Defektaufbau

Knochen und Antibiotika-Imprägnierung

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The best substitute for bone is ...

BONE
“Stationary phase” bacteria

- **SCV**
  - (Small Colony Variants)
  - Require up to 100x AB concentration

- **BIOFILM**
  - (sessile phenotypes in glycocalix)
  - Require up to 1000x AB concentration
5 Basic requirements for eliminating biofilm associated infection

1. LOCALIZE
   Localize habitats of microbes as exactly as possible.

2. REDUCE
   Drastically reduce their number and their means of livelihood by removing all identified avital material as radically as possible;

3. DISRUPT
   Disturb the community live of eventual remaining biofilm colonies by mechanically disrupting their established structures as thoroughly as possible;

4. FILL
   Avoid re-establishment of colonisation grounds by filling dead space with inaccessible material as completely as possible;

5. ELIMINATE
   Eliminate sessile bacteria inside remaining fragments using antimicrobial substances in concentrations as high and as consistent as possible.
Antibiotic loading of grafts for THERAPY*

*Cases WITH florid infection

✓ Markedly higher concentrations

✓ Sustained release over weeks

required
Vancomycin concentration through 24h

Bone marrow inside graft

- Possible source of disease transmission (HIV, hepatitis)
- Cells elicit immune response
- Fat elicits inflammatory response
- Tissue inhibits access of antibiotics
Remove bone marrow

✓ Solvents
  – Chloroform, ether
  – Acetone
  – Alcohols
  – Hydrogen peroxide (H2O2)
  – Sodium hydroxide (NaOH)
  – Urea
  – .......
Supercritical Carbon dioxide

✓ „Gas“:
  - Maximum penetration

✓ „Liquid“:
  - Maximum solvent

✓ Validated Virus Inactivation

Maximum penetration
Maximum solvent

50°C
260 bar
Additional Opportunity:

- Dead marrow cells and fat block revascularization
- must be eliminated by the host before neo-osteogenesis
- Revascularization stops after <10mm

Remodelling of purified grafts

✅ Re-Vascularization
  - faster
  - more complete

✅ Incorporation
  - more physiological
  - stronger
spongy bone without marrow = bony sponge

- Large surface
- Increased Storage capability (10x)
- High concentrations
- Prolonged release
- Biologically inert
- Remodelling (O-conduction)
- Mechanical support

IDEAL CARRIER
Bone processing

- Shaping
- Sc CO2
- drying
- gamma irradiation (25kGy)
- Impregnation, concentrated antibiotic solution
Antibiotics

✔ Vancomycin
  - gram positive pathogens
  - agent of choice for MRSA
  - intracellular activity (SCV)
  - rapid diffusion into biofilms

✔ Tobramycin
  - gram negative pathogens
  - agent of choice for pseudomonas

✔ Both
  - bactericidal
  - least cytotoxic effect
Elution: Human Bone - Vancomycin

- 1.day.: 20904,66 ± 1844,16 µg/ml
- 13.day: 4,43 ± 0,95 µg/ml

Elution: Human Bone - Tobramycin

- 1. day: \(13151.50 \pm 1677.48 \, \mu g/ml\)
- 28. day: \(1.39 \pm 0.94 \, \mu g/ml\)

Antibiotic impregnated bone

- Tobramycin (Gram -)
- Vancomycin (Gram +)
- Protects implant
- Decontaminates site
- Potential incorporation
# Antibiotic carriers

<table>
<thead>
<tr>
<th></th>
<th>AB Carrier</th>
<th>Purified Bone Graft *</th>
<th>PMMA</th>
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</thead>
<tbody>
<tr>
<td>Storage capacity / 10cc</td>
<td>1g</td>
<td>0.1g</td>
<td></td>
</tr>
<tr>
<td>Availability</td>
<td>&gt;90%</td>
<td>&lt;10%</td>
<td></td>
</tr>
<tr>
<td>Release 1.day</td>
<td>10,000 – 20,000mg/l</td>
<td>40 – 400mg/l</td>
<td></td>
</tr>
<tr>
<td>Release 6.day</td>
<td>60 – 130mg/l</td>
<td>&lt;5mg/l (Traces)</td>
<td></td>
</tr>
<tr>
<td>Release 100.day</td>
<td>0</td>
<td>Traces</td>
<td></td>
</tr>
</tbody>
</table>

Kinetics (Vancomycin) Cement versus Impregnated Bone

- bone
- cement
Principles of Septic Bone Surgery

- Removal of all avital material
- Radical debridement
- Dead space management
- Vascular supply
structural allografts

- Thorough cleaning only possible by supercritical-CO2
- Storage at room temperature
One stage exchange arthroplasty

