Effect of Gamma Irradiation and Irradiation Temperature on Hydrolytic Degradation of Synthetic Absorbable Sutures

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SYNOPSIS

The purpose of this study is to examine the effects of γ irradiation and the relative magnitude of T_{irr} to T_g on the physical, mechanical, thermal, morphological, and hydrolytic properties of two types of synthetic absorbable polymers. Polyglycolic acid (PGA) and glycolide-trimethylene carbonate block copolymer fibers in the form of 2/0 size Dexon and Maxon sutures from Davis/Geck were used in this study. In addition, injection-molded PGA disks were also used for determining how different polymer morphology affected the outcomes of γ irradiation and irradiation temperature. These two types of biomaterials were ^{60}Co γ irradiated at two irradiation temperatures (55 and $-78°C$ in dry ice). Both γ-irradiated and control specimens were immersed in a phosphate buffer solution of pH 7.44 at 37°C for various durations of hydrolysis. After each predetermined duration, the specimens were removed for subsequent testing which included determinations of tensile strength, weight loss, level of crystallinity, melting temperature, intrinsic viscosity, surface morphology, and infrared spectroscopic characteristics. γ irradiation at both irradiation temperature resulted in a faster hydrolytic degradation of these two biodegradable polymers. There was no apparent irradiation temperature effect in terms of mass loss, intrinsic viscosity, level of crystallinity, and melting temperature. However, irradiation temperature effect was evident in those properties that depended on the tie-chain segments located in the noncrystalline domains, such as tensile strength. The observed effect of irradiation temperature was attributed to chain mobility which could facilitate cage recombination of macromolecular radical pairs at the irradiation temperature lower than the glass transition temperature of the irradiated polymers. © 1995 John Wiley & Sons, Inc.

INTRODUCTION

The use of synthetic biodegradable polymers in surgery has become increasingly popular because they do not indefinitely elicit foreign body reactions during their presence in the human body. There are many experimental synthetic biodegradable polymers used for various clinical purposes. However, the most successful commercial use of this class of biomaterials is as sutures and clips/staples[1-3] in wound closures.

These commercial synthetic absorbable sutures belong to the class of linear aliphatic polyesters including polyglycolic acid homopolymer (Dexon®), glycolide-lactide random copolymer (Vicryl®), poly-*p*-dioxanone homopolymer (PDS), trimethylene carbonate-glycolide block copolymer (Maxon®), and a segmented block copolymer of glycolide and ϵ-caprolactone (Monocryl®). Their degradation mechanisms have been attributed to a simple hydrolytic process with possible enzymatic catalytic effects.

Recent research efforts in the development of new absorbable sutures include the random and segmented copolymerization of either existing absorbable suture components or new monomers chemically different from existing absorbable suture components, a concept similar to composite sutures. An example of such efforts up to now is the copolymerization of PDS suture with glycolides, lactides,

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or morpholine-2,5-dione (MD).[4-7] Copolymer of PDS and polyglycolic acid (PGA) (20%) has an absorption profile similar to Dexon and Vicryl sutures, but it has compliance similar to PDS. Copolymer of PDS and poly-L-lactic acid (PLLA) (15%) results in a more compliant suture than homopolymer PDS but with similar absorption profiles as PDS. Copolymer sutures made from PDS and morpholine-2,5-dione (MD/PD) exhibit rather interesting biodegradation properties.[5] Although MD/PD copolymer sutures were absorbed 10–25% earlier than PDS, the former retained tensile breaking strength profile similar to PDS with a slightly faster strength loss during the earlier stage, i.e., first 14 days. This ability to break the inherent fiber structure–property relationship through copolymerization is a major improvement in biodegradation property of absorbable sutures.

Recently, supercomputer molecular modeling of the effect of chemical structure of biodegradable polymers on their hydrolysis has been reported.[8,9] In these molecular modeling studies, the effects of steric hindrance and electron induction on the hydrolytic degradation were examined.

The chemical structure of these linear aliphatic polyesters suggests that they are sensitive to high-energy radiation, e.g., γ irradiation, induced degradation as evident in the premature loss of mechanical and biodegradation properties reported by several investigators.[4,10-17] As a result, these absorbable sutures must be sterilized by ethylene oxide gas. The γ-irradiation sensitivity of these absorbable suture fibers is due to the presence of oxygen atoms into the main-chain backbone (as part of the ester functional group), and such a presence has been shown to significantly increase the probability for main-chain scissions as found in the exceedingly high yields of radicals resulting from main-chain scission of polyoxymethylene.[18] However, due to the possible resonance stabilization of radical chain ends in ester functional group (i.e., $-COO^{\cdot}$), main-chain scissions in polyesters are expected to be less frequent than in polyethers. In addition, the lack of aromatic groups in these aliphatic polyesters makes them more prone to γ-irradiation degradation than aromatic polyesters. Thus, synthetic absorbable sutures based on aliphatic polyesters are generally sterilized by ethylene oxide.

