# PLEASE CLICK ON THE FOLLOWING LINK TO WATCH THE LECTURE ONLINE:-

https://www.youtube.com/watch?v= Ekw6Z6Nzg6A&list=PLuBRb5B7fa\_ey zMA0u7jajzWugcmiRi5s&index=3

# Pathological fracture and metastatic bone disease (SRE)

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# Objectives

- Review the symptoms and physical exam and presentation findings associated with pathologic fractures.
- Outline the approach and staging workup for the bony lesion resulting in a pathologic fracture.
- Summarize the surgical approach to fixation for pathologic fractures.
- Explain the importance of collaboration and communication in treating pathological and metastatic bone disease(skeletal related events) (SRE)



## Introduction

- A pathological fracture is a bone fracture which occurs without adequate trauma and is caused by a preexistent pathological bone lesion.
- The abnormal, weakened bone predisposes the patient for failure during normal activity or after minor (trivial) trauma

# **Demographics US**

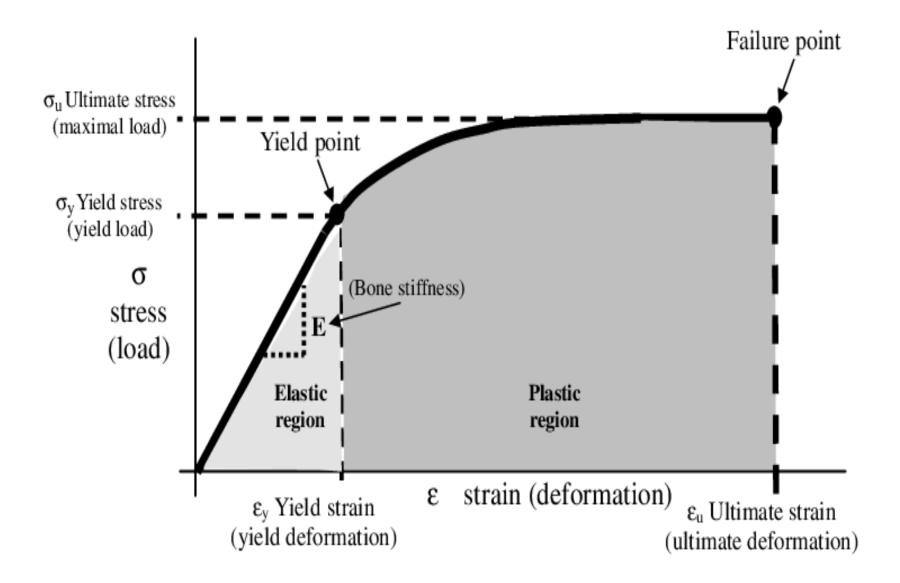
- 2 million people sustain a pathologic fracture related to osteoporosis each year.
- Of patients older than 50 years of age, 24% who sustain a hip fracture die within 1 year.
- One of every two women will have an osteoporosis-related fracture in her lifetime.

- Paget disease affect an estimated 1 million people in the United States.
- 20,000 to 50,000 Americans have osteogenesis imperfecta.
- The American Cancer Society predicts that over 1.8 million new cancer cases will be diagnosed in 2019, and nearly 50% of these tumors can metastasize to the skeleton.

- Stress (fatigue) fracture (normal bone).
- Insufficiency (fragility) fracture (metabolically weakened bone).
- Pathological fracture (weakened by tumor).



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- Why pathological fracture occur?
- Not enough time to the bone to remodel(plastic deformation)
- Abnormal bone micro and macrostructure

### Factors Suggesting a Pathologic Fracture

- Spontaneous fracture
- Fracture after minor trauma
- Pain at the site before the fracture
- Multiple recent fractures
- Unusual fracture pattern ("banana fracture")
- Patient older than 45 years (or 40)
- History of primary malignancy

# Etiology

- Congenital (developmental)
- Infectious
- Metabolic
- Neoplastic

- Correctable conditions:
- Renal osteodystrophy, hyperparathyroidism, osteomalacia, and disuse osteoporosis.

- Uncorrectable conditions:
- Osteogenesis imperfecta, polyostotic fibrous dysplasia, postmenopausal osteoporosis, Paget disease, osteopetrosis, and malignancy.

 What is in common between the two categories is that they are weak bones that are predisposed to fracture or plastic deformation, healing often occurs slowly, and may end up with nonunion.

### Osteoporosis

- The most common condition associated with pathologic fractures.
- Proximal femur, vertebrae, and distal radius.
- They only require minor modifications of typical fracture care.

1) Increase the risk of fracture from daily activities and low energy falls.

2) Higher rate of metal failure because of poor anchorage of implants in the weak bone .

- The fracture resistance of osteoporotic bone is a function of the third power of the bone mineral density (BMD)(a small change in bone density results in an exponentially large increase in fracture risk.)
- BMD is measured by dual-energy x-ray absorptiometry (DEXA).
- Quantitative CT (qCT) can detect local changes in BMD

- Use implants with sufficient fixation strength to support weight bearing.
- Failure of implants in osteoporotic bone occurs by loss of fixation in bone rather than by breakage of the implant.
- Screw fixation strength is highly dependent on cortical thickness.(A 1-mm loss in cortical thickness can result in a 50% decrease in the strength of screw fixation)

- Bicortical fixed angle locking screws in thin cortical bone improves the ability of a plate to resist loading, But may increase the risk of periprosthetic fractures in bending.
- It is often not possible for the elderly patient to limit loads postoperatively(WT bearing)

- Minimum Bone Mineral Density for Fixation Failure
- Location Minimum BMD for Implant Stability (mg/cm3)
- Proximal femur 250
- Proximal humerus 95
- Vertebral body (pedicle) 95
- Vertebral body 220

 Fixation strategies that emphasize placement of screws in the regions of strongest trabecular bone result in superior biomechanical and clinical results.(NOF, proximal humerus)

### How to approach

• History:

age ,sex, pain at rest, trauma scenario, Hx of other disease(breast, prostate, thyroid, kidney), medication(steroids, phyntoin, heparin),known previous lesion, review of systems, constitutional symptoms (recent weight loss, fevers, night sweats, and fatigue), Hx of irradiation, toxic exposures, smoking.

