Bone Grafting: Basic Science & Clinical Application

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Disclosures

- Lucas S. Marchand, MD: None
Introduction

- The basic science behind bone grafting
  - General overview

- Clinical Application: What are my options?
  - Autograft
  - Allograft
  - ‘Of the shelf’ products

- Take home points & conclusion
Introduction

- Bone grafting is a common adjunct procedure done in Orthopaedics
  - Fusion
  - Fracture care
  - Reconstruction
Introduction

- When do I need bone graft?
  - Non-union
  - Bone defect
Introduction

- When do I need bone graft?
  - Non-union
  - Bone defect

- Appropriate graft selection requires a thorough understanding of your patient
  - Bone healing needs of your patient VS
  - Bone healing properties of your graft

- Other considerations:
  - Diamond concept
  - Harvest site morbidity, mechanical stability, clinical results, and cost cost
Basic Science

- Critical components of fracture healing
  1. Osteogenesis (OG)
     - Stem cell delivery (capacity to differentiate)
  2. Osteoconduction (OC)
     - Scaffold to support bone/vascular growth
  3. Osteoinduction (OI)
     - Stimulation of bone formation (ie BMP’s)
  4. Vascularity*
     - Blood supply to the tissue
Basic Science

• Bone Grafting Options
  – 1. Autograft – Involves the transport of bone from donor site to another location in the same patient
    • Iliac Crest Autologous Bone Graft (Iliac Crest – ABG, Gold Standard)
    • Proximal Tibia
    • Reamed Sources of ABG (ie Reamer-Irrigator-Aspirator)
    • Iliac Crest Aspirate
    • Local Autograft
    • No risk of disease transmission
    • Inexpensive depending on the method of harvest
Basic Science

- Bone Grafting Options
  - 2. Allograft – Donor tissue
    - Crushed Cancellous
    - Demineralized Bone Matrix (DBM)
    - Structural/Cortical
    - Minimal risk of disease transmission
    - Intermediate expense
Basic Science

- Bone Grafting Options
  - 3. ‘Off the shelf’
    - BMP’s
    - Injectable Calcium Sulfate/Phosphates
    - No risk of disease transmission
    - Often the most expensive alternative
Graft Composition & Quality

- Cancellous graft
  - High surface area
  - Favorable handling properties
  - Tabecular bone allows for revascularization
  - Fast incorporation

- Cortical graft
  - Low surface area
  - Difficult handling properties
  - Slow revascularization
  - Delayed incorporation

- Vascularized Bone Graft
  - Applied w/ the expertise of a microvascular surgeon
  - Used when there is concern regarding native blood supply (osteonecrosis)
  - Ie. Free fibular & medial femoral condyle allografts
Iliac Crest ABG (Anterior or Posterior)

- Contains
  - OG: Bone forming MSC
  - OI: Growth factors including BMP’s
  - OC: Cancellous bone and/or tricortical graft
  - Vascularity: EPC’s, VEGF
  - Cost: Minimal
  - Donor Site Morbidity: Substantial
  - Graft Amount: ~40cc
  - Other: ‘Gold Standard’, Extensive support in the literature, Not available in all patients
  - Literature:

The Biology of Bone Grafting

Safdar N. Khan, MD, Frank P. Cammisa, Jr, MD, Harvinder S. Sandhu, MD, Ashish D. Diwan, MD, PhD, Federico P. Girardi, MD, and Joseph M. Lane, MD
Proximal Tibia ABG

- Contains
  - OG: Bone forming MSC
  - OI: Growth factors including BMP’s
  - OC: Cancellous bone
  - Vascularity: EPC’s, VEGF
  - Cost: Minimal
  - Donor Site Morbidity: Minimal (sub-q bone)
  - Graft Amount: ~25cc
  - Other: Easily accessible, risk of compartment syndrome
  - Literature:

Medial Approach for Tibial Bone Graft: Anatomic Study and Clinical Technique

Alan S. Herford, DDS, MD,* Brett J. King, DDS,†
Franco Audia, DDS, MS,‡ and Jonas Becktor, DDS§
Reamed ABG (ie RIA Harvest)