Studies of γ-irradiation effects on many nonabsorbable polymers have suggested that there are several environmental factors that could influence the rate and products of radiation-induced chemical reactions. These factors include oxygen, dose rate, linear energy transfer, and irradiation temperature, T_{irr}.[19] The effects of varying the irradiation temperature, especially with respect to the glass transition temperature, T_g, have probably been examined less than any of the other factors.

In theory, a pair of macromolecular radicals formed as a result of γ irradiation-induced main-chain scissions have a certain probability to recombine. The extent of recombination depends on molecular chain mobility. Chain segments with restricted segmental mobility due to crystalline structure, orientation, or being at a temperature below their T_g would be expected to facilitate the recombination of a pair of macromolecular radicals and hence would show less γ-irradiation-induced degradation. Previous published work on the effect of γ irradiation on synthetic absorbable sutures did not permit us to conclude whether this cage recombination of pairs of macromolecular radicals observed in nonabsorbable polymers also occurred in synthetic absorbable sutures. This was because of the lack of a systematic evaluation of T_{irr} effect by employing T_{irr} both significantly above and below the T_g of the γ-irradiated materials.[20-23]

In this study, we report the use of two types of synthetic absorbable sutures for examining the effects of γ irradiation and the relative magnitude of T_{irr} to T_g on their physical, mechanical, thermal, morphological, and hydrolytic properties.

MATERIALS AND METHODS

Two types of synthetic biodegradable polymers were used in this study: polyglycolic acid (PGA) and glycolide-trimethylene carbonate block copolymer. PGA chips with initial inherent viscosity of 1.4 dL/g were obtained from Boehringer Ingelheim in Germany. These PGA chips were fabricated into circular disks of 16 mm diameter and 0.5 mm thickness for subsequent γ irradiation and studies of *in vitro* degradation. The circular disk specimens were made by a laboratory size CSI injection mold under inert (N_2) environment to minimize undesirable degradation. The prepared disk samples were placed in vacuum-sealed plastic bags stored in a dry desiccator prior to γ-irradiation treatment and the degradation study.

PGA and glycolide-trimethylene carbonate block copolymer fibers in the form of 2/0 size Dexon and Maxon suture from Davis/Geck were also used in this study. These two types of biomaterials were sealed in plastic bags under low vacuum and ^{60}Co γ irradiated by Neutron Products in Dickerson, MD. Two irradiation temperatures (55 and $-78°C$ in dry ice) were used for the γ irradiation. These temper-

atures were chosen on the basis of the reported T_g's of 36°C for PGA[24] and 10°C for Maxon.[25] Thus, the two T_{irr} are, respectively, well above and well below the T_g's of the testing biomaterials. The γ-irradiation dosage for the fibrous biomaterials (i.e., Dexon and Maxon) were 2 and 10 Mrads, while 2 and 20 Mrads were used for the PGA disks. Because the specimens were vacuum sealed, γ-irradiation-induced oxidative degradation should have been minimized.

Both γ-irradiated and control specimens were immersed in a phosphate buffer solution of pH 7.44 at 37°C for various durations of hydrolysis. After each predetermined duration, the specimens were removed for subsequent testing which included determinations of tensile strength, weight loss, level of crystallinity, melting temperature, intrinsic viscosity, surface morphology, and infrared spectroscopic characteristics.

Weight Loss

The mass loss of the specimens was determined by the ratio of the dry weight after *in vitro* hydrolysis to the initial dry weight.

Tensile Strength Measurement

The tensile breaking force of the suture specimens was tested using an Instron testing machine (Model 1122). The gauge length was 50 mm and the crosshead speed was 10 mm/min. Five to 10 specimens were used for each test. The tensile breaking force data were expressed in terms of the percentage of retention of original tensile breaking force. No PGA disk tensile breaking strength was measured because there are no equivalent testing procedures for disk samples as for fiber specimens.

Thermal Property Determination

A Perkin-Elmer DSC-4 with a System 4 microprocessor controller and a Model 3700 data station was used in this study. The specimens were heated from 150 to 250°C at the rate of 20°C/min in a nitrogen atmosphere, and their melting characteristics (the melting temperature and the heat of fusion) were recorded. The heat of fusion per gram of samples calculated from the area under the peak was used to calculate the level of crystallinity of PGA disks and Dexon sutures by using a value of 49.34 cal/g for ΔH^* of 100% crystallized PGA.[26] However, a similar calculation could not be done with Maxon suture because the ΔH^* of 100% crystalline Maxon is not available in the literature, and hence only the experimental ΔH was used as an indirect indication of the level of the crystallinity in Maxon. The temperature at maximum endotherm was used as the melting temperature of the sample. The detailed procedures were given elsewhere.[27-29]

Intrinsic Viscosity Measurement

The intrinsic viscosity was measured in a water bath at room temperature (18°C) using an Ostwald-Cannon-Fenske (OCF) viscometer. It was determined by the following formulas:

$$\eta_r = t/t_0 \tag{1}$$

$$[\eta]_{int} = [(\ln \eta_r)/C]_{c\to 0} \tag{2}$$

where η_r is relative viscosity of a polymer solution, t is flow time (in seconds) of a polymer solution with a fixed concentration, t_0 is the flow time of hexafluoroisopropanol (HFIP) solvent, and C is the polymer concentration ranging from 0.2 to 0.6 g/dL. The intrinsic viscosity $[\eta]_{int}$ was obtained by plotting $(\ln \eta_r)/C$ vs. C and extrapolating to zero concentration through a linear regression.

