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Meniscal tissue regeneration in porous 50/50 copoly(L-lactide/ε-caprolactone) implants


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Porous materials of a high-molecular-weight 50/50 copolymer of L-lactide and ε-caprolactone with different compression moduli were used for meniscal repair. In contrast to the previously used 4,4'-diphenylmethane and 1,4-trans-cyclohexane diisocyanates containing polyurethanes, degradation products of the copolymer are non-toxic. Two series of porous materials with compression moduli of 40 and 100 kPa respectively were implanted in the knees of dogs using a new, less traumatizing suturing technique. A porous aliphatic polyurethane series with compression modulus of 150 kPa was implanted for comparison. Adhesion of the implant to meniscal tissue was found to be essential for healing of the longitudinal lesion. Copolymer implants showed better adhesion, probably due to the higher degradation rate of the copolymer. Fibrocartilage formation was found to be affected by the compression modulus of the implant. Implants with a modulus of 40 kPa did not show ingrowth of fibrocartilage, whereas implants with compression moduli of 100 and 150 kPa yielded 50–70 and 80–100% fibrocartilage respectively. During degradation the copolymer phase separated into a crystalline phase containing mainly L-lactide and an amorphous phase containing mainly ε-caprolactone. The copolymer degraded through bulk degradation.© 1997 Elsevier Science Limited. All rights reserved

Keywords: Meniscal repair, porous materials, polyester, degradation

Received 10 June 1996; accepted 22 September 1996

Since it is beyond doubt that menisci are important structures in the knee joint1−3, there is an increasing interest in methods which can preserve meniscal tissue to prevent degenerative changes of articular cartilage. Repair of meniscal lesions by simple suturing is limited to the vascularized outer 10–20% part of the meniscus4−6. For meniscal lesions situated in the avascular central part of the meniscus, new experimental techniques are in the process of being developed6−8. Previously, we have shown that healing of large lesions in the avascular part, occupying about 30% of the length of the meniscus, can be accomplished by implanting a porous poly(ester)urethane (PU) in a connecting wedge-shaped defect9−11. A degradable porous polymer implant acts as a temporary scaffold for the formation of blood vessels and tissue. The repaired tissue appeared to be fibrocartilage, on morphological and immunological grounds12,13.

PUs were used because of their excellent mechanical properties and relatively good blood compatibility. In a previous study14, an aliphatic PU based upon ε-caprolactone and trans-cyclohexane diisocyanate was used. Since diisocyanates may be converted into diamines during degradation15,16, it is important that the diamines formed are non-toxic. Although trans-cyclohexanediimine is probably less toxic than aromatic diamines15, the consequences of its toxicity must also be considered. Therefore, a polymer that possesses good mechanical properties and releases only non-toxic degradation products is preferred.

A polymer that fulfils these requirements is a high-molecular-weight 50/50 copolymer of L-lactide and ε-caprolactone. This copolymer appeared to be an elastomer with mechanical properties comparable to segmented PUs due to highly entangled polymer chains and the presence of crystallizable L-lactide sequences17. Upon degradation, the polymer will yield L-lactic acid and ω-hydroxyhexanoic acid as degradation products. This polymer has been implanted successfully as nerve guides, was found to be non-toxic and showed a minor foreign-body reaction18,19.

To examine the possibilities of using this copolymer for meniscal reconstruction, two series of porous materials with compression moduli of 40 and 100 kPa respectively were implanted. An aliphatic PU series, which was used in a previous study14, with a compression modulus of 150 kPa was implanted for comparison. The experiments were carried out using a...
new, less traumatizing surgical technique. In previous studies full-thickness defects were made to connect the experimental lesion to the vascular periphery. Although this technique proved to result in healing of a torn meniscus in a substantial number of cases, gap formation between meniscal tissue and implants was sometimes observed. By creating a partial-thickness defect, leaving an inferior part of the meniscus intact, this surgical technique is less damaging.

Since the implant acts as a temporary scaffold, it is critical to understand the degradation behaviour. In this study the in vivo hydrolytic degradability as well as the in vitro degradability was monitored by weight loss, variation of monomer contents by NMR, molecular mass changes by size exclusion chromatography (SEC) and variation of the crystallinity by differential scanning calorimetry (DSC). Surface degradation was investigated by Fourier transform infrared internal reflection spectroscopy (FTIR/ATR) and scanning electron microscopy (SEM).

