

Bone Grafting and Bone Graft Substitutes

Original Author: James Krieg, MD

Revision Author: David Hak, MD

Last Revision May 2010

Bone Graft Function

- Structural support of articular fracture
 - Tibial plateau fracture
 - Prevent post-op collapse
- Void filler to prevent fracture
 - Cyst excision
- Improved healing of fracture and nonunions
 - Speed healing
 - Fewer nonunions

Mechanisms of Bone Growth

- Osteoconduction
 - Provides matrix for bone growth
- Osteoinduction
 - Growth factors encourage mesenchymal cells to differentiate into osteoblastic lineages
- Osteogenesis
 - Transplanted osteoblasts and periosteal cells directly produce bone

Types of Bone Grafts

- Autograft
- Allograft
- Bone graft substitutes
 - Most have osteoconductive properties
- Osteoinductive agents
 - rhBMP-2 (Infuse) and rhBMP-7 (OP-1)

Autogenous Bone Graft

- “Gold standard”
 - Standard by which other materials are judged
- May provide osteoconduction, osteoinduction and osteogenesis
- Drawbacks
 - Limited supply
 - Donor site morbidity

Autogenous Bone Grafts

- Cancellous
- Cortical
- Free vascular transfers
- Bone marrow aspirate

Cancellous Bone Grafts

- Three dimensional scaffold (osteoconductive)
- Osteocytes and stem cells (osteogenic)
- A small quantity of growth factors (osteoinductive)

- Little initial structural support
- Can gain support quickly as bone is formed

Cortical Bone Grafts

- Less biologically active than cancellous bone
 - Less porous, less surface area, less cellular matrix
 - Prolonged time to revascularization
- Provides more structural support
 - Can be used to span defects
- Vascularized cortical grafts
 - Better structural support due to earlier incorporation
 - Also osteogenic, osteoinductive
 - Transported periosteum

Bone Marrow Aspirate

- Osteogenic
 - Mesenchymal stem cells (osteoprogenitor cells) exist in a 1:50,000 ratio to nucleated cells in marrow aspirate
 - Numbers decrease with advancing age
 - Can be used in combination with an osteoconductive matrix

Autograft Harvest

- Cancellous
 - Iliac crest (most common)
 - Anterior- taken from gluteus medius pillar
 - Posterior- taken from posterior ilium near SI joint
 - Metaphyseal bone
 - May offer local source for graft harvest
 - Greater trochanter, distal femur, proximal or distal tibia, calcaneus, olecranon, distal radius, proximal humerus

Autograft Harvest

- Cancellous harvest technique
 - Cortical window made with osteotomes
 - Cancellous bone harvested with gouge or curette
 - Can be done with trephine instrument
 - Circular drills for dowel harvest
 - Commercially available trephines or “harvesters”
 - Can be a percutaneous procedure

Autograft Harvest

- Cortical
 - Fibula common donor
 - Avoid distal fibula to protect ankle function
 - Preserve head to keep LCL, hamstrings intact
 - Iliac crest
 - Cortical or tricortical pieces can be harvested in shape to fill defect

Bone Allografts

- Cancellous or cortical
 - Plentiful supply
 - Limited infection risk (varies based on processing method)
 - Provide **osteoconductive** scaffold
 - May provide **structural support**

Bone Allografts

- Available in various forms
 - Processing methods may vary between companies / agencies
- Fresh
- Fresh Frozen
- Freeze Dried

Bone Allografts

- Fresh
 - Highly antigenic
 - Limited time to test for immunogenicity or diseases
 - Use limited to joint replacement using shape matched osteochondral allografts

Bone Allografts

- Fresh frozen
 - Less antigenic
 - Time to test for diseases
 - Strictly regulated by FDA
 - Preserves biomechanical properties
 - Good for structural grafts

Bone Allografts

- Freeze-dried
 - Even less antigenic
 - Time to test for diseases
 - Strictly regulated by FDA
 - Can be stored at room temperature up to 5 years
 - Mechanical properties degrade

Graft Incorporation

- Hematoma formation
 - Release of cytokines and growth factors

Graft Incorporation

- Hematoma formation
 - Release of cytokines and growth factors
- **Inflammation**
 - Development of fibrovascular tissue

