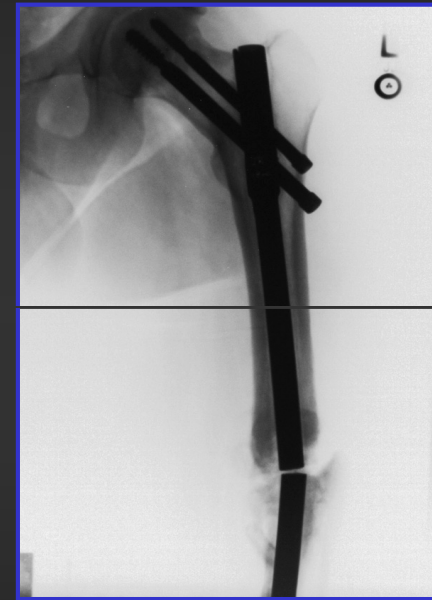


Biological enhancement of Aseptic Femoral Non-unions with BMP-7 – a multicenter experience.

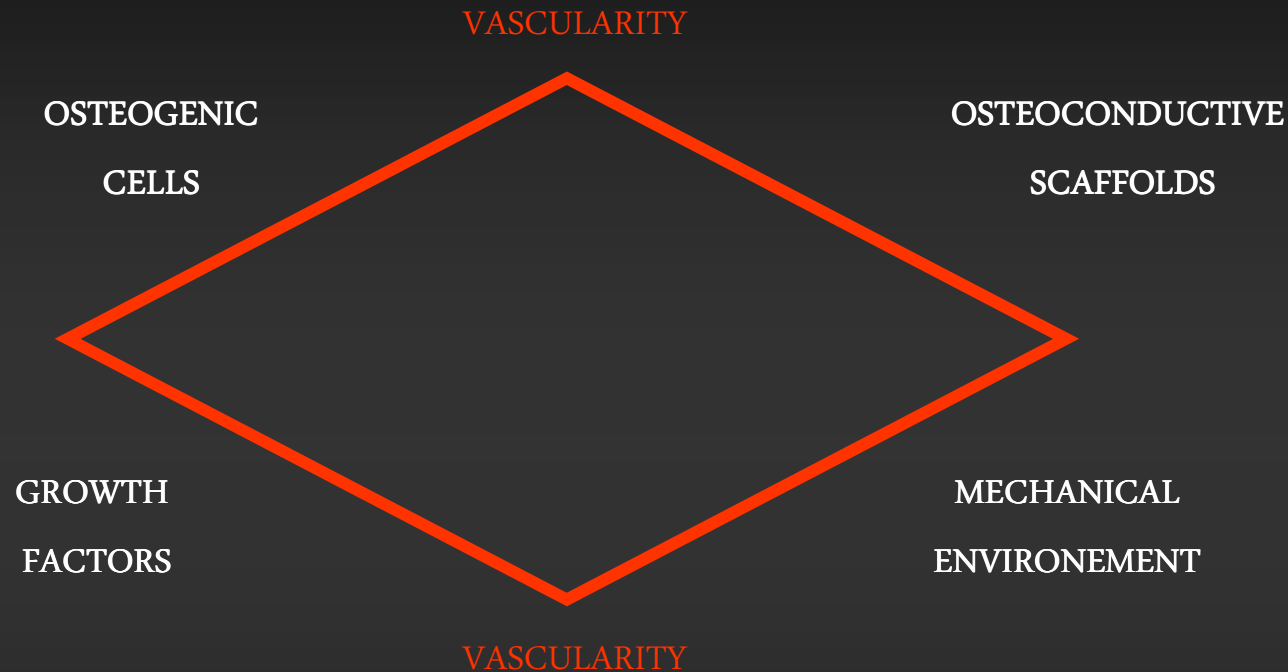


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Impaired Fracture Healing



**The Diamond
Concept**

1: [Injury](#). 2007 Sep;38 Suppl 4:S3-6.