Age	Well-defined	ill-defined	Sclerotic
	3		
0 - 10	EG SBC	EG - Ewing Osteosarcoma Leukemia	Osteosarcoma
10 - 20	NOF, Osteoblast Fibr dysplasia EG SBC ABC Chondroblast CMF	Ewing EG Osteosarcoma	Osteosarcoma Fibr dysplasia EG Osteoid osteo Osteoblastoma
20 - 40	Giant CT Enchondroma Chondrosarcoma (low grade) HPT - Brown tumor Osteblastoma	Giant CT	Enchondroma Osteoma Bone island Parosteal Osteosar Healed lesions: - NOF, EG - SBC, ABC - Chondroblast
40+	Metastases Myeloma Geode	Metastases Myeloma Chondrosarcoma (high grade)	Metastases Bone island
All ages	Infection	Infection	Infection

#### Physical examination:

- Thorough evaluation of the affected skeletal region.
- Detailed neurovascular examination of the extremities are essential.
- All extremities and the entire spine should be evaluated for additional lesions.
- Look for lymphadenopathy.
- Careful evaluation of all possible primary sites (breast, prostate, lung, thyroid)

# Laboratory studies

- CBC (Anemia)
- KFT, BUN
- ESR,CRP
- LFT
- PTH
- Albumin
- Calcium
- Phosphorus
- Alkaline phosphatase
- Urine analysis
- Serum and urine protein electrophoreses /Bence jones protien
- TFT, (CEA), CA125, and (PSA), CA15-3, CA19-9, serum markers for specific tumors

# **Disorders producing Osteopenia**

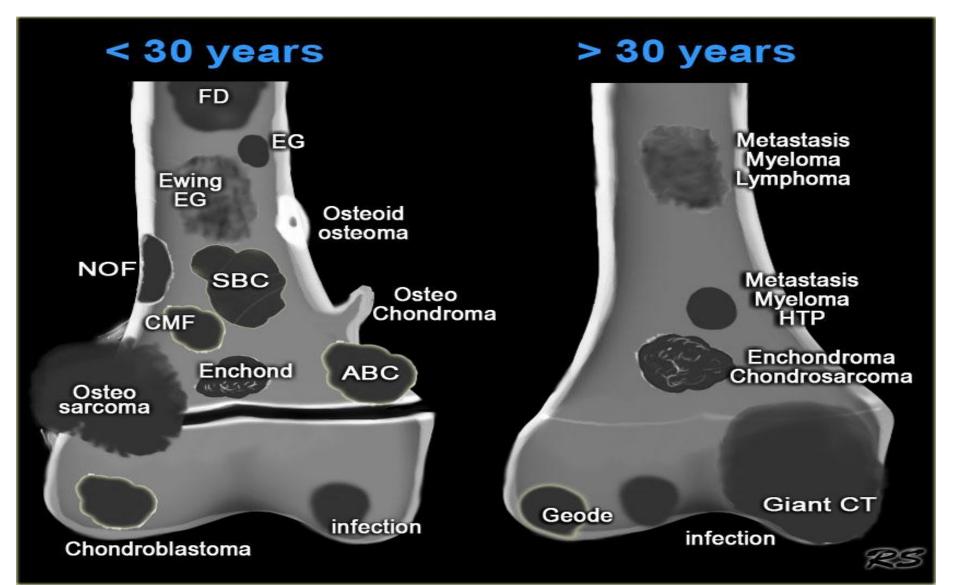
Disorder	Serum Calcium	S. Phosphorous	S. Alkaline phosphatase	Urine Calcium
Osteoporosis	N	Ν	N	Ν
Osteomalacia	Low	Low	High	Low
Hyperparathyroidism	High	Low	Normal	High
Renal Osteodystrophy	Low	High	High	
Pagets disease	Ν	Ν	High	Hydroxyproline
Myeloma	N	Ν	Ν	Light chains

# **Imaging Studies**

- Plain Radiographs :
- 2 planes AP,LAT , joint above and below
- Where is the lesion?
- What is the lesion doing to the bone ?
- What is the bone doing to the lesion?(Periosteal reaction)
- What are the clues to the tissue type within the lesion?

- Systematic approach:
- Location
- Pattern of bone destruction
- Visible tumor matrix
- Periosteal reaction
- Soft tissue component

