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Calcium-phosphate **biomaterials** *for bone healing*

practical guideline for implementation in clinical practice

SECOND EDITION

This publication was made possible by...

Colofon

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Contents

Preface

Dear reader,

The second edition of this booklet summarizes the basic terminology regarding material/mechanical properties of Ca-P ceramics and will explain their effect on biological and mechanical behaviour. Also the Diamond/Pentagon concept for bone healing is explained and supported by illustrative cases.

In this second edition, additional information is added on osteoinduction and additional biomaterials such as bioactive glass and bioactive peptides

As before, this book is by no means intended as a comprehensive overview but aims to raise awareness and stimulate discussion regarding Ca-P ceramics for bone healing in clinical practice. I trust you will find this a useful addition to your clinical practice and education.

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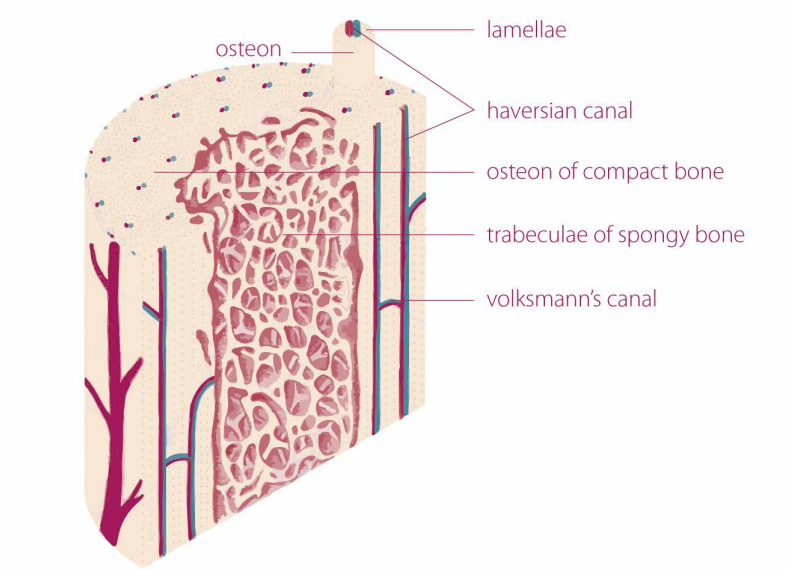
Definitions



Bone is a living tissue capable of self-repair

Bone only forms when mechanical loading is present (Wolff's law)

Bone is continuously being renewed; balance between osteoblasts forming bone and osteoclasts resorbing bone

This process of constant bone resorption and bone formation is called *bone remodeling*

Functions of bone

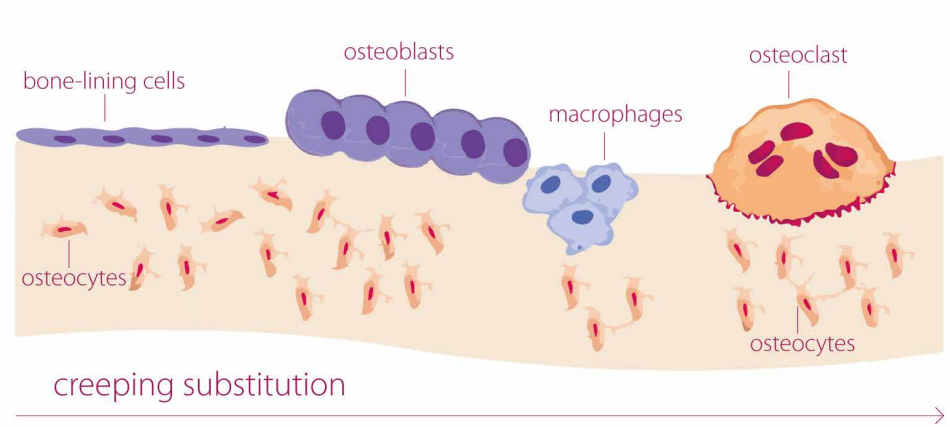
Stabilise and support body

Protection of internal organs and soft tissue

Rigid part of the human movement system

Storage of minerals and fatty acids

Production of blood cells through bone marrow haematopoiesis



The process of bone remodeling is also called *"creeping substitution"* [17]

The osteoclastic resorption of bone grafts or Ca-P materials and its replacement by new living bone made by osteoblasts from the host tissue

Gradual penetration across a fracture site by osteogenic tissue followed by bone formation

Biomaterial

A natural or synthetic material that is suitable for introduction into living tissue[1]

A synthetic material used to replace part of a living system or to function in intimate contact with living tissue. [2]

A biomaterial is a substance that has been engineered to take a form which, alone or a a part of a complex system is used to direct, by control of interactions with components of living systems, the course of any therapeutic or diagnostic procedure. [3]

Scaffold

Temporary framework used to support people and material in the construction or repair of buildings.

In regenerative medicine the more commonly used definition is: “An artificial structure capable of supporting 3-D tissue formation.”[4]

To allow bone formation a scaffold should allow : attachment, proliferation, migration, and phenotypic expression of bone cells leading to formation of new bone in direct apposition to the Ca-P biomaterial.[2,5]

Scaffold purpose[6-9]

Allow cell attachment and migration

Deliver and retain cells and biochemical factors

Enable diffusion of vital cell nutrients and expressed products

Exert certain mechanical and biological influences to modify the behaviour of the cell phase differentiation

A scaffold must be...[6-9]

~ Biocompatible and biodegradable

~ Mechanically stable over time

~ Able to incorporate any chemical, or biological cues desired

~ Adequate permeable to allow fluid flow and diffusion

~ Unable to elicit an inflammatory reaction

The ideal scaffold should be...

