Synthesis of Polyethylene Oxide Hydrogels by Electron Radiation

C. Branca,[1] S. Magazù,[1] G. Maisano,[1] L. Auditore,[2] R. C. Barnà,[2] D. De Pasquale,[2] U. Emanuele,[2] A. Trifirò,[2] M. Trimarchi[2]

[1]*Dipartimento di Fisica and INFM, Universita' di Messina, Papardo, 98166 Messina, Italy*
[2]*Dipartimento di Fisica, Università di Messina and INFN, Gruppo Collegato di Messina, Messina, Italy*

Received 21 October 2005; accepted 25 January 2006
DOI 10.1002/app.24238
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Poly(ethylene oxide) (PEO) hydrogels were prepared by crosslinking of aqueous PEO 35,000 solutions at a 30% concentration by using electron irradiation. Measurements were performed at different dose rates and irradiation doses. The swelling properties of each sample have been investigated and the network properties of the PEO hydrogels calculated. In particular, the effect of dose rate and dose irradiation on the crosslinking density were investigated. Finally, the experimental results illustrating the effects of the beam parameters on the network properties for a pulsed irradiation are compared to those of a continuum beam.
 J Appl Polym Sci 102: 820–824, 2006

Key words: poly(ethylene oxide); hydrogels; electron radiation

INTRODUCTION

Hydrogels are three dimensional hydrophilic polymeric networks capable of imbibing large amounts of water. Depending on the forces involved in the building up of networks, it is possible to classify hydrogels in two main groups: chemical hydrogels and physical hydrogels. In chemical hydrogels, the network of chemical links joining different chains can be obtained by crosslinking bulk polymers or polymers in solution, whereas in physical hydrogels, chains are held together by ionic, hydrogen bonding and/or dipolar interactions. In both cases, the density of crosslinks is crucial in determining the properties and applications of the gels, as it is responsible for the swelling behavior and consequently for the combined solid-like and liquid-like characteristics.

A common method of obtaining a randomly crosslinked network is by irradiation.[1,2] The use of radiation in the preparation of hydrogels has recently been reviewed by Rosiak and Olejnizak,[3] who have investigated the medical applications of radiation formed hydrogels. Pekala et al.[4] has investigated and prepared radiation crosslinked hydrogels as continuous release drug delivery systems. The controlled release of proteins and peptides from hydrogels synthesized by γ-ray induced polymerization was also studied.[5] Generally, the effects of electron irradiation on the structure, the conformation and the optical and mechanical properties of polymers have been widely studied and reported in literature.[6–13]

Among polymeric hydrogels, poly(ethylene oxide) (PEO) hydrogels are highly desirable in most biomedical applications requiring contact with physiological fluids, mostly because of their high biocompatibility and nontoxicity. For these reasons, PEO hydrogels are applied as wound coverings, drug delivery systems, hemodialysis membrane etc.[14,15] The chemical structure, H—(O—CH_2—CH_2)$_m$—OH, of this synthetic polymer includes two terminal groups, H and OH, which play an important role in short compounds. The hydrophobic ethylene units and the hydrophilic oxygens, which alternate along the chain, are responsible for its amphoteric character. The similarity of the ether oxygen spacing (2.88 Å) with that of the oxygens in water (2.85 Å) could explain the polymer solubility in water[16–18] which persists in all proportions at temperatures lower than the boiling point of water. Above this point it presents a miscibility gap that, by diminishing the polymerization degree, m, shifts towards greater temperatures and vanishes for $m < 48$. PEO is commercially available in an extremely broad molecular weight (M_w) range. PEO with $m < 150$ is generally called poly(ethylene glycol), or for short PEG.[18]

In view of the biomedical applications of PEO hydrogels, radiation crosslinking is particularly suitable since the network formation is completed without a potentially toxic crosslinking agent, and there are no chemical functional groups in the crosslinked structure. PEO appears to undergo both chain scission and crosslinking reactions when irradiated.[19] Crosslinking

Correspondence to: C. Branca (fisika@iol.it).