- Contains
  - OG: Bone forming MSC
  - OI: Growth factors including BMP’s
  - OC: Cancellous bone
  - Vascularity: EPC’s, VEGF
  - Cost: Moderate
  - Donor Site Morbidity: Minimal (certainly less than IC-ABG)
  - Graft Amount: ~60cc (Most)
  - Other: Easily accessible, risk of compartment syndrome, requires reaming, donor site fracture, The new ‘Gold Standard’
  - Literature:

The Reamer–Irrigator–Aspirator as a Device for Harvesting Bone Graft Compared With Iliac Crest Bone Graft: Union Rates and Complications

John Dawson, MD,* Dirk Kiner, MD,† Warren Gardner II, MD,† Rachel Swafford, MPH,† and Peter J. Nowotarski, MD†
Bone Marrow Aspirate

- Contains
  - OG: Bone forming mesenchymal stem cells (MSC)
    - Used as fresh aspirate or expanded as autologous stem cells
  - OI: Growth factors including BMP’s
  - OC: None
  - Vascularity: EPC’s
  - Cost: Minimal
  - Donor Site Morbidity: Minimal
  - Graft Amount: ~10cc
  - Other: Easily accessible, only studied in tibial non-unions
  - Literature:

Percutaneous Autologous Bone-Marrow Grafting for Nonunions

Influence of the number and concentration of progenitor cells

By Ph. Hernigou, MD, A. Poignard, MD, F. Beaujean, MD, and H. Rouard, MD

Investigation performed at the Service de Chirurgie Orthopédique, Hôpital Henri Mondor, Creteil, France
Local ABG

- Contains
  - OG: Bone forming mesenchymal stem cells (MSC)
  - OI: Growth factors including BMP’s
  - OC: Variable
  - Vascularity: EPC’s, VEGF
  - Cost: Minimal
  - Donor Site Morbidity: Minimal
  - Graft Amount: Variable
  - Other: Easily accessible, Often close to operative field & convenient
  - Literature:

Percutaneous Harvest of Calcaneal Bone Graft

Lawrence A. DiDomenico, DPM, FACFAS,¹ and Alfonso A. Haro III, DPM, FACFAS²
Crushed Cancellous Allograft

- Contains
  - OG: None
  - OI: None
  - OC: Cancellous bone
  - Vascularity: None
  - Cost: Minimal to Moderate
  - Donor Site Morbidity: None
  - Graft Amount: Variable
  - Other: Structure support only
  - Literature:

Particulate Bone Allograft Incorporation in Regeneration of Osseous Defects; Importance of Particle Sizes

Theodore I. Malinin*,1,2, Ellen M. Carpenter3 and H. Thomas Temple1
Demineralized Bone Matrix

- Contains
  - OG: None
  - OI: Trace amounts of GF’s
  - OC: Acid extracted organic matrix
  - Vascularity: VEGF (minimal)
  - Cost: High
  - Donor Site Morbidity: None
  - Graft Amount: Variable
  - Other: Questionable OI activity
  - Literature:

Demineralized bone matrix in bone repair: History and use

Elliott Gruskin, Bruce A. Doll, F. William Futrell, John P. Schmitz, Jeffrey O. Hollinger
Structural Bone Graft

- Contains
  - OG: None
  - OI: None
  - OC: Tricortical graft matrix
  - Vascularity: None
  - Cost: Moderate
  - Donor Site Morbidity: None
  - Graft Amount: Variable
  - Other: Structural support
  - Literature:

  **Tibiotalocalcaneal Arthrodesis With Bulk Femoral Head Allograft for Salvage of Large Defects in the Ankle**

  Clifford L. Jeng, MD¹, John T. Campbell, MD¹, Edward Y. Tang, MD², Rebecca A. Cerrato, MD¹, and Mark S. Myerson, MD¹
BMP

