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Evaluation of copolymers of polyethylene oxide and polybutylene terephthalate (polyactive): mechanical behaviour

R. J. B. SAKKERS*
Department of Orthopaedic Surgery, University Hospital Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands

J. R. de WIJN, R. A. J. DALMEYER, R. BRAND‡, C.A. van BLITTERSWIJK
Biomaterials Research Group and ‡ Department of Medical Statistics, University of Leiden, Leiden, The Netherlands

Polyether–polyester segmented block copolymers (Polyactive^R) on the basis of polybutylene terephthalate (PBT) and polyethylene oxide (PEO) were mechanically tested. Tensile strength and modulus of elasticity in compressive and tensile deformation were recorded according to ASTM standards. These tests were done *in vitro* under dry and wet conditions, and after 3, 9 and 25 wk subcutaneous implantation of these materials in goats. Strength and modulus of elasticity were higher with increased contents of PBT in the copolymers. After water uptake, the polymer displayed a lower strength and stiffness. Disintegration of the materials with 70% PEO content and dumb-bell shape was noted at 3 wk. Disintegration of the cylinders of the same material was seen after 25 wk implantation. Of the materials with 60% PEO content, only four of the five dumb-bells had disintegrated after 25 wk implantation. The *in vivo* test results of all other implants did not show a clinically relevant decrease of strength and stiffness with time after implantation of the copolymers in the goats. Mechanical behaviour of the various copolymers seemed mainly determined by the amount and integrity of the PBT phase.

1. Introduction

Polyactive^R is the brand name for a new generation of biomedical degradable elastomers. These recently developed copolymers have shown unexpected bone-bonding properties [1–5]. The microstructure of these copolymers consists of hard, crystalline polybutylene terephthalate (PBT) domains and soft, amorphous polyethylene oxide (PEO) domains, the latter being strongly hydrophillic. Polyactive^R can be synthesized with different ratios of PEO–PBT. With increase of the amount of PBT in the ratio PEO–PBT, the copolymer will increase its stiffness.

The block copolymers, when saturated with water, can be characterized as physically cross-linked hydrogels. When dry, the material can be processed by thermoplastic procedures like hot pressing, injection moulding, etc., so that the classification of thermoplastic hydrogels is also justified. Although Polyactive^R implants are already clinically used in ear, nose and throat medicine and orthopaedic surgery (ear-drum, biodegradable cement stop, porous bone filler) [6], its mechanical properties have not yet been determined in detail.

These biodegradable PEO–PBT copolymers are of special interest for possible use in orthopaedic surgery and dentistry because of their bone-bonding properties [6–8]. The mechanical characteristics of the different materials will be a major determinant for the suitability of these materials for various applications. Not only strength and stiffness are of importance, but also the relationship between these properties and the extent of degradation with time after implantation.

In this study, tensile strength and modulus of elasticity of copolymers with different ratios of PEO–PBT were measured under laboratory conditions and at several different time intervals after implantation in goats [9, 10].

2. Materials and methods

2.1. Test materials

For testing, Polyactive^R with five different ratios of polyethylene oxide (PEO) and polybuthylene terephthalate (PBT) was manufactured: PEO–PBT 30–70, 40–60, 55–45, 60–40, 70–30.

* Author to whom all correspondence should be addressed.
e-mail: orthopaedic@chir.azu.nl

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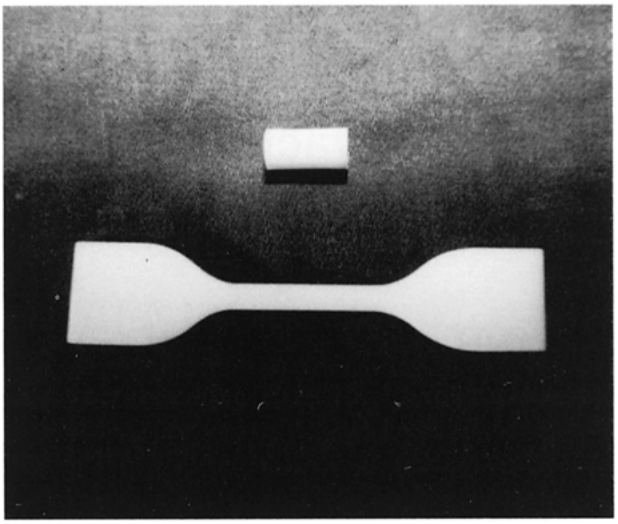

Figure 1 The polyethylene oxide and polybutylene terephthalate (PEO–PBT) cylinder and dumb-bell, shaped according to ASTM Standards [9].