EXPERIMENTAL

Materials

L-Lactide (Purac Biochem, Gorinchem, The Netherlands) was recrystallized from dry toluene under a nitrogen atmosphere. e-Caprolactone (Jansen Chimica, Belgium) was dried with CaH₂ and distilled under reduced nitrogen pressure prior to use. The catalyst, stannous octoate (Sigma Corp., USA), was used directly from the supplier without further purification.

Polymerization

Polymerization was carried out in silanized glass ampoules. L-Lactide and e-caprolactone were mixed to a 1:1 mole ratio and 1 x 10⁻³ moles of catalyst per mole of monomer were added. The ampoule was heat sealed under vacuum. The polymerization mixture was homogenized at the polymerization temperature. Polymerization was continued for 10 days at 110°C.

Polymer processing

Implants

Polymer was purified and freed from unreacted monomer by precipitating chloroform solution into a 40/60 mixture of acetone and hexane. Porous materials were prepared using a freeze-drying/salt-leaching technique. Series 1: a 5 wt% copolymer solution in 1,4-dioxane and c-hexane (90/10) was mixed with 30 wt% saccharose crystals (200–400 μm). After freezing the mixture at −15°C, the solvent was sublimated under reduced pressure and the crystals were leached out with water. Series 2: after mixing a 5 wt% copolymer solution in 1,4-dioxane and c-hexane (90/10) with 30 wt% saccharose crystals (200–400 μm), the polymer concentration was increased to 8% by slowly controlled evaporation of the solvent under reduced pressure at 60°C. The mixture was then frozen at −15°C, the solvent was removed at reduced pressure by sublimation, and the crystals were leached out with water. Series 3: the porous aliphatic PU materials were prepared as described elsewhere. Implants were disinfected with 70/30 vol% ethanol/water for 1 week.

Films

Copolymer, poly(l-lactide) and poly(e-caprolactone) films were cast from dioxane solution (3 wt%), resulting in a thickness of 0.15 mm. Copolymer films were also obtained by compression-moulding bulk-polymerized polymer samples at 170°C followed by cooling rapidly in a cold press (thickness 1.5 mm).

Surgery

Experiments were performed under aseptic conditions on 26 lateral menisci of 13 adult mongrel dogs weighing 25 kg or more. Anaesthesia was accomplished by intravenous administration of pentothal (30 mg kg⁻¹) and maintained after intubation with nitrous oxide (2:1) and halothane.

The surgical technique, according to Klompmaker, that was used is shown in Figure 1A. Full-thickness lesions were made which had a longitudinal extension into both the anterior and posterior sides of the meniscus. A rectangular partial-thickness defect was made, leaving the inferior meniscal part intact. In this defect an implant was sutured using mersilene sutures. The longitudinal tear was not sutured. Three series of implants were implanted: series 1 into 8 knees, series 2 into 6 knees and series 3 into 12 knees. Follow-up periods were between 4 and 26 weeks.

Degradation

In vitro

Porous copolymer (series 1) samples (40 x 6 x 6 mm³) and polymer films were subjected to degradation at 37 ± 1°C in iso-osmolar phosphate buffer solutions at pH 6.9. To ensure a constant pH, the buffer solutions were refreshed regularly.

In vivo

Porous copolymer (series 1) samples (15 x 15 x 5 mm³) and solid as-polymerized copolymer samples (half discs: diameter 15 mm, thickness 4 mm) were subcutaneously implanted on four sides of the back of
20 Wistar albino rats. The samples were removed after killing the rats. Follow-up periods were 1, 8, 16, 32 and 56 weeks. Porous samples for histological study were fixed in glutaraldehyde and other samples were washed with water and dried in a vacuum oven at 37°C.

Characterization
The intrinsic viscosities were measured in chloroform at 25°C with an Ubbelohde viscometer. Size exclusion chromatography (SEC) of polymer samples was carried out at 30°C on a Waters GPC 150 with chloroform as eluent. As estimate of the molecular weight was obtained by using the Mark–Houwink constants of polystyrene (\( K = 4.9 \times 10^{-5} \text{dg}^{-1} \text{m}^2 \text{mol}^{-1} \) and \( a = 0.790 \).