TABLE I
Major Features of the Employed 5 MeV Accelerator

Parameters of the accelerating structure	
Energy (MeV)	3.5–6.5
Max peak current (mA)	200
Repetition rate (Hz)	1–300
Pulse duration (μsec)	3
Peak power (MW)	1
Max average power (kW)	1
RF Frequency (GHz)	2.997
Structure type	SW OAC
Operating mode	$\pi/2$
Beam aperture size (mm)	10
N. accelerating cavities	9
Magnetic lenses	NO
Length (cm)	40
Weight (kg)	25

involves the loss of a hydrogen from a main chain carbon on two separate chains followed by the coupling of the two carbon radicals. Chain scission could take place by the abstraction of a hydrogen from a main chain carbon or by the breakage of a C—O bond to produce a pair of free radicals. Previous studies of bulk PEO irradiation have shown that chain scission predominates over crosslinking[20] whereas irradiation in aqueous solution increases the probability of free radical crosslinking.[19,21]

Most of previous works focused the attention on PEO hydrogels prepared by γ-irradiation.[14,19,21–23] The objective of this work is the development and optimization of an experimental method for the preparation of PEO hydrogels through electron irradiation. The effects of dose rate and total irradiation dose on the network properties have been studied through the analysis of the swelling behavior. Interjunction molecular weight, crosslinking density and mesh size were consequently determined at the different experimental conditions. Finally, the experimental results observed for the pulsed irradiation are compared to those of a continuum beam.

EXPERIMENTAL

Aqueous solutions of PEO 35,000 were prepared at a concentration of 30 wt % PEO. The solutions were prepared using double distilled deionized water. Once the aqueous solutions had formed, they were irradiated at different dose rates and total irradiation doses by electron beam at room temperature. The 1 kW autofocusing standing wave electron linac of the Physics Department of Messina University has been employed to accelerate electrons at 5 MeV energy with 1 mA/cm^2 current density and a beam energy stability better than 2%. Major features of the 5 MeV accelerator are summarized in Table I.

The beam spot on the target at a 10 cm distance is circular with 1 cm diameter. An accurate measurement of the irradiation dose per unit electron current has been performed, at different distances from the electron beam exit window, by means of Gafchromic® films. This allows us to measure the total dose provided to a given sample as a function of the total electron charge collected by a charge integrator, coupled with a toroidal ferrite, which continuously monitors the beam electron current stability.

Irradiation of PEO samples were performed at different dose rates by varying the pulse frequency between 1.5 and 6 Hz, and ranging the peak current between 5 and 30 mA. Under these experimental conditions the total dose ranges from 40 to 100 kGy. The list of samples along with the peak current, the pulse frequency employed and the corresponding dose rate and total irradiation dose is reported in Table II.

As reported in literature,[24] dissolved oxygen in the solution is rapidly scavenged by the hydroxyl radicals and under the high dose rates of the electron beam, redissolution of oxygen is inconsequential. Consequently, in our experiments, a negligible small fraction of the dose rate delivered is lost by reaction with dissolved oxygen.

RESULTS AND DISCUSSION

Characterization of PEO hydrogels

As above stressed, in the case of polymeric gels, properties such as swelling behavior, mechanical properties, optical properties, and permeability, are dependent on the gel network structure, which in turn depends on the conditions at gel preparation and conditions at measurements. It's therefore clear that, in view of a practical application, a characterization of the electron irradiation effects on the crosslinked network of polymeric hydrogels is to be considered as a preliminary step. To this purpose, the swelling properties of the polymeric hydrogels prepared at different dose rates and total irradiation doses have been first

TABLE II
List of Samples Along with the Peak Current, the Pulse Frequency Employed and the Corresponding Dose Rate and Total Irradiation Dose

Sample	Peak current (mA)	Pulse frequency (Hz)	Total irradiation Dose (kGy)	Dose rate (Gy/s)
A	5	1.5	40	5
B	5	3	40	10
C	30	1.5	40	30
D	5	6	60	20
E	5	6	80	20
F	5	6	100	20

evaluated by placing, after electron irradiation, dried PEO hydrogels into distilled water at room temperature. The degree of swelling Q, was calculated at different time intervals using the following equation[14]:

$$Q = \frac{(W_s - W_0)}{W_0}\% \quad (1)$$

where W_0 and W_s are the weights of gel before and after swelling, respectively.

The equilibrium swelling data were used to evaluate the network property of the PEO hydrogels. To determine the number average molecular weight between junction, $\bar{M}_c$ the following equation was used[14,22–25]:

$$\frac{1}{\overline{M}_c} = \frac{2}{\overline{M}_n} - \frac{1/d_p V_1[\ln(1 - v_{2,s}) + v_{2,s} + \chi v_{2,s}^2]}{v_{2,r}[(v_{2,s}/v_{2,r})^{1/3} - 1/2(v_{2,s}/v_{2,r})]} \quad (2)$$

here, $\bar{M}_n$ is the average molecular weight of the uncrosslinked PEO, χ is the Flory-Huggins coefficient (for the system PEO-water, $\chi = 0.45$[26]), V_1 is the molar volume of water (=18.1 cm^3/mol), $v_{2,s}$ is the polymer volume fraction in the state of equilibrium swelling: $v_{2,s} = d_w w_a/(d_w w_a + (w_s - w_a)d_p)$, where d_w and d_p are densities of water and polymer, $v_{2,r}$ is the polymer volume fraction after crosslinking but before swelling (the relaxed polymer volume fraction): $v_{2,r} = d_w w_a/(d_w w_a + (w_p - w_a)d_p)$, where w_p, w_a, and w_s are the mass of the polymer, gel, and swollen gel, respectively.