Fracture healing: the diamond concept.

[Giannoudis PV](#), [Einhorn TA](#), [Marsh D](#).

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Fracture healing is a complex physiological process. With the latest advances made in molecular biology and genetics it is now known that it involves the spatial and temporal coordinated action of several different cell types, proteins and the expression of hundreds of genes working towards restoring its structural integrity without scar formation. The standard tissue engineering approach to provide solutions for impaired fracture healing, bone restoration and regeneration includes the utilisation of growth factors, scaffolds and mesenchymal stem cells (triangular concept). However, although the mechanical environment is discussed and is considered as an important element in bone regeneration, its importance is often underestimated and it is not always given the necessary attention. The available scientific evidence supports the view that all the 4 known factors contributing to bone restoration should be given an equal acknowledgment and recognition. The traditional discussed triangular concept therefore should be reconsidered and be accepted as the 'diamond concept'.

PMID: 18224731 [PubMed - indexed for MEDLINE]

Femoral Non-Unions

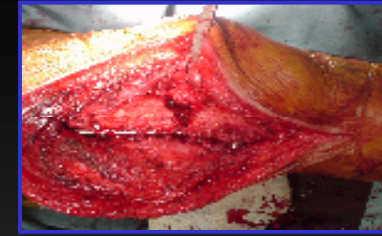
- Are rare
- Very challenging
- Treatment may be long lasting
- Utilisation of many resources



Reports of Femoral Fracture Treatments - *Results*

Author	Year	No of patients	Intervention	Nonunion (%)
Ruedi and Luscher	1979	131	Plating	7
Loomer et al.	1980	46	Plating	2
Alonso et al.	1989	24	External fixation	12
Wiss et al.	1990	112	Reamed antegrade nail	2
Riemer et al.	1992	141	Plating	7
Geissler et al.	1995	71	Plating	7
Mohr et al.	1995	17	External fixation	0
Wolinsky et al.	1999	551	Reamed antegrade nail	6
Nowotarski et al.	2000	54	External fixation then nailing	3
Ostrum et al.	2000	54	Retrograde nail	2
Tornetta & Tiburtzi	2000	83	Reamed antegrade nail	0
Tornetta & Tiburzi	2000	89	Unreamed antegrade nail	0
Ricci et al.	2001	134	Retrograde nail	6
Canadian Orthopaedic Trauma Society	2003	121	Reamed antegrade nail	2
Canadian Orthopaedic Trauma Society	2003	107	Unreamed antegrade nail	8

Patients and Methods

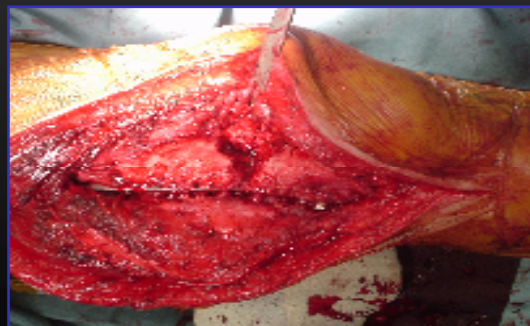


- Non-union was declared as healed in the absence of pain on loading and in the presence of bridging callus on 3 of the 4 cortices in two different planes on x-rays.
- One unit of BMP-7 per non-union was applied in all cases (Osigraft, by Stryker Biotech Hopkinton, Massachusetts, MA, USA) containing 3.5 milligrams of the rhBMP-7 mixed with 1 gram of type I bovine-derived collagen.
- The clinical and functional outcome assessed utilising parameters like union, complication, return-to-previous-occupation rates, and the EuroQol 5D

Patients and Methods



- A focused electronic databank has been created and updated constantly since January 2005
- Accumulation of clinical prospective and retrospective data regarding the use of BMPs
- 6 International specialised orthopaedic centres (3 Italian, 1 Belgian, 1 Dutch, 1 from UK - **University hospitals**)