Surface Morphology

The surface morphologic change of the specimens due to γ irradiation and hydrolysis was examined by using a JOEL JSM-5200 scanning electron microscope (SEM). The samples were mounted onto metal stubs, coated with a 60/40 gold/palladium alloy using a pulse plasma system and then examined by SEM.

FTIR Evaluation

Five types of PGA disk specimens were investigated using infrared (IR) spectroscopy. These were disks γ-irradiated at 2 Mrad at both dry ice temperature and 55°C, disks γ-irradiated at 20 Mrad at both dry ice and 55°C temperature, and unirradiated controls. Each type of specimen was examined prior to hydrolysis and after 2, 7, 21, and 28 (2-Mrad specimens only) days of hydrolysis. The excessive brittleness of the PGA disks after 28 days of hydrolysis necessitated the use of much smaller samples which yielded spectra with much smaller absorption intensities and consequently more artifacts and greater distortions in bandshape and intensity. Meaningful Fourier transform IR (FTIR) spectra of PGA disks with greater than 28 days of hydrolysis could not

be obtained due to excessive degradation of the samples.

The thoroughly dried disk specimens were clamped against a KRS-5 (thallium bromoiodide) internal reflection element and mounted in a Harrick Twin Parallel Mirror Reflection Attachment. The calculated theoretical depth of penetration of the evanescent wave was approximately 1.3 μm at 1600 cm^{-1} and 2.6 μm at 800 cm^{-1}. A minimum of 500 coadded scans were collected at 4 cm^{-1} resolution using a 710 Nicolet FTIR spectrometer.

All IR absorption bands found in the PGA disk samples were subject to changes in intensity and bandshape in the collected spectra due to the ongoing hydrolysis. However, it has been shown in another study that only minimal changes occur in crystalline IR bands during the early stages of hydrolysis of a similar suture material.[30] Therefore, an IR band at 806 cm^{-1} associated with the crystalline domains of PGA was chosen as an internal calibration standard, and all spectra were scaled to equal intensities for this band. The 806 cm^{-1} band displayed only minor changes in bandshape and bandwidth for the various spectra, did not overlap with neighboring IR vibrations, and was in the immediate vicinity of other IR bands of interest.

The constant intensities (as a result of the calibration technique) and shapes of this band and other crystalline IR bands did not preclude the possibility that some small changes in the crystalline domains of the PGA samples may have occurred during the early stages of hydrolysis. Any changes which did occur were surely minimal with respect to those occurring in the amorphous domains.

RESULTS AND DISCUSSION

Weight Loss Data

γ irradiation had a significant effect on the weight loss of Dexon sutures as shown in Figure 1(a). A higher irradiation dosage resulted in a very rapid loss of weight, which occurred at an earlier duration of hydrolysis than that of samples irradiated at a lower dosage. For example, the most dramatic weight loss of Dexon sutures irradiated at 2 Mrad occurred between 10 days (76% retention of original weight) and 14 days (24% retention of original weight) of hydrolysis, and there was little weight loss during the first 7 days, while the Dexon sutures irradiated at 10 Mrad showed the most dramatic weight loss between 3 days (74%) and 7 days (29%), although there was virtually no weight loss during the first 3 days of hydrolysis. The effect of T_{irr} on weight loss was, however, not apparent. The unirradiated Dexon sutures did not exhibit accelerated weight loss until after 14 days, and there was still 17% of its original weight remaining at the end of 42 days.

PGA disks, which have the same chemical structure as Dexon suture but different polymer morphology, however, exhibited different extents of γ-irradiation effects, as shown in Figure 1(b). The most significant difference between PGA disks and Dexon sutures was the slower rate of weight loss observed in PGA disks, irrespective of the fact that twice the γ irradiation dosage of Dexon sutures was used in PGA disks. All irradiated PGA disks still retained 45–52% of their original weight at the end of 28 days of hydrolysis, while there was no measurable weight observed in Dexon sutures at the same duration of hydrolysis. This is particularly significant when considering that the highest dosage of PGA disks used was twice the highest dosage used for the Dexon sutures. Thus, in terms of mass loss, γ irradiation results in a less profound effect on the subsequent hydrolysis of PGA disks than of Dexon sutures. Since it has been reported that hydrolytically induced mass loss of synthetic absorbable polymers mainly derive from the destruction and dissolution of crystalline domains,[23,29] the observed lengthier retention of mass of γ-irradiated PGA disks than of PGA sutures must be attributed to the presence of larger crystallites in PGA disks. The larger crystallites in PGA disks would lead to their slower hydrolytic destruction and dissolution. On the other hand, the drawing process in melt-spinning of fibers like Dexon sutures would break these larger laminar crystallites into smaller crystallites which facilitated the destruction and dissolution of crystalline domains. This is reflected in the observed faster mass loss in Dexon suture fibers. Again, the effect of T_{irr} appears to be insignificant in PGA disks.