> Implantable through a minimal surgical exposure

> Applicable for various indications

> Moldable to conform to and fill irregular defects

> In possession of roughly the same visco-elasticity as bone

> As rigid and strong as intact bone for immediate load-bearing capability

> Promote new bone formation and incorporation by host bone

> Available in large quantities

> Affordable

Bioactivity [2,11]

The ability of a material to have interaction with or effect on any cell tissue in the human body.[2]

The ability of a material to form a direct bonding with the host biological tissue

Biocompatibility [2,11]

The ability of a material to perform with an appropriate host response in a specific situation.

Ability of a material to be in contact with a living system without producing an adverse effect.

Biocompatibility of a material-host system[5]

During ESB 2014 in Liverpool Prof. D.F. Williams postulated that biocompatibility of a specific material does not exist. Instead the definition should be broadened and should state: biocompatibility of a material-host system.

Refers to the ability of a biomaterial to perform its desired function with respect to a medical therapy, without eliciting any undesirable local or systemic effects in the recipient or beneficiary of that therapy, but generating the most appropriate beneficial cellular or tissue response in that specific situation, and optimizing the clinically relevant performance of that therapy.[5]

Definitions

Calcium-phosphate biomaterials *for* bone healing

Osteointegration [2,12]

The property of a material that allows development of a direct, adherent and strong bond with the surrounding bone tissue.

The formation of a direct interface between an implant and bone, without intervening soft tissue.

Osteopromotive (DBMs)

Describes a material that promotes the de novo formation of bone. It will not contribute to de novo bone growth but serve to enhance the osteoinductivity of osteoinductive materials.

Osteostimulative (Bioactive glasses, ceramic BGS)

An osteostimulative material needs an osseous defect that provides nutrients (blood) to stimulate bone growth. Effectively promotes new bone growth, accelerating bone remodeling. In addition, a synthetic bone graft that is osteostimulative will not grow ectopic bone.

Osteoinduction [2,10-11]

The ability to induce new bone formation through molecular stimuli recruitment and differentiation in a controlled phenotype or particular lineage promote cellular functions leading to new bone formation

Active process

Osteoinduction is too widely defined and often used when not supported (DBMs). It should be defined according to location in the body and timeline!

Osteoconduction [2,10-11]

The ability of a scaffold to facilitate new bone formation by allowing bone cells to adhere, proliferate, and form extracellular matrix on its surface and pores

Passive process

Primarily based on mechanical stimuli as well as chemical composition surface properties and geometry of the material

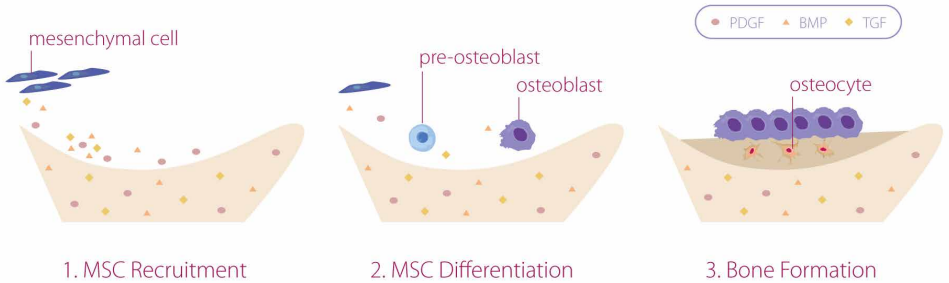
Definitions

Calcium-phosphate biomaterials *for* bone healing

PDGF Platelet-derived growth factor

BMP Bone morphogenetic protein

TGF Transforming growth factor



principles of osteoinductive materials

Osteoinduction [21-22]

Osteoinduction, as proposed by Friedenstein, was “the induction of undifferentiated inducible osteoprogenitor cells that are not yet committed to the osteogenic lineage to form osteoprogenitor cells” .

Urist defined the process of bone formation by autoinduction, or osteoinduction as “the mechanism of cellular differentiation towards bone of one tissue due to the physicochemical effect or contact with another tissue” .

Requirements

Capability of recruiting mesenchymal-type osteoprogenitor cells.

Capability of transforming an undifferentiated mesenchymal cell into a mature, bone forming osteoblast.

Capability of inducing bone formation when implanted in ectopic locations

Ca-P ceramics properties

Ca-P ceramics properties

Calcium-phosphate biomaterials for bone healing

Ca-P ceramics

Refers to ancient Greek “Keramos” which means “pottery”

Made from inorganic, non-metallic materials with a crystalline structure, usually produced by sintering (processing at high >1200° C temperature)

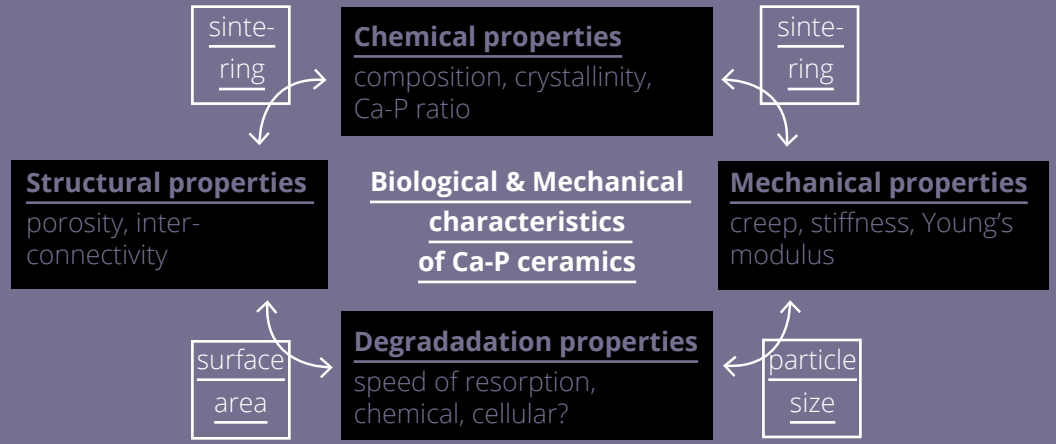
Most ceramics are hard, porous yet brittle