Graft Incorporation

- Hematoma formation
 - Release of cytokines and growth factors
- Inflammation
 - Development of fibrovascular tissue
- **Vascular ingrowth**
 - Often extending Haversian canals

Graft Incorporation

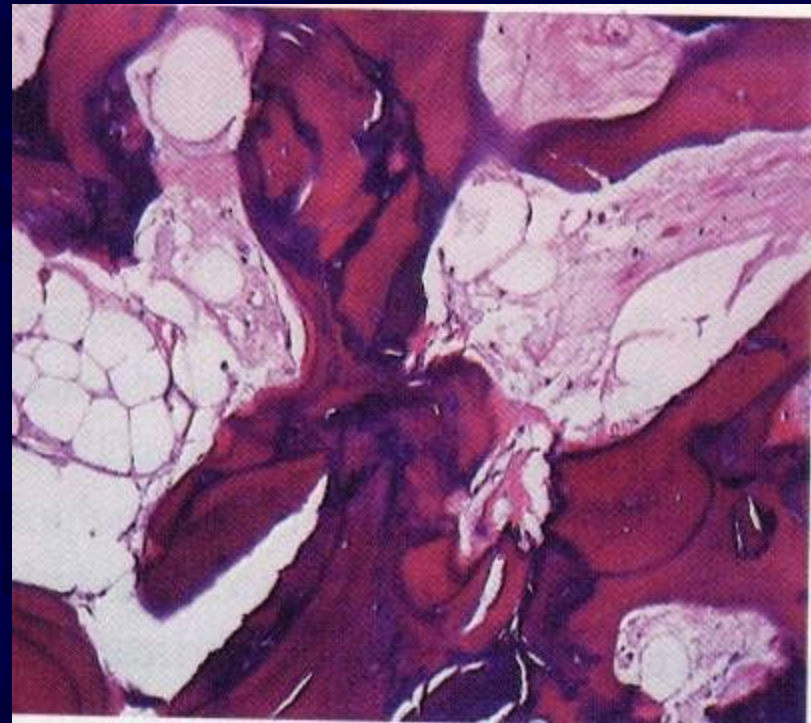
- Hematoma formation
 - Release of cytokines and growth factors
- Inflammation
 - Development of fibrovascular tissue
- Vascular ingrowth
 - Often extending Haversian canals
- Focal osteoclastic resorption of graft

Graft Incorporation

- Hematoma formation
 - Release of cytokines and growth factors
- Inflammation
 - Development of fibrovascular tissue
- Vascular ingrowth
 - Often extending Haversian canals
- Focal osteoclastic resorption of graft
- Intramembranous and/or endochondral bone formation on graft surfaces

