Bone Grafting and Bone Graft Substitutes

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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
  – Prologed time to revascularizarion

• 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
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• Inflammation
  – Development of fibrovascular tissue
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- Vascular ingrowth
  - Often extending Haversian canals
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• 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 lead 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
Deminerlized 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
Deminingeralized 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.

Hydroxyapatite

- Produced from marine coral exoskeletons that are hydrothermically 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 Therics (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

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

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

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