Because γ-irradiation sensitivity also depends on the chemical structure of materials, Maxon sutures were expected to behave differently from Dexon sutures even though both have fibrous morphology. Maxon sutures were found to be more resistant to γ-irradiation-induced degradation than Dexon sutures as shown in Figure 1(c). There was virtually no weight loss during the first 21 days of hydrolysis of Maxon irradiated at 2 Mrad and 14 days of hydrolysis of Maxon irradiated at 10 Mrad. Like Dexon sutures, Maxon sutures also exhibited a significant

loss of suture weight after a certain period of unmeasurable weight change. This period of hydrolysis without measurable weight loss became shorter as the γ irradiation dosage was increased. For example, the periods with the most significant reduction in weight occurred between 60 and 90 days in the unirradiated control, between 42 and 60 days in the 2-Mrad-treated sample, and between 28 and 42 days in the 10-Mrad-treated sample.

As in the PGA disks and sutures, no significant T_{irr} effects were observed in the weight loss data. This, however, should not be interpreted as the lack of a T_{irr} effect in this class of synthetic absorbable polymers. As described later, T_{irr} effect was pronounced in those properties that depend on the tie-chain segments located in noncrystalline domains, while mass loss is mainly derived from the crystalline domains of the materials.

Intrinsic Viscosity

The intrinsic viscosity, $[\eta]_{int}$, of the testing samples exhibited more profound changes with γ irradiation than mass loss data, particularly at the earlier stages of hydrolysis, as shown in Figure 2. As expected, a significant reduction in $[\eta]_{int}$ was observed due to γ irradiation alone (i.e., unhydrolyzed specimens). It appears that the most significant reduction in $[\eta]_{int}$ of unhydrolyzed specimens occurred at a dosage level of 2 Mrad. A further increase in γ-irradiation dosage resulted in an additional, but not a profound, reduction in $[\eta]_{int}$. The effect of T_{irr} on $[\eta]_{int}$ was not apparent in both Dexon and Maxon suture fibers.

A comparison between Figures 2(a) and 2(b) indicates that different polymer morphology of identical chemical species (i.e., Dexon fiber vs. PGA disk) showed different levels of γ-irradiation effects. This was particularly true in unhydrolyzed specimens. For examples, 2-Mrad-irradiated PGA disks lost more than 50% of their original $[\eta]_{int}$, while the corresponding Dexon fibers lost less than 15% of their original $[\eta]_{int}$. This observed morphologic effect is believed to be attributed to the relationship between cage recombination and orientation of chain segments.

In fibers, there is a considerable orientation of chain segments along the longitudinal fiber axis. This orientation could facilitate the cage recombination of a pair of macromolecular radicals produced from γ-irradiation scission. The effect of orientation on cage recombination of a pair of radicals is particularly important for chain segments located in noncrystalline domains. This is because amorphous domains do not have a crystalline lattice to serve as cages to immobilize chain segments for facilitating the recombination of pairs of radicals generated from γ irradiation. The only "cage" that could restrict the mobility of chain segments in amorphous domains is the orientation of chain segments. Thus, Dexon suture fibers were expected to show and indeed were found to have less γ-irradiation-induced chain scissions than PGA disks as reflected in the observed higher retention of $[\eta]_{int}$ in Dexon fibers. This theory should also predict that a higher degree of orientation in fibers would be expected to result in a lesser extent of γ-irradiation-induced chain scissions and hence a higher retention of $[\eta]_{int}$ and tensile breaking force. This is because more restrictions on chain mobility would be imposed at a higher degree of fiber orientation for facilitating better cage recombination of pairs of macromolecular radicals. A higher degree of fiber orientation should thus be expected to result in a smaller effect of the relative magnitude of T_{irr} to T_g on the extent of chain scissions.

Tensile Breaking Force

The tensile breaking force of both Dexon and Maxon sutures was significantly reduced by γ-irradiation treatment. The magnitude of reduction depended on the dosage level, T_{irr}, duration of hydrolysis, and the chemical structure of the suture fibers. Figure 3 summarizes these findings as a function of hydrolysis time.