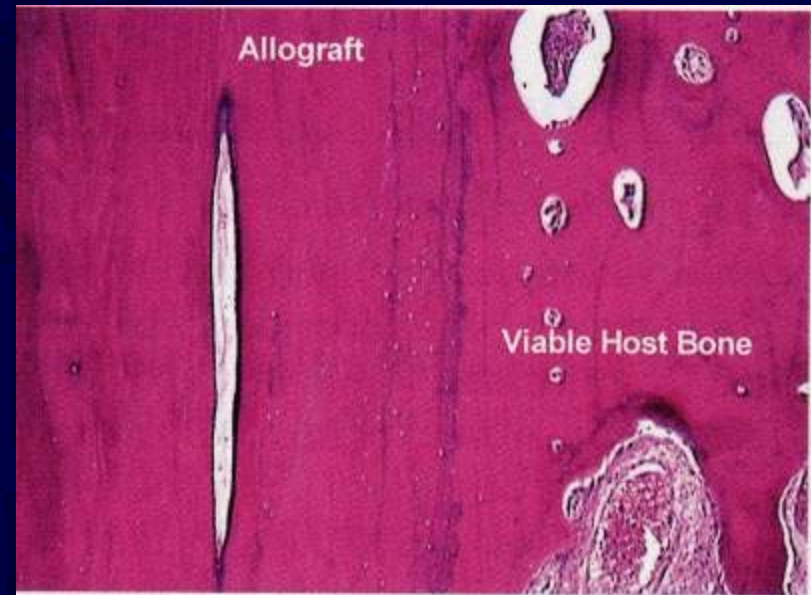
Graft Incorporation

- Cancellous bone interface between graft and host bone



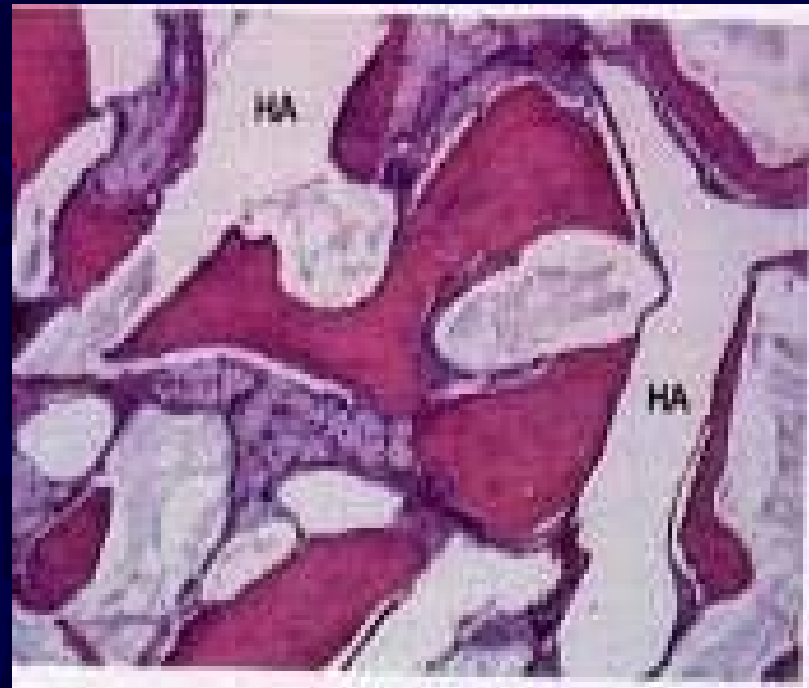
Graft Incorporation

- Cortical allograft strut graft placed next to cortex of host
- After 4 years of incorporation



Bone Graft Substitute Incorporation

- Partial incorporation of hydroxyapatite bone graft substitute\
- Biopsy of material obtained 1 year post-op



Bone Graft Substitutes

- Need for bone graft alternatives has led to development of numerous bone graft substitutes
- Avoid morbidity of autogenous bone graft harvest
- Mechanical properties vary
- Most offer osteoconductive properties
- Some provide osteoinductive properties

Bone Graft Substitutes

Potential Roles

- Extender for autogenous bone graft
 - Large defects
 - Multiple level spinal fusion
- Enhancer
 - To improve success of autogenous bone graft
- Substitute
 - To replace autogenous bone graft

Bone Graft Substitutes

- Calcium phosphate
- Calcium sulfate
- Collagen based matrices
- Demineralized bone matrix
- Hydroxyapatite
- Tricalcium phosphate
- Osteoinductive proteins

Bone Graft Substitutes

- Resorption rates vary widely
 - Dependant on composition
 - Calcium sulfate - very rapid
 - Hydroxyapatite (HA) – very, very slow
 - Some products may be combined to optimize resorption rate
 - Also dependant on porosity, geometry

Bone Graft Substitutes

- Mechanical properties vary widely
 - Dependant on composition
 - Calcium phosphate cement has highest compressive strength
 - Cancellous bone compressive strength is relatively low
 - Many substitutes have compressive strengths similar to cancellous bone
 - All designed to be used with internal fixation

Calcium Phosphate

- Injectable pastes of calcium and phosphate
 - Norian SRS (Synthes/Stratec)
 - Alpha BSM (Etex/Depuy)
 - Callos Bone Void Filler (Skeletal Kinetics)



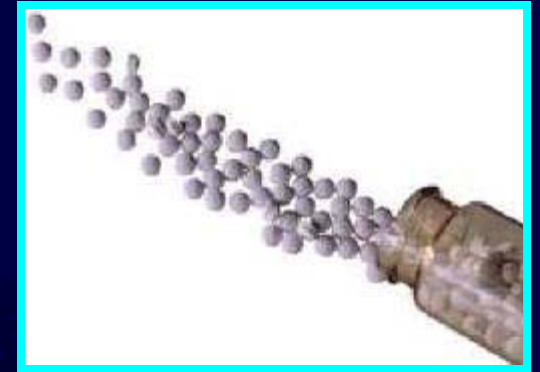
Calcium Phosphate

- Injectable
- Very high compressive strength once hardens
- Some studies of its use have allowed earlier weightbearing and range of motion





Calcium Sulfate



- Osteoconductive void filler
- Low compressive strength – no structural support
- Rapidly resorbs
- May be used as a autogenous graft extender
 - Available from numerous companies
 - Osteoset, Calceon 6, Bone Blast, etc.



