BMA & BMP: Alternative to Autologous BG?

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A "gift" you do ***not*** want…

Motion
Avascularity
Gap
Infection

Prognostic Issues

- Local factors
  - Soft tissue injury
  - Local blood supply/compromised vascular supply
  - Presence of interposed tissue
  - Open Fx, Bone Loss
  - Infection
  - ***Surgical Felony -- Don't do it!***

Vascularity

- Hypertrophic
  - Provide rigid mechanical stability ⇨ rapid biologic response
  - STABILITY - Decrease micromotion
  -
  - Endochondral ossification
  - ***No bone grafting required***

Vascularity

- Oligotrophic
  - Adequate vascularity
  - Viable bone ends
  - Inadequate stability
    - Less instability than HYPERTROPHIC

Vascularity

- Atrophic
  - ***Poor vascularity***
  - +/- inadequate stability

Vascularity

- Atrophic: Restricted blood supply
  - *Remove dead tissue*
    - *No reincarnation in the “Temple of Bone”*
  - ***Needs biological stimulus***
  - ***Needs stability***
  - Defect bridged with bone graft

Surgical Treatment

- Plate osteosynthesis
- Intramedullary nailing
- External fixation

+/- Bone Grafting

Deformity correction

Many nonunions have an associated MALALIGNMENT !!!

Graft Incorporation – shares early stages with INFLAMMATORY CASCADE

- ***Hematoma formation***
  - release of cytokines and growth factors
- ***Inflammation***
  - development of fibrovascular tissue
- ***Vascular ingrowth***
  - often extending Haversian canals
- ***Intramembranous and/or endochondral bone formation on graft surfaces***
  - new bone formation
- ***Focal osteoclastic resorption of graft***
  - Grafts replaced by bone

The Language of Fracture Healing and Bone Graft Requirements

- ***Osteogenesis***
  - Stem cells or osteoprogenitor cells
- ***Osteoinduction***
  - Precursor cells are *induced* to differentiate and form bone
- ***Osteoconduction***
  - Provide a 3-D scaffold

The Language of Fracture Healing and Bone Graft Requirements

- ***Osteogenesis – from the HOST***
  - Autograft
  - BMA
  - RIA
- ***Osteoinduction***
  - Autograft, BMA, RIA
  - Demineralized bone matrix*
  - Bone morphogenetic proteins (BMPs)
- ***Osteoconduction***
  - Calcium Phosphate, Calcium Sulfate
  - Demineralized bone matrix
  - Autograft / Allograft

Bone Marrow Aspirate

- Tools of the Trade
  - 4" long #8 Jamshidi needle
  - Heparin
  - 20 cc syringe

***Withdraw in 2-3 mL increments – Single port needle

***Withdraw up to 5mL increments – Multiport needle

Bone Marrow Aspirate

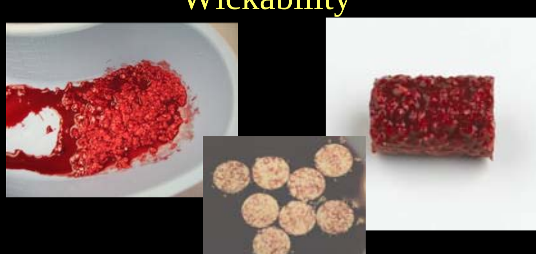
- Percutaneous bone marrow injected
- 9 of 10 delayed tibia fractures united
- 80% of 100 tibial fracture patients united when in conjunction with adequate fixation

Connolly J., CORR. 1995

Bone Marrow Aspirate (literature)

- Osteogenic
- Improve union w/
  - Fx's
    - Closed
    - ORIF
  - Spine Fusion
- May be combined w/ carrier or expander
- May be concentrated

Wickability



Often a DBM containing substrate

PERCUTANEOUS AUTOLOGOUS BONE-MARROW GRAFTING FOR NONUNIONS

INFLUENCE OF THE NUMBER AND CONCENTRATION OF PROGENITOR CELLS

-60 pts

-Tibia Aseptic Nonunions

-Union in 53/60

-Positive Correlation w/ Volume of Callus and CFUs

-7 who did not unite LOW CFUs

General Materials

- Vacuum (VacLok) syringes
- Multiport Jamshidi
- Scalpel
- Mallet
- Marking pen
- Dermabond (optional)
- Gauze/Tegaderm

