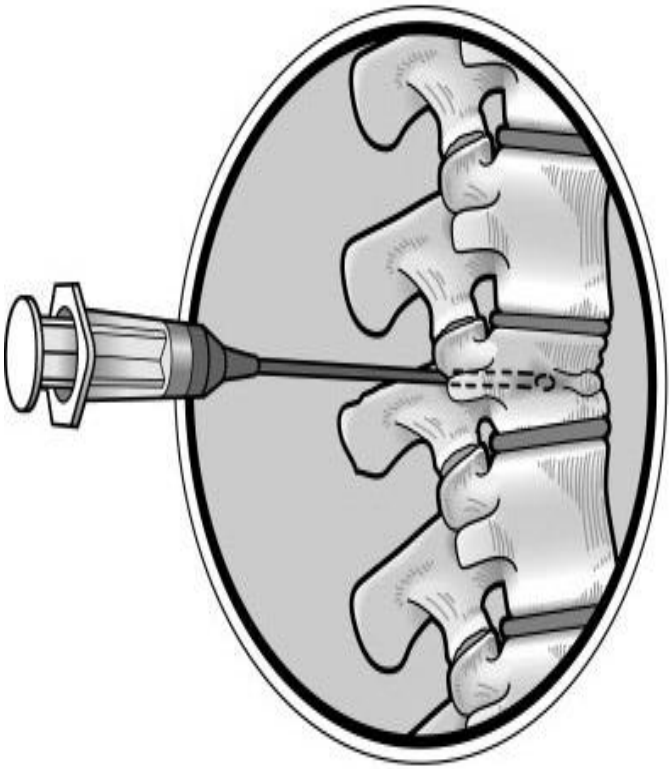
Class V: patients with vertebral collapse or instability with major neurological compromise.

Recommended treatment for Class IV & V: surgical management with adjuvant RT.

Percutaneous Vertebroplasty/Kyphoplasty

PMMA

(Polymethylmethacrylate)



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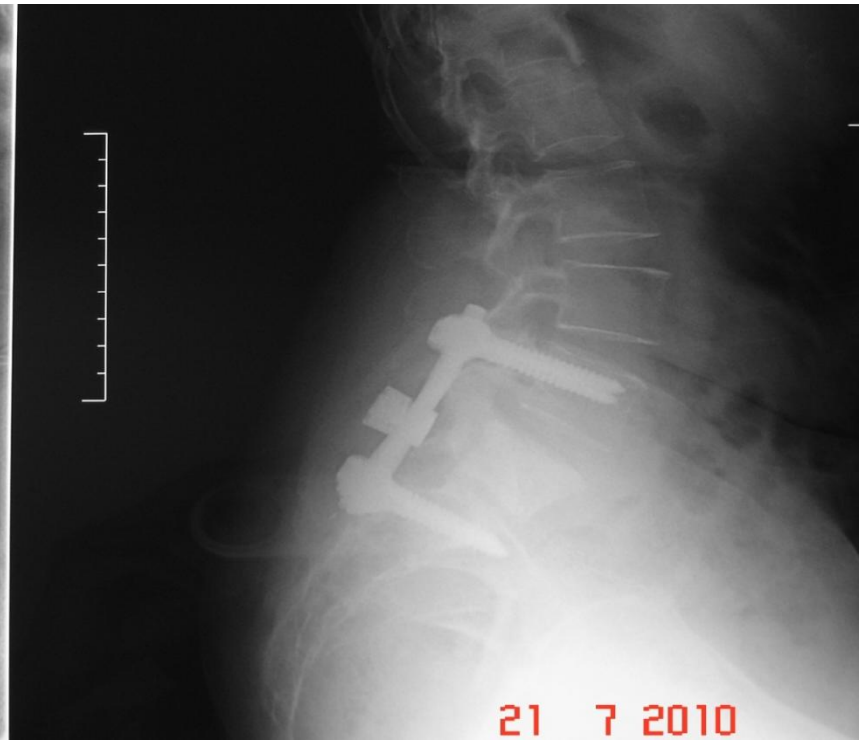
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Spine metastasis: Summary

- Single vertebral metastasis with cord compression: Surgery
- Impending fracture, better projected survival – Surgical fixation and RT
- Multiple spinal mets : RT
- Diffuse skeletal mets with severe pain : Radionuclide therapy

Approach to diagnosis of Metastatic lesion

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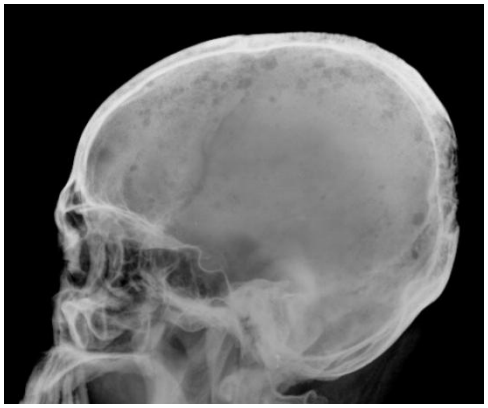
Multiple skeletal lesions

- Conventional approach

- Basic investigations
- MRI
- CT thorax/Abdomen/Pelvis/PET Scan
- Workup for Myeloma
- Tumor markers
- Endoscopy / Colonoscopy
- Biopsy

Investigations



- S. Alk Phosphatase
- Myeloma profile:
  - ESR
  - S. Electrophoresis
  - Bence Jones Proteins
  - Skeletal survey – Skull, pelvis, spine