From the molecular weight between crosslinks, the number of links along the polymer chain, n, was calculated as[22]:

$$n = \frac{3\overline{M}_c}{\overline{M}_r} \quad (3)$$

here, $\bar{M}_y$ is the molecular weight of the PEO repeating unit (=44 g/mol). The root-mean-square end-to-end distance of the PEO chain in freely joined state was calculated by[22]:

$$(\bar{r}^2)^{1/2} = l\, n^{1/2} \quad (4)$$

where l is the bond length along the polymer chain (=1.54 Å). Then, the root-mean-square end-to-end distance of the polymer chain in the unperturbed state was calculated as:

$$(\bar{r}_0^2)^{1/2} = (\bar{r}^2)^{1/2}\, C_n \quad (5)$$

where C_n is the PEO characteristic ratio (=3.8). The mesh size of the polymer network, ξ, was calculated by[22]:

TABLE III
Average Interjunction Molecular Weight, $\bar{M}_c$, Crosslinking Density, d_x, and Mesh Size of the Investigated Samples

Sample	$\bar{M}_c$	d_x (10^5 mol/cm^3)	Mesh size ξ (Å)
A	4000	29.5	83
B	2416	48.9	65
C	1763	67.1	55
D	2153	54.9	61
E	1774	66.7	55
F	948	124.8	40

$$\xi = v_{2,r}^{-1/3}\, (\bar{r}_0^2)^{1/2} \quad (6)$$

Finally the crosslinking density, d_x, was calculated using the equation[14]:

$$d_x = \frac{1}{v\overline{M}_c} \quad (7)$$

where v is the specific volume of the polymer. The values of $\bar{M}_c$, d_x, and ξ determined for all the samples investigated are summarized in Table III.

Dose rate and total irradiation dose effects

Let us first analyze the effects of dose rate on the network properties. Figure 1 shows the swelling behavior as a function of time for the PEO hydrogel samples A, B, and C prepared at different dose rates at the same total irradiation dose, $D_t = 40$ kGy. As can be seen, the samples swell in water rapidly at first and then gradually reach an equilibrium value. In agreement with previous experiments,[14] it can be observed that the lower the dose rate, the higher is the degree of swelling. According to eq. (2), this trend determines a decreasing in the average molecular weight between crosslinks with increasing dose rate, see Table III, and a consequent increasing of the crosslink density from 30 to around 67 $\times$ 10^5 mol/cm^3. This observation agrees with previous measurements performed on PEO hydrogels synthesized by γ-irradiation.[14] However, in this frame, it has to be stressed the great advantage offered by the pulsed electron accelerator in comparison with continuum one, that is the availability of a friendly user apparatus that allows us, by simply varying the pulse repetition rate or the peak current, to change the dose rate within broad ranges with a good reproducibility of the parameters.

Turning now the attention on the total irradiation dose effects, Figure 2 shows the swelling behavior of the PEO hydrogel samples D, E, and F, prepared at different total irradiation doses, but with the same dose rate, $D_r = 20$ Gy/s. Also in this case the PEO

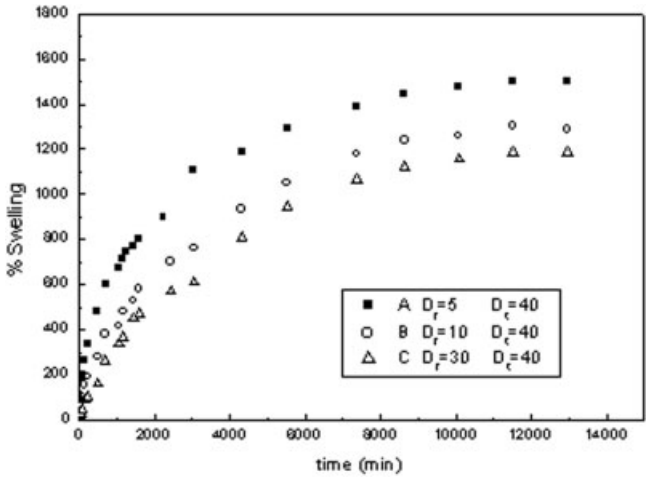

Figure 1 Swelling behavior as a function of time for the PEO hydrogel samples A, B, and C prepared at different dose rates at the same total irradiation dose, D_t = 40 kGy.