- Contains
  - OG: None
  - OI: BMP (the primary GFs driving OG)
  - OC: None
  - Vascularity: None
  - Cost: High
  - Donor Site Morbidity: None
  - Graft Amount: Variable
  - Other: Can be combined w/ other graft material to become OC, Ideal dosing (supra-physiologic)?, Timing?, will only work in the presence of MSC (OG cells), risk of malignancy
  - Literature:

Recombinant Human Bone Morphogenetic Protein-2 for Treatment of Open Tibial Fractures

A Prospective, Controlled, Randomized Study of Four Hundred and Fifty Patients

By the BMP-2 Evaluation in Surgery for Tibial Trauma (BESTT) Study Group, Shunmugam Govender, MD, Cristina Cismma, RPh, MHP, Harry K. Genant, MD, and Alexandre Valentin-Opran, MD
Injectable Calcium Phosphate/Sulfate

- Contains
  - OG: None
  - OI: None
  - OC: Synthetic implanted matrix
    - Mimics cancellous bone architecture
  - Vascularity: None
  - Cost: Moderate-High
  - Donor Site Morbidity: None
  - Graft Amount: Variable
  - Other: Calcium phosphate (non-porous) ceramics absorbs the fastest, calcium sulfate (porous) absorbs slower
  - Literature:

The Use of Calcium Phosphate Bone Cement in Fracture Treatment

A Meta-Analysis of Randomized Trials

By Sohail S. Bajammal, MBChB, MSc, FRCSC, Michael Zlowodzki, MD, Amy Lelewica, MD, Paul Tornetta III, MD, Thomas A. Einhorn, MD, Richard Buckley, MD, FRCSC, Ross Leighton, MD, FRCSC, Thomas A. Russell, MD, Sune Larsson, MD, PhD, and Mohit Bhandari, MD, MSc, FRCSC
<table>
<thead>
<tr>
<th>Bone Graft/Bone Graft Substitute</th>
<th>Osteogenesis</th>
<th>Osteoinduction</th>
<th>Osteoconduction</th>
<th>Vascularity</th>
<th>Mechanical Stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autogenous Iliac Crest Bone Graft (AICBG)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (EPCs, VEGF, HIF1α)</td>
<td>Yes (If Tricortical)</td>
</tr>
<tr>
<td>Reamer-Irrigator-Aspirator (RIA)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (EPCs, VEGF, HIF1α)</td>
<td>No</td>
</tr>
<tr>
<td>Allograft Bone</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No (If Allograft Strut)</td>
</tr>
<tr>
<td>Bone Marrow Aspirate</td>
<td>Yes</td>
<td>Yes</td>
<td>No (must be combined with osteoconductive scaffold)</td>
<td>Yes (EPCs)</td>
<td>No</td>
</tr>
<tr>
<td>Bone Morphogenetic Proteins</td>
<td>No</td>
<td>Yes</td>
<td>No (must be combined with osteoconductive scaffold)</td>
<td>?</td>
<td>No</td>
</tr>
<tr>
<td>Platelet Derived Growth Factor (PDGF)</td>
<td>No</td>
<td>Yes</td>
<td>No (must be combined with osteoconductive scaffold)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Calcium Phosphates</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes (compressive only)</td>
</tr>
<tr>
<td>Osteoset T (calcium sulfate pellets with Tobramycin)</td>
<td>No</td>
<td>No</td>
<td>Yes (plus local antibiotic delivery)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Demineralized Bone Matrix (DBM)</td>
<td>No</td>
<td>Yes (small amounts of osteoinductive proteins)</td>
<td>Yes</td>
<td>Maybe (small amounts of VEGF)</td>
<td>No</td>
</tr>
</tbody>
</table>
Conclusion

- Appropriate selection of bone graft or bone graft substitute requires an understanding of:
  - Patient's problem
  - Specific biological needs
  - Graft properties

- IC-ABG is the historical gold standard
  - This is likely changing
  - Many options can still achieve a successful result when applied in the appropriate setting