Soft tissue and cancellous bone reaction to the implantation of novel biodegradable pins and plates in rabbits

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Biodegradable implants for osteosynthesis have had insufficient strength and a fast degradation rate. We produced a polymer based lactide to increase the molecular weight and strength of the implant and delay the degradation rate. This novel fiber-reinforced material in the form of plates and pins was tested in vitro for mechanical performance and in vivo in a neutral mechanical environment to assess biocompatibility. 21 rabbits with implants in the tibia and femoral condyles were killed at 1, 6, 12 months after implantation. Only a mild foreign-body reaction was observed and the implant was encapsulated by a thin 0.8–1.6 mm layer of connective tissue. Only a few lymphocytes and giant cells were detected in the early stages, dense fibroblasts in the middle stage, and giant cells clearing material particles in the late stage. In conclusion, the novel fiber-reinforced polymer based on polylactides was found mechanically superior to former degradable implants and biocompatible, showing no late inflammatory tissue response.

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Plate osteosynthesis is a popular method of fracture fixation. The metallic plates used up to now offer a rather rigid fixation with 2 distinct disadvantages; stress protection osteopenia and possibly nonunion, underneath the plate, and often the need to remove the implants in a second operation.

To avoid such problems, new composite materials have been introduced with more a physiological Young's modulus (Hastings 1994). In addition, the introduction of biodegradable polymers has eliminated the need for metalwork removal. The gradual degradation of the material implies that it has initial strength and stiffness to act as a supporting scaffold, but with the time the tissue is able to regain natural function. The in vivo behavior of the biodegradable implants needs further research to identify the exact degradation rate, the local biological tolerance, as well as possible systemic effects.

We examined the biological response in situ of a novel continuous fiber reinforced resorbable material for osteosynthesis. The polymer was produced in collaboration with two institutes (ITV and ITF) and was implanted in the form of plates and pins in rabbits in a neutral mechanical environment.

Material and methods

21 mature white New Zealand rabbits (males and females with a body weight between 3–4.5 kg) were used. 3 died during general anesthesia (i.v. ketamine, 20 mg/kg BW), 2 died postoperatively and 1 was excluded due to infection. The remaining 15 rabbits were divided into 3 groups (A, B, C) of 5 animals each and were killed at 1, 6 and 12 months, respectively.

Implants were placed surgically under standard aseptic conditions on both tibiae and left femoral condyle of each animal. Tibiae were approached through a lateral skin incision via the intramuscular septum down to the bone. The periosteum was left intact.

The biodegradable plate (4.5 x 1.5 x 50 mm) was fixed to the left tibia with 2 AO screws and washers (1.5-mm screw core), which were inserted outside the plate pressing it firmly to the bone (Figure 1). This achieved a stable mechanical environment. The same surgical procedure was performed on the right tibia which was used as control.

The left femoral condyle was exposed through a medial parapatellar incision and a pin made by the same biodegradable material was inserted in horizon-

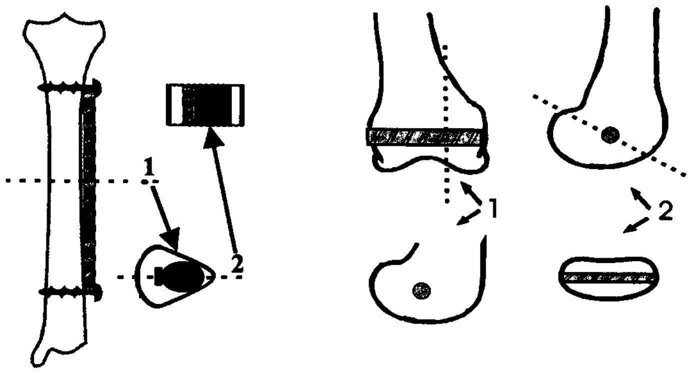

Figure 1. Diagrammatic presentation of implant application showing (left) the plate implant in a transverse view (1) and oblique view (2) on the tibia, and (right) pins in a transverse view (1) and oblique view (2) within the femoral condyles.

tally (medio-lateral) using a 3.0-mm drill bit. The pin had a diameter of 3.0 mm and its insertion was facilitated by a special instrument to prevent mishandling of the implant.