**Advantages:**
- Short treatment
- Quick rehabilitation
- Reduced costs

**Disadvantages:**
- So far only with AB loaded cement
- Higher risk?
Two stage with „Spacer“

- Case M.A.: male, 62yrs, immunocompromised (lymphoma), diabetes, obesity.
- 2 yrs after surface replacement right hip (Birmingham);
- postop. Infection; 2x debridement + synovectomy with retention of implants, 1x removal + Prostalac Spacer. 1x exchange of spacer.
- Ongoing infection with draining sinus.
- CNS (methicillin resistant), Mycoplasma hominis
- Massive bone defect
1998 – 2004: 37 Patients, uncemented

Follow up

✓ Min 2 years
✓ Max 8 years
✓ Mean 4.4 years
Success hips (n=37)

Lasting absence of signs of infection

1 Operation: 34
(>91%)

2 Operations: 36
(>97%)

Chronic Infection after Fracture

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Chronic Osteomyelitis: single stage surgery

- Exact preoperative identification of avital areas (MRI)
- Radical sequestrectomy preserving vital structures
- High speed burr sclerosis
- Pulsed lavage
- Bone grafts impacted into defects (intramedullary)
- Rigid internal fixation (nail, plate)
- Drainage
- Closure (flap)
Chronic infection in cortical / sklerotic bone

✔ Radical Debridement / sequestrectomy!
High speed burr, saline cooled

✓ Sclerotic bone
„Paprika sign“
Pulsed Lavage

✔ after debridement

✔ NOT after grafting!
Case S.F., 46yrs, male, smoker, 120 kg (B-host)

1998:
- Fracture bimal + Calcaneus
- Plate, K-wires
- Infection

2000:
- Revision, removal of osteosynthetic material, necrosectomy culture: CNS

2009:
- massive infection, sepsis,
- MRSA + Gram-,
- revision, AB-bead chains, multiple revisions, Vacuum closure
CT
Excision soft tissue
Necrosectomy bone

Jet lavage
RADICAL Debridement!

- Bleeding bone
- Removal of ALL granulation and scar tissue
Stabilization: NCB plate

- Locking plate
- Internal fixator
Impaction grafting
Flap

6 weeks
po
Postop

2 weeks bedrest

3 months partial weight bearing
1 year postop

- Graft incorporated
- Not remodelled
3 years postop
Graft + Nail

- Intramedullary filling
- (Reverse) reaming
- Insertion nail
- Interlocking
M.F., 21 yrs, male

- Car accident with open fracture 2009
- 2009 – 2012: 21 operations!
- Shortening -4cm
- MRSA
- E.Coli
After Bone transport -4cm
Radical Debridement
Nailing - Grafting
Latissimus Flap
POSTOPERATIVE

- 1 week bedrest
- 2 weeks hospital stay
- 6 weeks crutches

- 2 weeks Teicoplanin + Meropenem i.v.
- 4 weeks Fusidic acid + Ciproflaxacin oral
6 months postop
Case: R.E., m, 8a

- Hematogenous
- Staph. aureus
- 14 operations (debridement, bead chains, VAC, autologous bone)
- Massive defect
- Pathologic fracture
3yrs

4yrs
Chronic OM of long bones
2004 – 2007: 30 Patients

融合发展

- m:f 16 : 14
- age 16 - 67yrs (mean 40yrs)
- infection 0,5 - 57yrs (mean 11,6 yrs)
- previous operations 1 - 24 (mean 6,6)
<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Count</th>
</tr>
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<tbody>
<tr>
<td>&lt; 1 week</td>
<td>10</td>
</tr>
<tr>
<td>&lt; 2 weeks</td>
<td>8</td>
</tr>
<tr>
<td>&lt; 3 weeks</td>
<td>6 (flaps)</td>
</tr>
<tr>
<td>&gt; 3 weeks</td>
<td>6 (complications requiring additional surgery)</td>
</tr>
</tbody>
</table>
Follow up

Deceased (cardiac failure)  1
Lost to FU               0
Followed                29

✓ Min               1 yr
✓ Max              4 yrs
✓ Mean            2.3 yrs
Results after Φ 2,3a (n=29)

✓ Non-union (radiological) 1
✓ Persistent infection 1
✓ Painfree function 28
✓ No sign of infection 28
(=97%)
Conclusions

- Antibiotic impregnated allograft bone may provide protection against bacterial colonisation and optimum dead space management.
- Highly purified and high-dose impregnated allograft bone seems likely to provide sufficient antibiotic delivery to eliminate biofilm remnants after radical debridement.
- Same stage implantation of orthopaedic devices such becomes feasible.
- Defects may be reconstructed simultaneously with good chance of restoration.
Antibiotic impregnated allograft may grant

- Single stage supply of orthopaedic infections
- Short treatment, resulting in
  - Improved functional results
  - Reduced systemic antibiotics
  - Reduced costs
- Improved conditions in case of failure
Thank You!