γ irradiation reduced the tensile breaking force of unhydrolyzed Dexon sutures 6–34% from that of their unirradiated Dexon control. Similarly, γ irradiation reduced the tensile breaking strength of unhydrolyzed Maxon sutures 3–19% from that of their unirradiated Maxon controls. In both Dexon and Maxon sutures, those irradiated at $T_{irr} < T_g$ consistently showed higher tensile breaking force than those irradiated at $T_{irr} > T_g$. ANOVA statistical analysis of the effect of irradiation temperature on tensile breaking force indicated that there was a statistically significant effect of irradiation temperature on tensile breaking force ($P < 0.01$). For example, Dexon sutures irradiated at 55°C lost 17% (2 Mrad) and 34% (10 Mrad) of that of their unirradiated controls, while the same sutures irradiated at −78°C lost only 6% (2 Mrad) and 24% (10 Mrad) of that of their controls. A similar pattern was observed in Maxon sutures. It appeared also that a lower irradiation dosage resulted in a larger retention of breaking force when $T_{irr} < T_g$ than does a higher dosage. This suggested that an overwhelmingly high dosage of γ irradiation overpowered the propensity

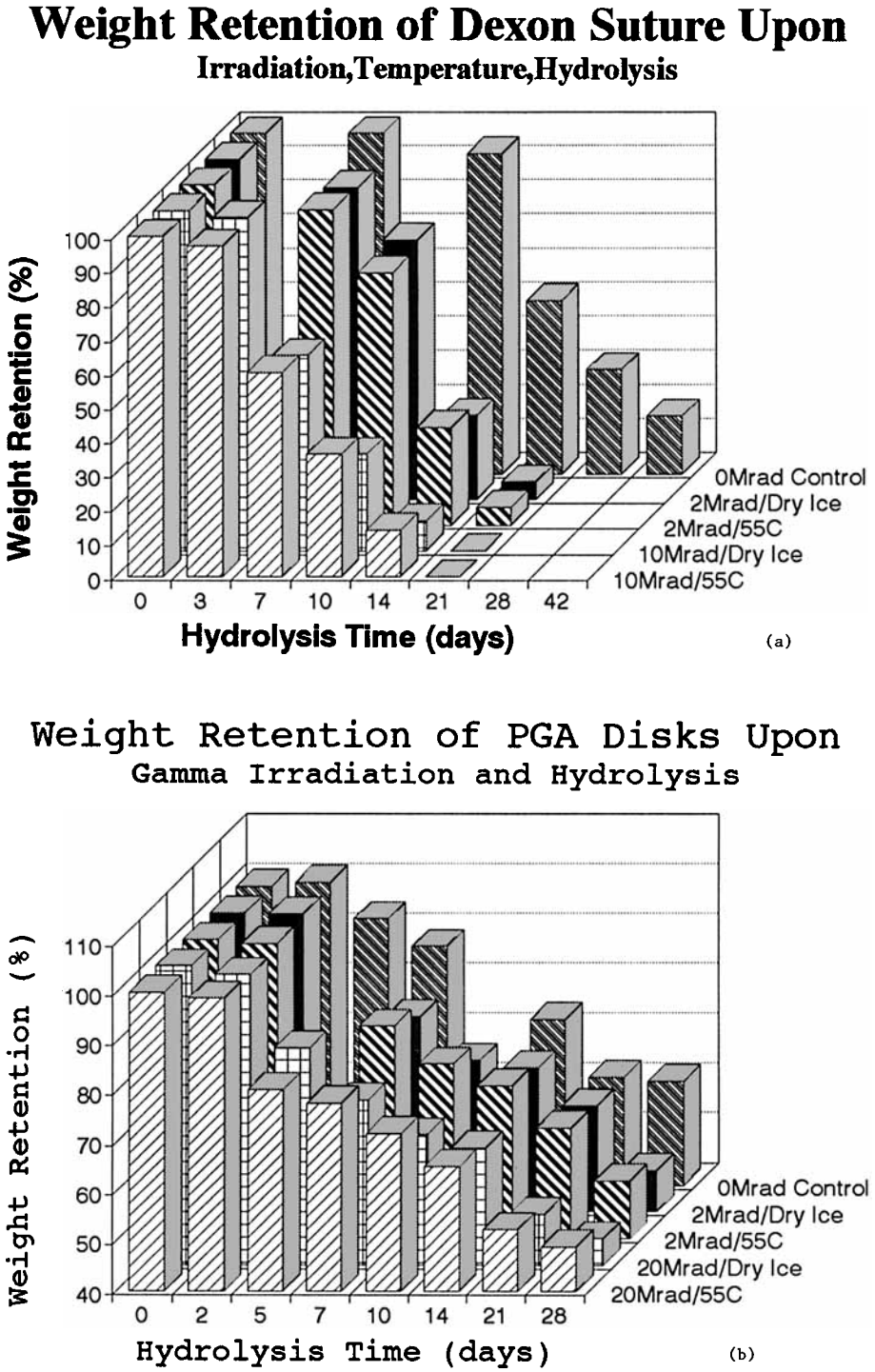


Figure 1 Effect of γ irradiation, irradiation temperature, and hydrolysis time on weight retention of synthetic absorbable sutures and disks. (a) Dexon suture, (b) PGA disk, (c) Maxon suture.

for cage recombination of pairs of macromolecular radicals at a T_{irr} below the T_g of the material since the rate of radical generation became much faster than the rate of cage recombination.