### Where is the lesion?

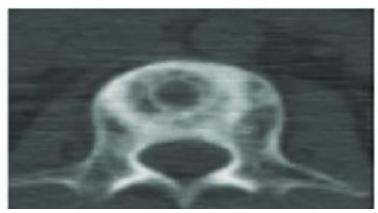


#### What is the lesion doing to the bone ?

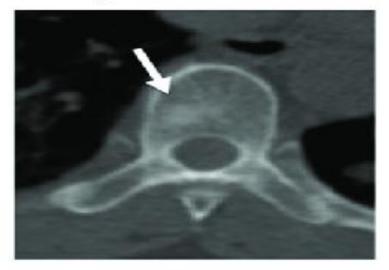
#### Osteoblastic



#### Mixed type



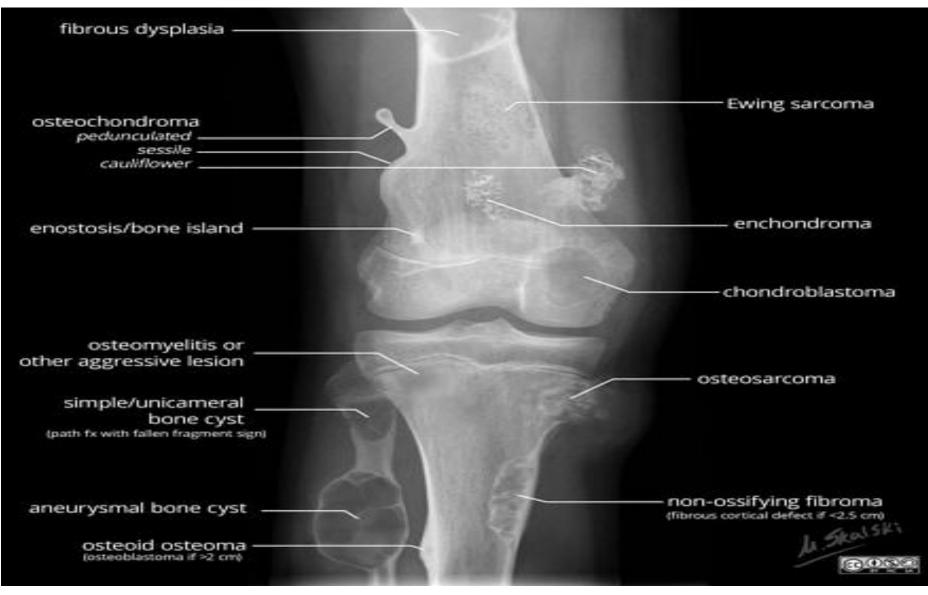
#### Mildly osteoblastic



#### Osteolytic

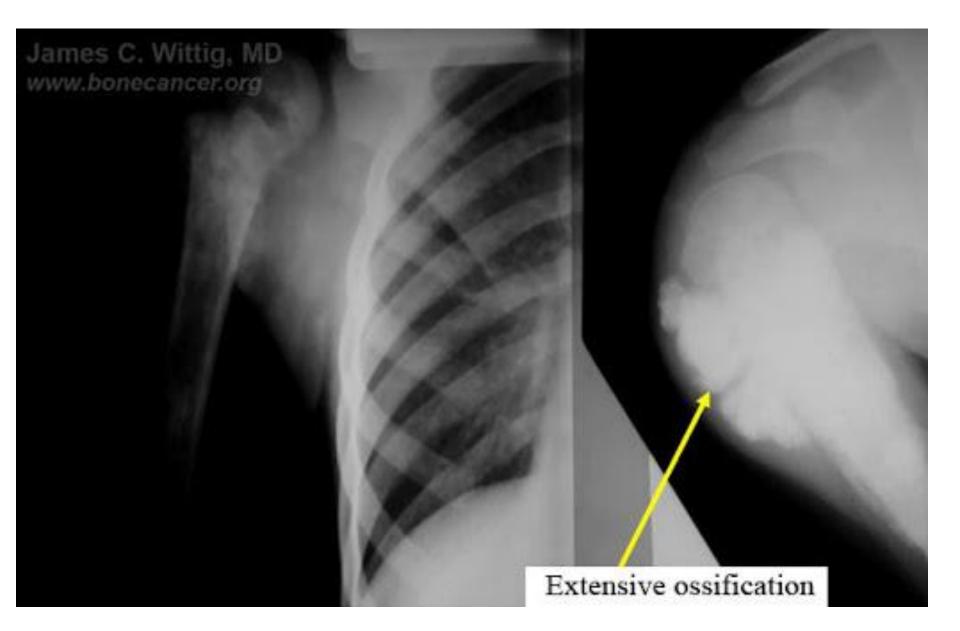


#### What is the bone doing to the lesion?



# What are the clues to the tissue type within the lesion?



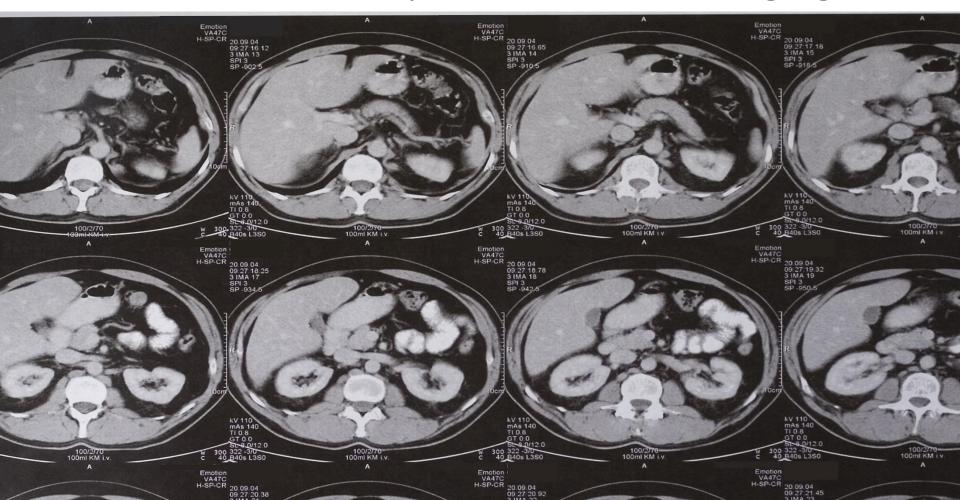


 When an osteolytic or osteoblastic lesion is noted in otherwise normal bone, the process is most likely neoplastic.



## Radiology

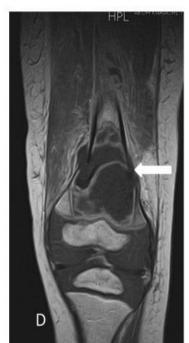
• Chest, abdomen, pelvic Ct scan for staging



- MRI :
- Detailed study of the involved lesion.



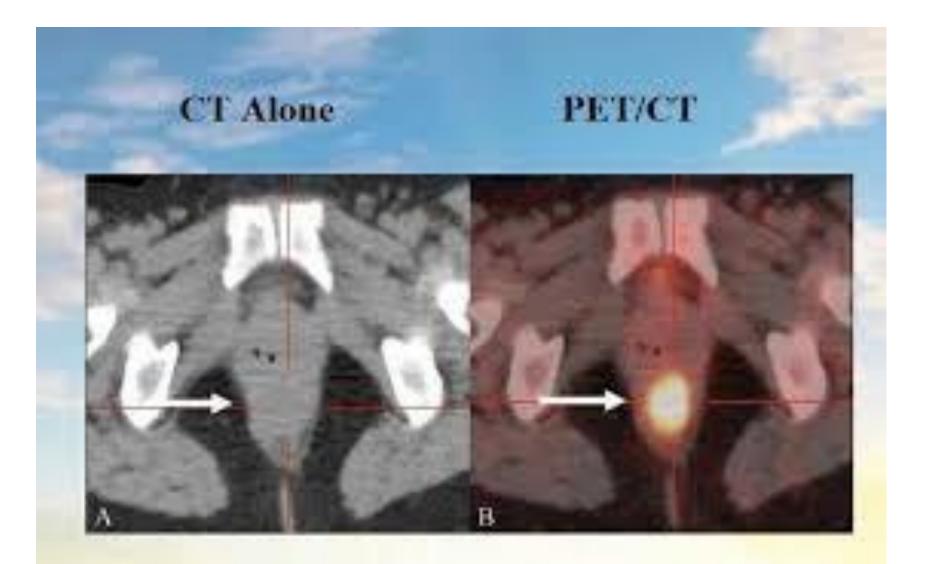




- Nuclear Medicine Studies :
- Technetium bone scintigraphy single or multiple lesions, Multiple myeloma and RCC are falsely negative on a bone scan.
- Positron emission tomography (PET) or correlated wit CT, lymphoma and lung CA.

 In a recent study, PET-CT scanning had higher sensitivity and specificity than PET scanning alone for detection of malignant bone lesions



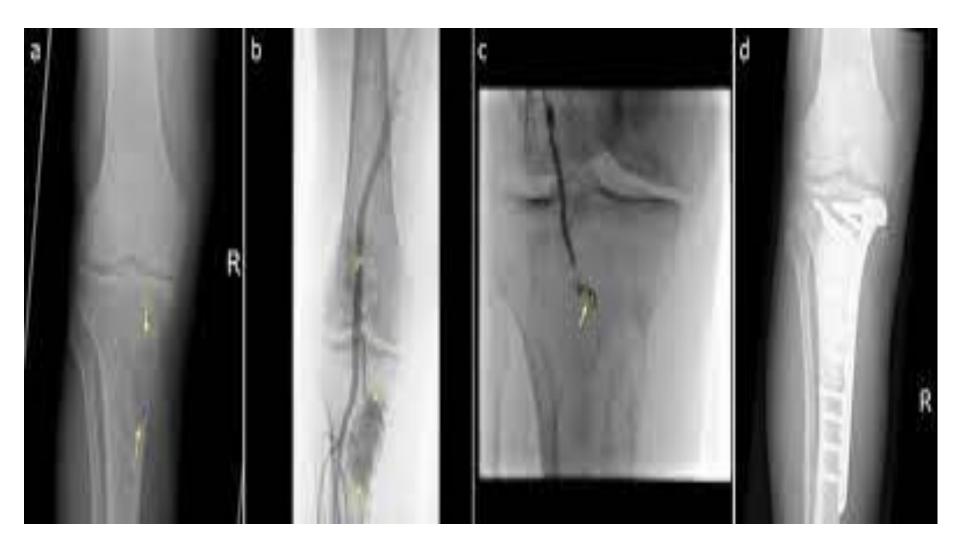


### SAE( selective arterial embolization)

 A standard angiogram is still useful when embolizing feeding tumor vessels in vascular lesions such as metastatic RCC or multiple myeloma or metastatic thyroid CA as definitive or adjuvant treatment before surgery.

### RCC mets to proximal femur





# Biopsy

- If we fail to reach a diagnosis after all the investigation were done a biopsy should be considered.
- a solitary bone lesion in a patient with or without a history of cancer should be biopsied to obtain an accurate diagnosis
- Patient older than 40years with pathological fracture upon trivial trauma should be labeled as mets until proven otherwise

 If the patient has a remote history of cancer or who has no known metastasis to bone, a biopsy should be performed to confirm that the lesion is not a primary sarcoma.