1. Dumb-bell shaped test specimens (type M II of ASTM D 638M) were made of PEO–PBT 30–70, 40–60, 55–45, 60–40 and 70–30 by injection moulding (Fig. 1). Of each PEO–PBT type, five specimens were tested *in vitro* under dry and wet conditions, and after 3, 9 and 25 wk subcutaneous implantation in goats, making the total of tested specimens 125. The test specimens were dried to constant weight and vaccum-sealed 24 h before testing.

2. For testing of the mechanical properties of Polyactive^{R} under compressive forces, cylinders of the various PEO–PBT types with a length of 20 mm and a diameter of 10 mm were made by injection moulding (Fig. 1). Again five specimens of each PEO–PBT type were tested *in vitro* under dry and wet conditions, and after 3, 9 and 25 wk subcutaneous implantation in goats, making the total of tested specimens 125. These specimens were dried to constant weight and vaccum-sealed 24 h before testing.

2.2. Test design for tensile properties

Tensile testing of PEO–PBT was done according to ASTM D 638M standards [9]. This test method covers the determination of the tensile properties of unreinforced and reinforced plastics in the form of standard dumb-bell shaped test specimens when tested under defined conditions. Testing of the materials was done in a Zwick test machine type 1400–661/01 under dry and wet conditions (for testing in a wet state, 25 dumb-bells were kept in saline at 37 °C for 5 d before being tested) as well as after 3, 9 and 25 wk implantation. The specimens were mounted in the test bench and tested on their tensile properties with a crosshead speed of 50 mm min^{-1}.

2.3. Test design for compressive properties

The PEO–PBT cylinders 30–70, 40–60, 55–45, 60–40 and 70–30 were tested in a Hounsfield test machine type H25KM under compression, in dry and wet states (for testing in the wet state, 25 cylinders were soaked according to the same procedure as the dumb-bells) and after 3, 9 and 25 wk implantation. The crosshead speed of the test machine was 5 mm min^{-1}.

2.4. Test design for determination of tensile and compressive properties as a function of time after implantation in goats

In all, 75 dumb-bells and 75 cylinders were implanted in a total of 15 goats: five goats for each follow-up time. All goats were female, mature (2–4 y in age), and weighing 40–80 kg. They were obtained from a professional stock breeder and examined by a veterinary surgeon. Blood samples were taken to ensure that the animals were CEA/CL arthritis free.

Dumb-bells and cylinders were implanted subcutaneously in the right side or in the left side of the back of the goats, respectively, using a scheme made by random permutations. The site for each of the five implant types in the cranio-caudal plane was determined by using latin squares.

After 3, 9 and 25 wk the animals were sacrificed with an overdose of Thiopental and potassium chloride. Subsequently, the test materials were removed from the backs of the goats and tested in the same way as the non-implanted implants.

2.5. Calculation of material properties

The tensile strength at yield was calculated by dividing the load in Newtons at yield point by the original cross-sectional area of the specimen in square metres. The modulus of elasticity was calculated as the slope of the initial linear portion of the load–extension curve.

2.6. Statistical analysis

For statistical analysis, several (unbalanced) repeated measures models were fit to the data using the BMDP 5V procedure [11]. Variables included in the various models were F (follow-up time 3, 9 or 25 wk, three categories), S (shape = dumb-bell or cylinder, two categories), R (ratio PEO–PBT, five categories). Because the position of implants in the goat was randomized, the actual subcutaneous location of the implant in the goat's back was not taken into account as a separate variable in the model, but its effect was assumed to be averaged out over the goats. As a significance test for each factor in the model (estimating its effect adjusted for all other effects in the model), the Wald test was used. The level of significance was put at 5% (two-sided).

