Osseointegration and adverse tissue reactions in clinical use of implants

Klemen Ravnihar

1st BioTiNet Workshop, October 2011, Ljubljana
Why to use implants in human medicine?
Why to use implants?

- for enhanced visual results

on different parts of the body…
Why to use implants?

- to sustain life when our hearts and vessels fail…
... to treat fractures and bone/joint diseases ...

- to fix fractures or replace joints
...instead of older methods...

- to reduce the downsides of conservative treatment with plaster and/or traction devices:
  - unacceptable position of bone
  - muscle atrophy
  - sores
  - loss of function
... leading to development of osteosynthesis...

- open/closed fracture - reduction
- fracture fixation - retention
- restoration of function - rehabilitation
...and to development of total joint endoprostheses.

- to replace damaged joints due to:
  - trauma (injury)
  - disease (arthritis)
  - developmental disorders
Joint arthroplasty – total joint replacement (TJR)

- 1930s – early designs with glass, teflon interface bearing, ivory heads…
- Charnley hip 1960s – cement fix., PE bearing
- 1980s – improvements of design, knee TJR
- 1990s – cementless design, porous coated implants
- 2000+ - ceramic bearings, HC HDPE, hip resurfacing, functional coatings
Issues of modern TJR surgery

Medical:
- procedure/technique
- choice of implant/fixation
- mechanical alignment
- infection
- blood replacement
- rehabilitation

Sociobiological:
- age and health of patient
- unique characteristics of anatomy, behavior and lifestyle

Technical:
- bone
- materials
- fixation
- coating
- bearing
Medical factors:

- procedure/technique:
  - aseptic environment
  - prophylactic dose of antibiotic
  - various surgical approaches
  - removal of damaged joint surfaces
  - reaming/preparation of bone
  - artificial joint components placement
  - reposition
  - closure
Medical factors:

- choice of implant/fixation:
  - implants available on the market, provided by healthcare insurance, clinics
  - professional standards – state of the art
  - choice of design and material
Medical factors:

- early complications:
  - intraoperative bone fracture
  - major blood loss
  - haematoma/infection
  - dislocation

"We can't give you blood transfusion Mr Dodds, your blood type has been discontinued."
Medical factors:

- late complications and concerns:
  - late infection (haematogenous)
  - periprosthetic bone fracture (injury)
  - persistent pain (scaring, fibrous tissue ingrowth)
  - loosening (mechanical problem, debris, tissue reactions, requires revision - exchange op.)
Medical factors:

- follow up:
  - checkup on 6W, 3M, 9M, 2Y, 3Y, 5Y
  - X-ray
  - CT scan
  - TJR register

Alloclassic® - Clinical Experience

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Clinical Cases</th>
<th>Follow-up (years)</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>Havelin et al. MC</td>
<td>333 avg.</td>
<td>3.9</td>
<td>99.1%</td>
</tr>
<tr>
<td>1995</td>
<td>Huo et al.</td>
<td>46 avg.</td>
<td>4.2</td>
<td>100%</td>
</tr>
<tr>
<td>1995</td>
<td>Baumgartner et al.</td>
<td>533 max.</td>
<td>7</td>
<td>98.9%</td>
</tr>
<tr>
<td>1995</td>
<td>Bohler et al.</td>
<td>104 avg.</td>
<td>4.3</td>
<td>100%</td>
</tr>
<tr>
<td>1996</td>
<td>Delaunay &amp; Kapandji</td>
<td>167 max.</td>
<td>8</td>
<td>99.3%</td>
</tr>
<tr>
<td>1996</td>
<td>Love</td>
<td>25 max.</td>
<td>7</td>
<td>100%</td>
</tr>
<tr>
<td>1997</td>
<td>Dorig et al.</td>
<td>331 max.</td>
<td>8</td>
<td>100%</td>
</tr>
<tr>
<td>1998</td>
<td>Delaunay et al.</td>
<td>116 max.</td>
<td>8</td>
<td>99.3%</td>
</tr>
</tbody>
</table>
### 15 most common implants