The benefit of irradiation at $T_{irr} < T_g$ also extended to hydrolyzed specimens. With a few exceptions, both Dexon and Maxon sutures consistently exhibited higher retention of tensile breaking force

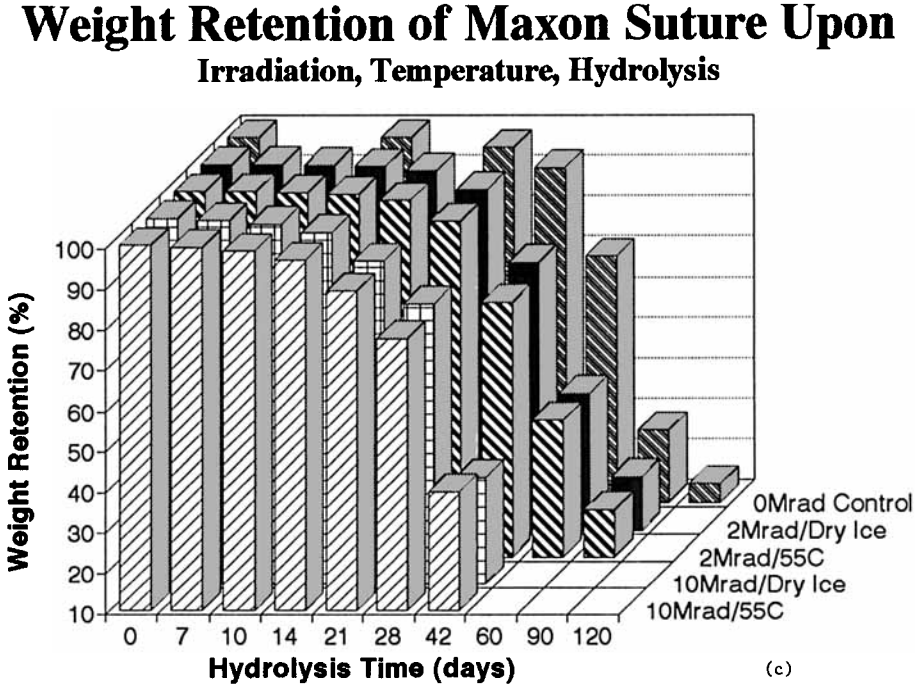
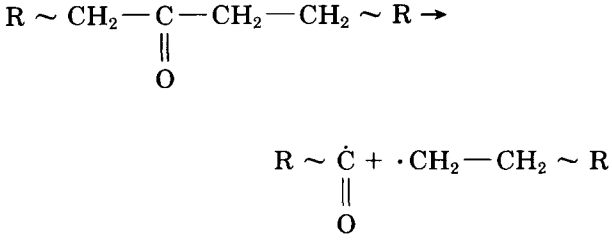


Figure 1 *(Continued from the previous page)*

over the specified hydrolysis periods when T_{irr} was less than T_g. However, it appeared that the benefit of irradiation at $T_{irr} < T_g$ became less obvious as the duration of hydrolysis increased or higher irradiation dosage was applied. For example, 10-Mrad irradiated Dexon suture fibers at either T_{irr} less than or greater than T_g all exhibited a nonmeasurable tensile breaking force at 7 days.

The observed effect of T_{irr} has also been observed in both photo and γ degradation of other types of polymers.[30-33,35] The effect was attributed to chain mobility. In studies of polyisobutylene, polymethyl methacrylate, polyethylene oxide, and various copolymers of styrene/phenylvinyl ketone, methylmethacrylate/methylvinyl ketone, the quantum yields of main-chain scission, $\phi(s)$, showed a sigmoidal relationship to T_{irr}. In other words, the number of main-chain scissions per photon (in the case of photodegradation) or per 100 eV (in the case of γ irradiation) energy absorbed by a polymer increased significantly when the polymer was irradiated at a temperature slightly above T_g. When T_{irr} was less than T_g, there was very little change in $\phi(s)$ with temperature. The effect of T_{irr} relative to T_g of the material is theoretically expected to be significant in the case of Norrish Type I chemical reactions (shown below) induced by either photo or γ irradiation.



Since γ- or photoinduced Norrish Type I chemical reactions on polymers with carbonyl groups in the backbone (e.g., polyesters) produce macromolecular radicals, the degree of chain mobility thus affects the efficacy of cage recombinations of macromolecular radical pairs. Increasing chain mobility of polymeric chain segments at a temperature higher than T_g reduces the probability for cage recombinations which subsequently leads to more main-chain scissions. It is known that fiber strength depends on the tie-chain segments located in the amorphous domains of microfibrils. When γ irradiation was done at −78°C (i.e., $T_{irr} < T_g$), the resulting Norrish Type I macromolecular radicals due to the chain scission of the tie-chain segments have a better opportunity to recombine than radicals produced from γ irradiation done at $T_{irr} > T_g$. This higher probability of macromolecular radicals recombination was further enhanced by the orientation effect of fibers