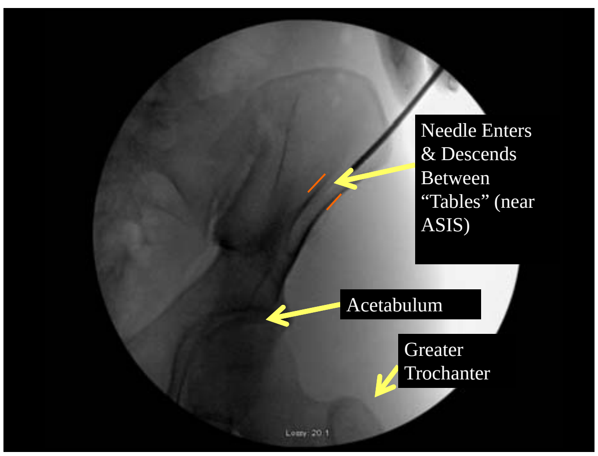
Not Shown Here:

- Fluoroscopy x-ray machine
- Radiolucent operating table
- Patient in supine position (anterior approach)

Needles/Syringes

- Multi-lock ports
  - Avoids having to redirect so often
  - Needs to be turned 90 degrees with each pull
- Vacuum syringes


Multiple
ports


Needle Enters
& Descends
Between
“Tables” (near
ASIS)
Acetabulum
Greater
Trochanter

Grafting Long Bone Fractures with DBM Putty Enriched with BMA

Lindsey, RW, Wood, GW, Sadasivian, KK, Stubbs, HA, Block, JE, Orthopedics, 29:10, 939-941, 2006

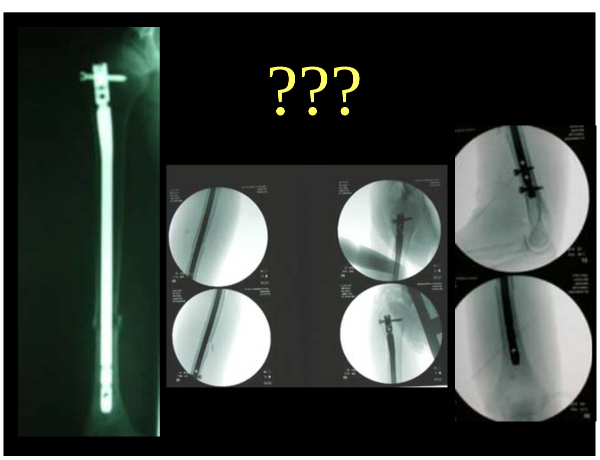
27

DBM Putty with BMA in Long Bone Fractures

Outcomes:

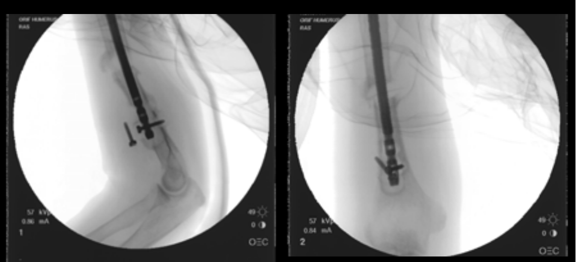
- 90% Achieved Full Bone Formation w/ DBM + BMA Group
  - 100% patients were healed
- 75% Achieved Full Bone Formation w/ Iliac Crest Group
  - 63% patients were healed

