2009 OTA Annual Meeting

Manchester Grand Hyatt
San Diego, CA

Symposium III: Graft Options for Bone Defects

Elizabeth Ballroom, Level II

8:00am – 9:30am
Saturday, October 10, 2009

Moderators: Paul Tornetta, III, MD

Faculty: **Michael J. Bosse, MD**
Clifford B. Jones, MD
H. Claude Sagi, MD
J. Tracy Watson, MD

Other Autologous Sources:
Crest Aspirate, Reamer Irrigator Aspirator, and Induced Membranes

HC Sagi, MD

Autogenous iliac crest bone graft (ICBG) remains the gold standard in the treatment of non-union as well as cortical defects. ICBG provides all of the necessary elements required for bone healing and regeneration: osteo-conductive scaffolding, osteo-inductive biochemical elements, and osteogenic stem and progenitor cells.

Because of the much-lamented incidence of donor site morbidity (as high as 20% for persistent chronic pain in some studies), other sources of bone graft, both autogenous and allogeneic, have been exploited.

It is important to understand that neither all non-unions nor bone graft sources are created equal. The clinical scenario that one particular graft source may be of benefit in may not (in fact probably won't) be amenable to treatment with other sources of graft material. The physiological state of the patietnt, type of non-union (atrophic/avascular versus hypertrophic/hypervascular) and presence of segmental defects are all important variables to consider when deciding on the type of graft to be used. Additionally, many of these techniques and products have very little clinical and/or basic science rational to support their use in any situation.

Iliac crest aspirate, based on the technique used for obtaining bone marrow is one alternative source of autologous bone graft. The technique was published in the American JBJS by Hernigou et al in 2006. Basic science data has verified the presence of osteo-progenitor stem cells within bone marrow aspirate from the iliac crest. However, multiple studies have shown that the quality of aspirate and concentrate is very technique dependent with significant patient to patient variability in terms of the number of colony forming units of progenitor cells. This is important because Hernigou also showed that those non-unions successfully treated with iliac crest aspirate had a threshold concentration of >1500 CFU per milliliter of concentrated buffy coat.

Only two clinical studies exist analyzing the use of aspirate on healing non-unions: 1) Hernigou et al with 60 tibial non-unions finding that atrophic non-unions with gaps less than 5mm were the ideal candidate, and 2) Matsuda et al with 7 femoral non-unions finding that non-infected hypertrophic non-unions were the ideal candidate.

It has been known for a number of years that the reamings from long-bone fracture intra-medullary nailing retain viable osteocytes, osteo-blasts, osteo-clasts and osteo-progenitor cells. It has also been shown in two separate studies that long bone reamings liberate angiogenic and osteogenic biological markers in equivalent amounts relative to ICBG.

For these reasons, it has been postulated that intra-medullary reamings in the absence of an acute fracture would be a good alternative source of autogenous bone graft material.

The device known a the Reamer Irrigator Aspirator © (Synthes USA) which was initially developed to prevent the systemic embolization of medullary contents into the blood stream, has in fact turned out to be an ideal device for implementing this technique. By filtering the debris obtained from reaming the tibia or femur, marrow and endosteal reamings can be collected in sterile fashion for later use as autogenous bone graft.

Animal studies performed in the 1990's studying the properties and biological characteristics of foreign body membranes was extrapolated for clinical use in humans with segmental cortical defects and non-unions. Masquelet and colleagues have described the technique of induced membrane formation around cement spacers in patients with cortical segmental defects of the tibia. It has been shown that this membrane liberates both angiogenic and osteogenic factors that inhibit resorption and promote vascularization of the graft material.

Interestingly, the technique of using induced membrane for treating segmental defects, while being developed separately and independently, has evolved along side the RIA graft harvesting technique, and many surgeons use them concurrently today.

Alternative sources of bone graft such as iliac crest aspirates and reaming debris aspirates have good support in the literature based on basic science studies examining their relative histological and biochemical characteristics. However, little to no clinical human data exists regarding the efficacy and/or complications relative to classical iliac crest bone graft harvesting.

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<u>**Graft Options for Bone Defects: The BMP's**</u>**, Clifford Jones, Grand Rapids, MI**

Mini-Symposium for 2009 OTA Annual Meeting

Graft Options for Bone Defects

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<u>**The BMP's, What is the Evidence?**</u> **15 min**

Clifford Jones, MD, FACS, Orthopaedic Associates of Michigan

- Evidence based Evaluation
  - Biology & History
    - 1965, M Urist, DBM induces new bone
    - 1971, M Urist, "Bone Morphogenic Proteins"
    - 1977, BMP extracted from bone is inductive(1)
    - 1988, First recombinant human BMP produced
    - 1996, M Urist, review of BMP (2)
    - 2001, Friedlaender, JBJS, OP-1, tibial nonunion treatment(3, 4)
    - 2001, H Reddi, clinical review(5, 6)
    - 2002, BESTT group, JBJS, open tibial fracture treatment(7)
    - 2004, INFUSE for open tibial fractures treated with IMN
  - Technique & Limitations
    - Bridging
    - Gap Filling
    - Carrier
      - Powder
      - Gel
      - Putty
      - Flexible Sheets
    - Preparation
  - Biologic Enhancement Results
    - <u>OP-1, Nonunion Treatment, BMP-7</u>
      - Concentration of BMP-7, 0.88 mg/ml
      - Product delivered 3.5 mg
      - Friedlaender, JBJS 2001(3, 4)
        - 85% healing nonunion compared to autograft
        - Similar adverse events
        - 10x less infection risk
        - Similar clinical and radiographic results
    - <u>INFUSE, Open Fracture Treatment, BMP-2</u>
      - Concentration of BMP-2, 1.5 mg/ml
      - Product delivered 12 mg
      - BESTT, Govender, JBJS, 2002(7)