The osteoconductive Ca-P biomaterials allow: attachment, proliferation, migration, phenotypic expression of bone cells leading to formation of new bone in direct apposition to the Ca-P biomaterial

Top sintering production of large HA blocks at high temperature

Bottom ceramic TCP-HA granules with macro-porosity

Property overview of Ca-P ceramics



Ca-P ceramics properties

Chemical properties

Composition refers to the original base components of the material

Hydroxyapatite (HA) [$Ca_{10}(PO_4)_6(OH)_2$]

Tri-calcium phosphate (TCP) [$Ca_3(PO_4)_2$]

Biphasic: percentage combination of HA & TCP in same material

Hybrid: One of the above with added material such as Si, Mg or Bioactive glass

Composition has an effect on

Mechanical properties (impactability strength, stiffness, Young's modulus)

Biological properties (osteoconduction)

Degradability speed

Rules of thumb

Strength	>	TCP less brittle in dry formulation compared to HA
Strength	>	TCP quicker loss of mechanical strength compared to HA in vivo
Resorption	>	TCP chemically less stable compared to HA
Resorption	>	TCP possesses high resolution characteristics compared to HA
Degradation	>	TCP easily resorbed by osteoclasts compared to HA
Degradation	>	TCP faster degradation (12-18 months) compared to HA (2-10 years)

Ca-P ceramics properties

Structural properties

Crystallinity refers to the degree of structural order in a material.

Less order provides a more amorphous material

crystalline structure

amorphous structure

Crystallinity has an effect on

Mechanical properties (hardness, density)

Biological properties (osteoconduction)

Degradation properties (speed and type of degradation)

Rules of thumb

Strength	> High crystallinity provides better stiffer material
Resorption	> Amorphous porous materials enhance bone ingrowth but also biological degradation
Degradability	> High crystallinity leads to slower degradablity due to resistance in dissolution

Calcium-phosphate (Ca/P) ratio refers to be a measurement of Ca-P ceramics composition

Name	Formula	Ca/P
Tetracalcium phosphate	$Ca_4(PO_4)_2O$	2.0
Hydroxyapatite	$Ca_{10}(PO_4)_6(OH)_2$	1.67
Calcium deficient hydroxyapatite	$Ca_9(HPO_4)(PO_4)_5(OH)$	<1.67
Tricalcium phosphate (α,β)	$Ca_3(PO_4)_2$	1.5
Dicalcum phosphate dihydrated (Brushite)	$CaHPO_4.2H_2O$	1.0

Ca/P ratio Ca-P granules between 1.67 (HA) and 1.5 (TCP)

Ca/P ratio Ca-P cements between 2.0 (TTCP) and 1,0 (DCPH)

Rules of thumb

Strength	> High Ca/P ratio provides higher strength when compared to low Ca/P ratio
Degradability	> High Ca/P ratio 1,67 (HA) leads to slower degradability as compared to Ca/P ratio of 1,5 (TCP)

Ca-P ceramics properties

Structural properties

Porosity [2,16-17] **refers to the fraction of the volume of voids within the material over the total material volume**

Macro porosity

- Pores > 100 µm -400 µm
- Provides a scaffold for bone cell colonization

Micro porosity

- Pores < 10 µm
- Allows body fluid circulation (proteins)
- Allows blood vessel ingrowth
- (< 30 µm decreased tissue infiltration)

Porosity ...

- **allows for mechanical interlocking between the implant biomaterials and host bone**
- **regulates cell reactions**
- **effects degradability**

Surface Porosity ...

- **pores only on surface area**
- **mechanically stronger**

Interconnective Porosity ...

- **pores throughout entire structure**
- **mechanical weaker**
- **direction dictates pathway for ingrowing cells**

Rules of thumb

Strength	> Interconnective porosity mechanical weaker compared to surface porosity
Resorption	> Interconnective porosity resorbs faster compared to surface porosity
Degradation	> Interconnective porosity degrades faster compared to surface porosity

Ca-P ceramics properties

Mechanical properties

Strength refers to the load carrying capacity of a material

Stiffness refers to the resistance to elastic deformation

Strain refers to the deformation of a material by a force acting on the material. Strain can be tensile or compressive (plastic or viscoelastic deformation)

Young's Modulus (modulus of elasticity) refers to the unique property of a material; measure of a material to resist deformation and return to its original shape

Creep refers to the permanent deformation under influence of mechanical stress

Mechanical property	Cortical bone	Cancellous bone	Ca-P ceramics
Tensile strength (MPa)	50-150	10-100	40-100
Elastic modulus (GPa)	3-20	8	
Compressive strength (MPa)	130-230	2-12	100-900
Young's modulus (GPa)	15-42	0,02 - 0,5	70-120

Ca-P ceramics properties

Mechanical properties

Strength refers to the load carrying capacity of a material

Elastic modulus, compressive strength and tensile strength are highly dependent on the position of the body and the condition of the individual. [11]

Mechanical properties of bone vary with depending on load orientation with respect to the orientation of tissue (anisotropy) and the speed to which the load is applied (viscoelasticity). [11]

Rules of thumb

Strength	> Material strength primarily dependent on composition, structure, porosity and elasticity
Strength	> Ca-P ceramics strong under compression and weak under torsion loads
Strength	> Ca-P cement compressive modulus stronger compared to Ha or TCP granules
Strength	> TCP quicker loss of mechanical strength compared to HA in vivo

Ca-P ceramics properties

Degradation properties

Degradation refers to a chemical process resulting in the cleavage of covalent bonds due to hydrolysis, oxidation or enzymatic processes