<http://www.bmpusergroup.co.uk>

Results

- 30 cases (22 males - 8 females)
- Median Age 42 (range 20-78)
- 9 Smokers - 1 DM
- Mechanism: 24 RTAS – 6 Falls
- Anatomic location:
 - 4 proximal 1/3
 - 17 mid-shaft
 - 9 distal 1/3



Results

- 22 closed – 8 open (3 I, 1 II & 4 III)
- Initial stabilisation 15 IMN - 10 ORIFs - 5 DCO
- Previous operations 1.6 (1-5)
- Time from injury to BMP-7 application 24 months
- 10 cases had implanted AICBG
(*Autogenous Iliac Crest Bone Graft*)



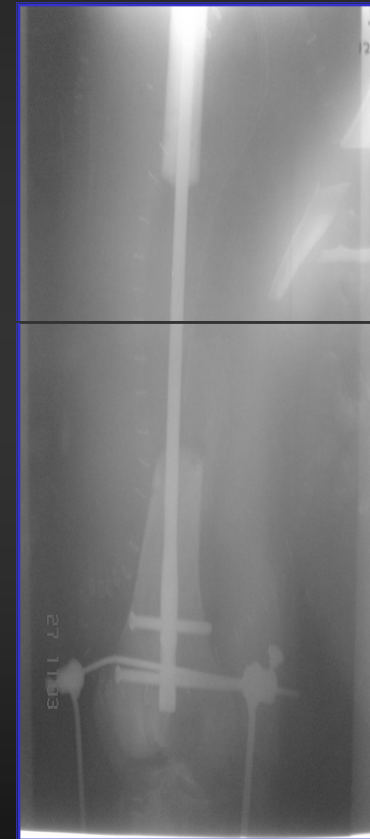
RESULTS

- 7 cases: BMP-7 implantation - no hardware removal
- 23 cases had revision of fixation & BMP-7
 - 14 exchange IMN (11 exchange nailings and 3 revisions from ORIF)
 - 6 ORIFs (1 from IMN, 5 ORIF exchange)
 - 3 Circular Frame (1 from IMN and 2 exchanges)
- 12 cases BMP-7 and AICBG
- Median follow up 30 months (12-46)



RESULTS

- Union rate 26/30 (86.7%)
- Time to union 6 months (4-10)
- 4 cases of re-operation
- 19 patients returned to work
- 7 changed occupation
- 1 retired
- EuroQ overall health state 82.5 points