Lindsey et al., Orthopedics, October 2006
28

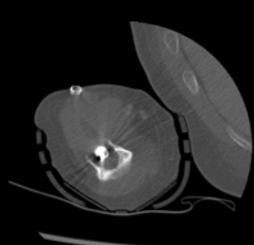


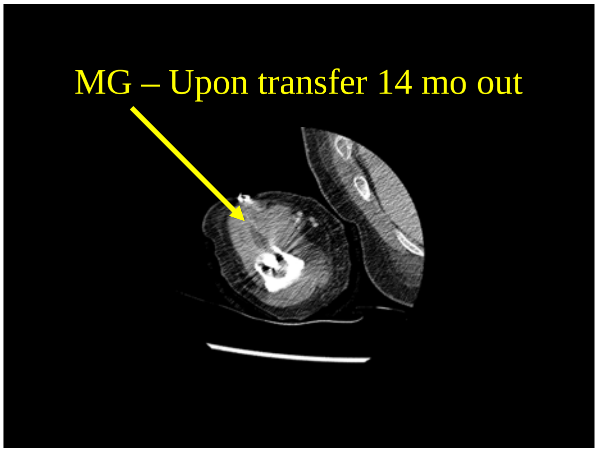
1 year post-op

Surgeon’s plan to “dynamize” but pus came out



MG – Upon transfer 14 mo out

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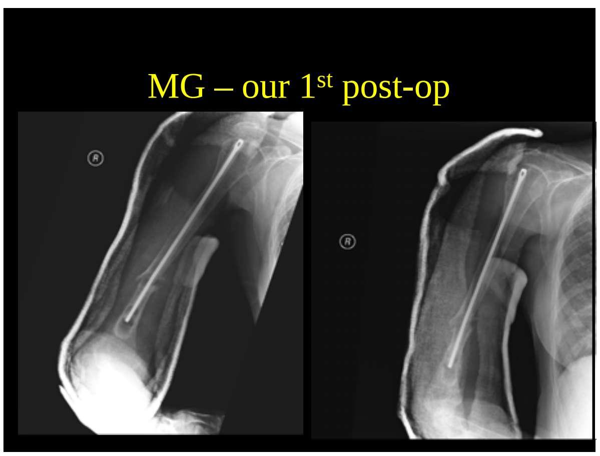
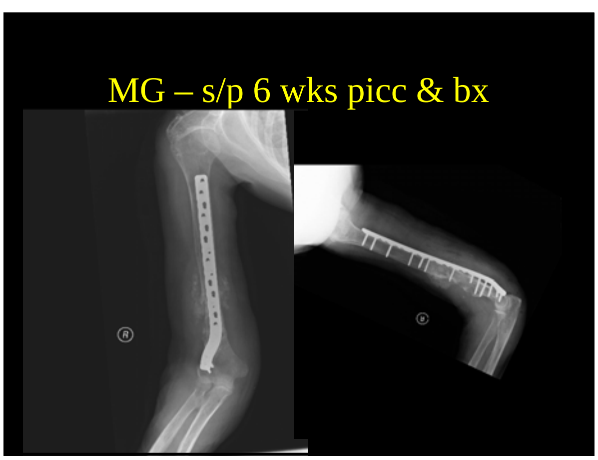

MG – our 1st post-op


MG – s/p 6 wks picc & bx

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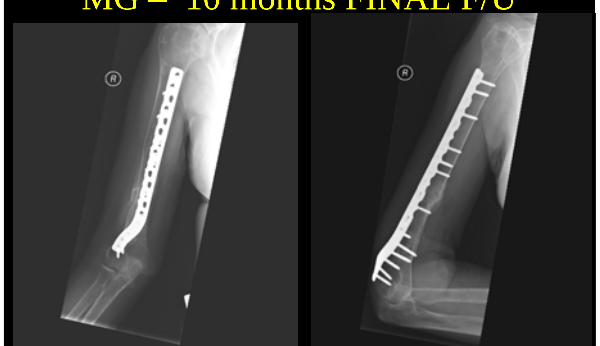
MG – 10 months FINAL F/U