- Reduce risk 2° interventions by 41%
- Reduce rate non-union by 29%
- No increase risk of infection
- Reduce rate of infection with Type III open fx

- Cost Evaluation
  - INFUSE, Medtronic, Memphis, TN
    - Manufactures' Charge $5500-6000
    - Hospitals' Charge $11-12,000
  - OP-1, Stryker, NJ
    - Manufactures' Charge $4500-5,000
    - Hospitals' Charge $10-12,000
  - Taylor Spatial Frame, Richards, Smith-Nephew, TN
    - $5-6,000 with hospital charge 2-3 x more
  - Variables
    - Operative Time
    - Cost/Charges with autografting
    - Graft extenders
    - Return to OR for complications
    - Time out of work
    - Visits to Office
    - Length of defect ~ Amount of BMP/Carrier
  - Supportive Literature
    - A Jones, JBJS(8-10)
    - J Keeling, JBJS(11)

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2009 OTA SYMPOSIUM

Graft Options for Bone Defects

BONE TRANSPORT

When considering bone transport in an acute situation it is paramount to determine if a biologically sound healing environment can be achieved at both the site of the proposed corticotomy and / or docking sites. The success of both corticotomy and solid docking involves well-vascularized segments of bone and soft tissue. If soft tissue incompetence (dysvascularity) is present at the proposed corticotomy site, the production of healthy regenerate may be in question. Severe open fractures with a wide zone of injury are often associated with very poor soft tissue coverage at the site of injury. Associated soft tissue compromise may be co-existent elsewhere in the limb, which may involve the site of the proposed corticotomy.

BIOLOGY

A. The periosteal blood supply is derived primarily from the surrounding soft tissue envelope. If this is inadequate and unable to provide a vascularized viable periosteal sleeve, the prospects for the development of an inadequate regenerate is very real. In these situations an alternative corticotomy site performed thru healthy tissues should be selected.

B. Influence of a stable mechanical environment facilitates docking site union. The hallmark of these events is the inflammatory phase of fracture healing which promotes the revascularization process. This area must be manipulated to provide the appropriate vascular response either thru aggressive debridement or soft tissue coverage techniques.

CLINICAL EVALUATION

A. MRI can be helpful to determine the extent of marrow dysvascularity found in a proposed transport segment or proposed docking site.

B. Arteriography may also be useful to determine distal vascularity (blush) with regard to docking segment viability as well as soft tissue viability.

C. Soft tissue loss without exposed bone… soft tissue transport in conjunction with the bone transport is possible.

D. Tissue loss that exposes bone is not amenable to combined soft tissue / bone transport without first addressing the exposed bone.

1. Free tissue transfer
2. Avoid local rotational flaps

TREATMENT OPTIONS

A. Acute or gradual shortening offers advantages over transport in the patient that presents with vascular insufficiency, i.e a one vessel leg where free vascularized tissue transfer is contraindicated.

1. Acute shortening 3-4 cm in the tibia and humerus.
2. Shortening acutely in a femoral defect up 5-7 cm.

3. Soft tissue coverage combined with vacuum assisted closure may allow wounds to be closed by delayed primary closure or healed by secondary intention or simple skin grafting.

4. Acute shortening > 4 cm can cause the development of tortuous vasculature and actually produce a low flow state with detrimental consequences.

5. Gradual shortening. Shortening at the rate of .5 cm per day in divided doses will rapidly oppose the skeletal defect as well as avoid the detrimental soft tissue consequences and vascular element kinking of acute defect compression.

6. Massive defects greater than 8-10 cm..combined treatment options

a. Acutely shortening can reduce the transport time

b. Docking is accomplished, then lengthening can then be carried out.

. Rapid lengthening over an IM nail using autodistractor devices.

i. Decrease the discomfort associated with traditional lengthening techniques.

ii. Internal lengthening nails. Transport over locking plates

c. Bifocal and trifocal strategies …. double level transport in combination with acute shortening

d. Transport over nails, as well as locking plates has also been employed for larger defects in both tibial and femoral deficiencies.

e. Free vascularized fibula combined with acute shortening and bone transport

f. Lastly, transverse ipsilateral fibular transport

COMPLICATIONS

A. Frame related complications,

B. Nonunion of the docking site.

1.Autogenous grafts alloplastic and recombinant materials have been used to augment and aid in the rapid consolidation of the docking site.

2. Ultrasound speed the consolidation of regenerate segments

3. Percutaneous augmentation of regenerate

FUTURE DIRECTIONS

A. Frame configurations with simplified mountings with multiple half-pin attachments.

B. Hexapod frames, as well as many monolateral transport constructs have devised less complex frame mountings that allow for simplistic application. These frames permit constant adjustment of the proposed docking site without the malalignment potential that can occur with traditional circular frame constructs.

C. Pin technologies

. 1. HA (hydroxy-appetite) coated pins

D. Alternative pin placement

1. Off set pin angle of 60 degrees

E. Orthobiologics…augment large regenerate segments / docking sites

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