RESULTS

Complications

- 2 superficial wound infections
- 1 haematoma
- 1 DVT
- 0 systemic reactions



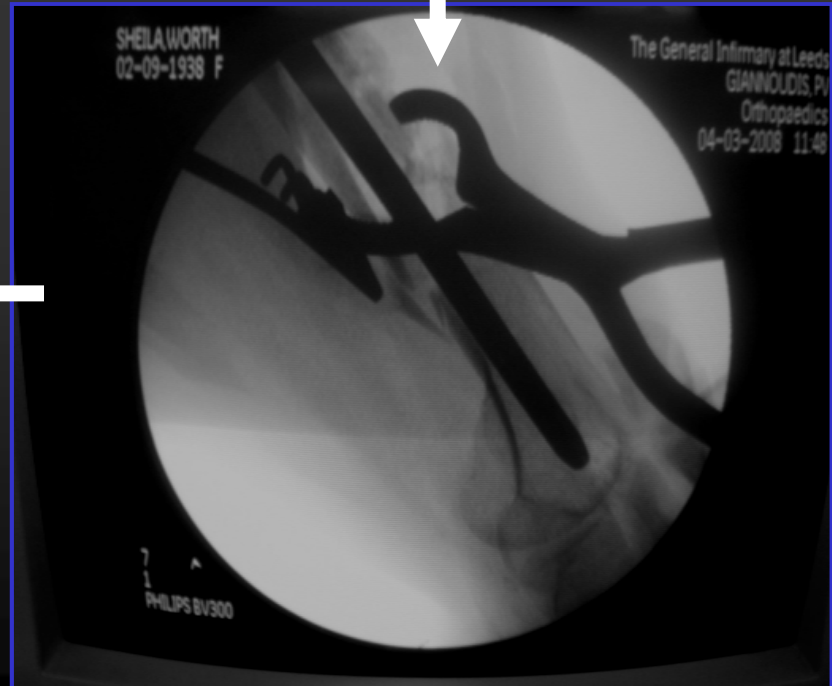
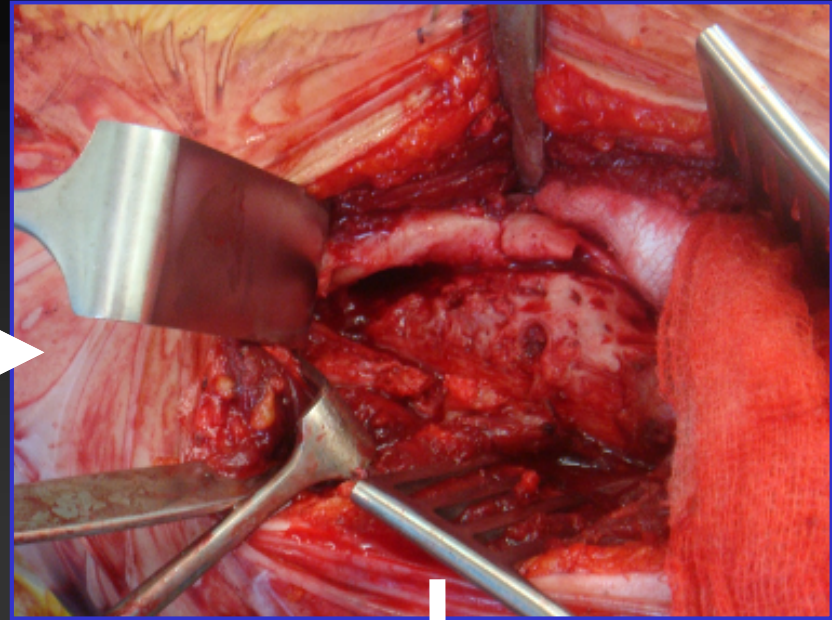
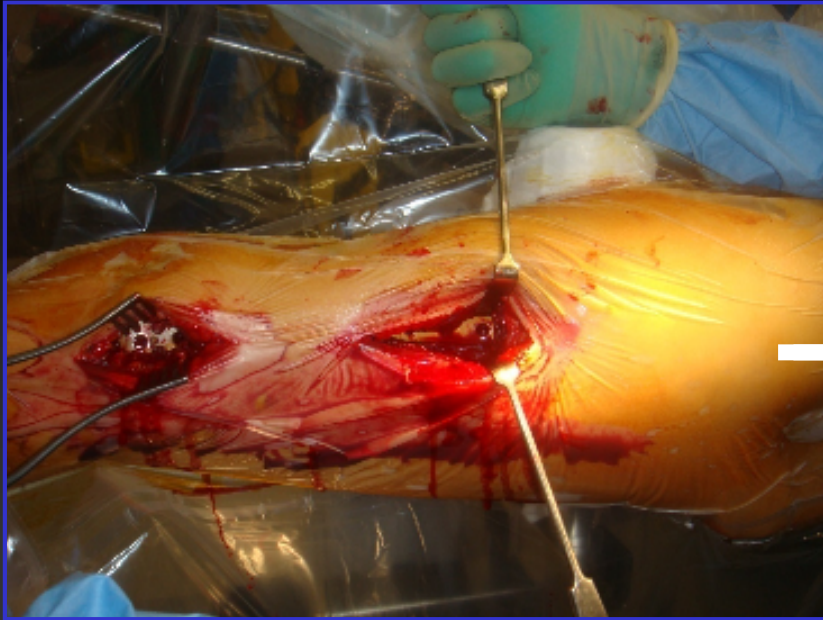
Authors Journal	LOE	Femoral nonunions & BMPs*	Site Indication Non-Union	Union Rates (Femur)	Mean time to Union	Re- Operations	Functional Outcome
Johnson EE 1992-CORR	(hBMP & allograft) <i>IV</i>	12 (25)	Tibial, Femoral, Humeral	75%	6 months (3-14)	20%	14 excellent 5 good 5 fair
Dimitriou R 2005-Injury	(BMP-7) <i>IV</i>	8 (25)	Tibial, Femoral, Humeral, Forearm, Clavicle	100%	5.6 months (2.5 - 11)	12%	n/a
Calori GM 2008 -Injury	(BMP-7 vs. PRP) <i>II-III</i>	5 (16)	Tibial, Femoral, Humeral, Forearm	100%	8 months (+ / - 0.43)	6.2%	n/a
Ronga M 2006-Injury	(BMP-7) <i>IV</i>	23 (105)	Tibial, Femoral, Humeral, Forearm, Clavicle	78.3%	7.9 months (2-21)	16.2%	n/a
Present Study	(BMP-7) <i>IV</i>	30	Femoral	86.7%	6 months (4-10)	13.3%	21 excellent 5 good 4 poor (re-operation)