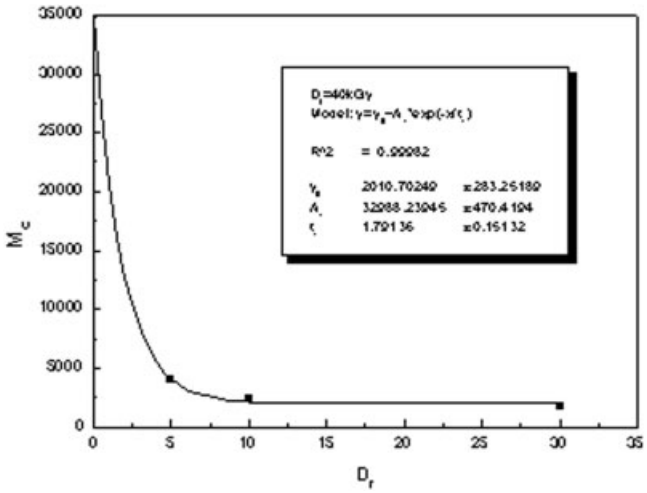

Figure 3 Dose rate dependence, D_r, of the average interjunction molecular weight, $\bar{M}_c$. The solid line is the fit result according to an exponential decay model (see text for details).

hydrogels put into water swell gradually reaching an equilibrium value. However, by comparing Figures 1 and 2 one can see that the time required by the samples to reach this equilibrium value is much longer for the samples prepared at different dose rates than for the samples prepared at different irradiation doses. Moreover, differently from the previous case, an anomalous behavior has been evidenced in the initial step of the swelling. In fact, notwithstanding, as expected, the higher the irradiation doses, the lower is the equilibrium swelling value, up to 900 min, one can observe an higher swelling rate for the sample with the higher irradiation dose, see the insert of Figure 2.

The values of $\bar{M}_c$ and d_x, summarized in Table III, evidence that, by increasing the irradiation dose, the average interjunction molecular weight decreases from around 2000 to 900, and the crosslink density increases, from 55 to 125 $\times$ 10^5 mol/cm^3 so leading to more densely crosslinked networks.

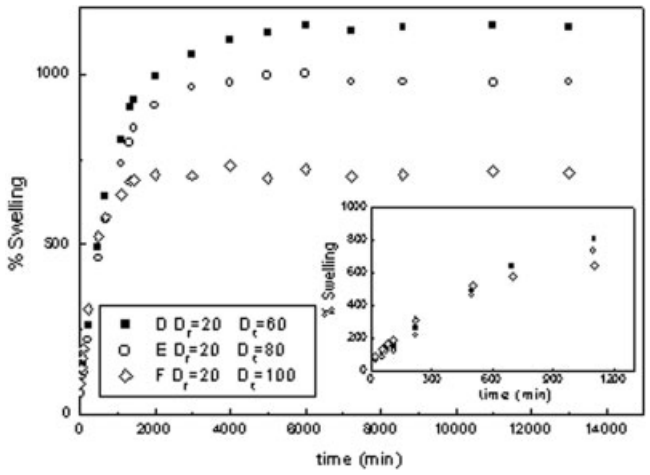

Figure 2 Swelling behavior of the PEO hydrogel samples D, E, and F, prepared at different total irradiation doses at the same dose rate, D_r = 20 Gy/s. In the insert, the initial swelling phase is enlarged.

It is interesting at this point to compare our experimental results to those reported in literature obtained by a continuous beam. In particular we refer to an experimental work on PEO hydrogels prepared by γ-irradiation at a dose rate of 4440 rad/min, corresponding to 0.74 Gy/s, with total dose varying between 3 and 10 Mrad, corresponding to 30–100 kGy.[22] To compare the interjunction molecular weight data for the aqueous PEO solutions at a same concentration (30 wt %), we follow a procedure that encompasses first the definition of an analytical expression for the dose rate dependence of $\bar{M}_c$. The observed experimental behavior for the samples A, B, and C, see Figure 3, suggests us to adopt an exponential decay model whose parameters are reported in the insert of the figure. Once the parameters have been defined, by adopting the same model, we obtain, by extrapolation, the $\bar{M}_c$ values for a dose rate of 0.74 Gy/s at different total doses. The comparison with the $\bar{M}_c$ values ob-