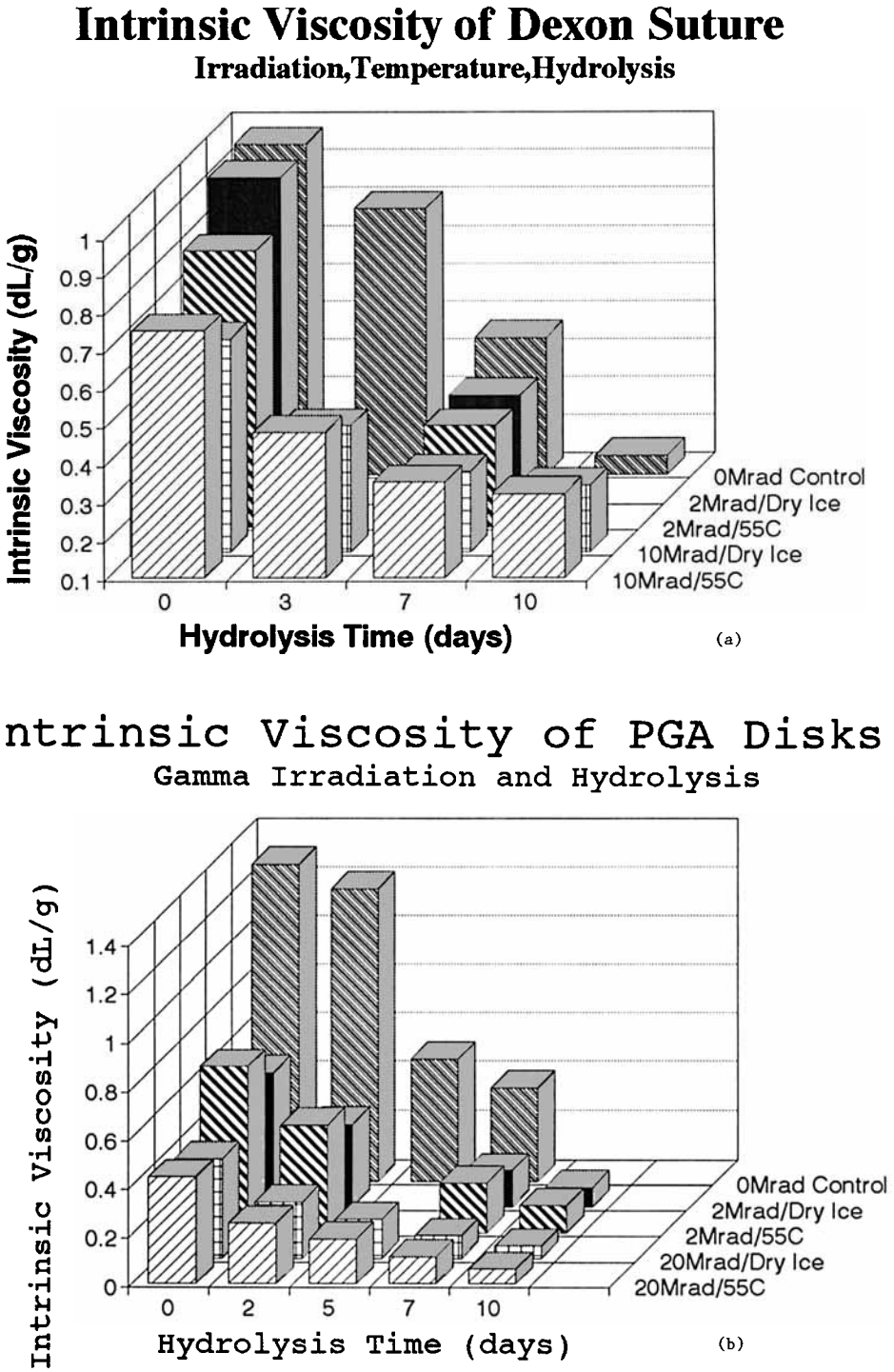


Figure 2 Effect of γ irradiation, irradiation temperature, and hydrolysis time on intrinsic viscosity of synthetic absorbable sutures and disks. (a) Dexon suture, (b) PGA disk, (c) Maxon suture.

and thus resulted in a better retention of tensile breaking force as observed in this study. However, when a high γ-irradiation dosage was applied, the recombined macromolecular radicals could be cleaved as soon as they were formed. As a result, the effect of the relative magnitude of T_{irr} to T_g became less apparent and less significant at a higher dosage of γ irradiation.