Calorimeter studies were carried out with a PerkinElmer DSC 7 calorimeter. The scanning rate was 10°C min\(^{-1}\) in the range from –100 to 260°C.

Changes in polymer composition were determined by 300 MHz\(^{1}\)H NMR (Varian VXR-300) solutions in deuterated chloroform. In vivo porous polymer samples were extracted with deuterated chloroform and filtered before measurement.

FTIR internal reflection spectra were collected using a Bruker IP88 FTIR spectrophotometer with an MCT-A detector at an incident angle of 45°. Cast films (thickness 0.15 mm) were pressed against KRS-5 reflection plates.

Compression curves were determined at room temperature using an Instron (4301) tensile tester equipped with a 100 N load-cell at a cross-head speed of 12 mm min\(^{-1}\). Cylindrical specimens with a diameter of 10 mm and a length of about 8 mm were cut out of the foams by cooling them with liquid nitrogen.

An ISI-DS-130 scanning electron microscope was used for studying the pore structure of the porous materials and the surface of the films.

For light microscopy, meniscal reconstruction implants and rat implants were fixed in formaldehyde and embedded in glycol methacrylate. Sections (2 μm) were stained with toluidine blue and Giesma.

Implant preparation
Implants were prepared using the freeze-drying/salt-leaching technique described earlier.\(^{18}\) A polymer solution was mixed with saccharose crystals (200–400 μm) and frozen. After removing the solvent by sublimation, the crystals were leached out with water. The porous structure contained channel-like micropores (<50 μm) as a result of freeze-drying the solvent\(^{21}\) and macropores as a result of leaching out the crystals. These macropores have proven to be very important for the formation of fibrocartilaginous tissue\(^{9,22}\). Due to the high molecular weight of the polymer, the maximal concentration of the polymer solution to which saccharose crystals could be added homogeneously was only 5%. This resulted in material with a lower compression modulus (40 kPa) compared to the previous successfully used PU implants (250 and 150 kPa). To increase the modulus of the implants, the polymer concentration had to be increased since the modulus \( E_t \) and density \( \rho_t \) are related through:\(^{23}\)

\[ E_t \propto (\rho_t)^2 \]

After mixing the solution with the crystals, the polymer concentration could be increased to 8% by slowly controlled evaporation of the solvent under reduced pressure. The maximal compression modulus of the copolymer materials using this technique was 100 kPa.

RESULTS AND DISCUSSION
\( L \)-Lactide and \( \varepsilon \)-caprolactone can be polymerized to a high molecular weight with intrinsic viscosities (\( \eta \)) up to 9.9 dl g\(^{-1}\). The average sequence length of \( L \)-lactide appeared to be 8.5. The presence of these relatively long, crystallizable \( L \)-lactide sequences is responsible for the excellent mechanical properties of the material. The ability to crystallize under strain results in a tensile strength of 34 MPa, which is comparable to the tensile strength of the aliphatic PU used in a previous study\(^{14}\). The combination of good mechanical properties and the fact that upon degradation only non-toxic products are released make this polymer suitable for use as a strong, degradable, biomedical elastomer.

<table>
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<tr>
<th>Table 1 Implant characteristics</th>
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<tr>
<td><strong>Series 1</strong></td>
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<tr>
<td>Polymer</td>
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<tr>
<td>Porosity (%)</td>
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<tr>
<td>Microporosity (%)</td>
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<tr>
<td>Macroporosity (%)</td>
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<tr>
<td>Macroporosity (%)</td>
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<tr>
<td>Compression modulus (kPa)</td>
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Implantation
The data of the different implant series are presented in Table 1. Two copolymer series were implanted into the knees of dogs. Series 1 and series 2 implants had respective compression moduli of 40 and 100 kPa and respective porosities of 96 and 90%. An aliphatic PU implant, series 3, with a compression modulus of 150 kPa and porosity of 86%, implanted previously, was used as comparison. The porous structures of the implants are presented in Figure 2.