3. Results

3.1. Tensile and compressive properties tested *in vitro*

The mean tensile strength and modulus of elasticity of the dumb-bells and the modulus of elasticity of the cylinders with various PEO–PBT ratios, tested dry and wet are represented in Tables I and II. The tensile

TABLE I Tensile and compressive properties, tested unimplanted. D = dumb-bell, C = cylinder, T = tensile strength, E_t = E modulus tension, E_c = E modulus compression. S.D. in parentheses

PEO–PBT dry	T(D) (MPa)	E_t(D) (MPa)	E_c(C) (MPa)
30–70	19.78 (0.52)	325.51 (10.30)	274.65 (18.55)
40–60	15.43 (0.18)	197.54 (8.30)	185.99 (4.84)
55–45	10.13 (0.06)	92.38 (1.72)	88.15 (2.56)
60–40	8.40 (0.03)	69.20 (2.71)	68.65 (0.74)
70–30	5.27 (0.10)	33.95 (5.27)	44.27 (0.62)

TABLE II Tensile and compressive properties, unimplanted. S.D. in parentheses

PEO–PBT wet	T(D) (MPa)	E_t(D) (MPa)	E_c(C) (MPa)
30–70	18.35 (0.60)	246.03 (5.59)	252.89 (15.56)
40–60	14.30 (0.30)	137.89 (3.16)	153.93 (3.96)
55–45	9.43 (0.08)	53.87 (3.00)	67.61 (1.78)
60–40	7.97 (0.12)	39.57 (2.45)	46.99 (1.70)
70–30	4.71 (0.05)	15.84 (0.30)	18.56 (0.36)

strength as well as the modulus of elasticity increased significantly with an increasingly higher PBT content: for tensile strength and PBT content we found a positive correlation averaging 3.5 MPa (S.D. 0.16) per 10% increase in PBT content; for the modulus of elasticity the difference averaged 61 MPa (S.D 5.3) per 10% increase. Both correlations are highly significant ($p < 0.001$). Averaged over all different PBT contents, both the tensile strength and the modulus of elasticity of the wet-test specimen was significantly lower than that of the dry specimen: we estimated a difference of 18 MPa (S.D. 1.7) for the modulus of elasticity and of 0.44 MPa (S.D. 0.05) for the tensile strength, respectively.

3.2. Tensile and compressive properties tested after implantation

One goat of the 3 wk group died a few days postoperatively. Therefore, every type of implant with a follow-up time of 3 wk was tested four times instead of five. The materials of the other groups were all harvested five times and tested at follow-up times of 9 and 25 wk.

All dumb-bells with a ratio PEO–PBT 70–30 had disintegrated after 3 wk implantation. After 25 wk, four of the dumb-bells with a PEO–PBT ratio of 60–40 had also disintegrated. The tensile strength and modulus of elasticity of all dumb-bells which were tested are shown in Tables III–V.

Within a certain PEO–PBT ratio, no clinically relevant change in tensile strength of the intact test specimens was found over the period of 25 wk (Figs 2 and 3, Tables III–V). The modulus of elasticity decreased slightly (but significantly) over the same period (decrease 3–9 wk: 7 MPa $p = 0.47$, decrease 9–25 wk: 20 MPa $p < 0.003$).

Of the cylinders, all specimens with a ratio PEO–PBT 70–30 at a follow-up time of 25 wk, had disintegrated. The modulus of elasticity of all cylinders tested in compression in listed in Tables III–V. It was not possible to determine a meaningful compression strength of the tested cylinders due to the extensive

TABLE III Tensile and compressive properties, tested after implantation. S.D. in parentheses

PEO–PBT 3 wk	T(D) (MPa)	E_t(D) (MPa)	E_c(C) (MPa)
30–70	18.69 (0.57)	247.61 (3.44)	239.83 (3.67)
40–60	14.16 (0.30)	143.66 (15.74)	154.68 (4.90)
55–45	9.35 (0.02)	58.63 (2.79)	63.95 (3.88)
60–40	8.18 (1.15)	46.96 (6.98)	43.95 (0.71)
70–30	0	0	17.54 (0.69)

TABLE IV Tensile and compressive properties, tested after implantation. S.D. in parentheses

