PROPERTIES OF GAMMA-IRRADIATED POLY(TRIMETHYLENE CARBONATE)

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Summary

In this study, poly(trimethylene carbonate) (PTMC) of various molecular weights is gamma-irradiated at doses ranging from 25 to 100 kGy. The influence of gamma-irradiation on creep resistance under static and dynamic conditions is investigated. Also, the influence on the in vivo degradation rate is studied. The results show that crosslinking is an attractive way to improve the properties of high molecular weight PTMC for applications as cardiovascular tissue engineering scaffolds.

Introduction

Cardiovascular tissue engineering requires the use of a porous scaffold in which cells are cultured. To provide mechanical stimuli to the cells, the scaffold is subjected to mechanical stresses in a bioreactor. As a result, the cells excrete highly organized extracellular matrix (ECM) [1,2]. The scaffold should be resistant to long-term cyclic loading; ideally it is constructed from a biodegradable elastomeric material.

We have shown that high molecular weight PTMC shows rubber-like properties despite being totally amorphous and not cross-linked [3]. However, creep resistance of the material is limited. The introduction of chemical and/or physical crosslinks should overcome these limitations. Gamma-irradiation introduces chemical crosslinkages into the polymer and simultaneously sterilizes the specimen. Furthermore, this method does not require additional chemicals.

Experimental methods

PTMC of various molecular weights was synthesized and purified as reported before [3]. Compression molded (140 °C, Fontijne laboratory press THB008, The Netherlands) films and discs were vacuum-packaged and gamma-irradiated at 0 (unirradiated), 25, 50 or 100 kGy from a ^{60}Co source (Isotron Nederland, The Netherlands).

Equilibrium swelling experiments in chloroform were performed at room temperature. Gel contents and swelling ratios were calculated from the initial weight, the swollen weight and the dry weight of the extracted specimens. The densities of chloroform and PTMC used in the calculations were 1.48 and 1.31 g/ml respectively.

Mechanical properties were determined in triplicate on films ($100\times5\times0.6$ mm^3).

Tensile tests were performed at a crosshead speed of 50 mm/min, with an initial grip-to-grip distance of 50 mm using a Zwick Z020 universal tensile testing machine (Germany) at room temperature.

Static creep tests were performed at 50% of the yield stress, by loading a sample with the appropriate weight and periodically measuring the elongation between two marks on the specimen. The permanent deformation of specimens loaded for three days was determined after a 1-week recovery period.

Dynamic creep tests were performed by cyclic loading (20 cycles) of films to 50% strain at a crosshead speed of 50 mm/min with an initial grip-to-grip distance of 50 mm. The 21st cycle was started after a 2-h recovery period, after which the permanent deformation was determined.

Circular compression molded and gamma-irradiated (25 kGy) PTMC films (1 cm in diameter, 500 μm thick) were subcutaneously implanted in rats (male Wistar rats of approximately 3 months of age). At predetermined times the films were explanted and their mass and thickness were determined.

Results and discussion

Physical properties

Gamma-irradiation of PTMC results in crosslinking. Fig. 1 shows the gel fraction of the resultant networks after irradiating PTMC of various molecular weights at 25 kGy. The figure shows that a minimum molecular weight is required to form a gel. The highest gel fractions are obtained for polymers with the highest molecular weights. The applied radiation dose also has an influence on the gel fraction: PTMC (M_n=300 kg/mol) irradiated at 25, 50, and 100 kGy had a gel fraction of 58%, 59%, and 76%, respectively.

The short-term mechanical properties of PTMC are affected to some extent by gamma-irradiation. Irradiation of PTMC (300 kg/mol) at 0, 25, 50 and 100 kGy results in a decrease in *E*-modulus (6.4, 6.6, 5.1 and 4.4 MPa, respectively), a decrease in stress at yield (2.1, 1.9, 1.5 and 1.1 MPa, respectively) and an increase in stress at break (500%, 800%, 850% and 900%, respectively).

