Enhancement of fracture healing-current trends

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Iliac crest: the gold standard

- **Osteogenicity**: ability to form bone
- **Osteoinductivity**: induce bone formation
- **Osteoconductivity**: allow bone to grow
- **Histocompatible & non immunogenic**

… Szapalski 2005
Autograft : problems

- Donor site morbidity: pain 31%, scarring
- Hernia, infection, nerve injury, iliac wing #s
- Blood loss, more operative time
- Low volume if previously used & In porosis
Bone growth stimulators

- **Biological methods**: growth factors, BMP
- **Biophysical methods**: UltraSound, electromagnets
- **Physical methods**: improved implants
- **Chemical methods**: Drugs: Simvastatin
Biological methods

• Bone induction principle
• Marshall Urist 1965: identified BMP

“Bone matrix contains proteins which induce new bone formation when implanted extraskeletally“
BMP
• Protein : belongs to TGF – B superfamily
• 20 BMPs are discovered currently
• Chondrogenic phase : BMP 2-6
• Osteogenic phase : BMP 7, 8
• Only 2 are clinically useful :
  - rh BMP-2 (Infuse , Medtronic )
  - rh BMP-7 (OP-1 , Stryker )
• Both are manufactured by gene recombination tech. from bovine sources
Method of use

- Both the products require a collagen sponge carrier delivery system
  - Scaffold for bone ingrowth
  - Concentrates BMP locally
- Necrotic & sclerotic tissue shld be debrided
- Should be in contact with viable fragment
- ORIF shld be done first
- No irrigation, drains after BMP

*Biological adjunct with no mechanical strength*
Clinical evidence

**BESTT study** Govender et al JBJS A 2002

Multicentre prospective RCT 450 open tibial #s

- Accelerated union time
- Improved wound healing
- Few secondary interventions
- Reduced infection rate

**Swiontkowski et al , Mckee et al OTA 2002**

- IIIa & IIIb open #s 145 pts
- Definitely less secondary interventions
BMP in nonunions

- **Frielernder et al JBJS A 2003**
  Multicentre prospective RCT on 122 NU
  Higher union rate with rhBMP 7.
- **Bilic et al Int Orth 2006 scaphoid NU**
- **Bull et al 2006 17 humeral NU**
  100% union with BMP 7
- **Giannoudis et al Injury 2007**
  Pelvic NU 78% good results.
Problems with BMP

• Heterotrophic ossification
  …*Boraiah Corr* 2009

• Bone resorption: stimulation of osteoclasts
  Esp in cancellous bone  …*Toth spine* 2009

• Local inflammatory response

• Local immune response

• Stimulation of cancer cells
  …*cochrane database* 2010

*Recommended use in atrophic nonunions only*
Biophysical methods

• Basset et al 1962

  Mechanical forces applied to healing bone generate local electric potentials which can cause cellular transduction

• A. electric
• B. magnetic
• C. ultrasound
Electrical stimulation

• **D C stimulation**: increase collagen & proteoglycan production by reducing local PO2

• **Pulsed electromagnetic stimulation**: Increase formation of BMP2 & BMP4
Magnetic stimulation

• Affects ion transport across cell mem
• Increase the formation of insulin like growth factor II which proliferates osteoblasts

... insufficient clinical evidence for commercial use.
Ultrasound stimulation

• Low intensity pulsed ultrasound :LIPUS
• Most extensively studied & reported
• Has adequate clinical evidence

• 1\textsuperscript{st} clinical study by Xavier & Duarte in 1983
• Published in AOTS 1983
• Based on the piezo electric properties of bone
LIPUS: MECHANISM

• 3 Fold increase in blood flow at # site
• Increased angiogenesis
• Increased chondrogenesis
• Increased intracellular calcium levels
• Facilitate adhesion of osteoblasts to the fracture site
• Increased osteogenesis
Clinical evidence

• Acute fractures:
  
  1. Heckmann et al JBJS A 1994
     RCT on 48 tibial #s: 46% faster healing
  
  2. Krisiantsen et al JBJS A 1997
     RCT on 85 distal radius #s: 35% faster healing
  
  3. Mayr et al JHMPS Germany 2000
     RCT on 30 scaphoid #s: 30% faster healing
Clinical evidence

- **Nonunions**

1. *Mayr et al AOTS 2000: retrospective study on 933 DU & 366 NU*

<table>
<thead>
<tr>
<th>Bone</th>
<th>Delayed union</th>
<th>Nonunion</th>
</tr>
</thead>
<tbody>
<tr>
<td>clavicle</td>
<td>95%</td>
<td>80%</td>
</tr>
<tr>
<td>humerus</td>
<td>76%</td>
<td>69%</td>
</tr>
<tr>
<td>radius</td>
<td>94%</td>
<td>95%</td>
</tr>
<tr>
<td>ulna</td>
<td>81%</td>
<td>85%</td>
</tr>
<tr>
<td>scaphoid</td>
<td>94%</td>
<td>98%</td>
</tr>
</tbody>
</table>

2. *P. Tornetta, M. Bhandari BMJ 2009 metanalysis of 158 pts in various studies*

36.9% decrease in healing time
Extended uses

- High energy open tibial fractures
  \textit{Leung et al UMB 2004}

- Failed arthrodesis – charcot neuropathy
  \textit{Strauss et al clin orthop 1998}

- Stress fractures of tibia
  \textit{Brand, Jensen Iowa J O 1998}

- Infected nonunions
  \textit{Romano et al oct 1999}
LIPUS

• APPROVED for use on patients by the FDA in 1994 for fresh fractures & 2000 for nonunions

• Has to be used at half hrly pulses for 6 weeks at least.

• Available as noninvasive home therapy: EXOGEN
Chemical agents

**Simvastatin** locally applied to fracture
- Between 28-42 days after #
- Increases angiogenesis locally
- Decreases bone resorption

*S Pauly, N.Haas Berlin, Bone 2009*

Studies on Rabbits & sheep
Newer agents

• **HE 800** a hyaluronic acid like bacterial exopolysaccharide

• **Amniotic fluid**: stem cells

• **PRP in collagen matrix**, hydroxyapatite

• **NMP**: N – methyl pyrrolidone

? Safe, human trials awaited
..........THANK YOU !!