(Bio)degradation or resorption is chemical breakdown of an implant by a chemical agent (enzyme, cell, organism)

Erosion refers to physical changes in size, shape or mass due to degradation, dissolution, ablation or wear

Erosion can be distinguished into surface erosion and bulk erosion

Degradation has an effect on

Mechanical properties (impactability strength, stiffnes, Young's modulus)

Biological properties (osteoconduction)

Degradability speed

Rules of thumb

Degradation	>	TCP chemically less stable compared to HA due to high resolution characteristics
Degradation	>	TCP easily resorbed by osteoclasts compared to HA
Degradation	>	TCP faster degradation (12-18 months) compared to HA (2-10 years

In vitro dissolution of Ca-P materials depends on

- Composition
- Crystallinity
- Ca/P ratio
- Interconnectivity
- Degradability / type and speed of resorption
- Mechanical properties
- Particle size
- Surface area
- Production process
- Patient characteristics: age, gender,
- Health status, co-morbidities

Ca-P bone substitutes have to be intact long enough for bone ongrowth to occur and to maintain stability

To achieve *balanced bone remodeling*, slow bone remodeling and to fast biomaterial resorption should be prevented

Ca-P ceramics design considerations [2,11]

Mechanical properties: mechanical properties such as elastic modulus, tensile strength, fracture toughness, fatigue, and elongation percentage should be as close as possible to the replaced tissue (mechanical compatibility) in order to prevent bone loss, osteopenia, or "stress shielding"

Ca-P ceramics must have enough mechanical strength to retain its structure in order to comply with its mechanical function after its implantation in the case of hard, load-bearing tissues as bone.

Pore size and porosity: a 3-D design affects the spatial distribution and location of cells, nutrients, and oxygen, thus affecting the viability of the new formed tissue. Porous scaffolds facilitate the migration and proliferation of cells, providing an appropriate microenvironment for cell proliferation and differentiation and allowing the mass transfer of nutrients, oxygen, and waste metabolic products within the structure.

Scaffolds should have a large internal surface area due to overall porosity and pore size. The surface to volume ratio of porous scaffolds depends on the size of the pores. A large surface area allows cell adhesion and proliferation, whereas a large pore volume is required to contain and later deliver a cell population sufficient for healing or regeneration process.

Bone healing

39 Bone healing
Diamond & Pentagon concept

Diamond concept **Bone healing is a multidimensional process requiring all elements of the Diamond concept** [18-19]

Pentagon concept **Multidimensional process requiring all elements of the Diamond concept combined with mechanical stability and vascularization** [18-19]

INJURY
INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED
www.elsevierhealth.com/locate/injury
Injury, Int. J. Care Injured (2007) 38S4, S3-S6
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Fracture healing: The diamond concept

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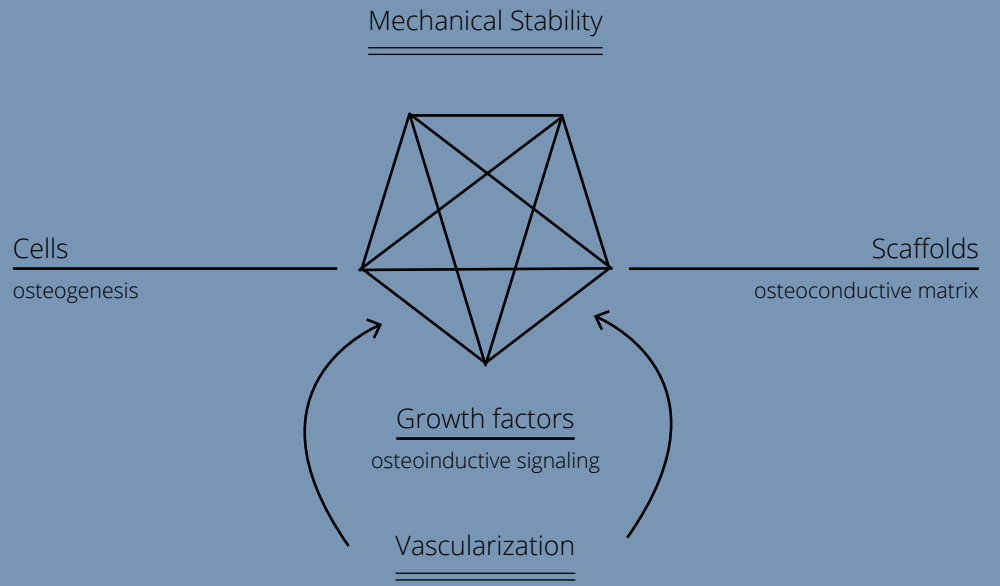
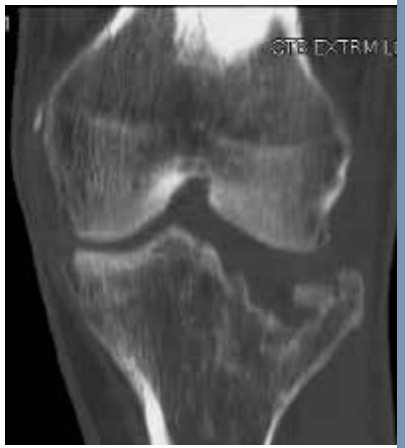


Stepwise assessment of bone defect

What would you do with this patient... And why?

