Bioresorption of Bioretec Activa Implants

Bioretec Research and Development

BIOABSORPTION OF BIORETEC ACTIVA IMPLANTS

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BACKGROUND

Oriented PLGA (poly(lactic-co-glycolic acid), polymer is a very strong and tough material. Therefore it is suitable raw material for manufacturing of bioabsorbable implants, like pins, screws, plates, tacks, suture anchors and arrows etc. for musculoskeletal applications.

Bioretec Activa -implants are manufactured of medical grade PLGA. Because of high strength and toughness of oriented implants, they can be sterilized with gamma radiation. In addition of giving the thorough sterility to implants, without any remnants from sterilization process, gamma radiation also reduces molecular weight of oriented PLGA implants. This is advantageous for controlled bioabsorption of oriented PLGA implants within approx. 2 years in vivo.

The strong and tough structure of oriented PLGA implants prevents their breaking prematurely to large and sharp -edged fragments. The disintegration of PLGA implants in vivo leads to small angular or rounded particles, which slowly disappear with a mild inflammatory reaction. [1]
DEGRADATION AND BIOABSORPTION OF PLGA IMPLANTS

Initial Mechanical Properties of PLGA Implants

Oriented PLGA implants have high strength and toughness. They deform at room temperature with a ductile mode, which makes them safe in selected clinical applications.

Non-oriented PLGA implants, like pins, are weak and brittle and they can be broken easily by bending.

Self-Locking™ and Auto-Compression™

After implantation Bioretec Activa -implants increase in diameter and decrease in length 1-2 % during first postoperative weeks as a consequence of water absorption and structural relaxation of the oriented molecular structure. These dimensional changes lock the implants effectively into bone. The contraction of the implant in length applies a predetermined stress to the healing tissue ensuring the firm contact and advantageous compression in the fracture or osteotomy line.

0-6 Months hydrolysis in vitro and in vivo

Visual appearance of Activa –products is transparent before hydrolysis

Figure 1.

Figure 1. Visual appearance of ActivaPin™ 3.2 mm before starting the hydrolysis testing.

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Tiainen et al. report no change in morphology of mini screws, made of oriented PLGA 80L/20G, in rabbit cranial bone after 2 weeks. Slight fibroblast proliferation, microvascularization and osteoblastic activity was seen at the edges of the screw. Macrophages were seen around the head of the screw.

Figure 2 [1].

![Histological view of a 1,5 mm PLGA screw 2 weeks after implantation in a rabbit cranial bone. (S = Screw, B = Bone, Masson-Goldner trichrome staining)[1]](image)

The absorbed water starts the hydrolysis of the implant material. This can be seen as the reduction of molecular weight and strength of the implant as a function of hydrolysis time. In vitro the visual appearance of the implant turns from transparent to whitish indicating degradation of the material. Figure 3. After 6 months of in vitro hydrolysis the material is still solid, but pieces of the implant can be fractured off the surface by using a substantial force.
Tiainen et al. report a significant change in morphology of miniscrews, made of oriented PLGA 80L/20G, in rabbit cranial bone after 24 weeks. Screws are mostly fragmented. Osteoblastic activity is seen along the screw shaft. Macrophages and giant cells were seen around the fragmented head of the screw

Figure 3  Visual appearance of ActivaPin™ 3.2 mm after 6 months of hydrolysis in vitro.

Figure 4  Histological view of a 1,5 mm PLGA screw 24 weeks after implantation in a rabbit cranial bone. (S = Screw, B = Bone, Masson-Goldner trichrome staining)
6-12 months hydrolysis in vitro and in vivo

After 1 year of in vitro hydrolysis the Activa –products are already weak and porous. They can be broken to powder or to small granules when pressing with a finger Figure 5.

Figure 5 Visual appearance of ActivaPin™ 3.2 mm after 1 year of hydrolysis. Pressing with a finger results breaking of the product into powder or small fragments.

After the loss of their strength oriented PLGA implants start to disintegrate to small particles. The implants do not break neither prematurely nor to large, sharp-edged particles, as can happen with non-oriented polylactide implants [2][3], leading to problems, like to the extrusion of implant fragments [3].

Tiainen et al. report to have still some PLGA material left of miniscrews implanted in rabbit cranial bone at 1 year follow up. The position of the screw was mostly filled with adipose (fat) tissue, fibrous tissue and foamy macrophages, which had intracellular polymer material. New bone islets were noted around the head area of the screw Figure 6. [1]
Figure 6  Histological view of a 1,5 mm PLGA screw 52 weeks after implantation in a rabbit cranial bone. The remnants of PLGA were mostly internalized by foamy macrophages, but some extracellular PLGA was also found. (S = Screw, B = Bone, * = PLGA, Masson-Goldner trichrome staining)[1]
1-2 years hydrolysis *in vitro* and *in vivo*

After two years of *in vitro* hydrolysis only small amount of powder or small granule-like material is left of Activa –products Figure 7.

![Figure 7 Visual appearance of ActivaPin™ 3.2 mm after 2 years of hydrolysis.](image)

Tianen et al. report that oriented PLGA screws implanted in the cranial bone of rabbits were largely degraded after 1.5 years, although microscopically some intracellular material could still be seen, but hardly any in the extracellular space Figure 8 [1].

![Figure 8 Histological view of a 1.5 mm PLGA screw 72 weeks after implantation in a rabbit cranial bone. New bone islets can be noticed at the location, where the screw head was before its degradation. (S = Screw, B = Bone, Masson-Goldner trichrome staining)[1](image)

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Landes et al. report complete degradation of PLGA 85L/15G screws and plates in a clinical setup in cranio-maxillofacial applications in 1 year. Degradation time determination is based on the palpability of the implants and analyzed data of explanted implant material. They also report screw locations to be filled with bone in 2 years, based on radiological evaluation. [4][5]
3. SUMMARY

Oriented PLGA implants degrade by disintegration to small rounded or angular particles, which are digested by a mild, clinically not detectable, inflammatory process in vivo [1].

Final bioabsorption takes 1 to 2 years in vivo, depending on implant size, geometry and tissue metabolism conditions at the implantation site.

Rozema et al. reported the formation of hydrolysis resistant, perfect crystal remnants in vivo, after biodegradation of as-polymerized, high molecular weight polylactide implants [6]. Such degradation remnants have not been found with PLGA implants, because of low crystallinity, non-perfect crystalline copolymer structure and low molecular weight of gamma sterilized, oriented PLGA implants.

4. REFERENCES


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