### Aspiration cytology (Fine Needle Aspiration Cytology (FNAC)

 This is a technique used to obtain material from organs or lesions by needle aspiration. It is valuable in diagnosis of lesions of the breast, thyroid, lymph nodes, liver, lung, soft tissue ...etc.



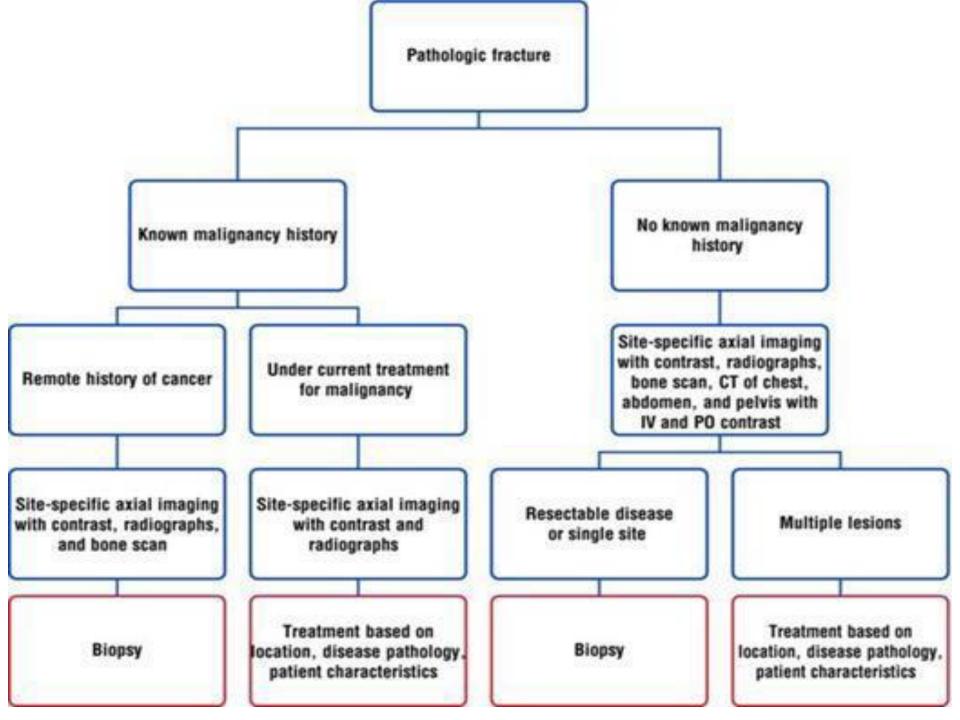
• Tru-cut needle



- Open Bx
- Stick to biopsy taking principle
- Cultures should always be sent at the time of biopsy to rule out infection.
- Frozen section can be used when taking the Bx

## Comprehensive Evaluation of a Patient with pathological fracture or impending

- History: Thyroid, breast, or prostate nodule
- Review of systems: Gastrointestinal symptoms, weight loss, flank pain, hematuria
- Physical examination: Lymph nodes, thyroid, breast, lungs, abdomen, prostate, testicles, rectum
- Plain x-rays: Chest, affected bone (additional sites as directed by bone scan findings)
- 99mTc total body bone scan (FDG-PET scan in selected cases such as lymphoma)
- CT scan with contrast: Chest, abdomen, pelvis
- Laboratory: Complete blood count, erythrocyte sedimentation rate, calcium, phosphate, urinalysis, prostate specific antigen, immunoelectrophoresis, and alkaline phosphatase
- Biopsy: Needle vs. open



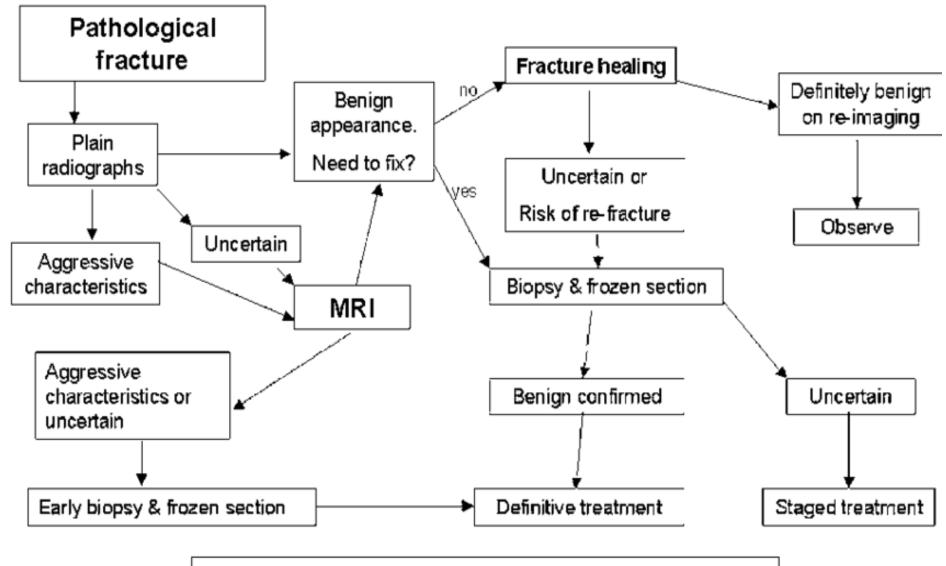
### Fractures Through Primary Benign Bone Tumors

- Most commonly in children and young adults.
- Most tumors gradually enlarge until the patient reaches skeletal maturity and then resolve or become inactive.
- Most can be treated nonoperatively in a cast until the fracture heals.

- Indications for surgical treatment:
- unacceptable deformity in a cast.
- Open fracture.
- Fracture nonunion.
- Aggressive lesions such as (GCT).
- Any lesion in proximal femur.

 In treating ABC Bx should be taken as telangiectatic osteosarcomas can appear radiographically similar.

### Algorithm



NO FIXATION UNTIL HISTOLOGICAL DIAGNOSIS

### Impending Pathologic Fractures

(CT-based structural rigidity analysis (CTRA))

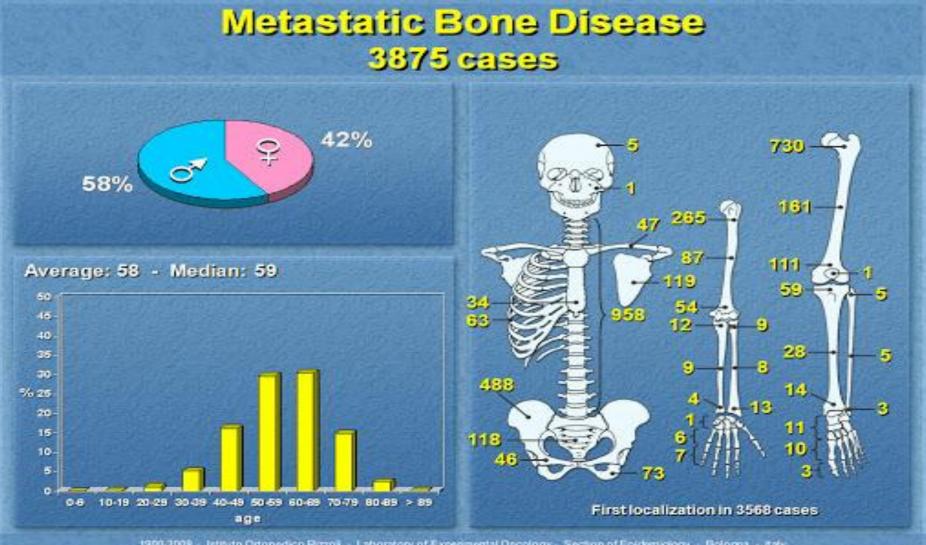
Mirel's criteria score > 8 suggests prophylactic fixation						
Score	1	2	3			
Site	upper limb	lower limb	peritrochanteric			
Pain	mild	moderate	functional			
Lesion	blastic	mixed	lytic			
Size	< 1/3	1/3 to 2/3	> 2/3			