Calcium Sulfate



- Pellets
 - Pellet injectors
- Bead kits
 - Allows addition of antibiotics
- Injectable
 - May be used to augment screw purchase



Collagen Based Matrices

- Highly purified Type 1 bovine dermal fibrillar collagen
- Bone marrow is added to provide bone forming cells
- Collagraft (Zimmer)
 - Collagen / HA / Tricalcium phosphate
- Healos (Depuy)
 - Collagen / HA



Demineralized Bone Matrix



- Prepared from cadaveric human bone
- Acid extraction of bone leaving
 - Collagen
 - Noncollagenous proteins
 - Bone growth factors
 - BMP quantity extremely low and variable
- Sterilized which may decrease the availability of BMP

Demineralized Bone Matrix



- Available from multiple vendors in multiple preparations
 - Gel
 - Putty
 - Strip
 - Combination products with cancellous bone and other bone graft substitute products

Demineralized Bone Matrix



- Growth factor activity varies between tissue banks and between batches
- While they may offer some osteoinductive potential because of available growth factors, they mainly act as an osteoconductive agents

Han B et al. J Orthop Res. 21(4):648-54, 2003.

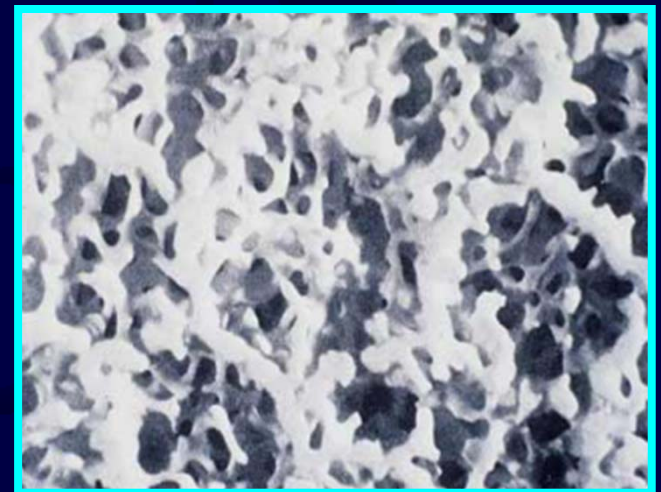
Blum B, et al. Orthopedics. 27 (1 Suppl): S161 – S165, 2004.

Hydroxyapatite

- Produced from marine coral exoskeletons that are hydrothermally converted to hydroxyapatite, the natural mineral composition of bone
- Interconnected porous structure closely resembles the porosity of human cancellous bone



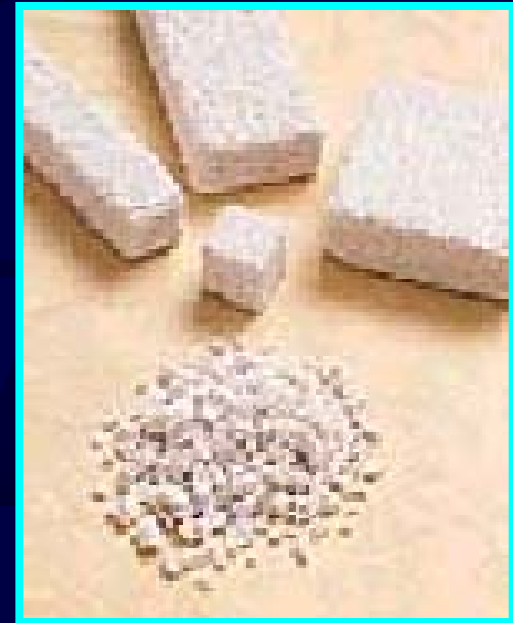
Cancellous Bone



Coralline hydroxyapatite

Hydroxyapatite

- Marketed as ProOsteon by Interpore Cross
- Available in various size blocks & granules
- ProOsteon 500
 - Very slow resorption
- ProOsteon 500 R
 - Only a thin layer of HA
 - Faster resorption