PEO–PBT 9 wk	T(D) (MPa)	E_t(D) (MPa)	E_c(C) (MPa)
30–70	18.20 (0.73)	212.09 (14.65)	237.03 (33.82)
40–60	14.55 (0.12)	146.47 (26.36)	159.27 (5.68)
55–45	9.39 (0.10)	59.57 (3.21)	66.00 (1.15)
60–40	7.42 (0.14)	40.03 (0.89)	44.87 (0.78)
70–30	0	0	15.84 (0.24)

TABLE V Tensile and compressive properties, tested after implantation. S.D. in parentheses

PEO–PBT 25 wk	T(D) (MPa)	E_t(D) (MPa)	E_c(C) (MPa)
30–70	18.18 (0.57)	205.91 (13.66)	237.45 (13.08)
40–60	14.28 (0.66)	132.32 (11.00)	144.92 (10.02)
55–45	8.60 (0.80)	55.12 (6.13)	62.81 (2.32)
60–40	(4): 0 (1): 8.40	(4): 0 (1): 41.49	42.41 (1.94)
70–30	0	0	0

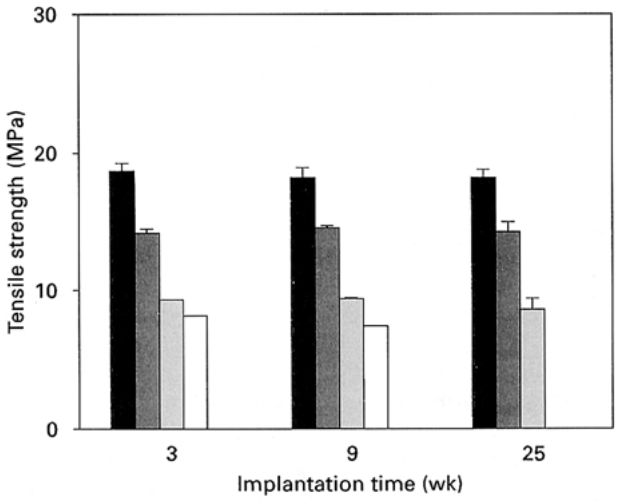

Figure 2 Tensile strength (at yield) of PEO–PBT 30–70 (black columns), 60–40 (dark grey columns), 55–45 (grey columns), 60–40 (light-grey columns), and 70–30 (white columns) with tensile testing at 3, 9 and 25 wk.

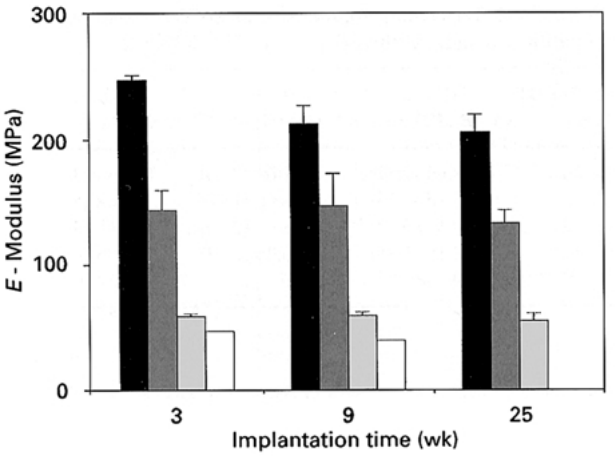

Figure 3 *E*-modulus of PEO–PBT 30–70 (black columns), 60–40 (dark grey columns), 55–45 (grey columns), 60–40 (light-grey columns) and 70–30 (white columns) with tensile testing at 3, 9 and 25 wk.