The biodegradable material was a polylactide polymer. High modulus fibers were produced by melt spinning and then embedded in a poly L/DL-lactide copolymer by compression moulding (Dauner et al. 1996). All material was sterilized by ethylenoxide in temperatures up to 50 °C and humid atmosphere. Mechanical properties and inherent viscosity were evaluated before and after the sterilization process.

The animals were free to move in individual cages, following routine closure and draping. No antibiotics were given.

Histology: The animals were killed at 1, 6, 12 months and the tibiae and left femoral condyle were disarticulated; after removal of the skin, they were fixed in buffer formalin for 24 hours. Specimens were obtained from the diaphysis of the tibiae transversely and longitudinally, as well as the femoral condyle longitudinally and obliquely. Half of the samples were used for conventional histology and were set with paraffin.

The remaining samples were set in embedding plastic undecalcified, proceeded by a methylmethacrylate medium for exothermic polymerization as described by Veld (1977). 4-μm thick sections were cut on a motorized Tung K heavy duty microtome. Histochemical staining with hematoxylin and eosin was done for conventional histology and with Masson-Goldner and toluidine blue for undecalcified sections. Histological examination was performed under light microscope and polarized light. The soft tissues around the plate were also assessed by conventional histology.

Results

No disturbances of wound-healing or other macroscopic signs of inflammation were detected on gross examination.

Group A (1 month): At 1 month after plate implantation, a few small lymphocytes and plasma cells were observed around the plate. No macrophages, giant cells, or histiocytes were noted. Fibrous and loose connective tissue had begun to appear close to the implant, which macroscopically appeared undamaged.

At 1 month after pin implantation, fibrous connective tissue was observed around the pins with a few giant cells. New bone had formed around the pins within the osseous tunnel without osteolysis.

Group B (6 months): At 6 months after plate implantation, histological analysis showed a typical nonspecific foreign-body reaction with mature connective tissue. No macrophages, and very few giant cells, histiocytes and lymphocytes were detected. A thin layer of connective tissue, 1.0–1.6 mm wide, had formed around the implants which were white macroscopically (hygroscopic effect). There was some separation of the fibers, especially at both ends (Figure 3).

At 6 months after pin implantation, fibrous connective tissue with a few macrophages and giant cells were observed. Approximately one third of the pins had broken down to fibers with macrophages and giant cells initiating phagocytosis of particles. Most of the matrix material had been replaced by fibrous type cellular connective tissue. Mixed areas of woven and mature bone, as well as hematopoietic bone marrow appeared to fill the osseous tunnel.

Group C (12 months): At 12 months, macrophages and giant cells appeared phagocytosing particles of the implant material. Most cells were of the epithelioid type (Figure 3). Fibrous connective tissue (0.8–1.2 mm wide) had formed around the plate. Whenever the plate was in complete contact to the bone (left tibia)

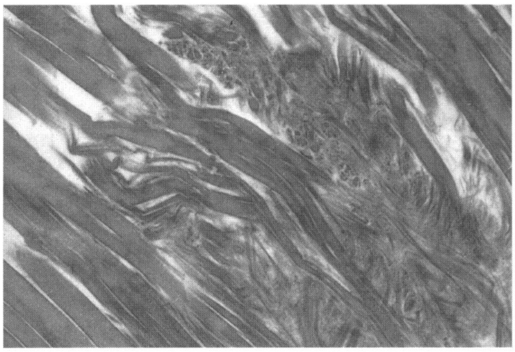

Figure 2. Histologic section at 6 months showing distinct invasion of the connective tissue into the end of the polymer plate underneath the screw-head (Masson-Goldner trichrome stain x160).

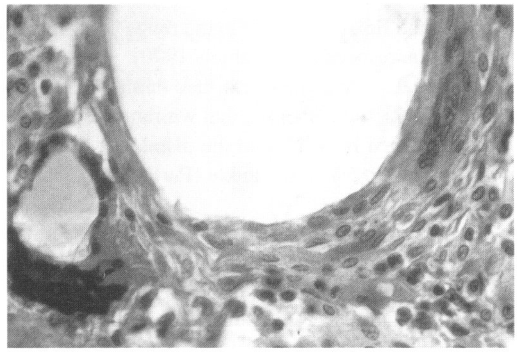

Figure 3. Histologic section at 12 months under light microscopy showing a fiber of the material surrounded by lympocytes and a released particle in phagocytosing process by a giant cell (Masson-Goldner trichrome x400).

