TISSUE REACTION TO POLYLACTIDE CHIPS PRE-DEGRADED BY GAMMA IRRADIATION TO A LOW MOLECULAR WEIGHT

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INTRODUCTION: Complete resorption of implants from polylactides may take up to a few years. In the late phase of degradation remnants of low molecular weight with an increased surface area are usually present at the implantation site[1]. In this study an experimental model was developed attempting to mimic the late stage of degradation of two polylactides with varying chemical composition. This stage is namely manifested by the presence at the implantation site of small polymeric particles having low molecular weight and a highly developed surface area.

METHODS: Chips from poly(L/DL-lactide) 80/20% (PLA80/20) and 70/30% (PLA70/30) (Boehringer Ingelheim) were used as purchased. The specimens were gamma irradiated in 6 cycles of 8 hours each using a dose of 2.5 Mrad. The molecular weight of the original and irradiated materials was determined by gel permeation chromatography. For animal experiments the chips of polymers were loaded in gelatin capsules (0.4 g polymer per capsule). The capsules were implanted subcutaneously for 9 weeks in ICR mice (permit GR16/95). Empty gelatin capsules served as control. The implants with the surrounding tissues harvested at 9 weeks were embedded in a polymer and cut with a Zeiss microtome into 6 micrometer sections. After Giemsa staining, a morphometric determination of chip geometry, amount of tissue between the chips, the number of cells, and a differentiation of cell types was performed.

RESULTS: Gamma irradiation reduced the molecular weight of materials from originally 92.800 to 8.400 Daltons and from 196.700 to 9.300 Daltons for PLA80/20 and PLA70/30, respectively. Control gelatin capsules were no longer palpable after 2 weeks, and their site could no longer be identified after 9 weeks. Histology revealed inflammatory-free tissue, and no scar tissue was visible. In the experimental groups no remainders of the gelatin capsule were detectable, and the agglomeration of polymer chips was flattened. The 80/20 chips were smaller, thus more chips per implantation site were counted. All chips were encapsulated by connective tissue, revealing a higher number of cells than in the control. The area of tissue between the chips was the same for both polymers, with higher cell content than in the control. The cell types for PLA80/20 and 70/30 were identical. The experimental groups had a significantly higher content of macrophages and lymphocytes than the control.

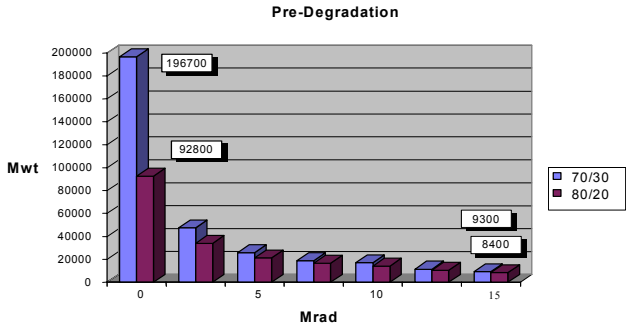

Fig. 1: Pre-degradation of polylacide chips by gamma radiation. After six cycles both types of polymer have reached a similar molecular weight

DISCUSSION & CONCLUSIONS: The model seems to be suited for rapid estimation of tissue reactions to degradable polymers at late stage of degradation. The histological appearance is that of a classical foreign body reaction, similar to earlier investigations with higher molecular weights polymers[2]. No signs of an increased inflammatory reaction were observed, which could be attributed to low molecular weight and to higher surface to volume ratio. In both polymers the cellular reaction was identical in respect to cell type. These findings suggest, that PLA80/20 presents compatibility characteristics comparable to those already established for late PLA70/30. PLA80/20 offers advantages on the mechanical side and in processing technology. These results encourage the development of the latter towards clinical applications.

REFERENCES: [1]J.E.Bergsma, F.R.Rozema, R.R.Bos, G.Boering, C.A.P.Joziasse, A.J.Pennings (1995) In vitro predegradation at elevated temperatures of poly(lactide, *J. Mat Science* **6**:642-646. [2] S.Gogolewski, M.Jovanovic, S.M.Perren, J.G.Dillon, M.K.Hughes (1993) *J Biomed Mater Res* **27**:1135-48.

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