Tricalcium Phosphate

- Wet compressive strength slightly less than cancellous bone
- Available as blocks, wedges, and granules
- Numerous tradenames
 - Vitoss (Orthovita)
 - ChronOS (Synthes)
 - Conduit (DePuy)
 - Cellplex TCP (Wright Medical)
 - Various Theri__ names (Therics)



Bone Morphogenetic Proteins

- Produced by recombinant technology
- Two most extensively studied and commercially available
 - BMP-2 (Infuse) Medtronic
 - BMP-7 (OP-1) Stryker Biotech

BMP-2 for Open Tibial Fractures

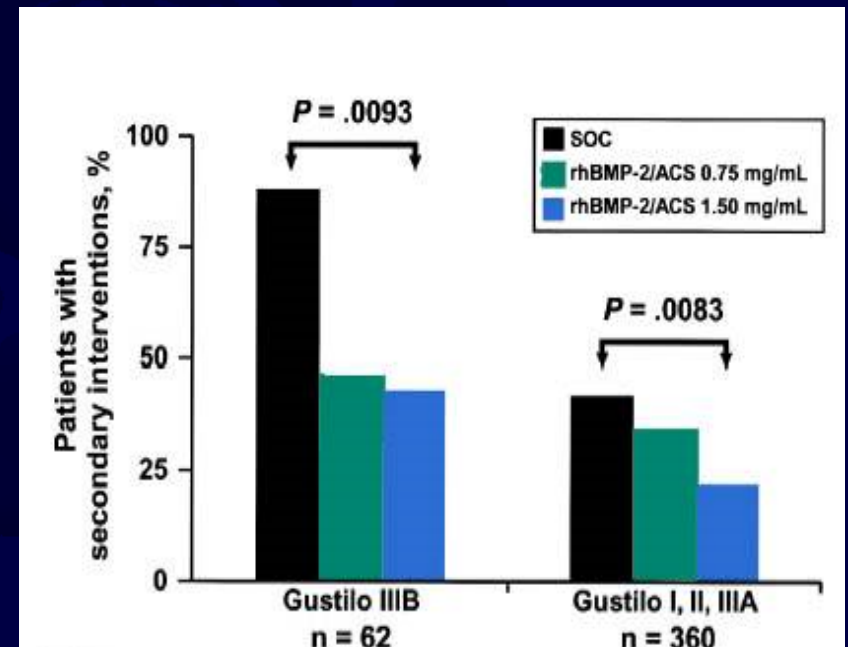
- Prospective, randomized study
- 450 patients
- All received IM nail (vast majority with UNREAMED technique) and appropriate soft tissue management
- Randomized to 3 treatments at time of definitive wound closure
 - Placebo
 - 0.75 mg/ml BMP-2/ACS
 - 1.50 mg/ml BMP-2/ACS



BESTT Study Group, et al. J Bone Joint Surg 84A: 2123, 2002.

Results

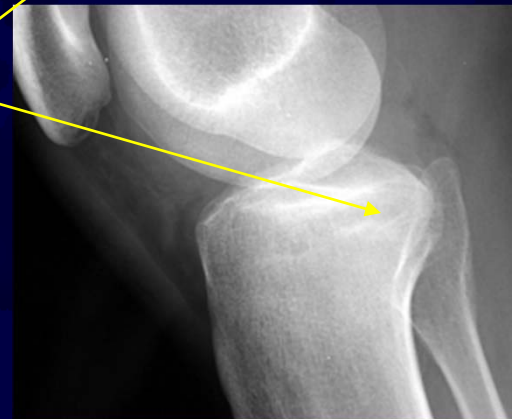
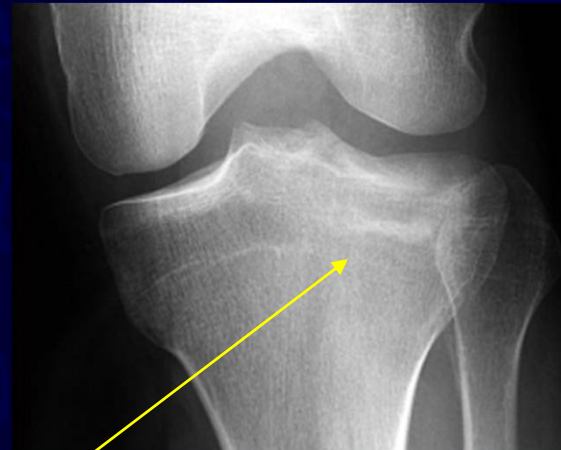
- 44% reduction in risk of nonunion/delayed union with high dose BMP-2
- Significantly faster fracture healing
- Significantly fewer
 - invasive interventions
 - hardware failures
 - infections