All experiments described up to now were carried out using the surgical technique as shown in Figure 1A1.2. A full-thickness defect was made to connect the
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Figure 2 Scanning electron micrographs of: a, copolymer implant series 1; b, copolymer implant series 2; c, PU implant series 3.

that they are running parallel to one another in the direction of the principal tensile stress, similar to tendons and ligaments. By creating a full-thickness defect, the old technique results in an interruption of the important collagen fibre structure and, after implantation, all the forces are directed across the implant and its contact area with meniscal tissue. This increases the possibility of tearing the connection between the implant and the meniscal tissue.

To overcome this drawback, a new, less traumatizing technique, according to Klompmaker, which leaves the collagen fibre structure intact as much as possible, has been developed. The technique is shown in Figure 1B1,2. Instead of creating a full-thickness defect to connect the lesion to the periphery, a partial-thickness defect was made to prevent movement between the implant and adjacent meniscal horn. Moreover, it appeared that healing of a tear is better when intimate contact exists between lesion and implant. Therefore, a rectangular defect was made instead of a wedge-shaped one, in order to provide a greater contact area between lesion and implant.

With this technique, gap formation between implant sides and meniscal tissue could be prevented, but the adherence of the implant to the underlying meniscal tissue has been found to be a problem. The implantation results are presented in Table 2. The copolymer implant series provide better adhesion than PU implants, showing complete or partial adhesion in 7/8, 5/6 and 7/12 of the cases respectively. The explanation for this phenomenon is probably the higher degradation rate of the copolymer. Upon degradation, carboxylic groups are formed which are able to stick to the meniscal tissue.

Healing of the lesion using series 1 and 3 implants was inventoried. Series 1 provides better results than series 3 implants, showing complete or partial healing in 75 and 25% of cases, respectively. This is an indication that the adherence of the implant to meniscal tissue is essential for healing of the lesion.

Series 1 showed the fastest ingrowth of fibrous tissue, probably due to the high porosity. After 12 weeks, ingrowth was complete. Ingrowth of fibrous tissue of series 2 and 3 was comparable and was complete after 20 weeks. The tissue response was equal for all three series.

Although series 1 showed the fastest ingrowth of fibrous tissue, fibrocartilage formation in these implants was never observed. In series 2 and 3, maximal 50-70 and 80-100% fibrocartilage was observed after 12 weeks, respectively. It appears that the formation of fibrocartilaginous tissue is affected by the modulus and density of the implant and not by the adherence of the implant to the underlying meniscal tissue. In other words, a higher compression modulus

<table>
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<th>Table 2 Implantation results</th>
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<tr>
<td>Implants</td>
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<tr>
<td>Adhesion to the lower meniscal part:</td>
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<tr>
<td>Healing</td>
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<tr>
<td>longitudinal lesion</td>
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<td>Fibrocartilage (%)</td>
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longitudinal lesion with the vascularized periphery. However, gap formation between the implant and the meniscal anterior and posterior horns could be observed in a number of cases. It seems likely that this gap formation was a result of the large circumferential forces in the meniscus during weight bearing. As a result of their concave wedge shape, axial loading of the joint causes the menisci to be displaced radially from the knee during weight bearing. Because they are anchored to the bone by the anterior and posterior horn attachments, this displacement generates large circumferential tensile stresses within the meniscal matrix. The arrangements of the collagen fibres is such
of the implant stimulates the formation of fibrocartilage. The fact that adhesion is not necessary for the formation of fibrocartilaginous tissue is indicative of fibrocartilage being formed by transformation rather than by direct ingrowth from meniscal tissue. It is known that fibrocartilage is formed after metaplasia of fibrous tissue and apparently this differentiation does not take place in implants with high porosity and low compression modulus.

