**Biology of Bone Healing in Membrane-Protected Defects**

Bone Grafts, Bone Substitutes and Barrier Membranes

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**Bone Deficiencies**

**Bone Loss due to Periodontitis**

Bone Loss due to Tooth Extraction

Critical region = facial bone plate

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**Bone Healing in Membrane-Protected Defects**

1. Barrier Membranes
2. Bone Fillers
3. Sinus Floor Elevation
4. Summary & Clinical Relevance

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**Bone Deficiencies**

Requirements in Implant Dentistry

- Enough bone volume
- Many recipient sites lack sufficient width or height of bone
- A bone augmentation procedure may be indicated

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**GBR Principle**

- A mechanical barrier membrane is used to direct bone regeneration
- The principle is to physically seal off an anatomic site for improved bone healing
1. Barrier Membranes

Membrane Types

- Polytetrafluoroethylene (PTFE)
- Expanded PTFE (ePTFE)
- Titanium-reinforced ePTFE
- Micro titanium mesh
- Titanium foils
- Collagen
- Freeze-dried fascia lata
- Freeze-dried dura mater allografts
- Polyglycolic acid (PGA)
- Polylactic acid (PLA)
- Trimethylene carbonate (TMC)
- Polytetrafluoroethylene glycol (PEG)
- Polythoroester
- Polyurethane
- Polynhdroxybutyrate
- Calcium sulfate

1. Barrier Membranes

Advantages & Disadvantages

Non-Resorbable Membranes
- Prolonged barrier function
- Second surgical procedure to remove the membrane
- Technique-sensitive
- Membrane exposure and infection

Resorbable Membranes
- No need for second surgery, decreased patient morbidity
- Simplified surgical procedure
- May elicit unfavorable tissue reactions
- Uncontrolled duration of barrier function
- Need for mechanical stabilization

1. Barrier Membranes - Collagen

How to increase the barrier function?

- Cross-linking (glutaraldehyde, UV-radiation, acidic agents, enzymatic)
- Increased thickness of barrier membrane
- Double layer (Kim et al. 2009, Kozlovsky et al. 2009)


1. Barrier Membranes

Examples

Healing Pattern of Bone Regeneration in Membrane-Protected Defects

- Saddle-type defects in dog mandible
- Test sites: membrane-protected with e-PTFE
- Control sites: without membrane
- Healing periods: 2 and 4 months
2. Bone Fillers

Classification of Bone Augmentation Materials

- **Autografts**
  - from same individual
  - Block grafts
  - Particulate grafts

- **Allografts**
  - from another individual, same species
  - Fresh frozen bone (FFB)
  - Freeze-dried bone allograft (FDBA)
  - Demineralized freeze-dried bone allograft (DFDBA)
  - Bone mineral from animals
  - From calcifying corals
  - From calcifying algae

- **Xenografts**
  - from another species
  - From calcifying algae

- **Alloplasts**
  - Synthetic
  - CaP
  - Polymers
  - Bioactive glasses

Is the autograft still the gold standard?

**Advantages**
- Osteoconductive scaffold
- Osteoinductive growth factors
- Osteogenic cells

**Limitations & Complications**
- Pronounced resorption
- Second surgery & donor site morbidity (pain, cosmetic disadvantages, haematoma formation, blood loss, nerve injury, haemato formation, infection, arterial injury, etc.)
- Graft availability (limited donor resources)
- Time & costs

**What are the requirements?**
- Safe, non-toxic, biocompatible
- Provide mechanical support
- Provide an osteoconductive scaffold
- Become osseointegrated or replaced
- Allow ingrowth of blood vessels
- Easy to use
- Cost-effective

**Mechanical Support of Membrane**
2. Bone Fillers

Osteoinduction

Which bone filler?

Bio-Oss
Bio-Oss Collagen
chronOs
Osteoinductive cement
BioResorb
Osteoinductive special
Skelite
Targobone
Osteon
Collagen
Fisiograft
Colloidal
PeriGlas
Osteograf
OsSatura TCP
Pepgen P-15
Biogran
Ossaplast
Nanobone
OsSatura BCP
Biogran
Tutodent Chips
Bio-Base

Is there a magic formula?

\[ X = \sqrt{\frac{C-H}{3}} \times \left( \frac{K+G+2C-E}{2-3D-A-2(F-C)} \right)^2 - K \]

X = Performance

How to evaluate bone fillers?

- Mechanical testing
- In vitro tests:
  - Cell migration
  - Cell attachment
  - Cell proliferation
  - Cell differentiation
  - Gene expression & synthesis of macromolecules
- In vivo validation tests:
  - Clinical experience
  - Histology
  - Histomorphometry
  - Immunohistochemistry

Histology

DBBM
Bone
2. Bone Fillers

Histochemistry - TRAP

2. Bone Fillers

New Bone – Qualitative Differences?

Autograft

Xenograft

2. Bone Fillers

New Bone – Quantitative Differences?