1. Observe
   - Changed anatomy > correct
   - Instability > stabilise
   - Bone loss, CT? > restore 3-D
2. Think } structure
3. Plan } structure
4. Operate
5. Clinical follow-up of cases

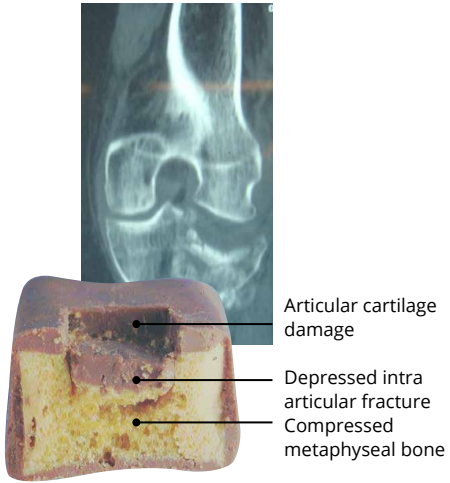


Stepwise bone defect assessment considerations

1. Changed anatomy
   - > correct
     - alignment mechanical/anatomical axis
     - articular surface
2. Instability
   - > stabilise
     - rigid or dynamic fixation
     - minimal invasive or open exposure
     - choice fixation
3. Biological capacity
   - > assess regenerative capacity
     - availability of stem cells
     - availability of vascularisation
4. Patient
   - > assess regenerative capacity
     - co-morbidity
     - post-op compliance

Rules of Thumb

> defect location, size, local mechanical (loading regime, stability) and biological environment (cells, osteoinductive signaling, vascularisation)
> determine what bone substitute material can be used



Biomaterial choice considerations

1. Material	> biocompatibility / osteoconductivity / osteoinductivity > handling (injectability) > mechanical properties material and mechanical load on bone defect
2. Surgical	> resorption speed > containment in defect (metal, periost flap, muscle, bone)
3. Mechanical	> connection (interdigitation) with host tissue > mechanical stability
4. Biological	> adequate fixation (preferably dynamic) > availability of stem cells > availability of vascularisation
5. Patient	> co-morbidity > post-op compliance
6. Literature	> large differences in level of evidence between products
7. Surgeon	> personal preference > experience

Bone healing

Biomaterial choice considerations

Focus on **Autograft**

Composition **Donor bone from patient's own iliac crest (gold standard?)**

PROS

Cheap (but prolonged surgery time)

Osteogenic, oteoconductive and osteoinductive

Extensive clinical experience

CONS

Pain from harvest[6-8] and donor site morbidity[6-8]

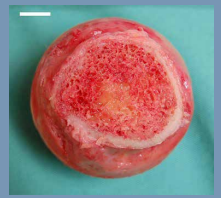
Quality and regenerative capacity donor depend

- stem cells ↑ with age
- growth factors ↓ with age

Limited availability

Focus on **Allograft**

Composition **Donor bone from another patient (femoral heads)**



PROS

Osteoconductive

No pain complications

Good availability

Extensive clinical experience

CONS

Risk of disease/ virus transfer / graft rejection

Variable quality (donor dependent)

Regenerative capacity donor dependent cancellous bone > cortical bone

Expensive (>600 Euro/femoral head)

Bone healing

Biomaterial choice considerations

Focus on **DBM**

Composition **Exposing allograft bone to demineralizing agents**

(hydrochloric acid) affecting handling, osteoconductive / osteoinductive potential

PROS

- Good handling properties (easy to mold/shape)
- Various growth factors in material
- Extensive clinical experience

CONS

- Risk of disease / virus transmission
- Variable quality
- Inconsistent osteoinductive
- Minimal osteoconductive
- No FDA device approval

Focus on **Ca-P ceramics**

Composition **Hydroxylapatite (HA), Tricalcium phosphate (TCP), Biphasic, one of the above with added material Si, Mg**

PROS

- Osteoconductive
- No risk of disease/ virus transfer
- Availability every shape, porosity, composition
- Unlimited supply / long shelf life

CONS

- Handling differs among products
- Never osteoinductive by themselves
- Large variance material properties, level of evidence

Focus on **BMPs**

Composition **Re-combinant produced materials in Chinese hamster ovaries**

PROS

Osteoinductive and somewhat osteoconductive carrier

Effective (Fusion levels PLIF 60-100%) [15]

Extensive clinical experience

CONS

Expensive

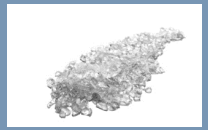
Dose not optimal (super physiological)

Can have both anabolic (osteoblasts) or catabolic (osteoclasts) effect on bone regeneration

High complications rate

Focus on **Bioactive glass**

Composition **Silicate & sodium dioxide, calcium oxide, phosphorous**



PROS

Osteostimulative (osteoconductive and effect on angiogenesis)

High ability to firmly attach to living tissue and facilitate tissue growth

Antimicrobial properties (S53P4)

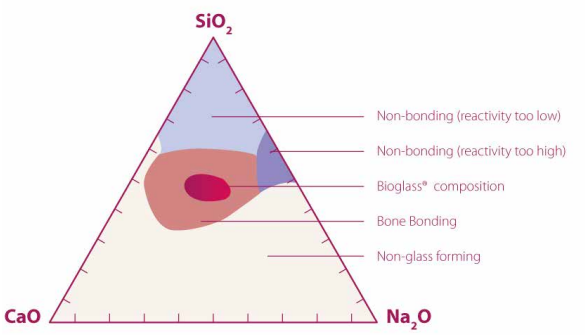
Proven effect on stem cell

CONS

More expensive that standard osteoconductive scaffolds

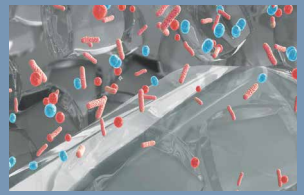
Limited product forms

Bioactive glass: mechanism of action

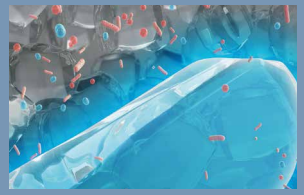


When S53P4 bioactive glass is implanted in a septic bone defect it will exchange alkali from the glass surface with the hydronium in the surrounding microenvironment, which will increase the local pH. The release of ions of the glass surface will also increase the osmotic pressure locally.