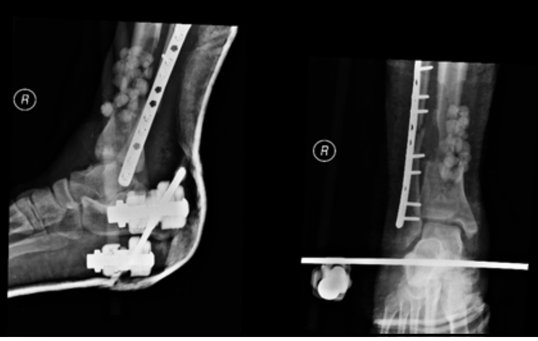


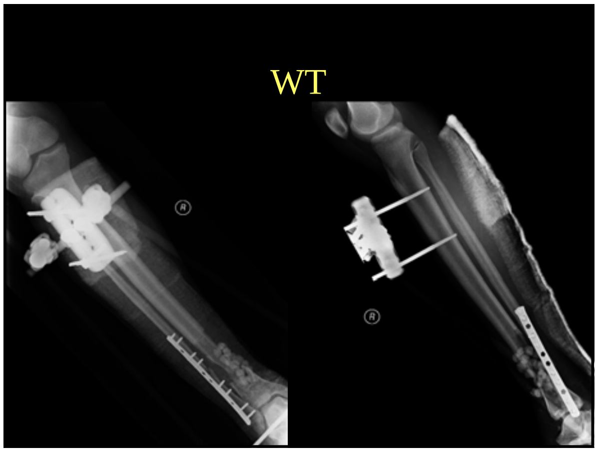
MG – 10 months FINAL F/U

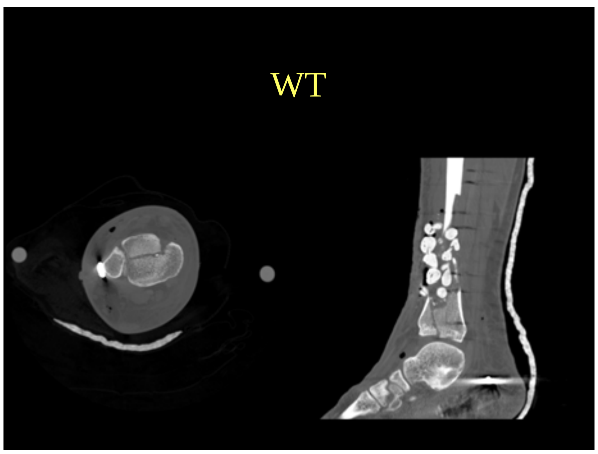
WORKS ALL OVER THE BODY !!!

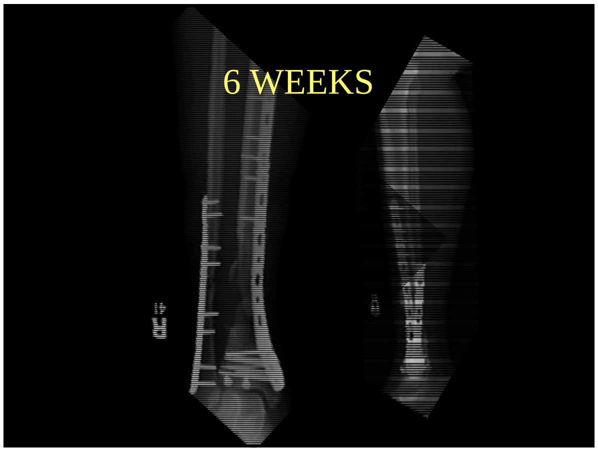
Nonuinon Tibia in Poor Host w/ Poor Soft Tissue & Contamination