BESTT Study Group, et al. J Bone Joint Surg 84A: 2123, 2002.

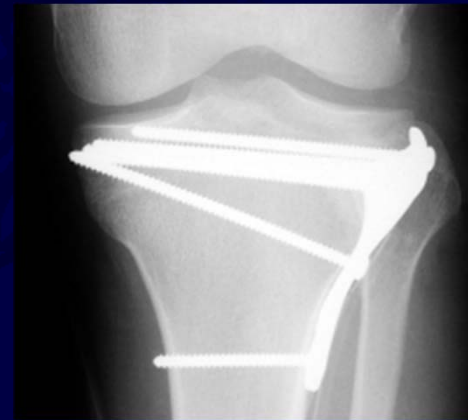
Indications for Bone Graft

- Provide mechanical support
 - **Metaphyseal impaction**
 - 27 y.o male with lateral split/depression tibial plateau fracture. Note posterolateral depression.



Indications for Bone Graft

- Provide mechanical support
 - **Metaphyseal impaction**
 - ORIF with allograft cancellous bone chips to fill defect and support depressed area
 - Alternatively could use any osteoconductive substitute with similar compressive strength



Indications for Bone Graft

- Provide mechanical support
 - **Metaphyseal impaction**
 - 4 months s/p surgery and the graft is well incorporated.



Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - **Cortical or segmental defect**
 - 29 y.o male with defect s/p IMN Type IIIB open tibia fracture. Gentamicin PMMA beads were used as spacers and removed.



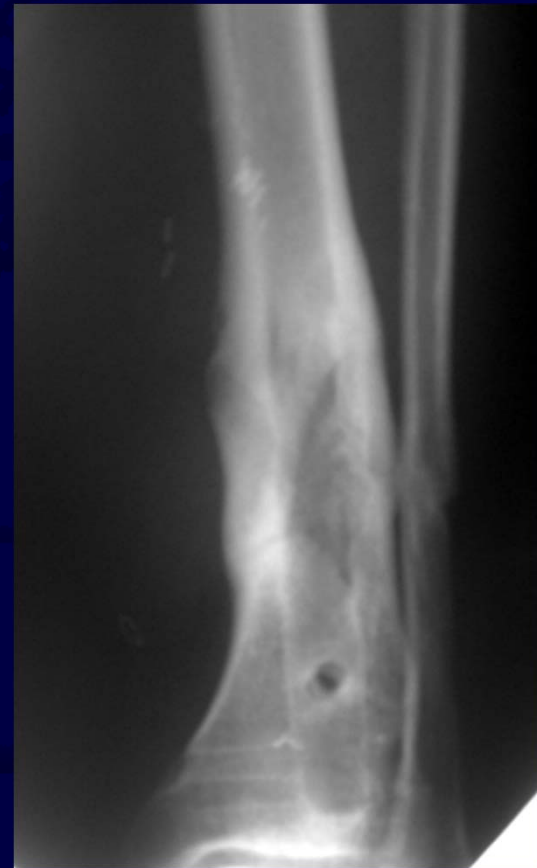
Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
 - s/p bone grafting with iliac crest autograft.



Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - **Cortical or segmental defect**
 - 14 months after injury, the fracture is healed and the nail removed.



