e-Manufacturing in Medical Device Industry using Additive Manufacturing

Bullemer Martin, Bob Evans
EOS

Medical Prototyping Conference – Minneapolis, September 8th 2011
Agenda

e-Manufacturing in Medical Device Industry using Additive Manufacturing

1. EOS and Additive Manufacturing (AM)

2. The Medical Market for AM / Success in Manufacturing

3. Custom-IMD – PEEK Cranial Implant R&D Project
   - Custom-IMD
   - EOSINT P800 (High Temperature Laser-Sintering System)
   - design evaluation
   - mechanical properties and FEM
   - polymer infiltration trials
   - sterilisation and biocompatibility testing
   - animal studies
   - socio-economic evaluation

4. Conclusions
EOS at a Glance

EOS worldwide

- EOS Founding 1989 (pilot customer BMW)
- Solution provider for plastic and metal laser sintering
- Worldwide recognized technology leader for high-end systems for e-Manufacturing™
- More than 1000 systems installed
- EOS offices and partners in more than 30 countries
- Vision to establish AM as proven manufacturing solution

Source: EOS
e-Manufacturing - fast, flexible and cost-effective manufacturing directly from CAD data

Laser-Sintering: key technology for e-Manufacturing

from 3D CAD data… …via Laser-Sintering… …to final parts & products

Quelle: EOS

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Additive Manufacturing (AM) addresses all major customer challenges:

- **Freedom of Design**
  - Lightweight
  - Optimized functionality
  - New materials / new properties

- **Cost advantage**
  - Small production series
  - Integrated functionality

- **Productivity advantage**
  - Time-to-market flexibility

- **Customization**
  - Individualized parts

![Images of 3D printed parts]
Integration of individual competencies to complete solutions generate customer value

EOS core know how

- Parameter
- System & Software
- Material
- Process

End - to - End solution

Design & Data Generation
- Design rules
- User interface (intelligent, seamless, automated)

DMLS-Manufacturing
- Application development (parameter, building strategy)
- Part production

Post Processing
- Heat Treatment
- Post machining
- Finishing

Design
Production
Finishing

Quality assurance

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The Medical Market for EOS

- **Dental Market**
  - Copings
  - Bridges
  - Implants
  - ...

- **Medical Device Orthopedics**
  - Hip, Knee
  - Trauma
  - Spine
  - ...

- **Medical Device**
  - Machine devices
  - Instruments
  - Endoscope
  - ...

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Dental Copings and Bridges Manufacturing

- Complete and well accepted manufacturing solution.
- CoCr SP2 certified according to MDD 93/42/EEC and its amendment.
- Installed base > 35 M270
- Production of 200 to 250 units / 11h
- > 1,500,000 Mio units produced/a

Source: EOS
Laser-sintered disposable surgical devices at Smith & Nephew

**Disposable Instruments in plastics**

**Application:**
- patient specific knee surgery guides

**Manufacturing Solution:**
- Data generation by CT
- Design of patient specific instruments (e.g. Materialise)
- Laser-sintering using PA 2200 (Nylon 12)
- Quality Control and Sterilization

**Material information:**
- biocompatibility of the powder (ISO 10993 and/or USP6)
- Mechanical properties sufficient
- sterilization possible (here just one time)

**Customer:**

Source: EOS, Smith& Nephew

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Certified Dental Implant “TiXos” by Leader Italia

- Component inherently decontaminated because manufactured through a laser in a clean environment.
- Possibility to create hybrid structure through the exact control of the laser power.
- Surface net structure precisely defined through the process without applying specific coating.

1. Surface determinated by the laser process. Pores are interconnected.

2. Immediate 3D organization of fibrin network and high cell activity

Source: EOS, Novaxa

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EOS and Custom-IMD

A research project funded by the EC in the FP6 program

**SME supply chain integration for enhanced fully customizable implants**

- Cranial (EOS involved), dental, spinal
- 22 partners from 7 European countries
  (12 SMEs, 8 Research institutions, 2 hospitals)

**Why PEEK (polyetherketone)?**

- Surgeons chose PEEK over PEEKHT due to years of proven implant performance and existing FDA Masterfile
- one of the bio-passive (non-interacting with body tissues) polymers of particular interest to the project
- biocompatible; x-ray and CT translucent; chemically resistant / bio-stable; easily sterilizable (radiation, gas and steam); has excellent wear properties and does not induce osteolysis (macrophage induce bone degeneration)

Source: EOS GmbH

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EOSINT P 800

High Temperature Laser-Sintering System

Developed for processing high temperature melting polymers

Supported by the EC in the Sixth Framework program

Source: EOS GmbH
EOSINT P 800

High Temperature Laser-Sintering System

Exposure

Recoating device

Front window

System GUI

Exchangeable build frame

Optical window

Source: EOS GmbH
Cranial implant geometry

Design evaluation

Idea: a solid PEEK plate similar to the titanium bone plates already known

Source: EOS, AZM
Medical Prototyping Conference; Minneapolis – September 8th 2011 - EOS
Cranial implant geometry