Most used during the past 10 years

<table>
<thead>
<tr>
<th>Cap (Stem)</th>
<th>1979-2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>Total</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lubinus All-Poly (Lubinus SP II)</td>
<td>46,720</td>
<td>4,712</td>
<td>5,395</td>
<td>5,705</td>
<td>5,529</td>
<td>5,226</td>
<td>67,287</td>
<td>36.1%</td>
</tr>
<tr>
<td>Exeter Durante (Exeter Polished)</td>
<td>5,293</td>
<td>1,170</td>
<td>1,289</td>
<td>1,121</td>
<td>1,122</td>
<td>618</td>
<td>11,095</td>
<td>0.8%</td>
</tr>
<tr>
<td>Charnley (Charnley)</td>
<td>55,125</td>
<td>802</td>
<td>81</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>55,581</td>
<td>0.3%</td>
</tr>
<tr>
<td>Charnley Elite (Exeter Polished)</td>
<td>2,353</td>
<td>1,062</td>
<td>998</td>
<td>900</td>
<td>1,143</td>
<td>1,151</td>
<td>7,707</td>
<td>0.1%</td>
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<tr>
<td>Reflection (Spectrum EF Primary)</td>
<td>7,276</td>
<td>3,089</td>
<td>871</td>
<td>788</td>
<td>671</td>
<td>285</td>
<td>7,220</td>
<td>5.2%</td>
</tr>
<tr>
<td>FAL (Lubinus SP II)</td>
<td>1,389</td>
<td>831</td>
<td>706</td>
<td>599</td>
<td>534</td>
<td>444</td>
<td>4,560</td>
<td>3.0%</td>
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<tr>
<td>Contemporary Headed Durante (Exeter Polished)</td>
<td>296</td>
<td>561</td>
<td>514</td>
<td>574</td>
<td>607</td>
<td>762</td>
<td>3,314</td>
<td>2.6%</td>
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<tr>
<td>Charnley (Exeter Polished)</td>
<td>0</td>
<td>201</td>
<td>435</td>
<td>518</td>
<td>282</td>
<td>205</td>
<td>2,539</td>
<td>1.7%</td>
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<tr>
<td>Exeter All-Poly (Exeter Polished)</td>
<td>0</td>
<td>10</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>6,565</td>
<td>0.4%</td>
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<tr>
<td>OPTICUP (Stern Hip II Collar)</td>
<td>1,044</td>
<td>125</td>
<td>10</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1,980</td>
<td>1.4%</td>
</tr>
<tr>
<td>Weber All-Poly cap (Straight-stem standard)</td>
<td>337</td>
<td>137</td>
<td>196</td>
<td>144</td>
<td>125</td>
<td>191</td>
<td>1,150</td>
<td>0.9%</td>
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<tr>
<td>Charnley Elite (Lubinus SP II)</td>
<td>505</td>
<td>140</td>
<td>176</td>
<td>187</td>
<td>124</td>
<td>96</td>
<td>1,228</td>
<td>0.9%</td>
</tr>
<tr>
<td>Trilogy HA (Spectrum EF Primary)</td>
<td>767</td>
<td>127</td>
<td>107</td>
<td>88</td>
<td>102</td>
<td>24</td>
<td>1,215</td>
<td>0.9%</td>
</tr>
<tr>
<td>Charnley (Charnley Elite Plus)</td>
<td>1,516</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trilogy HA (CLS Spotorno)</td>
<td>29</td>
<td>24</td>
<td>80</td>
<td>178</td>
<td>284</td>
<td>347</td>
<td>942</td>
<td>13.7%</td>
</tr>
<tr>
<td>Others (total 1,121)</td>
<td>95,229</td>
<td>2,083</td>
<td>2,486</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>216,490</td>
<td>12,602</td>
<td>13,394</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 15 most common uncemented implants