WT

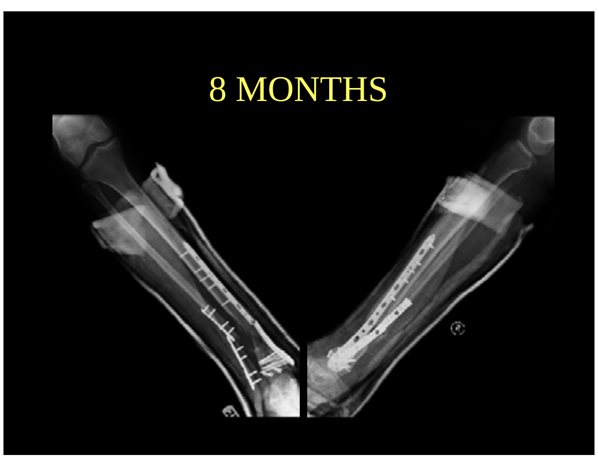



WT

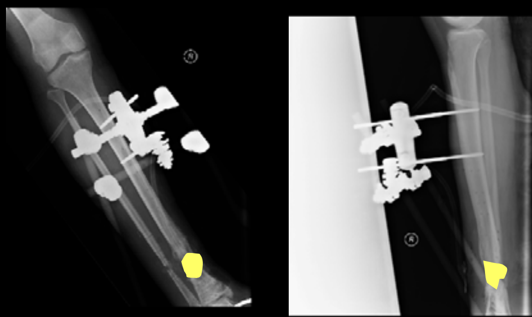

WT


6 WEEKS


2.5 MONTHS

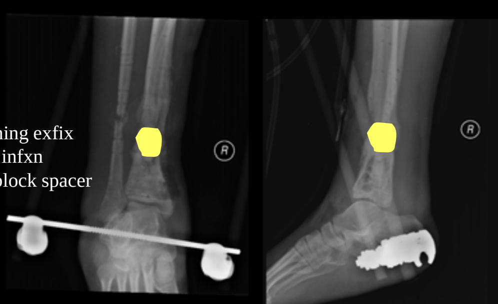

8 MONTHS

ROH & Infection & Nonunion



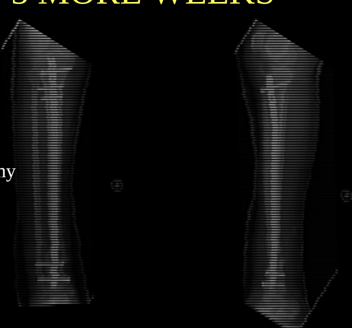
ROH & Infection & Nonunion

Spanning exfix
Clear infxn
Abx block spacer



5 MORE WEEKS

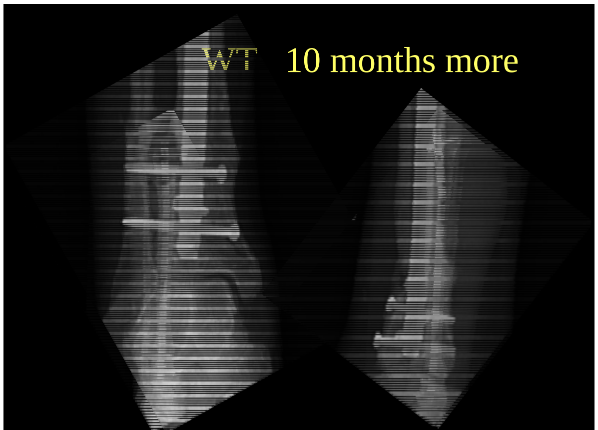
Fibula osteotomy
BMA
Grafting



Post-revision 10 weeks

Fibula osteotomy
BMA
Grafting

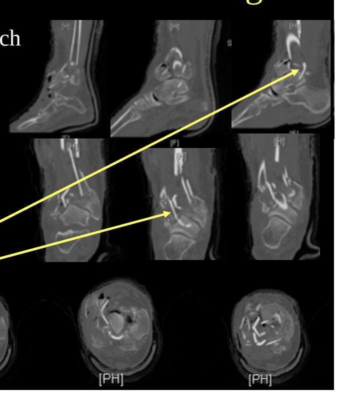
WT 10 months more



Large Defect Tx’ d w/ Grafting

- Sometimes the approach is done for you!
- 70 year old multi-trauma w/ 20 x 30cm open wound

Yes, part of the pilon is in the talus !!!



Large Defect Tx' d w/ Grafting

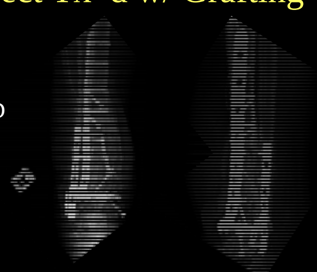
- Stick to the principles
- Ex-fix
- Lateral column recon
- I&D, I&D, I&D
- Fix & Flap

Large Defect Tx' d w/ Grafting

- Stick to the principles
- Ex-fix
- Lateral column reconstruction
- I&D, I&D, I&D
- Fix & Flap

Large Defect Tx' d w/ Grafting

- Pus, Pus, Pus
- I&D, I&D, I&D
- Picc Line
- IV Abx
- BONE GRAFT
- BMA



80 y.o. f
One year s/p Grade IIIB Tibia
W/U (-)

Good Nails / Poor Host

80 y.o. f
One year s/p Grade IIIB Tibia
W/U (-)