Design evaluation

<table>
<thead>
<tr>
<th>First version</th>
</tr>
</thead>
<tbody>
<tr>
<td>- design from Ti could not be transferred 1:1</td>
</tr>
<tr>
<td>- thickness and fixing had to be modified (patent pending AZM)</td>
</tr>
</tbody>
</table>

Source: EOS, AZM
Cranial implant geometry

Design evaluation

<table>
<thead>
<tr>
<th>Second version</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PEEK scaffold for improved bone in-growth</strong></td>
</tr>
<tr>
<td>- variation of different mesh designs and sizes</td>
</tr>
<tr>
<td>- goals: high strength, small deformation, infiltration ability, bone growth</td>
</tr>
</tbody>
</table>

Source: EOS, AZM
Cranial implant geometry

Design evaluation

<table>
<thead>
<tr>
<th>Iterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>various software applications, new mesh design</td>
</tr>
<tr>
<td>• solid border (rim) for better fitting into the skull and higher strength</td>
</tr>
<tr>
<td>• contour following mesh – no stress peaks</td>
</tr>
</tbody>
</table>

Source: EOS, AZM
Cranial implant geometry

Design evaluation

<table>
<thead>
<tr>
<th>Final version</th>
</tr>
</thead>
<tbody>
<tr>
<td>design with discontinuous rim</td>
</tr>
<tr>
<td>- high strength, low deformation</td>
</tr>
<tr>
<td>- perfect fit and excellent bone in-growth expected</td>
</tr>
</tbody>
</table>

Source: EOS, AZM

Medical Prototyping Conference; Minneapolis – September 8th 2011 - EOS
Cranial implant geometry

Mechanical properties and FEM

<table>
<thead>
<tr>
<th>Value</th>
<th>Unit</th>
<th>Value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compression strength</td>
<td>[MPa]</td>
<td>133</td>
<td>According to ISO 604</td>
</tr>
<tr>
<td>Tensile strength</td>
<td>[MPa]</td>
<td>72.73 (e=1.95%)</td>
<td>According to DIN EN ISO 527-1A</td>
</tr>
<tr>
<td>density</td>
<td>[g/cm³]</td>
<td>1.30</td>
<td></td>
</tr>
<tr>
<td>Tensile modulus</td>
<td>[MPa]</td>
<td>4.184</td>
<td>According to DIN EN ISO 527-1A</td>
</tr>
<tr>
<td>Flexural strength</td>
<td>[MPa]</td>
<td>108</td>
<td>According to ISO 178</td>
</tr>
</tbody>
</table>

Source: EOS

Medical Prototyping Conference; Minneapolis – September 8th 2011 - EOS
Cranial implant geometry

Mechanical properties and FEM

Stress distribution when applying 70 MPa

Source: EOS, Within

Medical Prototyping Conference; Minneapolis – September 8th 2011 - EOS
Cranial implant geometry

Mechanical properties and FEM

Displacement under load (70 MPa)

Source: EOS, Within

Medical Prototyping Conference; Minneapolis – September 8th 2011 - EOS
Cranial implant geometry

Mechanical properties and FEM

**Experimental testing**

- results range from 16-20 MPa for first mesh up to >100 MPa for the final version
# Cranial implant geometry

## Polymer infiltration

<table>
<thead>
<tr>
<th>Polymer infiltration trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>- SupraB bio-absorbable polymer/osteoconductive hydroxylapatite compound infiltration into different mesh geometry</td>
</tr>
</tbody>
</table>

![Image of cranial implant geometries]
# Cranial implant geometry

Polymer infiltration

<table>
<thead>
<tr>
<th>Polymer infiltration in real geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound infiltration into the final geometry by hot pressing performed by TNO</td>
</tr>
<tr>
<td>- Only possible due to the unprecedented low melt viscosity of the SupraB polymer</td>
</tr>
</tbody>
</table>

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Source: EOS, TNO, Suprapolix, Xpand

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Cranial implant geometry

Sterilization

**PEEK samples of representative shape, from laser-sintering, cleaned, vacuum packed**

6MeV EB accelerator at TU of Lodz, standard sterilization dose of 25 kGy ± 0.6 kGy

- despite the fact that PEEK can withstand all common sterilization techniques without abrupt changes in its properties
- that was mainly due to high reliability, short time of sterilization and parametric release of EB technique

<table>
<thead>
<tr>
<th>Value</th>
<th>Unit</th>
<th>Before sterilization</th>
<th>After sterilization</th>
<th>Remarks</th>
</tr>
</thead>
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<td>Compression strength</td>
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</table>
Cranial implant geometry

Sterilization

Chemical Verification: High temperature Gel Permeation Chromatography (GPC)

“… the sterilization process used in this case has not affected the molecular weight of the PEEK samples and so it can be concluded that no detectable degradation (chain scission or cross-linking) has resulted.”