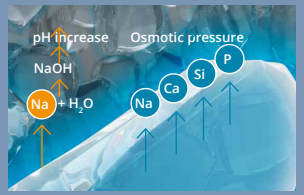
A silica gel layer will be formed near the glass surface to which amorphous calcium phosphate precipitates and subsequently will crystallize into natural hydroxyapatite. The hydroxyapatite will induce the osteostimulative effect by activating osteogenic cells.



1. In septic bone surgery bacteria are present in the bone defect



2. Upon implantation the surface reactions start on the bioacive glass S53P4 granules



3. Release of ions that increase pH and osmotic pressure of the microenvironment of the granules

4. Formation of silica gel and precipitation of calcium phosphate on bioactive glass surface

5. Calcium phosphate crystallises to natural hydroxyapatite

6. Hydroxyapatite layer will initiate osseointegration and thereafter the osteostimulative process

Bone healing

Biomaterial choice considerations

Focus on **Bioactive peptides**

Composition **i-FACTOR P-15 peptide. Type 1 collagen derivative**

Potential BMP drawbacks can be waylaid using bioactive peptides

PROS

Osteoconductive with added osteoinductive properties

Effective

Safe: high degree of biological specificity > can only target osteoblasts

Prove: extensive clinical experience, Level I data

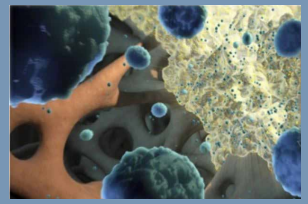
CONS

More expensive that standard osteoconductive scaffolds

Limited product forms

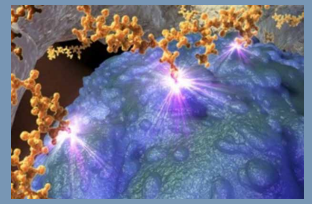
i-FACTOR P-15: mechanism of action

1. ATTRACT



Recruitment osteogenic precursor cells by making P-15 binding sites available for cellular adhesion

2. ATTACH



The high affinity between cells and the P-15 peptide supports the natural physiological mechanism by which cells attachment and interact with Type I collagen.

3. ACTIVATE

The P-15 peptide enhances bone formation by activation natural mechanical and chemical signalling pathways within the cell stimulating the release of specific growth factors and creating a microenvironment conductive to new bone formation.

Bone healing

Clinical indications

1. Bone graft extender

In case insufficient bone graft volume is available

- Autograft, allograft, DBM, Ca-P granules, bioactive glass and bioactive peptides can be used
- TCP resorption time < HA & bioactive glass
- Ca-P cement, BMP should not be used

2. Small contained bone defects

Filling of small Ø <2cm 'unloaded' defects when fixation/stabilisation is absent

- Autograft, Allograft, DBM, Ca-P granules, bioactive glass and bioactive peptides can be used
- TCP resorption time < HA * bioactive glass
- Ca-P ceramic/bone graft mixtures result in a more homogeneous mixture
- Ca-P cement, BMP should not be used

3. Smaller non-load bearing defects

Filling of larger Ø <2cm 'unloaded' defects when fixation/stabilisation is absent

- Autograft, allograft, Ca-P granules, bioactive glass and bioactive peptides can be used (provide structural integrity)
- Use of DBM is not advocated, due to lack of structural integrity
- Ca-P weight bearing granules made of HA or biphasic HA-TCP (resorb faster than Ca-P cement)
- Ca-P cements > stable but slower resorption
- BMP should not be used

4. Larger stabilised defects

tibia plateau #, distal radius #, distal/ proximal femur #, open wedge osteotomy

- Autograft, allograft, Ca-P granules, bioactive glass and bioactive peptides can be used (they provide structural integrity)
- Use Ca-P cements > stability for bone fragments, but slow resorption
- Do not use BMPs or DBMs as standalone materials (no structural integrity / stability of fragments)

5. Weight-bearing defects

Bone impaction grafting in TKA & THA, large acetabular #, segmental defects

- Osteosynthesis must come first
- Use materials that provide structural integrity (bone grafts, Ca-P ceramics, bioactive glass)
- Can use Ca-P cements > stability for fragments but slow resorption
- Defect closure for material containment is essential

6. Infected defects

In general Ca-P materials as standalone are a contra-indication when not combined with antibiotics

- Local (and systematic) antibiotic therapy must be used
- Use S53P4 bioactive glass or bone grafts / Ca-P ceramics loaded with high dose antibiotics
- S53P4 bioactive glass successful in one-stage treatment in osteomyelitis
- Cave: adequate debridement is essential for treatment success

Bone healing

Take home messages [10,21]

message **Bone substitute materials vary in composition, mechanical strength and biological mechanism of function, each having their own advantages and disadvantages**

message **Large variance in bone substitute materials, material properties, indications and level of evidence**

message **Not all bone graft substitutes will perform the same way, and their performance in one clinical site may not necessarily predict their performance in another site**

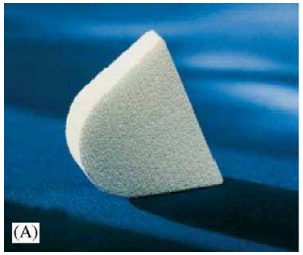
message **The choice of the optimal bone substitute is therefore not always an easy one, and largely depends on the clinical application and its associated biological and mechanical needs. Mechanical stability should primarily always be the predominant factor**

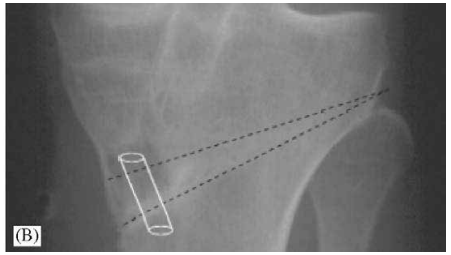
message **Pentagon / Diamond concepts are useful tools for planning surgery with bone substitute materials**