Good Nails / Poor Host

Exchange Nail
Percutaneous BMA

Open Injury, Poor Soft Tissue, Good Host

LD – 80 mph MCA crash

LD – 80 mph MCA crash

LD – 80 mph MCA crash

LD – 80 mph MCA crash

LD – NIGHT 1

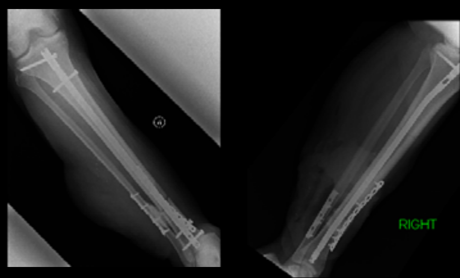
LD – 80 mph MCA crash

LD – NIGHT 1

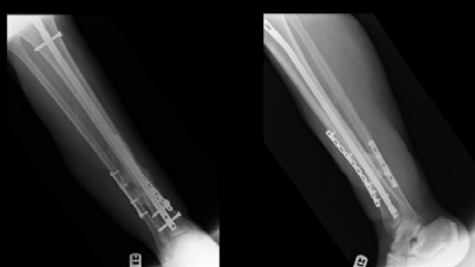
LD – DAY 5 after q48h I&D's

LD – DAY 7 + free flap + Abx spacer

LD – 6 weeks post-injury (remove spacer, BMA, DBM, cancellous chips)



LD – 3 months after grafting



LD – 6 months after grafting

RR – 25 yrs s/p ORIF open bimal – possible SAD

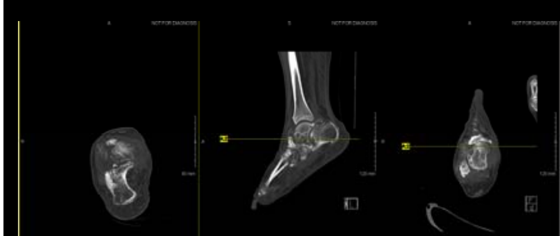
RR

RR – 3 months walking / painless

8 months

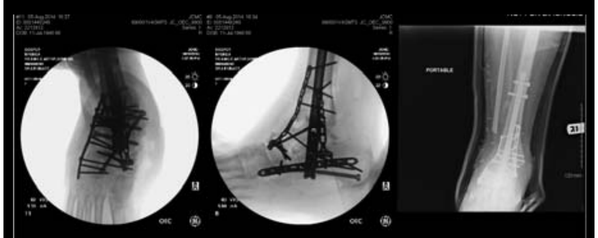
BC – DM, Charcot

July 2013



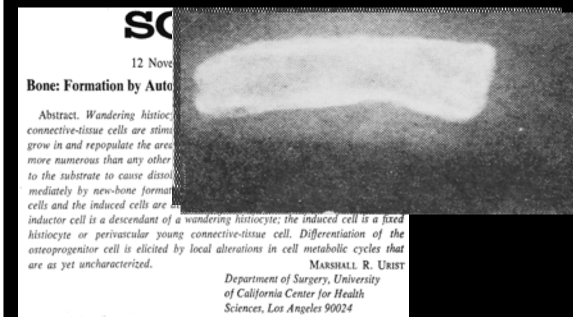
July 2014

Aug 2014

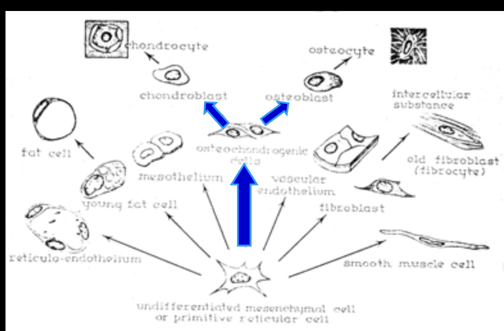


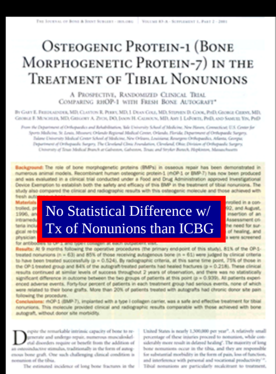
January 2015

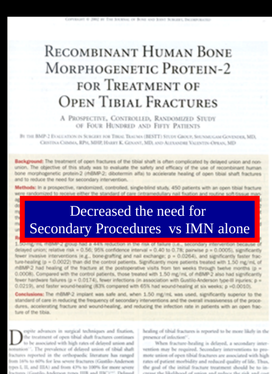
BMPs ?