- Instrument: Polymer Laboratories GPC120, with PL GPC-AS MT heated autosampler
- Columns: PLgel guard plus 2 x mixed bed-B, 30 cm, 10 µm
- Solvent: 50:50 (w/w) 1,2,4-trichlorobenzene:phenol with anti-oxidant
- Flow-rate: 0.8 mL/min (nominal)
- Temperature: PL GPC120: 115oC (nominal)
- PL GPC-AS MT: 80oC (nominal)
- Detector: refractive index
Cranial implant geometry

Sterilization

"It has not been possible using either ATR IR or Pyrolysis IR, to detect any chemical differences between the sterilized and unsterilized PEEK samples. There are no apparent differences in molecular weight, or molecular weight distribution, between the sterilized and unsterilized PEEK samples as well."

Source: EOS, LasMed, Rapra

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Cranial implant geometry

Sterilization

**Conclusion**

- The conclusions withdrawn stated that laser-sintered PEEK material has perfect properties for application as biomaterial for various purposes that include cranial implant.
- Sterilisation by EB irradiation at 25 kGy does not affect the physical and chemical properties of the polymer, nor influence in any way its faultless biocompatibility and bioinertness.
Cranial implant geometry

<table>
<thead>
<tr>
<th>Summarized results of the biocompatibility testing</th>
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<tbody>
<tr>
<td>▪ <strong>non-cytotoxic</strong> according to ISO standard 10993-5 “Biological evaluation of medical devices - Part 5: Test for in vitro cytotoxicity”</td>
</tr>
<tr>
<td>▪ <strong>non-haemolytic properties</strong> according to ISO standard 10993-4 “Biological evaluation of medical devices - Part 4: Selection of test for interactions with blood” and ASTM 756-00 “Standard Practice for Assessment of Hemolytic Properties of Materials”.</td>
</tr>
<tr>
<td>▪ <strong>not causing pyrogenicity</strong> according to FDA limits, procedure following the recommendations in ISO standard 10993-12 “Sample Preparation and Reference Materials”</td>
</tr>
<tr>
<td>▪ <strong>non-irritant</strong> according to Inasmet inner procedure, based on ISO 10993-11, and EpiDermTM kit supplied from MatTek corporation company (USA)</td>
</tr>
<tr>
<td>▪ This test was validated by ECVAM (European Centre for the Validation of Alternative Methods) in November 2008, in replacement of in vivo rabbit Draize test</td>
</tr>
<tr>
<td>▪ <strong>not causing any sensitization response</strong> according to ISO standard 10993-10</td>
</tr>
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Cranial implant geometry

Animal testing

Geometry to be implanted in mini pigs skull

- solid,
- Open mesh,
- mesh with compound infiltration

Source: EOS, AZM, Suprapolix, Xpand

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Cranial implant geometry

Animal testing
Cranial implant geometry

Animal testing
Cranial implant geometry

Animal testing

Skull with 4 drill holes to insert implants

flap
Cranial implant geometry

Animal testing

Reference hole left empty

Implants inserted into the skull, fixed with titanium perforated sheet to avoid friction caused inflammation.
Cranial implant geometry

Animal testing

Source: EOS, AZM
Cranial implant geometry

Animal testing
Cranial implant geometry

Animal testing

Scanning Electron Microscopy

Analysis of surface roughness

Source: University Hasselt
Cranial implant geometry

Animal testing
### Cranial implant geometry

#### Socio-economic evaluation

<table>
<thead>
<tr>
<th>Compared to current care, a custom IMD implant has the potential to:</th>
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<tbody>
<tr>
<td>improve health gain</td>
</tr>
<tr>
<td>increase patient satisfaction</td>
</tr>
<tr>
<td>reduce costs</td>
</tr>
<tr>
<td>be more cost-effective</td>
</tr>
<tr>
<td>become the preferred treatment</td>
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<tr>
<td><strong>4</strong></td>
<td><strong>Conclusions</strong></td>
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Conclusions

General:

- Laser-Sintering already a proven AM manufacturing solution for medical applications

PEEK Laser-Sintering:

- Laser-Sintering of PEEK implant geometry was successfully performed for the first time.
- All requirements were met regarding strength, sterilizations and biocompatibility.
- Scaffold implant structures could be built that are impossible using conventional technology.
- The concept of hybrid cranial implants (composite of polymers and ceramics) opens new ways in the reconstruction of skull defects.
- Introduction of laser-sintered PEEK, polymer-ceramic composites and new design techniques was proven to be an excellent combination for reconstruction of skull defects.
Thanks to…

**Partners**

- AZM University hospital Maastricht (The Netherlands) & the University of Hasselt (Belgium) for the medical advise and analysis.
- Suprapolix & Xpand biotechnology (The Netherlands) for providing bio-absorbable polymers and bioceramics.
- ASCAMM (Spain) for the biomechanical validation of cranial implants.
- TNO (The Netherlands) for the scaffold ideas and the infiltration trials.
- LasMed (Poland), Tecnalia (Spain) and Rapra (United Kingdom) for providing consultancy and tests on sterilization methods and biocompatibility.
- Within (United Kingdom) for providing designs and FEM analysis.