## Benefits of prophylactic stabilization of an impending fracture

- Shorter hospitalization (average 2 days)
- Discharge to home more likely (40%)
- Immediate pain relief
- Faster and less complicated surgery
- less blood loss
- Quicker return to premorbid function
- Improved survival
- Fewer hardware complications
- Fracture risk is greatest during surgical positioning, preparation, and draping.

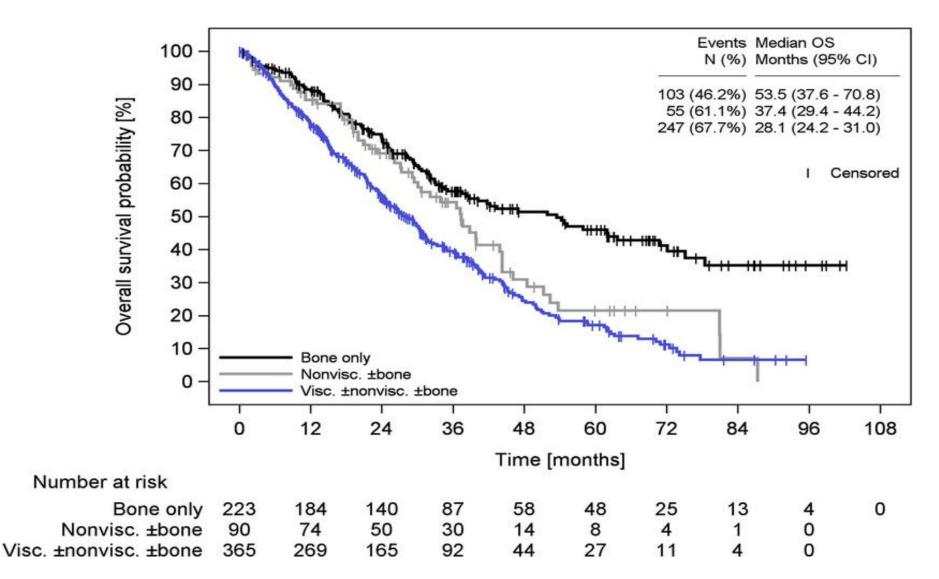
# Treatment Options for Metastatic (pathological) fracture

- Patients with cancer tend to be living longer.
- Advances in systemic treatment, pain control, and local modalities including radiation and surgery.
- Improve the quality of remaining life.
- They require multidisciplinary care.
- Nutrition is of particular concern.
- Higher chance of embolic events and liable for infection.



1950-2009 - Istitute Ortopedico Rizzoli - Laboratory of Experimental Oncology - Section of Epidemiology - Bologna - Italy

# Metastatic load & the length of survival.





#### Tuble 0

Mean Survival by Tumor Histology in Patients Treated for Metastatic Spine Disease<sup>23</sup>

Histology	Survival (mo)
Thyroid	26
Breast	19
Prostate	18
Rectal	18
Renal	10
Lung	6
Unidentified carcinoma	5

### Metastatic Bone Disease Is Prevalent in Patients With Lung Cancer

		5-year world prevalence, thousands <sup>1</sup>	Incidence of bone metastases in cancers <sup>2</sup>	Median survival, months <sup>2-4</sup>	
More lytic	Myeloma	144	70 - 95	6 - 54	
	Renal	480	20 - 25	12	
	Melanoma	533	14 - 45	6	tic
	Bladder	1,000	40	6 - 9	blastic
	Thyroid	475	60	48	More b
	Lung	1,394	30 - 40	6 - 7	Me
	Breast	3,860	65 - 75	19 - 25 🚽	
	Prostate	1,555	65 - 75	12 - 53	$\mathbf{\nabla}$

1. Ferlay J, et al. *IARC Globocan 2002*. http://www-dep.iarc.fr; 2. Coleman RE. *Cancer Treat Rev.* 2001;27(3):165-176; 3. Coleman RE. *Cancer.* 1997;80(8 suppl):1588-1594; 4. Zekri J, et al. *Int J Oncol.* 2001;19(2):379-382.

- N-telopeptide of type I collagen (NTX) identified as a bone marker for skeletal metastases.
- Elevated urinary levels of NTX increased the risk of (SREs).
- Prognostic factor(survival rate)

- Skeletal related events (SREs) :
- Pathological fracture.
- Spinal cord compression.
- Bone pain.
- Hypercalcemia

Treatment Options for Metastatic (pathological) fracture

- Non-operative
- Operative

### Non-operative

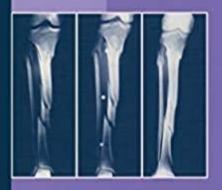
- Bracing
- Nonsurgical candidates :
- limited life expectancies <6 weeks</li>
- Severe comorbidities.
- Small lesions.
- Radiosensitive tumors
- More applicable in upper extremity lesions.
- Bone may or may not heal.



#### A. Sarmiento · L. L. Latta

### Functional Fracture Bracing

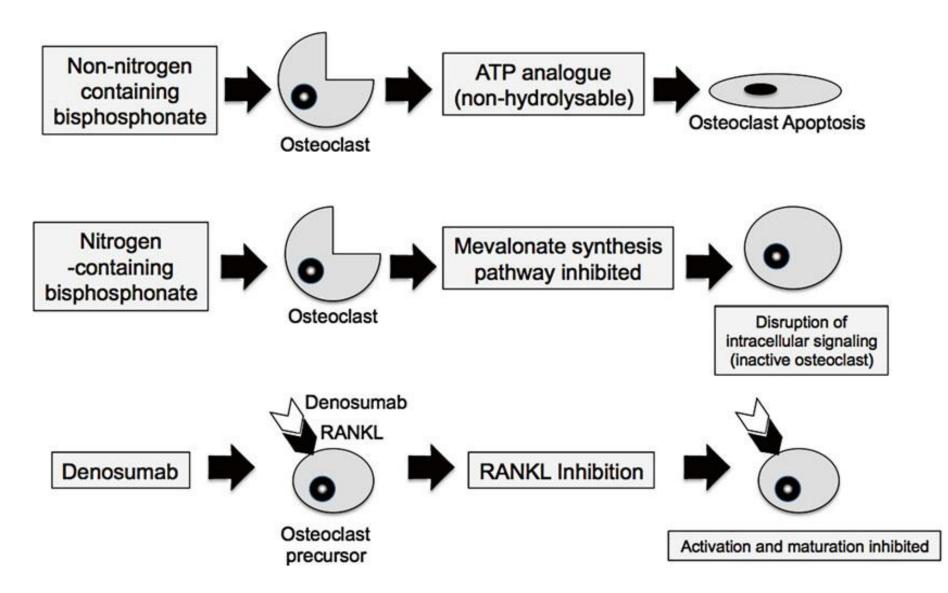
Tibia Humerus Ulna





### Medications

- Biphosphonates
- Denosumab



### Bisphosphonates

- One of the key pharmaceutical treatments that assist in the prevention of pathologic fractures in patients with bone metastases.
- Zoledronic acid was shown to effectively decrease the rate of SREs.
- Bisphosphonates is known as a mainstay pharmaceutical agent in decreasing the risk of pathologic fracture, SRE.
- Normalizing the levels of NTX.