TABLE IV
Comparison of the $\bar{M}_c$ Values Obtained by γ-Irradiation[14] and by Electron Irradiation (Present Work) at a Same Dose Rate, D_r = 0.74 (Gy/s), and at Different Irradiation Doses

Dose rate (Gy/s)	Irradiation dose (KGy)	$\bar{M}_c$ Ref. 14	$\bar{M}_c$ Present work
0.74	50	16,000	15,124
0.74	80	15,300	14,252
0.74	100	12,750	12,700

tained by γ-irradiation, reported in Table IV, evidence a good agreement, so supporting the goodness of the followed approach.

A last comment refers to the equivalent mesh sizes that, within the experimental beam parameters employed, vary from 40 to 83 Å. Such mesh sizes indicate that very small molecular weight solutes can penetrate the membranes relatively fast and are not affected by the crosslinked structure.

References

1. Peppas, N. A. Hydrogels in Medicine and Pharmacy, Vol. 1: Fundamentals; CRC Press: Boca Raton, FL, 1986.
2. Rosiak, J. M.; Ulanski, P. Radiat Phys Chem 1999, 55, 139.
3. Rosiak, J. M.; Olejniczak, J. Radiat Phys Chem 1993, 42, 903.
4. Pekala, W.; Rosiak, J.; Rucinska-Rybus, A.; Burczak, K.; Galant, S.; Czolczynska, T. Radiat Phys Chem 1986, 27, 275.
5. Caliceti, P.; Veronese, F. M.; Schiavon, O.; Lora, S.; Carenza, M. Farmaco 1992, 47, 275.
6. Li, H. L.; Ujihira, Y.; Shukushima, S.; Ueno, K. Polymer 2000, 41, 93.
7. Xu, H. S.; Shanthi, G.; Bearti, V.; Zhang, Q. M.; Ramotowski, T. Macromolecules 2000, 33, 4125.
8. Ravat, B.; Grivet, M.; Grohens, Y.; Chambaudet, A. Radiat Meas 2001, 34, 31.
9. Arndt, K. F.; Schmidt, T.; Reichelt, R. Polymer 2001, 42, 6785.
10. Alegaonkar, P. S.; Bhoraskar, V. N. Radiat Eff Defects Solids 2004, 159, 511.
11. Torrisi, L.; Visco, A. M.; Barna, R.; De Pasquale, D.; Campo, N.; Di Marco, G.; Trimarchi, M.; Trifiro, A. Radiat Eff Defects Solids 2004, 159, 259.
12. Othon, C. M.; Bateman, F. B.; Ducharme, S. J App Phys 2005, 98, 014106.
13. Cho, S. O.; Jun, H. Y. Nucl Instrum Methods Phys Res Sect B 2005, 237, 525.
14. Savaş, H.; Guven, O. J Pharm 2001, 224, 151.
15. Korsmeyer, R. W.; Peppas, N. A. In Controlled Release Delivery System; Roseman, T. J., Mansdorf, S. Z., Eds.; Marcel Dekker: New York, 1983; pp 77–90.
16. Branca, C.; Magazù, S.; Malsano, G.; Migliardo, P.; Villari, V. J Phys: Condens Matter 1998, 10, 10141.
17. Bieze, T. W. N.; Barnes, A. C.; Huige, C. J. M.; Enderby, J. E.; Leyte, JC. J Phys Chem 1994, 98, 6568.
18. Bailey, F. E.; Koleske, J. V. Poly(Ethylene Oxide); Academic Press: New York, 1976.
19. Grollman, U.; Schnabel, W. Makromol Chem 1980, 181, 1215.
20. Merrill, E. W.; Dennison, K. A.; Sung, C. Biomaterials 1993, 14, 1117.
21. Matheson, M. S.; Mamou, A.; Silverman, J.; Rabani, J. J Phys Chem 1973, 77, 2420.
22. Stringer, J. L.; Peppas, N. A. J Controlled Release 1996, 42, 195.
23. Peppas, N. A.; Merril, E. W. J Polym Sci Part A: Polym Chem 1976, 14, 441.
24. Kofinas, P.; Athanassiou, V.; Merrill, E. W. Biomaterials 1996, 17, 1547.
25. Bray, J. C.; Merril, E. W. J Appl Polym Sci 1973, 17, 3779.
26. Brandrup, J.; Immergut, E. H., Eds. Polymer Handbook; Interscience: New York, 1976.