In the literature several factors affecting the differentiation are described. *In vitro* formation of chondrocytes, cartilage cells, was determined by chick limb mesenchymal cells. These are cells that can differentiate to chondrocytes under the right circumstances. The differentiation was controlled by the initial plating density. At high density most cells became chondrocytes, at intermediate density only a few chondrocytes developed and at low density no development could be observed. The differentiation was affected by the oxygen level and chemical factors. It was also shown that, when exposed to intermittent compressive forces, high-density chondrocyte cultures showed an increase in cartilage production. Additionally, chondrocytes can be grown in a three-dimensional matrix of an agarose, collagen gel or porous polymer scaffold, but when they are grown in a monolayer they differentiate in cells with a fibroblast-like appearance. It may be possible that an implant stimulates chondrogenesis from precursor cells by local alteration of cell density, by offering the cells a three-dimensional matrix to grow and by adding compressive forces to the cells. In addition, when the defect is not filled with an implant, the repair tissue appeared to be inferior fibrous tissue. Probably due to the very high porosity of the implant series 1, this situation is approached and no fibrocartilage is formed.

Figure 3 shows the fibrocartilage formation in the copolymer implant series 2 and PU implant series 3 after 20 weeks. Noteworthy is the very small amount of polymer left in the case of the copolymer implant. In the case of the PU implant the initial porous structure is still visible. The degradation rate of the copolymer is evidently higher.

**Degradation**

Since the implant acts as a temporary scaffold for the ingrowth of fibrocartilaginous tissue, it is critical to understand the degradation behaviour. When fibrocartilage formation and healing of the longitudinal lesion are complete, degradation of the material is desired to obtain a completely healed meniscus. On the other hand, since fibrocartilage is formed after a certain induction time, the degradation rate of the polymer should not be too fast.

The compression modulus and density of the implant have been found to affect the fibrocartilage formation, and the degradation rate of the polymer determines the maintenance of these properties during implantation. Furthermore, the adhesion between implant and meniscal tissue, which is essential for the healing of the lesion, is affected by the degradation rate. Finally, the tissue response and degradation mechanism of biodegradable polymers can be of great consequence. For instance, three years after treatment with as-

In vitro

Porous copolymer samples of series 1 and polymer films were subjected to degradation at 37 ± 1°C in phosphate buffer solutions of pH 6.9.

In vivo

Porous copolymer samples of series 1 were subcutaneously implanted on two sides of the back of rats. Since, in the case of the porous copolymer, the characterization of the polymer is difficult due to ingrown tissue, solid as-polymerized copolymer samples were also subcutaneously implanted on two sides of the back of rats. Changes in intrinsic viscosity, mass, polymer composition and crystallinity were monitored as a function of degradation time. The surface of the copolymer films was characterized by SEM and FTIR during degradation.

In Figure 4 the remaining mass is plotted as function of the degradation time. After 6 months, the *in vivo* degradation of the porous material was monitored.
porous material showed a mass loss of 75%. This percentage is much higher than in the case of the aliphatic PU degradation, which in a previous study showed a mass loss of only 30% after 1 year\textsuperscript{14}. Difference in mass loss can be observed between in vivo and in vitro. It appears that the biological surroundings influence the degradation rate. The cause can be enzymatic, mechanical, chemical or a combination of the three. Figure 5 shows transmission electron micrographs of in vivo porous copolymer at different stages of degradation, showing a mild foreign-body reaction which was comparable to the PU implants used previously\textsuperscript{11}. Mass loss of the polymer is apparent. In vitro, this porous material showed fragmentation upon degradation, as presented in Figure 6. Notable is the presence of cracks on the fragments. Fragmentation was also observed for the solid material after in vivo degradation. Before implantation, the material was transparent. After implantation, the material became opaque until it fragmented after 56 weeks into white crystalline-like fragments.

In Figure 7 the intrinsic viscosity of in vitro porous and in vivo solid materials as a function of degradation time is shown. The initial value decreased rapidly from 9.1 and 5.9 dL g\(^{-1}\) to 1 and 0.2 dL g\(^{-1}\) after 16 weeks for in vitro porous and in vivo solid materials respectively. Mass loss was not simultaneous with loss of molecular weight, but lagged behind, indicating bulk erosion of the polymer samples. This is also confirmed by the single peak observed in SEC experiments for all three series. This single peak shifts towards lower molecular weight during degradation. In the case of surface erosion the molecular weight of the bulk is not expected to change during degradation.