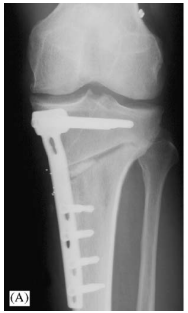
Cases

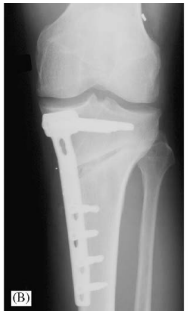
Cases

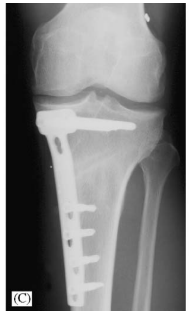
Case 1 Tibia Osteotomy [20]

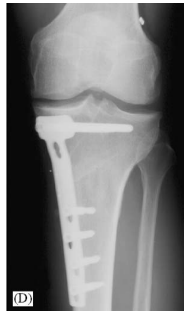












Top (left). B-TCP wedge and (right) location of osteotomy and biopsy.

Bottom Bone remodeling at different follow-up times after open wedge osteotomy filled with TCP.
(A) at 6 weeks, (B) at 3 months, (C) at 6 months, (D) at 12 months.

Details

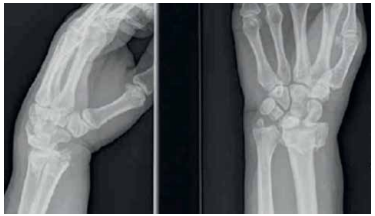
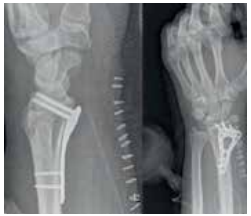
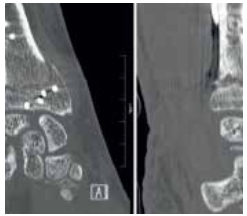
- Porous β-TCP (Ca3(PO4)2 with 70% interconnected macropores with a size of 100–500 µm and micropores of 1–10 µm (ChronOS, Synthes)
- 16 patients (17 osteotomies) : core biopsies for histology of bone remodeling at different follow-up periods
- X-rays at 6 weeks, 3 months, 6 months and 1 year postoperative

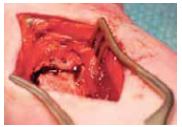
Results

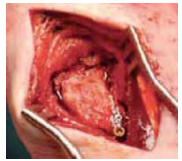
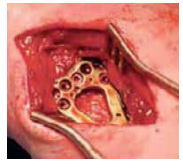
- Complete consolidation at 12 months in all cases
- 16 patients (17 osteotomies) : core biopsies at different follow-up periods
- Note: although the B-TCP wedge is almost completely resorbed at 12 months and bone is remodeling, the plate is still providing mechanical stability
- The newly formed bone is a mixture of woven and lamellar bone and it's not as strong as completely remodeled bone

Lessons learned

- This case illustrates the importance of the element mechanical stability of the Pentagon concept



Top Details first surgery

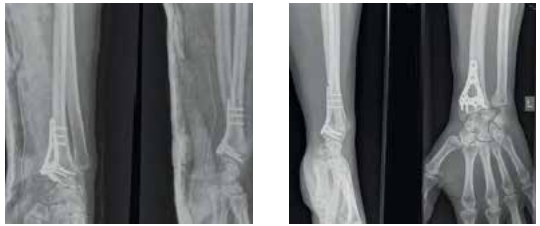
Bottom Details second surgery

Details 1st surgery

- 43-year-old male presented with a fracture to the left wrist.
- Clinical examination revealed painful range of motion with dorsal inclination and shortening (left)
- 1st intervention ORIF (middle)
- Post-operative a distal radius non-union developed within 8 weeks (right)

Details 2st surgery

- Debridement of non-union fibrous tissue, ORIF revision (left)
- Fill of defect with i-FACTOR FLEX strip filled the defect and was saturated with autologous blood (middle)
- i-FACTOR FLEX combines an anorganic bone matrix (ABM) with P-15 peptide (Cerapedics, USA)
- Reduction and internal fixation of the non-union site was performed using the same distal radius plate with new locking screws

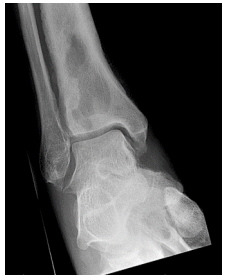


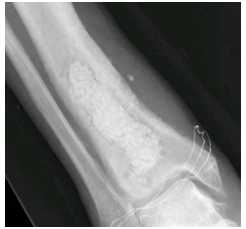
Results

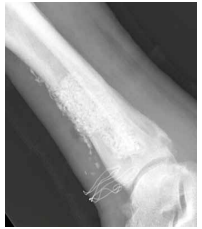
- Post-op X-ray (left) and 8 week post-op X-rays (right)
- X-rays showed consolidation of the non-union site and an increase in bone mineralisation

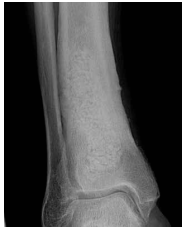
Lessons learned

- This case illustrates the importance of the elements cells (osteogenesis), scaffold (osteoconductive matrix), growth factors (osteoinductive signaling) and mechanical stability of the Pentagon concept









Details

- Patient distal tibia osteomyelitis > Brodie's abscess
- One-stage intervention: debridement surgery and defect filling with S53P4 bioactive glass (Bonalive, Finland)