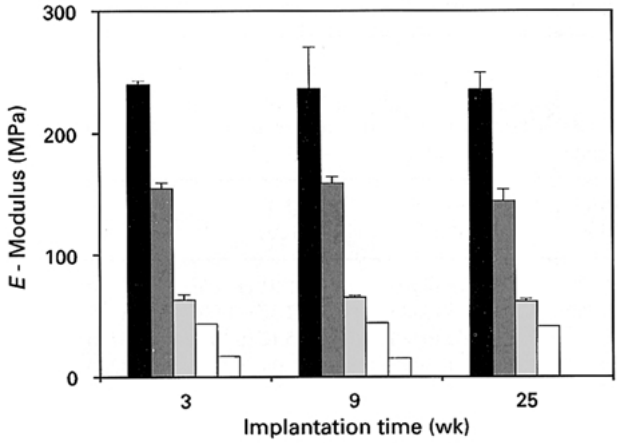

Figure 4 *E*-modulus of PEO–PBT 30–70 (black columns), 60–40 (dark grey columns), 55–45 (grey columns), 60–40 (light-grey columns) and 70–30 (white columns) with compression testing at 3, 9 and 25 wk.

elastic and plastic deformation before fracture. Within the different ratios, the modulus of elasticity decreased only marginally (decrease 9–25 wk: 6 MPa $p < 0.01$) with time over the period studied (Fig. 4, Tables III–V).

4. Discussion

Polyethylene oxide–polybutylene terephthalate copolymers (Polyactive^R) have shown favourable bone-bonding capacities [1–5]. To determine their suitability for use in orthopaedic surgery and dentistry, the mechanical characteristics of this material were investigated.

In PEO–PBT implants, the speed of disintegration is not only dependent on its PEO–PBT ratio, but also on its shape and volume. The type of test animal and site of implantation also most likely have their influence. The influence of shape and volume can be seen in this study because the bulky cylinders with a lower surface volume ratio stay intact longer than the dumb-bells of the same type of Polyactive^R.

The hard, crystalline polybutylene terephthalate domains in the polyethylene oxide–polybutylene terephthalate copolymers are the main determinants for the polymer's mechanical strength. The initial strength and modulus of elasticity of Polyactive^R will, therefore, be dependent on the percentage of PBT. This was also clear from the results of the mechanical testing described in this paper.

The soft, amorphous polyethylene oxide domains are strongly hydrophilic. In an aqueous environment, these domains will be responsible for the water uptake of the copolymer. In a swollen state, the amount of PBT cross-links per square metre will be decreased, resulting in a decreased strength and modulus of elasticity of the wet copolymer (Tables I and II).

However, it was remarkable to observe that the modulus of elasticity of intact test samples changed only slightly with time after subcutaneous implantation (Figs 2–4), especially in case of the PEO–PBT 60–40 materials of which four of the five dumb-bells had disintegrated after 25 wk implantation: the dumb-bell that was still intact had hardly changed in its mechanical behaviour. This mechanical behaviour *in vivo* is different from that of other, clinically used, degradable polymers like polylactide, that show a gradual decrease in strength after implantation [12, 13]. In earlier work, at longer follow-up times, fragmented Polyactive^R implants with PEO–PBT ratio 55–45 have been reported in human studies, indicating that degradation had taken place [14]. A possible explanation is that degradation of Polyactive^R starts with disappearance of PEO components by hydrolysis or oxidation. The PBT skeleton, which is the main determinant for the mechanical characteristics of Polyactive^R, remains intact in the initial phase of degradation. At a certain stage, by the time that hydrolysis of the PBT domains starts, the implant loses its coherency and disintegrates into smaller fragments. As long as the PBT skeleton is intact, the mechanical characteristics of the implant will remain relatively unimpaired.

It can be expected that Polyactive^R will behave differently after implantation in bone. By calcification, a composite will be formed with an increased modulus of elasticity. Recent investigations in dentistry have shown promising results with the use of a (flexible) coating of this type of elastomer on loaded implants [7, 8].

5. Conclusions

1. The amount of water uptake of Polyactive^R, *in vitro* or after implantation, will increase with an increase in percentage of PEO content of the copolymer and will result in a decrease of tensile strength and modulus of elasticity.

2. The "soft" types of Polyactive^R, 70–30 and 60–40, were the only copolymers that showed disintegration in the follow-up time of 25 wk. As long as the specimens are intact, no or only slight decrease in mechanical properties is observed when tested at follow-up times of 3, 9 and 25 wk.

3. The "harder" Polyactive^R test specimens, 55–45, 40–60 and 30–70, do not show a gradual decrease in

mechanical properties when tested at follow-up times of 3, 9 and 25 wk after implantation in goats.

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