- Because these drugs are retained in the bone, they characteristically have a half-life spanning multiple years and may have effects lasting for years after administration.
- Treatment with them should be initiated when bone metastases are diagnosed.
- Remember the risk of atypical fracture, jaw necrosis.

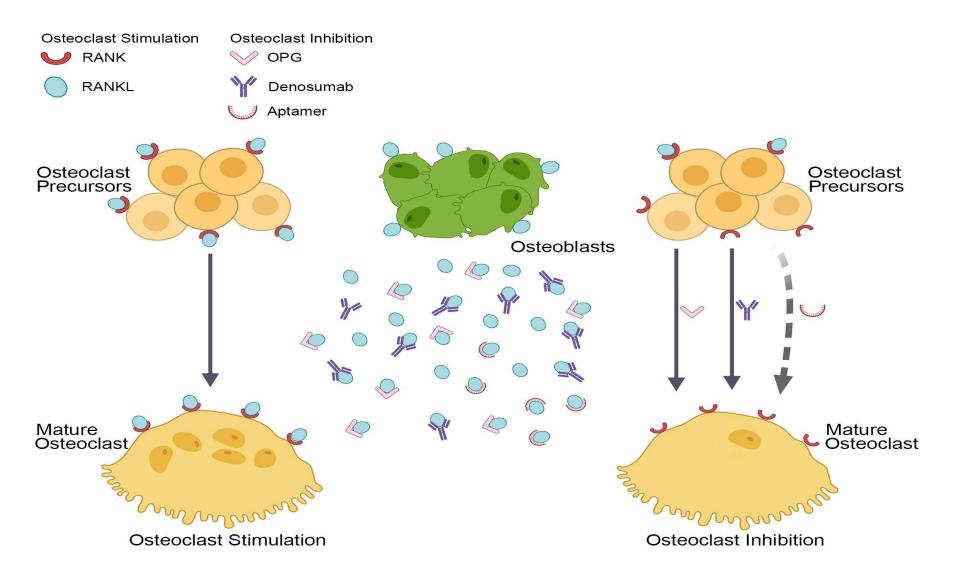
### pre-existing stress fracture. Pain always precede the fracture .

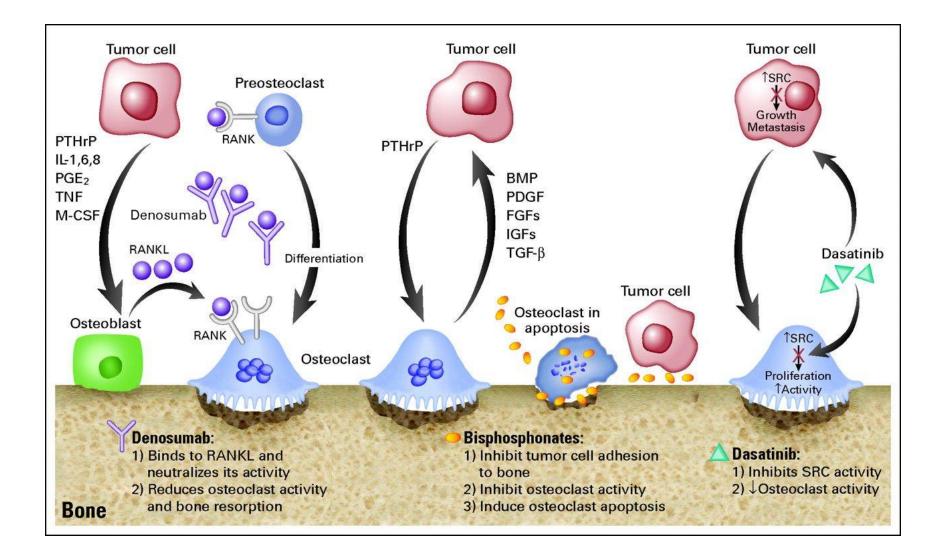




### Denosumab

- Fully human monoclonal antibodies against RANKL.
- A key cytokine in recruiting osteoclasts for bone resorption.
- Denosumab binds to and inhibits RANKL, which inhibits osteoclast maturation and activation.





 In most comparisons studies Denosumab appears to be more effective than bisphosphonates with the exception of multiple myeloma.

# **Radiation Therapy**

- External beam irradiation is the most common treatment used for palliation of bone metastases(treat pain).
- Studies have shown that external beam irradiation provides relief in patients with metastatic bone pain.
- local radiation therapy typically results in partial relief in over 80% of patients with bone metastasis and complete pain relief in 50% to 60% of cases.

- Retrospective data have shown that postoperative radiation improves limb function and decreases the rates of second orthopedic procedures.
- Radiation can usually begin 2 weeks after the surgical procedure.

# Radiofrequency Ablation and Cryoablation

- RFA uses a radiofrequency probe placed directly at the lesion site, typically under CT guidance(IR).
- A recent study of patients with pelvic and sacral metastasis treated with RFA showed a clinical benefit with significant pain relief in 95% of patients.

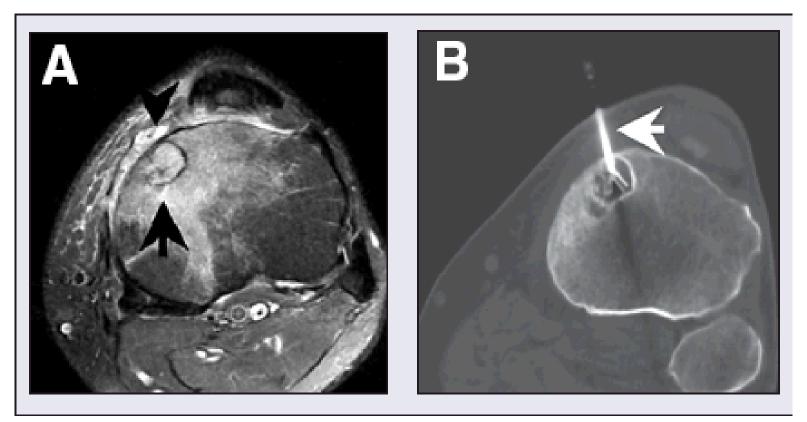
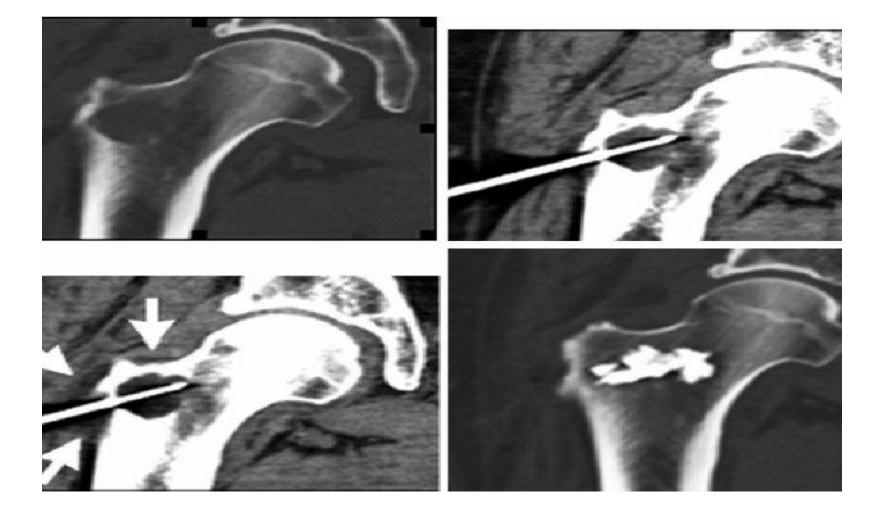