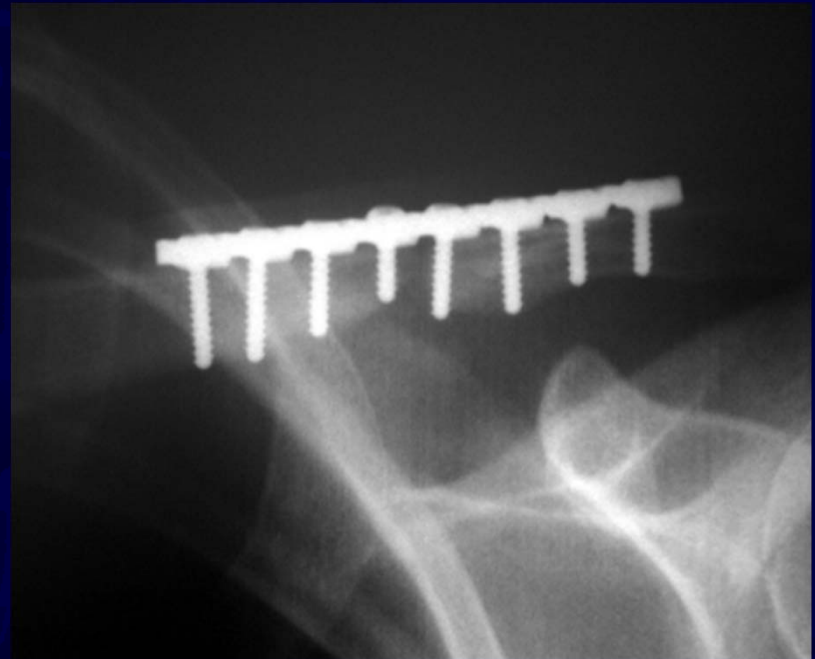
Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
- Stimulate healing
 - **Atrophic and Oligotrophic Nonunions**
 - 26 y.o. woman with established atrophic nonunion of the clavicle.



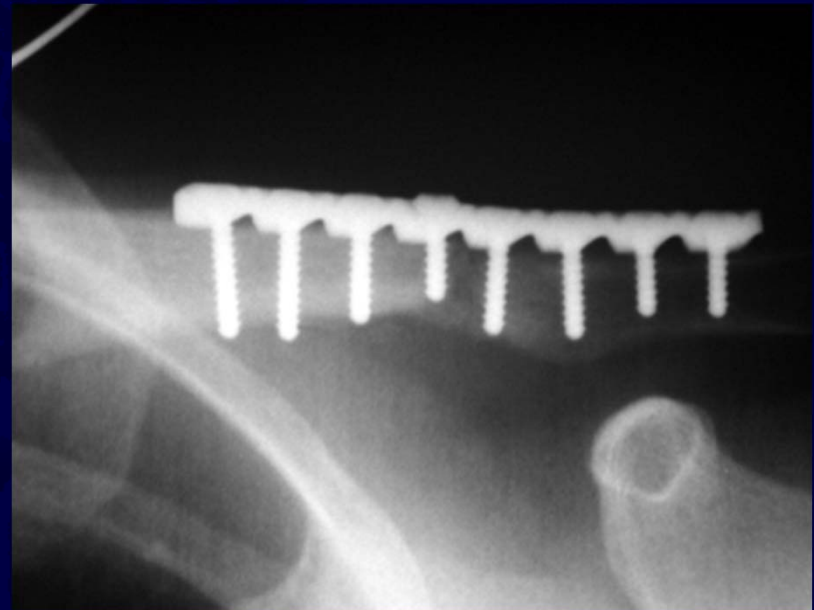
Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
- Stimulate healing
 - **Atrophic and Oligotrophic Nonunions**
 - Plating with cancellous iliac crest autograft.



Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
- Stimulate healing
 - **Atrophic and Oligotrophic Nonunions**
 - 6 months after surgery, she is healed and asymptomatic.



Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
- Stimulate healing
 - Nonunions
 - **Arthrodesis**
 - Failed subtalar arthrodesis



Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
- Stimulate healing
 - Nonunions
 - **Arthrodesis**
- Repeat fusion with autogenous iliac crest.



Indications for Bone Graft

- Provide mechanical support
 - Metaphyseal impaction
- Replace bone
 - Cortical or segmental defect
- Stimulate healing
 - Nonunions
 - **Arthrodesis**
 - 6 months after surgery, fused successfully





Thank You

If you would like to volunteer as an author for the Resident Slide Project or recommend updates to any of the following slides, please send an e-mail to ota@ota.org

Return to
General/Principles
Index