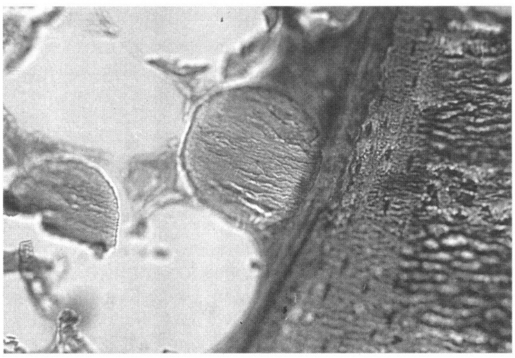

Figure 4. Histologic section at 12 months showing only one fiber intactand in contact to the cortical bone. The remaining fibers are degraded surrounded by a thin layer of connective tissue (Toluidine blue x 160).

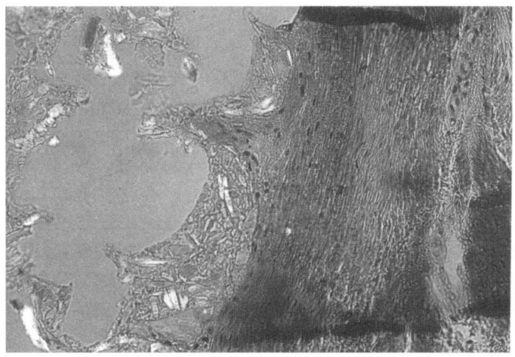

Figure 5. Histologic section at 12 months under polirized light showing many particles of fiber of the materials encapsulated within connective tissue and surrounded by giant cells (Masson-Goldner trichrome stam x160).

the encapsulating membrane was very thin, in contrast to the gap which was filled with adipose tissue and connective tissue (right tibia). Degradation was observed to have started from both ends of the plate with the invasion of vascularized connective tissue. 30–40% of the plate had been destroyed (Figure 4). Polarized light microscopy easily demonstrated the distribution of the particles (Figure 5). Osteolysis was detected around both screws in 3 cases.

At 12 months after pin implantation, the histological picture was similar to that observed at 6 months, but 90% of the pins had been broken down to fibers (about 0.15 mm in diameter). Several macrophages and giant cells were observed phagocytozing particles. The osseous tunnel was in the process of filling up with mature and woven bone.

Discussion

Polymers can be used for fracture fixation provided that they are biocompatible and mechanically adequate with a predictable degradation rate. To be biocompatible, they should have no adverse effects on the implant recipient by inducing adverse inflammatory reactions and not being carcinogenic, teratogenic, or toxic (Gogolewski 1992). Similarly, they must be reproducibly processed into desired form and sterilized without being degraded.

To date, the mechanical properties of the resorbable internal fixation implants developed had only 36% of the tensile strength, 54% of the bending stress and up to 3% of Young's modulus of stainless steel. The highest values of tensile and flexural moduli were 0.6–4 GPa and 2–10 GPa, respectively. Fiber-reinforced resorbable polymers, e.g. polylactides, showed a tensile and flexural moduli in the range of 6–30 and 4–124 GPa, respectively (Daniels 1990).

In clinical studies, the rate of late noninfectious inflammatory tissue responses that warranted operative drainage varied from 25% in the distal part of radius and scaphoid to 5% in the ankle (Partio 1990, Boestman 1991).

In our study, a novel polymer based on polylactides was synthesized by melt spinning and compression moulding. This produced a higher molecular weight and modulus of elasticity (Dauner et al. 1996).

The in vivo application of the implant onto the tibia and within the femoral condyles produced only a mild inflammatory tissue reaction with no sinus formation. The material was encapsulated by a thin layer of connective tissue, with more than 60% of the fibers remaining undamaged a year after the implantation.

These findings indicate that this novel material is biocompatible. Since it is also mechanically superior to previous materials, this suggests that it could be used for the manufacture of plates and pins for osteosynthesis. Further studies are needed, however, to produce appropriate designs which fulfill the criteria for a less rigid fixation which is well-known to enhance fracture healing.

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