Figure 2: RF Electrode Placement—(A) Fat-suppressed T2-weighted axial magnetic resonance image of upper tibia and fibula. Metastatic malignant melanoma lesion contained within the tibia (arrow) with surrounding bony edema. Metastatic melanoma is also present in soft tissues overlying the anterior aspect of the tibia (arrowhead). (B) Axial CT image at corresponding level with RF electrode (arrow) placed within the osteolytic metastatic tumor. CT = computed tomography; RF = radiofrequency.



# **Operative Treatment**

- General consideration:
- Maximizing pain control should be the primary goal.
- A construct should provide immediate stability and allow full weight bearing.
- Durable enough to last for the increased total life span of patients with metastatic bone disease.

- In most patients, physicians should avoid fixation methods that require bone healing, porous ingrowths, and bone grafting.
- Use load bearing device (NAIL bettrer than PLATES).
- An intramedullary device or modular prosthesis provides more definitive stability.
- Assume this is his final surgery(no role for revision)

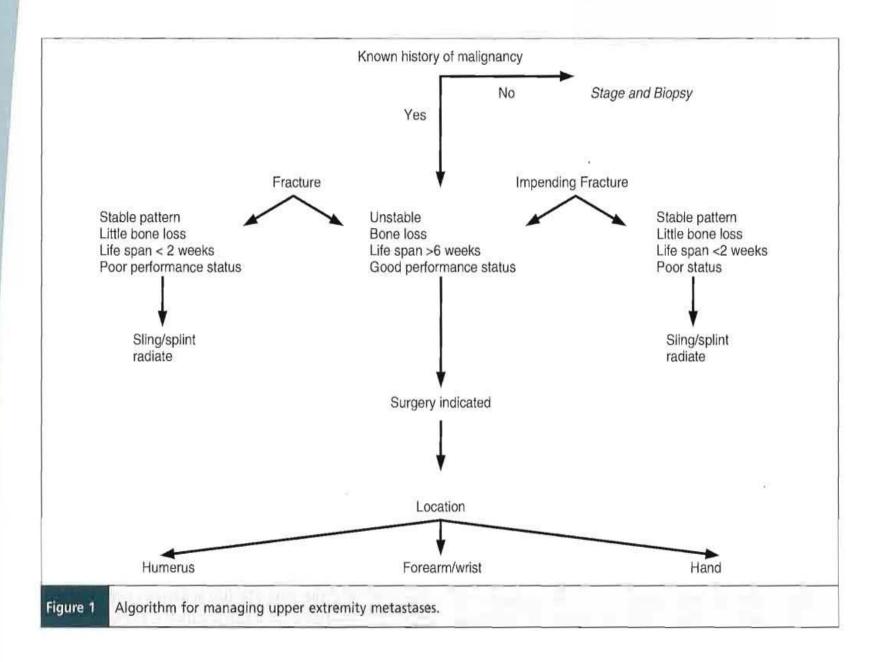
- For femoral lesions, historically a reconstruction nail is used to stabilize the femoral neck even if no lesion is present there at the time of surgery.
- Postoperative Radiation Therapy Following Stabilization:
- Increase the chances of achieving normal function status
- An overall decrease in the failure rate

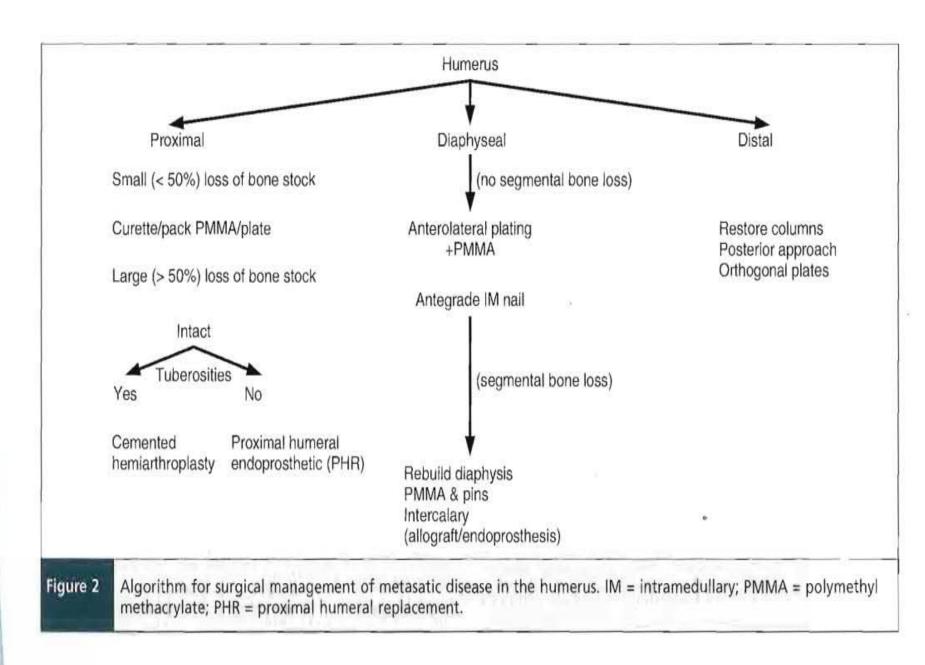
# Polymethyl Methacrylate(PMMA)

- Immediate stability following surgery.
- Easily applicable to fill the defects.
- Provides immediate rigidity, increase the strength of the fixation
- Generates an exothermic reaction that has shown to cause local tumor necrosis.
- It does not affect the use of therapeutic radiation.