In Figures 8–12 the respective variations of \(T_g\), \(T_m\), heat of fusion, and polymer composition as a function of degradation time are shown. Due to ingrown tissue in the porous in vivo material, the changes in the morphology of the polymer could not be determined for this case. Before degradation the materials showed a single \(T_g\) peak at \(-14^\circ C\) between the values for poly(l-caprolactone) of \(-60^\circ C\) and poly(l-lactide) of \(57^\circ C\), indicating that the lactide and caprolactone sequences are mixed to a certain degree. During degradation the \(T_g\) decreased and an increasing melting endotherm appeared between 100 and 120°C. As the fusion temperature of the poly(l-caprolactone) is 64°C, this melting temperature corresponds to crystallized l-lactide sequences. The decreasing \(T_g\) is an indication that the amorphous phase becomes richer in l-caprolactone. Since the amorphous phase is more susceptible to hydrolysis, the percentage of l-lactide increases with degradation time. Notable is the difference between the definite amounts of l-lactide in

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**Figure 4** Mass loss as a function of degradation time: O, in vivo porous; •, in vivo solid; ↗, in vitro porous.

**Figure 5** Porous copolymer series 2 after: a, 6 weeks; b, 18 weeks; c, 24 weeks implantation. The light-coloured areas represent polymer.
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Figure 6 Fragmentation of porous copolymer after in vitro degradation after: a, 8 weeks; b, 26 weeks; c, 47 weeks. d, Detail of a fragment after 47 weeks.

the case of porous in vivo and solid in vivo, which are 68 and 85%, respectively. Furthermore, narrowing of the melting endotherm at long degradation time is observed, indicating that 1-lactide crystallites have a narrow size distribution. Upon degradation the crystallinity increased to 43%.

An increase in crystallinity is also observed for high-molecular-weight as-polymerized bone plates and screws after implantation. After a postoperative period of 3 years, the poly(l-lactide) remnants revealed a heat of fusion of 96 J g⁻¹ and a melting temperature of 184°C, indicating that they are highly perfected, which makes them not very susceptible to hydrolysis. The copolymer crystallites are expected to be more susceptible to

Figure 7 Intrinsic viscosity of copolymer as a function of degradation time: ●, in vivo porous; •, in vivo solid; ▼, in vitro porous.

Figure 8 Tg as a function of degradation time: ●, in vivo solid; ▼, in vitro porous.
hydrolysis considering the lower melting temperature, indicating smaller dimensions of the crystallites. Swelling in the last stage of degradation of poly(l-lactide) was not attended by an increased cellular or foreign-body reaction, indicating that the swelling is induced by degradation of the polymer. An explanation for this phenomenon is the increase in osmotic pressure as a result of carboxylic and hydroxylic group formation during degradation\(^\text{34}\). The surrounding tissue capsule acts as a semipermeable membrane allowing water to pass which causes an increase in the volume. Up to 1 year no swelling at the implant sides was observed for both the porous and solid copolymers. It may be possible that at a later stage of degradation the solid copolymer gives rise to the same problems, but in the case of the porous copolymer this is not expected since the amount of polymer left is very small and a tissue capsule is absent.

**Surface degradation**

An FTIR internal reflection technique was used to provide information about the change in surface composition of cast copolymer films during degradation. The surface depth that the infrared beam penetrated was about 2\(\mu\)m. Figure 13 compares the spectra of the copolymer film before degradation and 4 weeks after degradation considering the lower melting temperature, indicating smaller dimensions of the crystallites. Swelling in the last stage of degradation of poly(l-lactide) was not attended by an increased cellular or foreign-body reaction, indicating that the swelling is induced by degradation of the polymer. An explanation for this phenomenon is the increase in osmotic pressure as a result of carboxylic and hydroxylic group formation during degradation\(^\text{34}\). The surrounding tissue capsule acts as a semipermeable membrane allowing water to pass which causes an increase in the volume. Up to 1 year no swelling at the implant sides was observed for both the porous and solid copolymers. It may be possible that at a later stage of degradation the solid copolymer gives rise to the same problems, but in the case of the porous copolymer this is not expected since the amount of polymer left is very small and a tissue capsule is absent.