Case 1

(female - 73 years old - RTA)

- A. Left Spiral shaft femoral fracture treated with locking LISS MIPPO plating
- B. Nine months later no progress of healing.
- C. Intramedullary nail fixation and BMP7 application (9 months post injury).
- D. Five months later, pain free function of the extremity and radiological healing.





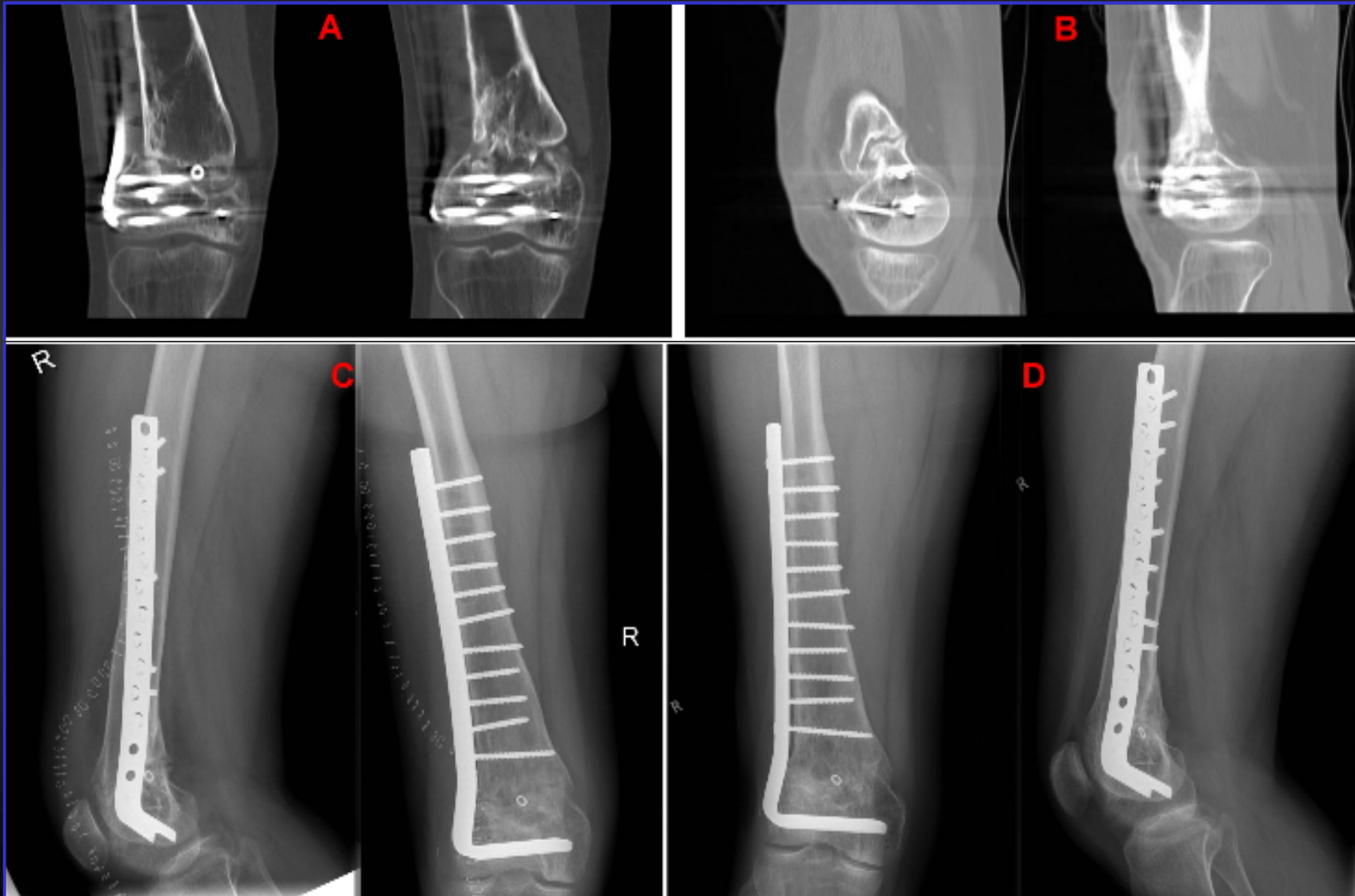
Case 2

(male - 24 years old - RTA)

