

Bioactive implant coating for local drug delivery

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Demographic data reveal that due to the increasing aging of the population, complications with the musculoskeletal system will increase in the next years.

One major problem in orthopedic and trauma surgery are the delayed healing or non-unions of long bone fractures. The exogenous application of growth factors can stimulate the bone healing to reduce this complication. Beside the choice of the optimal growth factor the application system is important.

Therefore, we developed a new bioactive coating method for implants, which is based on a biodegradable poly(D,L-lactide) (PDLLA, coating thickness: 10 µm) [1]. This coating allows the incorporation of growth factors and the controlled release of substances during the healing process without the need of further devices. The effect of different growth factors such as IGF-I and TGF-β1 locally released from coated intramedullary implants on fracture healing was investigated in a rat fracture model. Radiologically an enhanced healing was detectable due to the growth factor application (Fig. 1). The biomechanical and histomorphometrical results demonstrate a significant stimulation of the fracture healing due to the locally applied growth factors compared to control at days 28 and 42. At the latest investigated time point, 84 days after fracture, no differences were measurable in the biomechanical stability and the callus composition between the groups. The callus was consistently in the late phase of remodeling without any cartilage left. These results demonstrate, that the local growth factor application enhances the healing in the early phase without alteration of the normal healing process.

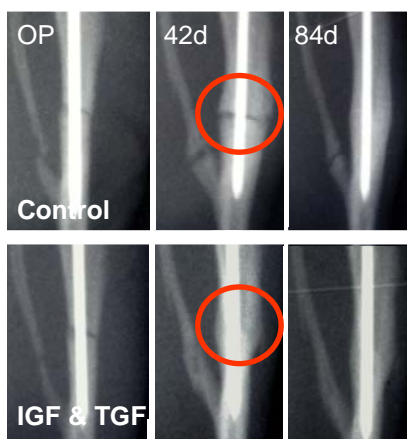


Figure 1
X-rays of fracture healing with and without growth factors
Day 42:
Better consolidation in the animals treated with IGF & TGF [2]

Besides delayed healing are implant related infections a feared complication in orthopedic and trauma surgery with tremendous consequences for the patient. To reduce this risk, administration of perioperative antibiotic prophylaxis is a routine procedure in orthopedic surgery. To optimize the prophylaxis the above mentioned local delivery system based on a polymer implant coating was used for antibiotics application.

In an animal experiment the efficacy of local prophylaxis was investigated. At surgery the medullary cavities of the rat tibiae were contaminated with *Staph. aureus* and titanium Kirschner wires were implanted. For local antibiotic therapy the implants were coated with PDLLA + gentamicin. All animals treated without local application of the antibiotic developed osteomyelitis (Fig. 2) and all cultures of implants were tested positive on *Staph. aureus* 42 days after surgery. The local application of gentamicin delivered from the PDLLA coating reduced significantly the signs of osteomyelitis in all animals and three of ten implants remained sterile in the microbiological analysis.

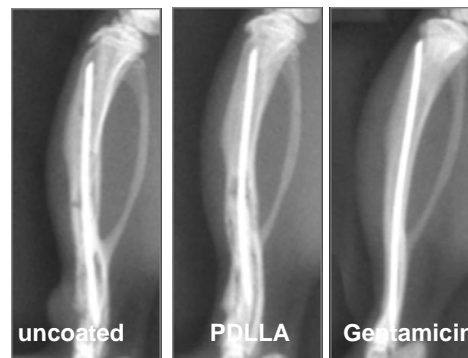


Figure 2 X-rays of implant related infection in a rat model 42 days after surgery. Local gentamicin application prevents the infection [3].

Bioactive coating of mechanical well established implants could on the one hand stabilize the fracture and on the other hand serve as a local drug delivery system. The use of gentamicin coated tibial nails is approved in Europe and Canada and the first patients have been treated.

1) Schmidmaier G. et al, J Biomed Mater Res 2001, 58:449-455

2) Schmidmaier G. et al, JOR 2004, 22:514-519

3) Lucke M. et al, Bone 2003, 32:521-531