- True cut core needle biopsy
- Bone marrow aspiration and biopsy

Annals of Oncology 19 (Supplement 2): ii106–ii107, 2008
doi:10.1093/annonc/mdn104

Cancers of unknown primary site: ESMO Clinical Recommendation for diagnosis, treatment and follow-up

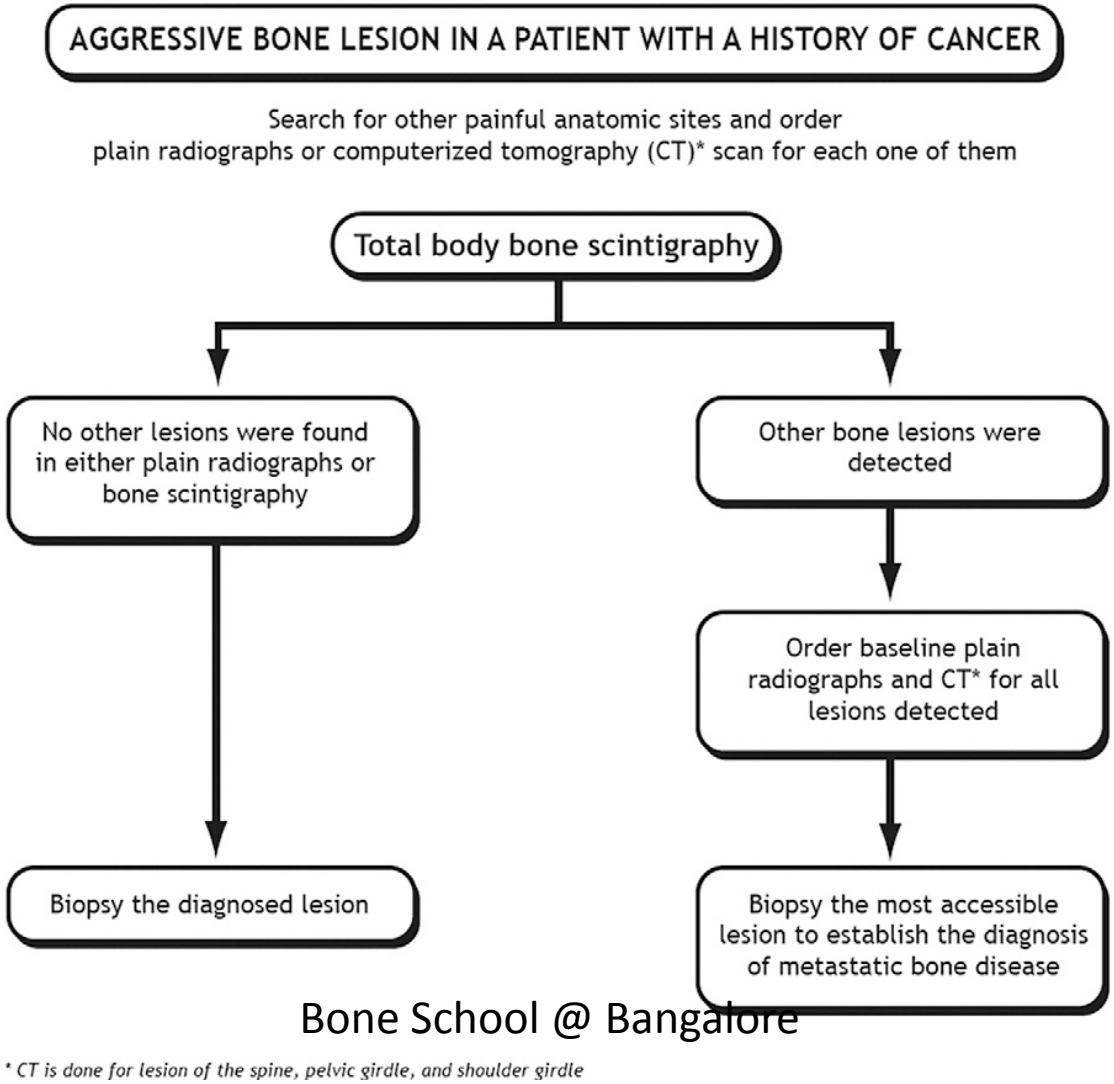
E. Briasoulis[1], N. Pavlidis[2] & E. Felip[3]
On behalf of the ESMO Guidelines Working Group*

[1]Department of Medical Oncology, University of Ioannina, Ioannina Ipiros, Greece; [2]Departr
[3]Medical Oncology Service, Vall d'Hebron University Hospital, Barcelona, Spain

CUP: 3 – 4% of all malignancies

Assessment suggested	Target patient population
Minimal standard work-up	
Thorough medical history and physical examination	All patients
Basic blood and biochemistry survey	All patients
Urinalysis and testing for fecal occult blood	All patients
CT scans thorax, abdomen and pelvis	All patients
Work-up for clinicopathological subsets	
Mammography or breast MRI (optional)	Female with axillary adenopathy
Serum aFP and bHCG	Patients with midline metastatic disease
Serum PSA	Male with adenocarcinoma bone metastases
Head and neck CT scan or CT/PET scan (optional)	Cervical adenopathies with squamous cell carcinoma
Endoscopies	Must be sign or symptom oriented

Algorithm for evaluation of a patient with a known history of Cancer



Never ever give up !

Thank you

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