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hydrolytic degradation. Significant differences in the carbonyl stretching band can be observed before and after degradation. Before degradation two C=O stretching peaks can be observed, one at 1758 cm\(^{-1}\) corresponding to the poly(L-lactide) carbonyl and a smaller one at 1737 cm\(^{-1}\) corresponding to the poly(ε-caprolactone) carbonyl. After degradation the relative intensity of the ε-caprolactone carbonyl has increased, indicating that the percentage of ε-caprolactone at the surface has increased. The difference spectrum for the copolymer before and after degradation strongly resembles the spectrum of poly(ε-caprolactone). Thus, the amorphous phase rich in ε-caprolactone tends to migrate to the surface. A similar phenomenon is observed for PUs. The flexible, soft segments are more abundant at the surface and the crystalline, hard segments are in the bulk.\(^{35,36}\) Since the amorphous phase is susceptible to hydrolysis, it is expected that carboxylic groups can be formed easily at the surface of the copolymer and contribute to adhesion between the implant and the meniscal tissue.

Figure 14 shows a scanning electron micrograph of the surface of a cast film after 4 weeks hydrolytic degradation. Many cracks are visible with widths ranging from 14 to 250 nm. Cracks are formed due to residual stresses in the material. In these regions the polymer chains are stressed and more susceptible to hydrolytic degradation.

**Figure 14** Scanning electron micrograph of the surface of a cast copolymer film, 4 weeks after hydrolytic degradation.

Figure 15 shows a scanning electron micrograph of the surface of compression-moulded film 4 weeks after hydrolytic degradation. The crack density is much smaller and the width of the cracks is 14 nm. Apparently, during compression moulding less residual stresses are left than after solvent evaporation. The surfaces of both films contain spherical structures of about 30 nm which are more pronounced for compression-moulded film. The spherical structures seem to be a result of phase separation. After 4 months of hydrolytic degradation, the cracks grew very large to widths of 5–20 µm and lengths of 10–300 µm. The crack morphology of the compression-moulded film is very different from the cast film. The presence of cracks enables the water to reach the inner parts of the material and it is therefore obvious that these materials degrade through bulk degradation rather than surface erosion.

**CONCLUSIONS**

Porous materials of a high-molecular-weight 50/50 copolymer of ε-caprolactone and L-lactide can be used for meniscal reconstruction utilizing a new, less traumatizing surgical technique. With this technique, gap formation between implant sides and meniscal tissue could be prevented, but implant adherence to the underlying meniscal tissue was found to be a problem. Copolymer implants showed better adhesion than PU implants, probably due to the higher degradation rate of the copolymer, and therefore yielding an increased number of carboxylic groups. Adhesion appeared to be important for healing of the longitudinal lesion. It is, however, not necessary for the formation of fibrocartilaginous tissue in the implant. Fibrocartilage formation was affected by the compression modulus of the implant. Implants with a compression modulus of 40 kPa never showed ingrowth of fibrocartilage, while the implants with compression moduli of 100 kPa showed 50–70% fibrocartilage after 12 weeks. The largest percentage of fibrocartilage (80–100%) was observed in PU implants with a compression modulus of 150 kPa.

The copolymer degrades through bulk degradation because the material easily forms cracks in the early stages of degradation. During degradation the material phase separated into a crystalline phase containing mainly L-lactide and an amorphous phase containing mainly ε-caprolactone, which tends to migrate to the surface. As the amorphous phase is more susceptible to hydrolysis, the percentage of L-lactide increased during degradation. Up to 1 year, no swelling of the polymer was observed and no problems are expected for porous implants in the later stages of degradation.

Since a high compression modulus of the implant was found to be crucial for fibrocartilage formation and the degradation rate of the copolymer is rather high compared to PU, the compression modulus of copolymer implants should be increased considerably in order to accomplish 100% fibrocartilage formation. However, using the freeze-drying/salt-leaching technique, materials with a maximal compression modulus of only 100 kPa could be prepared due to the molecular weight of the copolymer. Another technique has to be developed to further increase the compression modulus of the materials.
ACKNOWLEDGEMENTS

The authors wish to thank Dr E. A. Syed of Akzo Nobel Chemicals for supplying Elate prepolymer and Mr H. Nijland for the electron microscope work.

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