

Degradation *in vitro* of New Bioresorbable Terpolymers of Lactides

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Introduction: Times to complete resorption of bioresorbable implants from lactide copolymers with a molecular weight of 200.000 dalton or higher often exceed 3 years. For implants from poly(L-lactide) the time to complete resorption may exceed 15 years in human patients.¹ This may raise the question whether there is any advantage in using resorbable implants with this type of degradation pattern, especially for maxillofacial and/or paediatric applications. With this in mind we recently designed new terpolymers consisting of lactides, glycolide and ϵ -caprolactone, assuming that the time to complete resorption of these terpolymers will be significantly shortened due to the disturbed chain regularity. The foreseen application of these new terpolymers is for internal fixation devices and microporous membranes for guided bone regeneration.

The purpose of the present study was to evaluate the *in vitro* degradation of one these new terpolymers.

Materials and methods: Resorbable pins (3.2 x 50.0 mm) produced by injection-moulding from poly(L-lactide-co-DL-lactide-co-glycolide) 80-10-10%. The viscosity-average molecular weights were 255.000 dalton and 55.000 dalton for the raw polymer and the pins, respectively. *Degradation in vitro:* Phosphate buffer solution, pH=7.4, 37°C, 4, 8, 12, 16, 20, 24, 28, 32 and 36 weeks. "Static" mode, the pH of the ageing medium was not adjusted over the whole test period. "Pseudodynamic" mode, the ageing medium was replaced if the pH dropped more than 0.5. *Samples evaluation:* Molecular weights and the polydispersity index Q estimated from viscosity measurements and size exclusion chromatography; mechanical properties of wet samples (bending strengths and moduli) measured in 4-point-bending mode (ASTM D790M); crystallinity changes assessed from the heat of melting (DSC, heating rate 10°C/min); the samples appearance observed under SEM.

Results and Discussion: Injection-moulding of the polymer caused an extensive thermo-oxidative degradation of the material (75%). This significantly affected the behaviour of the polymeric implants during *in vitro* degradation. From the first week of the experiment there was a progressive drop in the molecular weight which at 4 weeks was 40% and at 16 weeks 15% of the initial value. At 28 weeks the remnants of the implant were powderlike.

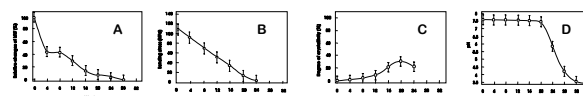


Fig. 1. Changes of molecular weight (A); bending strength (B); crystallinity (C) and pH (D) upon degradation of the samples.

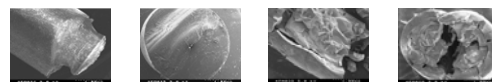


Fig. 2. SEM images of the pins before (A and B) and after 28 weeks *in vitro* degradation (C and D).

There was a progressive drop in mechanical properties of the samples from the first week of ageing. At 16 weeks the pins retained 31% of the initial strength, but at 24 weeks it was not possible to measure the strength due to pin fragmentation.

The crystallinity of the polymer used in the study increased during the first few weeks of the experiment from an initial value of 0.0% to 10% at 12 weeks, 21 at 16 weeks and 30% at 20 weeks. At 24 weeks the crystallinity was reduced to 22%. Similar behaviour has already been reported for other polyhydroxyacids. There was no change in the pH of the medium upon *in vitro* degradation of the samples in the pseudodynamic mode, and there was a decrease in the pH from week 20 through 36 from 7.5 to 3.5 in the static mode.

The polymer could be transformed into microporous membranes for guided bone regeneration using a phase-inverse process.

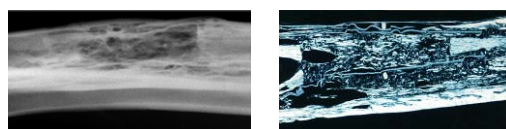


Fig. 2. Bone regeneration in critical-size defects in the rabbit radius covered with a microporous polylactide membrane.

Conclusions: Experimental implants produced from the new bioresorbable terpolymer show much higher susceptibility to degradation *in vitro* than implants from commonly used polyhydroxyacids. This is not only due to the chemical composition of the polymer, but also results from the low initial molecular weight of the samples used in the study. It is prerequisite that thermo-oxidative degradation of the polymer upon processing is avoided if the melt-processed implants are used *in vivo* for bone fracture fixation. The polymer can, however, be used for the preparation of the microporous bone regeneration membranes as solution-processing does not degrade the material.

References: Bos RRM, Presentation at the AO Maxillofacial Course, Davos, December 2003.