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Basic Science Focus Forum

Bone grafting Symposium #3

Bone Graft Extenders: Which Ones Work?

INTRODUCTION AND BASIC SCIENCE OVERVIEW

There are clearly no well defined indications for use of a specific type of bone graft substitute or use of inductive factor when dealing with complex fractures or nonunions. This is especially true when dealing with acute bone and soft tissue defects. The use of all of these materials should be based on contemporary fracture management principles and current levels of evidence for use of these materials

1) Common biological requirements for bone regeneration
   a) Cells: Adult progenitor cells from the marrow, periosteum, and other sources
   b) Blood supply: For the delivery of nutrients, oxygen, and systemic factors required for cell survival
   c) Molecules and their receptors: Provides for the induction of cells to proliferate and differentiate into osseous tissue (osteoinduction)
   d) Extracellular matrix: To provide a scaffold for cells (osteoconduction), and storage site for growth factors

DO THEY WORK?.....WHAT DO YOU WANT THEM TO DO?

-Simple void filler? (dead space management)(delivery vehicle)
-Mechanical support?
-Augment routine bone graft i.e bone graft extender? With inductive potential?

2) Extracellular matrix:
   a) Properties for function
      i) Space filler (biocompatibility)
      ii) Structural properties (mechanical)
      iii) Microstructural (biological for cell surface adhesion/healing)
   b) ECM scaffolding characteristics
      i) Substrates for bone replacement
      ii) Resorption over time
      iii) Requires cells for cytokines or potency
      iv) Dependent upon defect types or loads
      v) Clinical studies frequently compare efficacy of osteobiologics to cancellous autograft as gold standard
         (a) Late subsidence reported with autograft when used as bone void filler for plateau / pilon fx.
      vi) DBM as bone void filler
         (a) Conductive due to tremendous surface area afforded by particulate nature of material

(b) No inherent mechanical stability
1) Cannot be utilized as bone void filler in ***wt. bearing locations***…
2) Satisfactory for "contained " defects i.e solitary bone cyst.

3) Metaphyseal defects
a) Experimentally it has been shown that a simple cancellous void will reconstitute on its own and heal completely given a sound biologic environment without the addition of any further grafting material. The danger here is that the subchondral surface will collapse if this defect does not reconstitute fast enough to provide subchondral support with the initiation of wt. bearing
i) Conductive substrates
(1) Ca ceramics. $CaSO^4$ / $CaPO^4$ / Ca PO^3Si / composite SO^4- PO^4
(a) Incorporation characteristics…i.e rates of osteointegration
(b) Ultimate compressive strength mPa
(c) Delivery mechanism. Particulate vs self setting "cements"
(d) Incorporation time vs bone regenerated into defect
(i) Cellular mediated vs chemical degradation of materials
(ii) Use of marrow concentrates to accelerate incorporation characteristics. "seeding the graft"
(e) Multiple studies with good Level I and II evidence support use of both sulfate and phosphate materials for contained metaphyseal defects.
(i) Demonstrated superiority over autogenous graft materials.
(2) Allograft / Allograft composites
(a) Conductive substrate
(b) Moldable / may instrument and provide mechanical support metaphyseal cortical defects , transitional zone from metaphysis to diaphysis
(c) Compressive strength approximates cancellous bone for wt. bearing
(i) Relative mechanical deficientcy of Allograft "croutons" for bone void filler in peri-articular situations (i.e plateau fx void filler)
(3) MECHANICAL Factors. Use of conductive substrate materials in metaphyseal defects augmented with use of locking plates for plateau, distal femoral, and pilon fractures
(a) MINIMAL evidence currently avail for use of supplementary locking plates in these locations.
4) Diaphyseal fractures
a) Use of adjuvant *EXTENDER* materials in this location depends on numerous factors
i) Evaluation of fx site. Mid shaft tibia fracture is usually a biologically "challenged" region
(1) The appropriate migration of cellular components to the site of bone graft or fracture is crucial in continuing the progression of the fracture healing cascade. Consideration of delivering these cells to the region in question.
(2) Acute bone loss vs non-union defect
(3) Condition of soft tissues and "zone of injury" local environment

(a) Flap / soft tissue coverage…..reconstitution of inflammatory phase of Fx healing (neo vascularization)

(4) Graft *EXTENDER* options

(a) Composite grafts

(i) DBM + Autogenous cellular concentrates, +, - platelet gels (as carrier)

1. Limited success with centrifuged aspirate alone (Connelly, Watson)
2. Concentration of CFU’s in conjunction with carrier materials (Hernigou) (Jimenez….Astrom technique)

ii) Acute critical sized defect / nonunion. (segmental loss <4cm)

(1) Graft options

(a) BMP-2 implantation at time of wound closure (open tibia fx) (BESTT study results)

(b) Segmental defects up to 4 cm (Bucholz, Jones et.al)

(c) OP-1 (McKee ..Canadian open tibial shaft study

(d) OP-1 for nonunions (equivalent efficacy between autograft and OP-1)

(e) Providing scaffolding for mesenchymal cell infiltration. Depending on the temporal relationship of the delivery of the inductive factor to the cell population in question, will determine the specific effect that each protein has on the fracture healing cascade. It is important that these stem cells have the appropriate conductive surface to migrate on to initiate the further production of their specific induced function.

(f) Providing Colony forming units (CFU’s) (Hernigou)

iii) Large segmental defects

(1) Staged reconstruction

(a) Antibiotic spacer / beads / rods

(i) Carrier for inductive materials

(ii) Carrier for antibiotics

1. PMA
2. $CaSO^4$

(b) Development of vascularized pseudo-membranes.. Masquelet technique)

(i) Grafting directly into vascularized pseudo membrane
Using RIA derived bone graft.

(ii) Membrane directed bone regeneration

(2) Bone transport

(3) Free tissue transfer

(a) Combination methodologies with bone transport and inductive factor augmentation

(b) Vascularized fibula

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