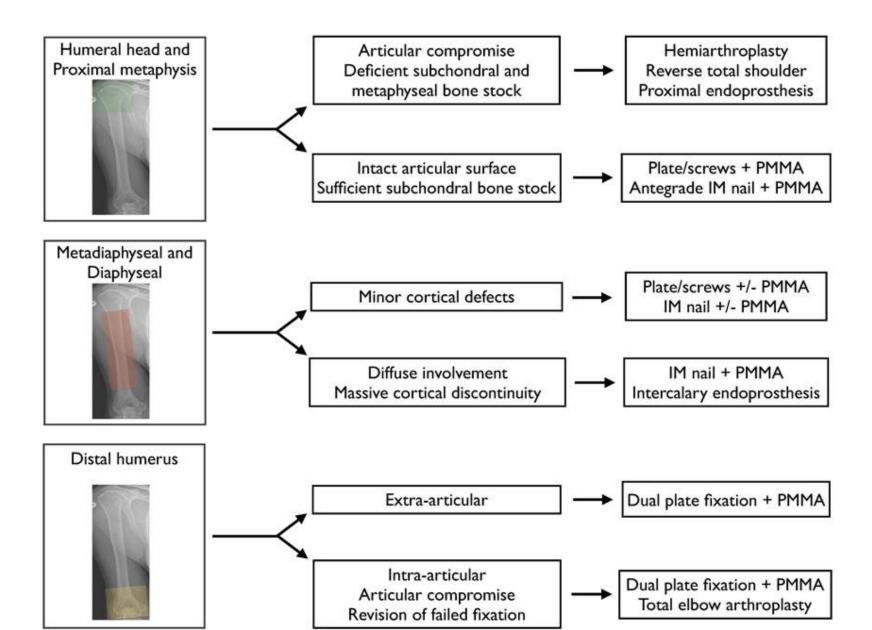
Bone	Location	Pathological Fracture Treatment	Impending Fracture Treatment
Humerus	Proximal	Proximal humerus replacement or proximal Proximal humerus plate or l humerus plate with cement proximal humerus nail	
	Diaphyseal	IM nail with cement	IM nail
	Distal	Total elbow arthropalsty or distal humerus replacement with cement	Distal humerus plate
Radius	Proximal	Small fragment T plate with cement or proximal radial replacementSmall fragment T plate or r head arthroplasty	
	Diaphyseal	Small fragment plate or flexible nail, with cement	Small fragment plate or flexible nail
	Distal	Distal radius plate with cement, or wrist fusion to ulna	Distal radius plate
Ulna	Proximal	Olecranon plate with cement or total elbow arthropalsty	Olecranon plate
	Diaphyseal	Small fragment plate or flexible nail, with cement	Small fragment plate or flexible nail
	Distal	Small fragment plate with cement or resection	Small fragment plate
	Proximal	Head or neck: Proximal femoral repalcement, or calcar-replacing THA	
Femur		Peritrochanteric: Long cephalomedullary nail with cement, or proximal femur replacement	Long cephalomedullary nail or cemented hemiarthroplasty
	Diaphyseal	Long cephalomedullary nail with cement	Long cephalomedullary nail
	Distal	Distal femoral replacement, or distal femoral plate with cement	Distal femoral plate or long retrograde supracondylar nail
Tibia	Proximal	Proximal tibia plate with cement, or proximal tibia replacement	Proximal tibia plate
	Diaphyseal	IM nail with cement	IM nail
	Distal	Distal tibia plate, or amputation	Distal tibia plate
Fibula	Proximal	Nonsurgical	Nonsurgical
	Diaphyseal	Nonsurgical	Nonsurgical
	Distal	Distal fibula plate or ankle fusion	Distal fibula plate

#### Section 5: Metastatic Disease to Bone





segmental resection is recommended with a proximal possible, because a proximal humeral replacement de-



#### Lower extremity lesions

- Pathologic fractures of the femoral head and neck rarely heal, and progressive disease, Therefore The procedure of choice for patients with metastatic disease to the femoral head or neck is a cemented replacement prosthesis.
- In femur nail are superior to plates

- In Femur fractures use a nail with largest diameter because the device will be load bearing and fracture usually doesn't unite.
- In distal femur lesion A retrograde nail has the drawback of potentially seeding the knee joint with tumor while failing to provide fixation to the femoral neck and epicondylar region.

- Most common complications are:
- Tumor progression with resultant hardware failure .
- Cardiopulmonary compromise.
- Hypercoagulable state.
- Fat emboli.

# Pelvic and actabulum

- Many bone metastasis or pathologic fractures in the bony pelvis do not affect weight-bearing functions; consequently, they do not require surgical intervention.
- Acetabuloplasty .

# Periacetabular lesions or fractures

Harrington Classification		Treatment
Class I	Disruption of lateral cortices with intact superior and medial wall	Conventional acetabular component +/- cement
Class II	Deficient medial wall	Antiprotrusion device/medial mesh
Class III	Disruption of lateral cortices and superior wall	Acetabular cage with long screw fixation into pubis, illium, or ischium +/-cement and Steinmann pins
Class IV	Pelvic Discontinuity	Saddle prosthesis versus resection arthroplasty

Туре	X-rays	Description	Management
Ι		Segmental/cavitary defects	Tumor curettage
		Intact acetabular dome	Cemented acetabular cup
		Intact anterior and posterior columns	Bone grafting
II		Medial wall defect	Antiprotrusio cage
	the for	Intact anterior and posterior columns	±Cementation of medial wall
	(C)		$\pm$ Bone graft to medial wall acetabular socket

Combined dome and column defects Intact posterior column Antiprotrusio cup Stabilization with retrograde screws into intact iliac wing

Pelvic discontinuity

Posterior column integrity disrupted

As type III

+Antegrade Steinmann pins via iliac wing into the ischium and/or the anterior column

Columns should be stabilized first

IV



A

# Hypercalcemia

#### Symptoms

- Fatigue or lethargy
- Confusion
- Thirst
- Muscle pain
- Abdominal pain
- Nausea or vomiting
- Anorexia
- Constipation
- Palpitations

#### Signs

- Altered mental state
- Polyuria (if diabetes insipidus)
- Oliguria (if acute kidney injury)
- Renal angle tenderness or haematuria (if renal calculi)
- Myopathy
- Reduced bowel sounds
- Arrhythmia (also demonstrates short QT interval on ECG)
- Dehydration
- Band keratopathy

ECG = electrocardiography.

### Hpercalcemia

Constitution symptoms	Weakness, fatigue, anorexia
CNS	Drowsiness, lethargy, altered mental status, stupor, coma
Cardiac	Short QT interval
Eye	Band keratopathy*
GI	Constipation, abdominal pain, peptic ulcer
Pancreas	Pancreatitis
Renal	Polyuria, nephrogenic DI, ARF, CKD, nephrocalcinosis, Nephrolithiasis

ARF- acute renal failure, CKD- chronic kidney disease, DI- diabetes insipidus; \* calcium deposits in cornea

# Hypercalcemia

- The most common complication in adults with osseous metastases.
- Hypercalcemia is not usually the presenting sign of malignancy, but it has a poor prognosis for the patient. As many as 60% of patients with hypercalcemia will survive less than 3 months, and only 20% will be alive at 1 year.
- Hydration (volume expansion)
- Loop diuretics
- Bisphosphonates

- A cortical lesion in an adult>40ys is usually a metastasis, most commonly from lung cancer.
- Any metastatic lesion distal to elbow and knee think of lung origin.
- Patient older than 40years with pathological fracture upon trivial trauma should be labeled as mets until proven otherwise

### Take home message

- It is important that all orthopedic surgeons have a basic understanding of the principles involved in the care of pathological fracture so they are well recognized and appropriate treatment is initiated.
- A pathologic fracture through a primary malignant bone tumor is treated much differently than a fracture through a metastatic lesion.