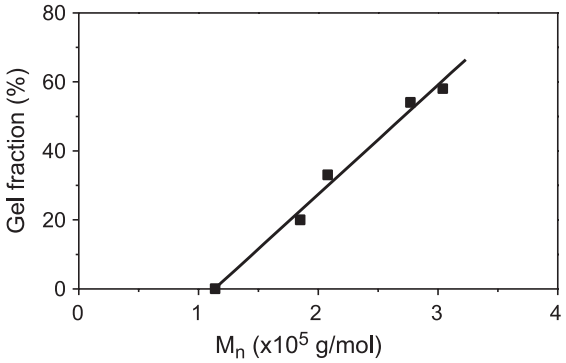

Fig. 1. Effect of PTMC molecular weight on the gel fraction after gamma-irradiation at 25 kGy.

Gamma-irradiation has a more significant effect on long-term mechanical properties of PTMC. The creep resistance under static and dynamic conditions is much improved upon crosslinking, as can be seen from Table 1. The ability to precondition a scaffold mechanically in a bioreactor highly depends on these parameters.

Table 1
Static and dynamic creep behavior of PTMC before and after gamma-irradiation

Radiation dose (kGy)	M_n=110 kg/mol			M_n=300 kg/mol		
	Static		Dynamic	Static		Dynamic
	Creep rate ($\times 10^{-5}$ s^{-1})	Permanent deformation (%)	Permanent deformation (%)	Creep rate ($\times 10^{-5}$ s^{-1})	Permanent deformation (%)	Permanent deformation (%)
0	146	329	11.6	16.6	350	0.6
25	134	[d]	2.1	2	57	0
50	127	27	1	0.5	14	0.5
100	45	9	0.3	0.3	3.4	0.05

[d]Sample fractured during creep test.

In vivo degradation

In a 2-year time period, noncrosslinked high molecular weight PTMC did not degrade in vitro [3], whereas in vivo (in subcutaneous implantations in rats) it degraded in 3–4 weeks [4]. Figs. 2 and 3 present the results of in vivo degradation experiments of high molecular weight PTMC after gamma-irradiation at 25 kGy.

Fig. 2 shows the effect of gamma-irradiation on the change in mass and thickness during in vivo degradation. It can be seen that the degradation of PTMC is retarded upon irradiation, resulting in a degradation time of approximately 6–7 weeks. Irradiated and nonirradiated PTMC degrade by surface erosion, as follows from the linear decrease in mass and thickness observed. This can be beneficial for tissue engineering applications.

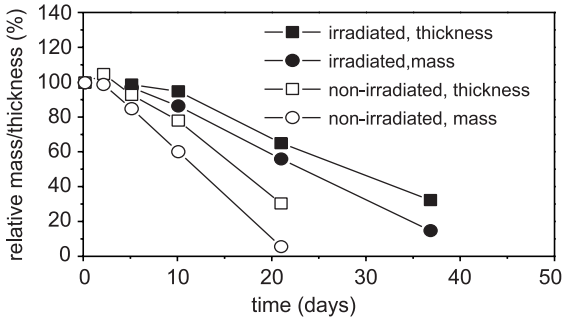

Fig. 2. In vivo degradation of PTMC. The M_n of nonirradiated PTMC is 320 kg/mol, the M_n of the irradiated PTMC was 480 kg/mol before irradiation.

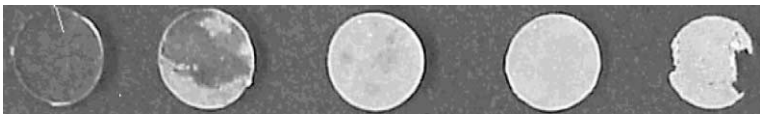

Fig. 3. Gamma-irradiated (25 kGy) high molecular weight PTMC specimens after explantation at 0, 5, 10, 21 and 37 days.

Conclusion

Gamma-irradiation induces crosslinking of PTMC. Increasing the molecular weight of the polymer and the radiation dose results in higher gel fractions. Short-term mechanical properties are affected to some extent by gamma-irradiation, creep resistance under static and dynamic conditions is much improved. Gamma-irradiation decreases the rate of in vivo degradation of PTMC; complete degradation is expected at 6–7 weeks.

References

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