Antiinfektive Beschichtungen von medizinischen Implantaten

Innovativer regionaler Wachstumskern

BIO-ANALYTICS AND SURFACES FOR INTEGRATION IN SYSTEMS

Steffi Grohmann, Manuela Menne, Holger Rothe und Klaus Liefeith, Institut für Bioprozess- und Analysenmesstechnik e.V. (iba), Fachbereich Biowerkstoffe, Heilbad Heiligenstadt
Motivation:

- Failure rate of load bearing bone implants still too high
  (~2% of all total hip prosthesis within the first 2 years post op.; according to the Swedish Hip Arthroplasty Register 2011)

- Major reasons for revision surgery:
  - Aseptic loosening
  - Implant-associated infections
    (z.B. ~15% of all above mentioned above)
**Motivation:**

**Race for the surface ...**

Gristina, Science (1987)

Major Goal I:
Fast and stable integration into the surrounding tissue

Supported by a biomimetic, bioactive surface coating

Major Goal II:
Effective Inhibition of implant associated infections

Supported by the local delivery of a broad band antibiotic
**Motivation:**

Bioactive, Biomimetic Polyelectrolyte Multilayer coating

Bioactive Compounds
- Antibiotic Gentamicin
- Growth factor $\text{rhBMP-2}$

Chondroitin sulfate and Heparin

Rider & Mulloy (2010)
**Motivation:**

Neutral environment (pH 7.4)

Acidic environment (pH 4.0)

- Demonstrated by Jiang, *et al.* (2009) for coatings composed of the polypeptides poly-L-glutamic acid and poly-L-Lysine

→ Applicability for multilayers composed of glycosamino glycans not investigated, yet
**Results:**

Film construction in acidic and pH neutral buffers

![Graph showing film mass (µg/cm²) vs. number of double layers at pH 4.0 and pH 7.4 for different polymers: PGA, CS, HEP.](image)
**Results:**

**Loading with the antibiotic**

- Highest concentration in PGA based coatings (none in CS based coatings)
- Concentration depends on the film thickness
Results: Release of the antibiotic

Concentration of released Gentamicin [µg/ml]

PGA

HEP

1d 2d 3d 4d 7d 14d

(PLL-PA)$_{10}$ mit PA = PGA bzw. PA = HEP
Results: In vivo experiment

Implantation of coated Titanium samples into the tibia to evaluate the effects on:

A) Infection
B) Osseointegration

Implants:
- „Kirschner“ wires, with one tip sharpened (Ø 0.8 mm, length 12 and 25 mm)
- Titanium, blasted and etched surface

Sprague-Dawley rat
Results: In vivo, Implant-associated infection

- All coatings reduce the severeness of the implant associated infection
- Best results for HEP30-GS (HEP based coating, composed of 30 double layers, loaded with gentamicin)
- PGA based coatings less effective though they delivered higher concentrations of the antibiotic
**Results:**

In vivo, Implant-associated infection

- Pronounced reduction in the amount of bacteria on and surrounding the implant
**Summary and Outlook:**

**Summary**
- Gentamicin-loaded Heparin-coatings (with high film thickness) reveal good anti-infective properties.
- Coatings composed of GAG reveal better anti-infective properties (despite a lower concentration of delivered antibiotic) and support osseointegration.

Promising results in vitro and in vivo, high potential for the implantology market.

**Outlook**
- The preparation conditions for the two-fold bioactive coatings need to be improved:
  - Higher quality of growth factor (eukariotic expression system).
  - Optimized sterilisation regime.
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