"Osteoconductivity-Test" = % Particle Surface Covered by Bone

% Volume Density in the Defect Area

2. Bone Fillers

Evaluation in Membrane-Protected Defects


2. Bone Fillers

New Bone – Evaluation in the Minipig

Membrane-protected defects in the mandible

> Autogenous bone chips
> Coral-derived HA
> Collagen sponge
> DFDBA
> β-TCP
> DBBM (bovine HA)
> BCP (biphasic CaP)
> Healing periods: 2-52 weeks

2. Bone Fillers

Bone Volume (% New Bone)
2. Bone Fillers

Osteoconductivity

![Graph showing osteoconductivity of bone fillers](image)


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2. Bone Fillers

Residual Bone Filler Volume

![Graph showing residual bone filler volume over time](image)

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2. Bone Fillers

Harvesting Technique of Autograft


- Cortico-cancellous blocks **particulated** by a bone mill
- Bone harvested with a **scraper**
- Bone harvested with a **piezosurgery device**
- Bone slurry **collected** from a filter-device upon drilling
- Placement in mandibular bone defects in minipigs; healing periods: 1, 2, 4, 8 weeks
- Histology, histomorphometry

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2. Bone Fillers

Resorption & Bone Formation of Autograft

![Graph showing resorption and bone formation](image)


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2. Bone Fillers

Resorption of Autograft

![Graph showing resorption of autograft over time](image)


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2. Bone Fillers

Resorption of Bone Substitutes

![Graph showing resorption of bone substitutes](image)


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2. Bone Fillers

Resorption of Bone Substitutes

![Image](Jensen, Gruber, Buser, Bosshardt: Clin Oral Implants Res 2014)

Bone Fillers - Contour Augmentation

Biomaterials with Low Degradation

Clinical & Radiographic Studies

- Bears little risk of recession of the facial mucosa
- Sustains long-term stability of the augmented volume, as documented clinically and radiographically with CBCT


Buser et al. J Periodontol 2009
Buser et al. J Periodontol 2011
Buser et al. J Periodontol 2013

2. Bone Fillers - Contour Augmentation

Preclinical Studies


![Image](Stricker et al. Clin Oral Implants Res (in print))

2. Bone Fillers - Contour Augmentation

Preclinical Studies

4 weeks

![Image](Janner et al. (in preparation))

2. Bone Fillers - Contour Augmentation

Human Biopsies – Histology & Morphometry

![Image](% of Bone and DBBM)

Long-term stability of contour augmentation in the aesthetic zone. Histologic and histomorphometric evaluation of 12 human biopsies after 14 to 80 months of healing. Jensen et al. (in revision)

3. Sinus Floor Elevation – Lateral Approach

Human Biopsies

![Image](Human Biopsies – Histology & Morphometry)
3. Sinus Floor Elevation – Lateral Approach

**Alloplast vs. Xenograft**

Reference

<table>
<thead>
<tr>
<th>Reference</th>
<th>BCP</th>
<th>DBBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Froum et al. Int J Periodontics Restorative Dent 2008 (6-8 months)</td>
<td>28.4 ± 23.8</td>
<td>22.3 ± 6.4</td>
</tr>
<tr>
<td>Busenlechner et al. Clin Oral Implants Res 2009</td>
<td>28.6 (6 months)</td>
<td>41.6 (9 months)</td>
</tr>
</tbody>
</table>

% New Bone

**Mixing Autograft with Bone Substitutes**

The graft volume is better preserved, when DBBM is added. (Jensen et al. Clin Oral Implants Res 2012;23:902)

More AB increases bone-to-implant contact (BIC). All mixtures had a sign. higher BIC than DBBM alone. (Jensen et al. Clin Oral Implants Res 2013;24:635)

**Is a Membrane Needed?**

- No effects of a membrane on bone formation, when autografts are used alone (Klijn et al. 2010) or combined with a xenograft (Barone et al. 2013)
- A tendency for more new bone, when a membrane was used (Tarnow et al. 2000, Wallace et al. 2005)
- More fibrous tissue without a membrane, when DBBM is used alone (Choi et al. 2009) or autograft is used combined with a xenograft (Barone et al. 2013)

**Summary & Clinical Relevance**

**Barrier Membranes**

- In the Dept. of Oral Surgery and Stomatology, bioreabsorbable collagen membranes are used for all horizontal GBR and all SFE surgeries
  - Favorable clinical handling
  - Low risk of postoperative complications
  - No need for a second surgery
- Non-resorbable ePTFE membranes are used only for selected vertical augmentation procedures

**Autogenous Bone & Bone Substitutes**

- Autogenous bone particles have excellent osteoconductive and osteogenic properties and contain osteoinductive growth factors
  - They enhance new bone formation
- Some HA-based fillers such as DBBM or BCP have a good osteoconductivity and a low substitution rate
  - They stay in place
- Pure β-TCP fillers have a good osteoconductivity and a high substitution rate
  - They quickly resorb
4. Summary & Clinical Relevance

**Autogenous Bone & Bone Substitutes**

- None of the current bone fillers fulfills all requirements
- A combination of autogenous bone AND a bone substitute material is synergistic and beneficial!

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Thank you!

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