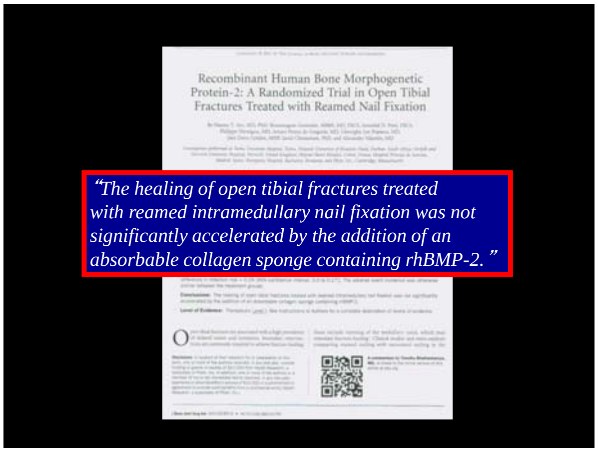


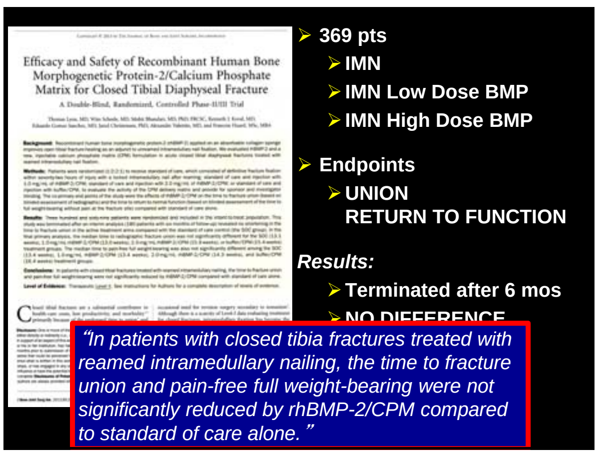
The Mesengenic Lineage

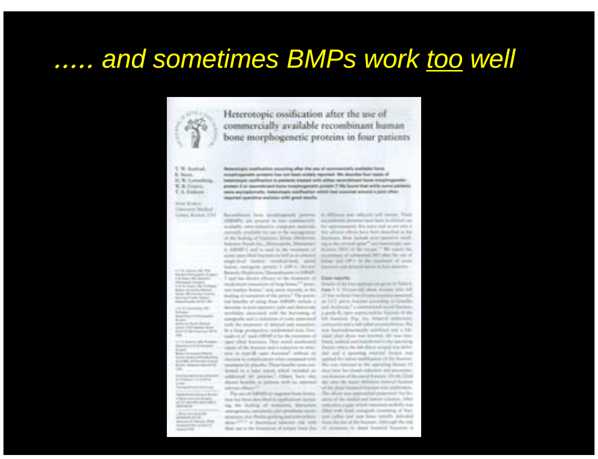




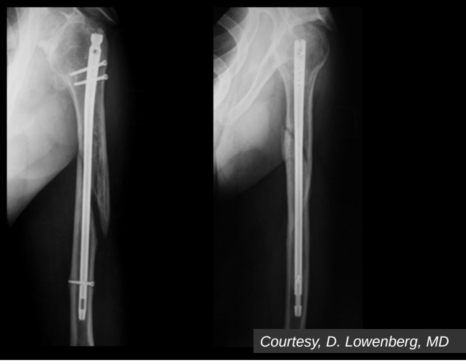



Recombinant Human Bone Morphogenetic Protein-2: A Randomized Trial in Open Tibial Fractures Treated with Reamed Nail Fixation
"The healing of open tibial fractures treated with reamed intramedullary nail fixation was not significantly accelerated by the addition of an absorbable collagen sponge containing rhBMP-2."