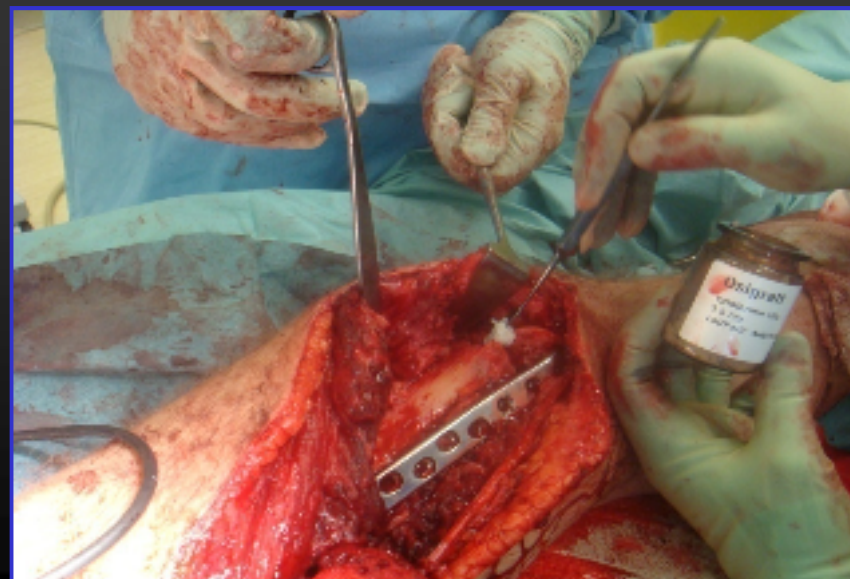
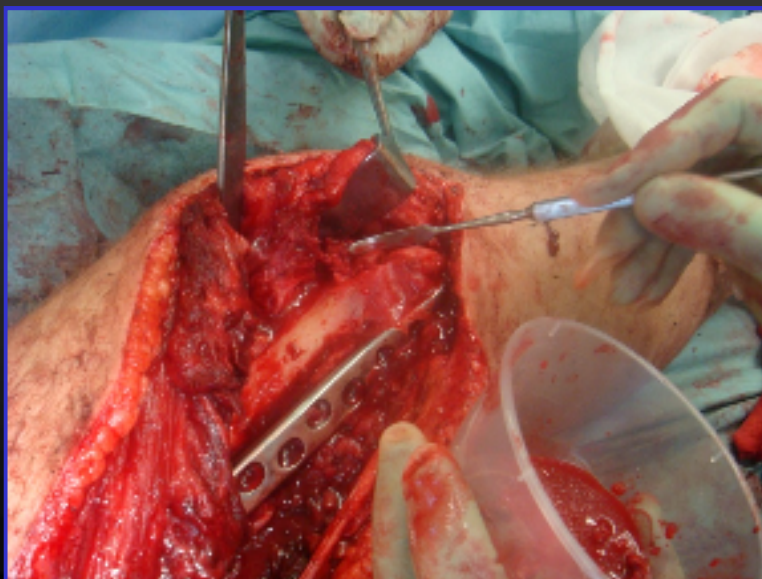
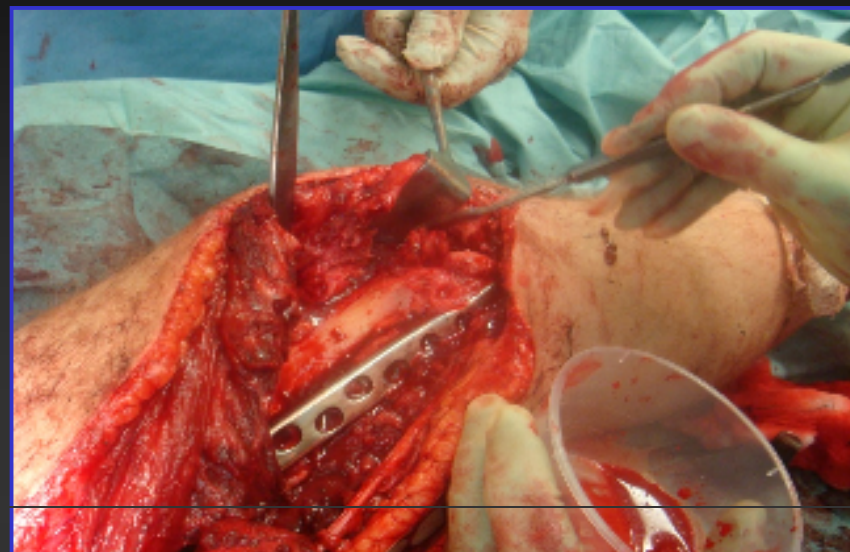
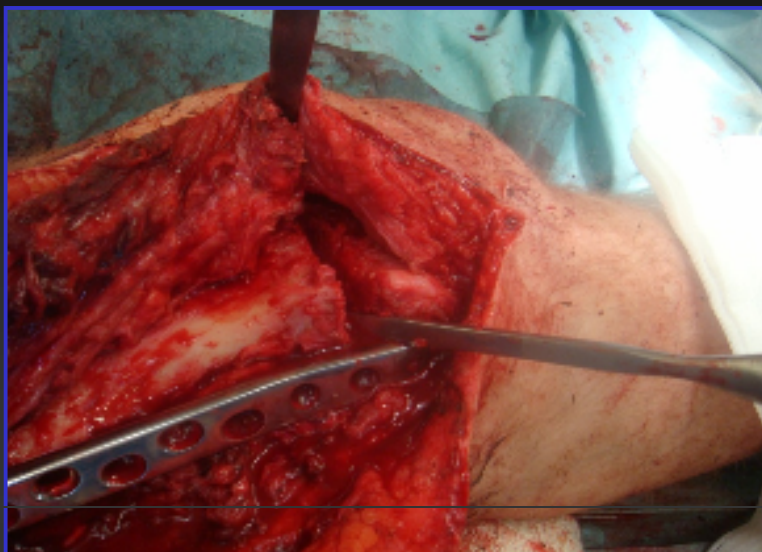
A-B. Femoral supracondylar fracture 12 months post injury and after an original ORIF and a first revision ORIF with locking LISS plate.

