Orthopaedica Belgica Course 2018

Natural or synthetic bone substitutes

Prof O Cornu

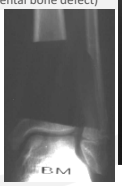
Cliniques universitaires SAINT-LUC UCL BRUXELLES

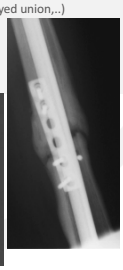
Need for bone substitution

Cavitary bone filler (metaphyseal defect, tumor,..)

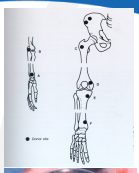
Bone healing promoter (bone volume expander, delayed union,..)

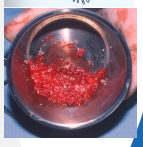
Bone and joint replacement material (Segmental bone defect)





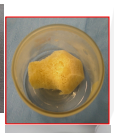
Bone Substitutes





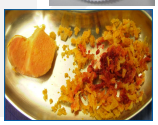
➢ ***Human***

Bone auto- and allo-grafts



donor site morbidity
limited availability

risk of disease transmission
immune response



incomplete integration

Alternatives ?

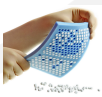
Bone Substitutes

➢ ***Animal***

Bone xenograft (Bovine/Coral)
Hydroxapatite (Endobon® ; ProOsteon®)

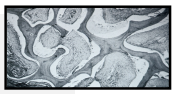
Synthetic

Calcium phosphate
Collagen (Healos® ; Collagraft®)
Calcium sulfate (Osteoset® ; Stimulan®)
Calcium silicate (bioglass) (Bonalive®)

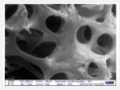


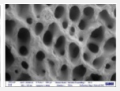
Animal bone substitutes

➢ **Bovine bone** : anecdotal use (Isobone®,Lubboc®)
concerns about non-union
intense inflammation



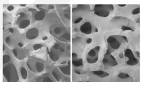
➢ **Hydroxyapatite from animal origin**
Solvent and high temperature process (>1100 °C)
Bovine - Endobon® - animal origin bone structure
- concerns about porosity / remodeling





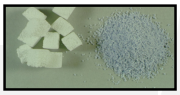
porosity (< 1 µm / > 0,2 mm)

Coral - ProOsteon® - calcium carbonate / thin HA layer
- interconnectivity



Filling material – dental applications
Biological degradation of the materials does not occur even during long-term follow-up.

Synthetic bone substitutes – Calcium Phosphate – World of ceramics

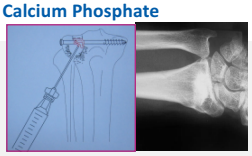


➢ **Calcium phosphate Ceramic**
Calcium phosphate powder ; Process : calcination (<900°C), compaction (high pressure), Sintering (1100-1500°C)
Porosity - microporosity : depending on physical parameters ; < 5 µm
- macroporosity : naphtalen ; high temperature sublimation ; > 100 µm
Ca/P HAP – 1,67 ; ßTCP – 1,5 ; BPC – variable (Bone Ca/P 1,61)

ADVANTAGES	LIMITS
Osteoconductive	Resorption varying on crystal size and composition
Promote cellular function (strong bone-implant interface)	Brittle ; structural strength varying for each formulation
Able to bind and concentrate BMP's and become osteoinductive	Limited non comparative studies as bone substitute (mainly bone void filler)
Similar to bone mineral	

Synthetic bone substitutes – Calcium Phosphate

➢ **Calcium phosphate Cement**



\+ Excellent biological properties
Injectable, moulded into the bone defect
ability to harden in situ at body temperature

\- Brittle, with low cohesion and no macroporosity
non loadbearing application **"NOT A GLUE"** **Need fixation**

Metaphyseal bone defect
Reinforcing osteoporotic bone
Bone augmentation

➢ **Apatite** HAP :
Better osteointegration
Stable in time
Higher mechanical properties

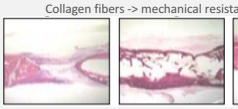
Long setting time
Low injectability
Biobon ®, BoneSource ®, Calcibon ®,Cementek ®, Norian SRS ®

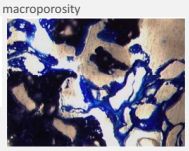
➢ **Brushite ßTCP** :
More degradable
Quick setting time

Poor mechanical properties
Low injectability
ChronOs inject®, Eurobone®, Vitalos®