Most used during the past 10 years

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<tr>
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<th>2007</th>
<th>Total</th>
<th>Annel (b)</th>
</tr>
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<tbody>
<tr>
<td>Trilogy HA (CLS Spotorno)</td>
<td>29</td>
<td>24</td>
<td>80</td>
<td>178</td>
<td>284</td>
<td>347</td>
<td>942</td>
<td>13.7%</td>
</tr>
<tr>
<td>CLS Spotorno (CLS Spotorno)</td>
<td>490</td>
<td>69</td>
<td>68</td>
<td>110</td>
<td>163</td>
<td>193</td>
<td>1,093</td>
<td>11.7%</td>
</tr>
<tr>
<td>Allliat (CLS Spotorno)</td>
<td>126</td>
<td>94</td>
<td>87</td>
<td>127</td>
<td>128</td>
<td>128</td>
<td>690</td>
<td>10.0%</td>
</tr>
<tr>
<td>Trilogy (CLS Spotorno)</td>
<td>76</td>
<td>58</td>
<td>78</td>
<td>86</td>
<td>88</td>
<td>93</td>
<td>479</td>
<td>7.0%</td>
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<tr>
<td>Trident HA (Acolade)</td>
<td>0</td>
<td>0</td>
<td>33</td>
<td>70</td>
<td>132</td>
<td>133</td>
<td>360</td>
<td>5.3%</td>
</tr>
<tr>
<td>Trilogy HA (Versys stern)</td>
<td>68</td>
<td>00</td>
<td>75</td>
<td>25</td>
<td>0</td>
<td>257</td>
<td>3.2%</td>
<td></td>
</tr>
<tr>
<td>Trilogy (Wagner Canou Prosthesis)</td>
<td>86</td>
<td>15</td>
<td>35</td>
<td>23</td>
<td>23</td>
<td>37</td>
<td>219</td>
<td>3.2%</td>
</tr>
<tr>
<td>ABS II HA (ABS uncom.)</td>
<td>145</td>
<td>19</td>
<td>18</td>
<td>18</td>
<td>3</td>
<td>0</td>
<td>198</td>
<td>2.8%</td>
</tr>
<tr>
<td>Trilogy HA (Bi-Metric HA uncom.)</td>
<td>73</td>
<td>61</td>
<td>28</td>
<td>22</td>
<td>4</td>
<td>3</td>
<td>191</td>
<td>2.8%</td>
</tr>
<tr>
<td>Trident HA (Symax)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>17</td>
<td>68</td>
<td>70</td>
<td>164</td>
<td>2.0%</td>
</tr>
<tr>
<td>Trilogy HA (ABG II HA)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24</td>
<td>30</td>
<td>107</td>
<td>161</td>
<td>2.3%</td>
</tr>
<tr>
<td>Kermans HA (Bi-Metric HA uncom.)</td>
<td>253</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>262</td>
<td>2.1%</td>
<td></td>
</tr>
<tr>
<td>M2a (Bi-Metric HA lat.)</td>
<td>0</td>
<td>7</td>
<td>21</td>
<td>26</td>
<td>47</td>
<td>36</td>
<td>137</td>
<td>2.0%</td>
</tr>
<tr>
<td>Trilogy (SL plus stem uncom.)</td>
<td>52</td>
<td>17</td>
<td>26</td>
<td>31</td>
<td>9</td>
<td>0</td>
<td>135</td>
<td>1.9%</td>
</tr>
<tr>
<td>Trilogy HA (Bi-Metric lat.)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>19</td>
<td>51</td>
<td>50</td>
<td>122</td>
<td>1.8%</td>
</tr>
<tr>
<td>Others (total 226)</td>
<td>5,539</td>
<td>130</td>
<td>202</td>
<td>220</td>
<td>319</td>
<td>460</td>
<td>6,871</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6,927</td>
<td>577</td>
<td>753</td>
<td>990</td>
<td>1,357</td>
<td>1,646</td>
<td>12,289</td>
<td></td>
</tr>
</tbody>
</table>
Issues of modern THR surgery

**Medical:**
- procedure/technique
- choice of implant/fixation
- mechanical alignment
- infection
- blood replacement
- rehabilitation

**Technical:**
- bone
- materials
- fixation
- coating
- bearing

**Sociobiological:**
- age and health of patient
- unique characteristics of anatomy, behavior and lifestyle
Sociobiological factors

- joint replacement surgery is an accepted form of treatment for advanced joint disease with very good results

- careful patient selection (age, activity status, social status, comorbidity)

- requires high standard of healthcare system

- high cost of direct treatment but is the most cost effective treatment of arthritis and joint disease on a long-term scale

- should be subjected to quality control
Issues of modern THR surgery

Medical:
- procedure/technique
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Sociobiological:
- age and health of patient
- unique characteristics of anatomy, behavior and lifestyle

Technical:
- bone
- materials
- fixation
- coating
- bearing
Technical factors:

- **properties of bone:**
  - *cancellous* (softer, more remodeling and metabolism),
  - *cortical* (80%, resistance to stress)
  - *metaphysis* (softer bone, better, blood supply, faster healing, *diaphysis* (mechanical properties),
  - *epiphysis* (joint surface)
  - blood perfusion (endosteal↑, periosteal)
Technical factors:

- properties of bone:
  - constant formation and degradation (P, Ca)
  - stress remodelling (piezoelectricity)
  - bone healing
  - bone grafting
Technical factors:

- **implant fixation:**

  - cemented (bone cement, non-biologic fixation, immediate stability)

  - noncemented (press fit, screws, threaded - for primary stability, later bone grows into the surface - secondary stability)
Technical factors:

- **uncemented implant fixation:**
  - shear stresses
  - stress shielding
Technical factors:

- metallic implant materials:
  - stainless steel (iron, chromium, nickel, Mn, Mo...)
  - CoCrMo alloy (+iron, nickel, carbon...)
  - Titanium based alloys (Ti6Al4V)
  - pure Titanium and Tantalum – 3D structures
Osseointegration – bone ingrowth

Metal surface pressed directly against bone structure

- Blood-borne cells and proteins form haematoma
- Migration of inflammatory cells to the surface
- Attraction of multipotent cells from bloodstream
- Cell differentiation to osteoblasts

Formation of new bone on the metal surface

Remodelation of bone to solid structure
Osseointegration – bone ingrowth

- we need a mechanically **resilient** implant (not to much elasticity, no shear stresses – e.g. Ti alloy)
- **good position** and **primary stability** after op. (good bone contact, micromotion must be kept below 150 µm (prefer 50-100 µm), greater motion will result in development of fibrous tissue around the prosthesis and it will be mechanically unstable
- start **weightbearing** early – micromotion up to 50 µm ▲ bone ingrowth
- we need to avoid **soft tissue problems** (no inflammation, infection)
Fibrous tissue ingrowth
Tissue differentiation around a short stemmed metaphyseal loading implant employing a modified mechanoregulatory algorithm: a finite element study.

What really happens?

- osseointegration occurs over an average 35% of the porous surface
- bone bridges form
- bone remodelation occurs with stress transfer over these bridges
- decrease in bone mineral content proximally (mean 23% loss)


Advanced surface options…

- grit blasted metallic – widely used today, roughened surface that allows bony on-growth fixation, surface roughness is directly proportional to interface shear strength (roughness defined as average distance from peak to valley)

- plasma sprayed porous coated Ti - porous covered surface that allows bone ingrowth fixation, optimal characteristics of porous coating:
  - optimal pore size for 50-300 µm (preferably 50-150 µm)
  - optimal porosity of 40-50% (above this can lead to shearing off metal particles)
  - optimal gaps between bone and prosthesis < 50 µm
Advanced surface options...

- Hydroxyapatite - osteoconductive agent used as an adjunct to porous coated and grit blasted surfaces, promotes more rapid closure of gaps (disadvantage is potential to delaminate from surface coating, success depends on high crystalinity and optimal thickness of 50 μm)

- Bioglass – basis for functional coatings, possibility of elution of diff. growth factors and other agents

- Carbon nanotubes – higher level of osseointegration in early studies, possible drug delivery


Biemond J. E., Aquarius R., Verdonschot N., Buma P.: 
Mobile parts of TJR - bearings

- Bearings and wear
Particle disease

- particles <12 µm bioactive
- modulated by immune response of the host
- keep PE wear under 0.1 mm/year!
- Ti particles affect osteoblast function directly

- osteolysis
- implant loosening
Aseptic loosening

- destruction of bone adjacent to the implant

- particles
- failed biomechanics
- overload
- immunological processes
- joint fluid pressure
Infection

- catastrophic event in TJR surgery, low incidence 0.1 – 1%
- early (0-3M) – connected to procedure, usually airborne, highly virulent bacteria, debride + ATB
- midterm (3-24M) – connected to procedure or haematogenous, debride and treat if symptoms<3W
- late (>24M) – haematogenous, consider loose implant, exchange op.

- asepsis in OR, prehospital decolonization of carriers important

Hypersensitivity

- due to metallic particles and corrosion dependent ion elution
- rare cause of Ti based implant failure
- often cause of cutaneous allergic reactions


Perspectives and conclusion

- Use of orthopaedic implants is medically and biologically complex process.
- Adverse reactions are relatively rare but serious.
- There is currently no good alternative to metallic implants.
- Material science can use potential for improving coating and bearing materials.

- Is there a different tissue reaction for every different material surface?
- Can we append specific human protein to metallic surface?
- Bioengineering – bio joints?
Thank you.