C. Postoperative films after revision ORIF with a blade plate and BMP-7 application.

D. 8 months post BMP7 application evident radiological healing, pain free FWB.



Case 2



Case 3

(male - 62 years old - fall)

- A. Subtrochanteric right femoral fracture.
- B. Initial IMN fixation. Malreduction in varus angulation and distraction.
- C. 18 months post initial fixation and after a failed exchange nailing.
- D. Revision of the nail and application of BMP7 and Autograft.
- E. 6 months post BMP7 application, evident radiological and clinical healing.



Literature

- No statistical differences between cases treated with BMP-7 or Autologous Bone Graft in tibia non-unions

Osteogenic protein-1 (bone morphogenetic protein-7) in the treatment of tibial nonunions.
Friedlaender GE, Perry CR, Cole JD, et al. - *J Bone Joint Surg Am* 2001;83-A (Suppl. 1 (Pt2)):S151-8

- Osteomyelitis at the fracture site in 21 % of patients treated with ABG but only in 3 % of those treated with BMP-7

Osteogenic protein-1 (bone morphogenetic protein-7) in the treatment of tibial nonunions.
Friedlaender GE, Perry CR, Cole JD, et al. - *J Bone Joint Surg Am* 2001;83-A (Suppl. 1 (Pt2)):S151-8

- BMP-7 reduces consolidation time in the scaphoid non-union compared to the time needed after the use of ABG.

Osteogenic protein-1 (BMP-7) accelerates healing of scaphoid non-union with proximal pole sclerosis.
Bilic R, Simic P, Jelic M, et al. - *Int Orthop* 2006;30(April (2)):128—34.

- Clinical and radiological union at a percentage of 92.3 % in persistent upper and lower limb non-unions

Application of recombinant BMP-7 on persistent upper and lower limb non-unions.
Dimitriou R, Dahabreh Z, Katsoulis E, et al. - *Injury* 2005; 36 Suppl 4 S51-9.

- The implantation of BMP-7 in pelvic reconstruction procedures adds another alternative to the treatment methods of contemporary orthopaedic

Biological enhancement of bone healing with Bone Morphogenetic Protein-7 at the clinical setting of pelvic girdle non-unions.
Giannoudis PV, Psarakis S, Kanakaris NK, Pape HC. - *Injury* 2007; 38 Suppl 4 S43-8

- Treating fracture non-unions is costly, but this could be reduced by early BMP-7 administration when a complex or persistent fracture non-union is present or anticipated.

Biological enhancement of bone healing with Bone Morphogenetic Protein-7 at the clinical setting of pelvic girdle non-unions.
Giannoudis PV, Psarakis S, Kanakaris NK, Pape HC. - *Injury* 2007; 38 Suppl 4 S43-8

Comclusions

- The implantation of BMP-7 as a biological stimulant appears to offer a good alternative option to AICBG.
- Use them in an early stage to avoid many re-operations
- No donor site morbidity – ABG harvesting
- Union rates as good as other series - No systemic effects.
- Need for multicenter supported databanks



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Application of BMP-7 to femoral non-unions: A 4-year multicentre experience

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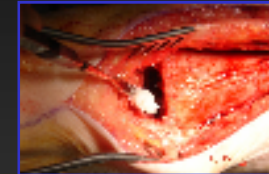
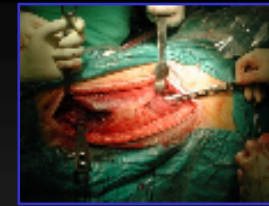
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THANK YOU



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