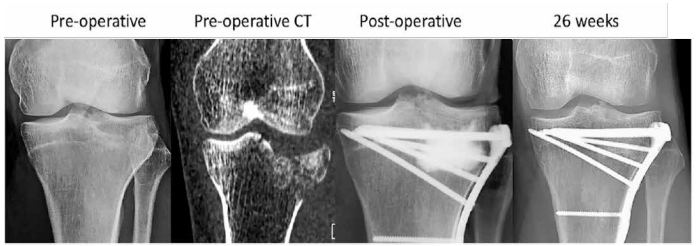
Results

- Bottom images left and middle: post-operative status showing S53P4 bioactive glass in defect and soft tissue envelope
- Bottom image right: 1 year clinical follow-up showing complete eradication of infection, S53P4 bioactive glass granules integrated in a mature bone matrix and previous detected granules in soft tissue envelope are fully remodeled

Lessons learned

- This case illustrates the importance of the element scaffold (osteoconductive matrix) and mechanical stability of the Pentagon concept
- This case also illustrates that S53P4 bioactive glass biomaterials result in complete infection eradication while also stimulating bone remodeling

Case 4 Tibia plateau fracture[23]



Details

- Depression tibia plateau fracture (OTA/AO 41-B2, Schatzker type 3)

Results

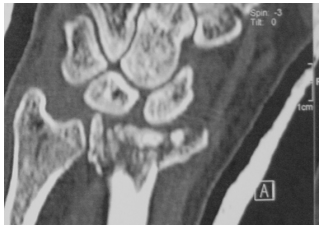
- Mechanical stabilisation with plate and lag-screws.
- Used biomaterial for bone void filling > Cerament: Hybrid Ca-P / Ca-S bone cement. (Cerament BVF, Bonesupport, Sweden)
- Post-operative, the radiopaque area in the lateral metaphysis corresponds to the contrast agent in the applied bone cement that diffuses away from the cement within 2 to 3 days
- At 26 weeks, bone defect healing with directional formation of bone trabecula was noticed on AP X-ray.

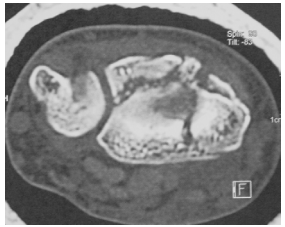
Lessons learned

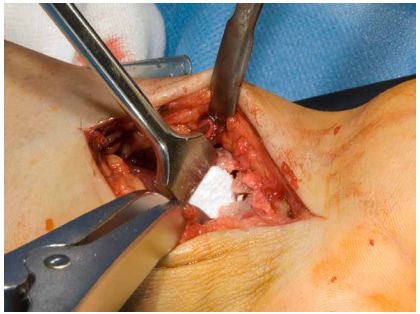
- This case illustrates the importance of the elements mechanical stability and scafolds (osteoconductive matrix) of the Pentagon concept

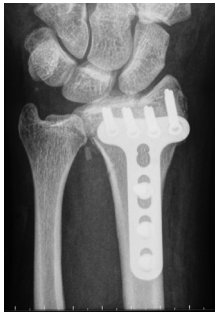
Cases

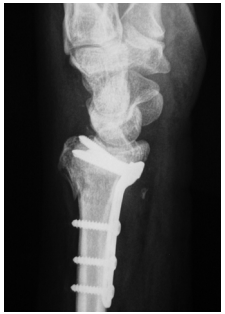
Case 5 Distal Radius Fracture **











Details

- Porous bi-phasic ceramic strip) 80% β-TCP [Ca_3 (PO_4)$_2$] and type-1 bovine collagen (Vitoss strip, Stryker)
- Single patient n=1 case
- X-rays at 12 weeks

Results

- Fracture stabilized with plate > osteosynthesis must come first!
- Bone void filled with TCP strip (Vitoss)
- Bone healing at 12 weeks follow-up
- The newly formed bone is a mixture of woven and lamellar bone and is not as strong as completely remodeled bone

Lessons learned

- This case illustrates the importance of the element scaffold of the Pentagon concept

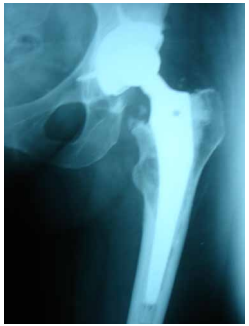
**Courtesy to Prof. Dr. Med. G.Zimmerman, Theresien Krankenhaus Mannheim, Germany for sharing the case

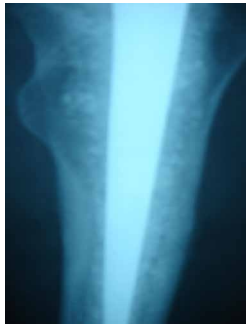
150 Acta Orthopaedica 2009; 80 (2): 150–154

Impaction bone grafting of the acetabulum at hip revision using a mix of bone chips and a biphasic porous ceramic bone graft substitute

Good outcome in 43 patients followed for a mean of 2 years

Ashley W Blom[1,2], Vikki Wylde[1], Christine Livesey[1], Michael R Whitehouse[1,2], Steve Eastaugh-Waring[2], Gordon C Bannister[2], and Ian D Learmonth[1]





Details

- Porous bi-phasic TCP-HA granule) 80% β-TCP [$Ca_3(PO_4)_2$] 20% HA [$Ca_{10}(PO_4)_6(OH)_2$] with not interconnected macropores with a size of 300–600µm and micropores of 2–80µm (BoneSave, Stryker)
- Revision total hip arthroplasty > TCP-HA granules as bone void filler in load-bearing bone defect

Results

- Biphasic TCP-HA (BoneSave) granules are strong enough to be used in load-bearing applications
- Gradual remodeling into a new bone structure over time
- Advise: neo vascularisation cannot span a graft layer thickness larger than 12-14 mm within 6 months

Lessons learned

- This case illustrates the importance of the element scaffold of the Pentagon concept

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