Synthetic bone substitutes – Calcium Phosphate

➢ **HA/ ßTCP +Collagen** (Healos® ; Collagraft®; Collapat II®; CopiOs®;VitOss®)
Highly purified bovine dermal collagen type I and HA/ßTCP
Collagen fibers -> mechanical resistance enhancement, macroporosity





Alvis M et al. 46th Meeting, Orthopaedic Research Society, March 12-15, 2000, Orlando, Florida

Must be used with: autologous bone savings or PRP (Platelet Rich Plasma) or autogenous bone marrow

-> questionable results
"not inferior to autologous iliac crest bone as a graft material in posterolateral lumbar spine fusions but are radiographically ineffective in lumbar interbody fusions."
Neen D et al. Spine 2006;31:636-40.

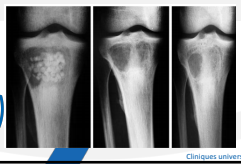
-> Bone graft expander

Synthetic bone substitutes – Calcium Sulfate

➢ **Surgical grade Calcium Sulfate**
First application in tuberculosis 1892 - Dreesman
Bone defect filler/graft expander 1959 - Peltier LF. *Clinical Orthopaedics*. 1961;21:1-31.

rapid resorption and poor mechanical performance -> Antibiotic carrier (***Osteoset T®, Herafill G®***)

D Donati et al. Adult osteomyelitis : Debridement versus debridement plus Osteoset T® pellets. Acta Orthop. Belg., 2007, 73, 238-244
No difference debridement versus debridement and Osteoset T unless within the subgroup of 39 patients with Cierny-Mader type IA (medullary osteomyelitis and normal immune system)
Most common complication: aseptic serous discharge (20%)



Synthetic bone substitutes – Calcium Sulfate

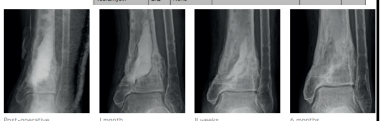
➢ **Surgical grade Calcium Sulfate**

New formulations (Stimulan®, *Cerament G and V®*)

physiologic pH, Hydrophilic
any antibiotic (termostable/thermolabile)
Pellets <-> injectable cement

Phase analysis	Commercial Calcium Sulphate	Medical / Surgical Grade	Stimulan® implant Grade
$CaSO_4 \cdot 2H_2O$	80-94%>	98%>	100%
$CaCO_3 MgCO_3$*	5.1%	0.5%	Nd
$CaCO_3$	1.0%	0.3%	Nd
Aggregate**	4.5%	0.3%	Nd

Single Antimicrobial Agents			Combined Antimicrobial Agents		
Amikacin	LIQ	LG	Gentamicin/Cefazolin	LIQ/POW	None
Amphotericin-B	POW	LG	Vancomycin/Amikacin	POW/LIQ	LG
Cefazolin	POW	LG	Vancomycin/Amphotericin-B	POW/POW	LG+S
Cefotaxime	POW	LG	Vancomycin/Fluconazole	POW/POW	LG
Ciprofloxacin	POW	LG	Vancomycin/Gentamicin	POW/LIQ	None
Clarithromycin	POW	LG+S	Vancomycin/Gentamicin/ Amphotericin-B	POW/LIQ/PO W	None
Fluconazole	POW	LG	Vancomycin/Piperacillin-Tazobactam	POW/POW	LG+S
Gentamicin	LIQ	None	Vancomycin/Tobramycin	POW/LIQ	None
Meropenem	POW	LG+S	Vancomycin/Tobramycin/ Amphotericin-B	POW/LIQ/PO W	None
Rifampin	POW	LG			
Tobramycin	LIQ	None			



Synthetic bone substitutes – Calcium Silicate

➢ **Bioactive Glass** (Actifuse ®; VitOss BA®; BonAlive®)
Bone filler
Remineralising agent
Angiogenic properties
Antibacterial agent: sodium released -> increase in pH
release of silicon, calcium, and phosphorous ions
increases osmotic pressure

Conclusions

➢Numerous synthetic bone substitutes solutions

➢Limited clinical reports (mostly non comparative, non randomised, limited cohorts)

➢Bone filler / Bone graft expander

To be used with Bone Marrow Aspirate/Autograft

Non loadbearing application

➢May act as drug carrier/ biological properties enhancement
(surface treatment, adjunctive proteins or growth factors)

➢Antibacterial properties