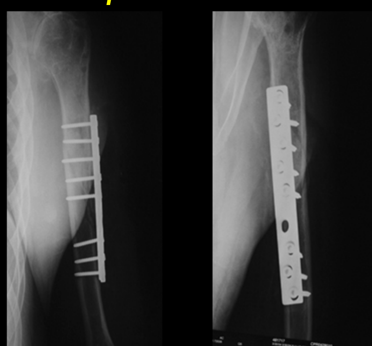

Efficacy and Safety of Recombinant Human Bone Morphogenetic Protein-2/Calcium Phosphate Matrix for Closed Tibial Diaphyseal Fracture
A Double-Blind, Randomized, Controlled Phase-II/III Trial
369 pts
IMN
IMN Low Dose BMP
IMN High Dose BMP
Endpoints
UNION
RETURN TO FUNCTION
Results:
Terminated after 6 mos
NO DIFFERENCE
"In patients with closed tibia fractures treated with reamed intramedullary nailing, the time to fracture union and pain-free full weight-bearing were not significantly reduced by rhBMP-2/CPM compared to standard of care alone."


….. and sometimes BMPs work too well
Heterotopic ossification after the use of commercially available recombinant human bone morphogenetic proteins in four patients

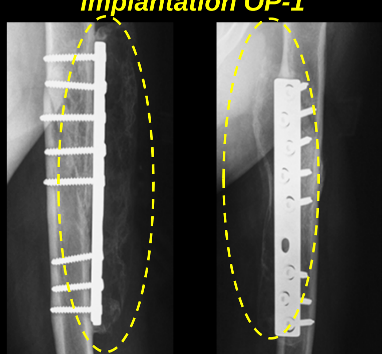
Fifty-four year-old man with a six-month old humeral nonunion



Five-weeks post-op plate fixation and implantation OP-1



Five-months post-op plate fixation and implantation OP-1

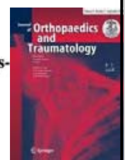


J Orthopaed Traumatol (2015) 16:151–159
DOI 10.1007/s10195-014-0327-6

CrossMark

ORIGINAL ARTICLE

The effect of locally delivered recombinant human bone morphogenetic protein-2 with hydroxyapatite/tri-calcium phosphate on the biomechanical properties of bone in diabetes-related osteoporosis



Frank A. Liporace · Eric A. Breitbart ·
Richard S. Yoon · Erin Doyle · David N. Paglia ·
Sheldon Lin

Conclusions Groups treated with rhBMP-2 demonstrated improved bone mineral density at both 4 and 8 weeks compared to control saline groups, in addition to strong trends towards improvement of intrinsic and extrinsic biomechanical properties when compared to control groups. Data revealed trends toward dose-dependent increases in peak torque, torsional rigidity, shear stress, and shear modulus 4 weeks after rhBMP-2 treatment.

HSSJ (2015) 11:104–111
DOI 10.1007/s11420-015-9432-1

HSS Journal®
The Musculoskeletal Journal of Hospital for Special Surgery

ORIGINAL ARTICLE

Bone Mesenchymal Stem Cells with Growth Factors Successfully Treat Nonunions and Delayed Unions

Pingal Desai, MD · Saad Mumtaz Hasan, MD · Lester Zambrana, BA · Vishal Hegde, MD · Anas Saleh, MD · Matthew R. Cohn, BS · Joseph M. Lane, MD

[BMA + DBM] vs [BMA + BMP]

49 TIBIA NONUNION

Results

Although both with success in tx'ing nonunions

There was no difference in the healing rate ($p = 0.81$) between patients with fracture gaps less than and greater than 5 mm. On multivariate analysis, the use of rhBMP-2 was associated with a lower healing rate compared to DBM ($p = 0.036$). Patients who underwent early intervention (within 6 months of fixation) had higher union rates ($p = 0.04$).

TAKE HOME POINTS !

100% Nonunions caused by:

- Motion
- Avascularity
- Gap
- Infection

PLAN to:
REVERSE THE PROBLEM(s) to have a chance for SUCCESS!

Personal Tx Algorithm

- Resect avascular segments
- Treat Infection
- Correct Deformity
- Provide Mechanical Stability

- Graft
  - Osteoconductive, Osteoindcutive, Osteogenic
- BMA + DBM + Crushed Cancellous graft + Powder Antibiotic