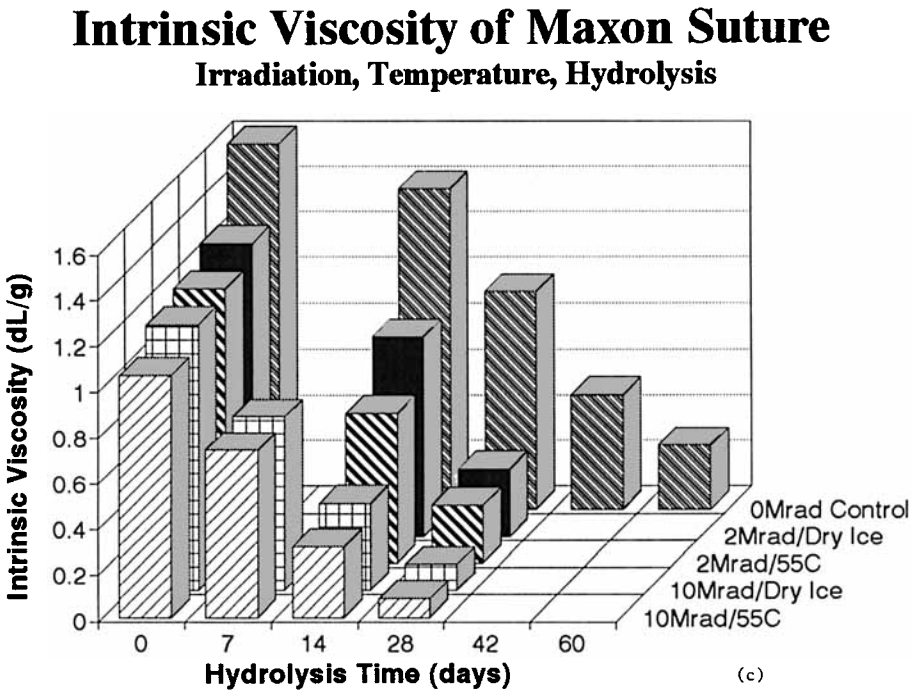


Figure 2 *(Continued from the previous page)*

Thermal Property

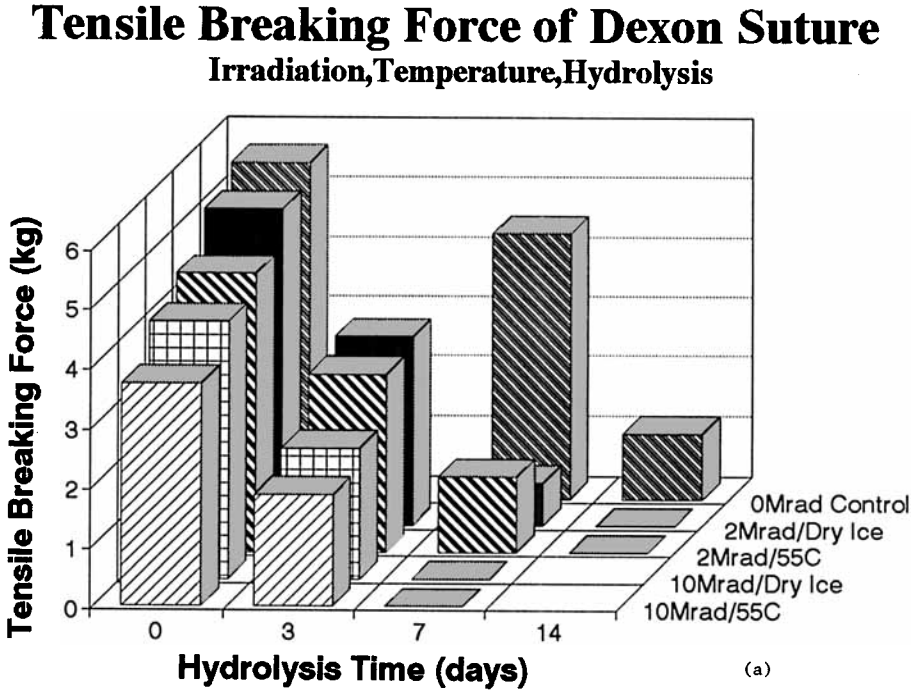
Within experimental error, the level of crystallinity and melting temperature of all three types of unhydrolyzed specimens appeared not to be significantly affected by γ irradiation alone at the dosage levels used in this study. For examples, both unhydrolyzed Dexon and Maxon suture fibers showed less than 1% change in their T_m solely due to γ irradiation. This suggests that most of the γ-irradiation-induced main-chain scissions within the dosages studied occurred in the noncrystalline domains. The observed reduction in tensile breaking force is consistent with this conclusion. Dosages as high as 50–100 Mrads are required to observe significant changes in the thermal property of polymers.[34]

When the factor of hydrolysis was considered, both irradiated and unirradiated specimens exhibited a continuous increase in their levels of crystallinity and T_m with hydrolysis time, reached a maximum and then decreased thereafter. However, the peak crystallinity (or T_m) of γ-irradiated specimens occurred at an earlier hydrolysis time than that of the unirradiated controls. Figure 4 illustrates this phenomenon. The peak ΔH of unirradiated Maxon suture fiber occurred at about 42 days of hydrolysis, while the peak ΔH of both 2- and 10-Mrad irradiated Maxon fibers occurred between 21 and 28 days of hydrolysis. Similar changes in thermal properties with hydrolysis time were also reported by others in their studies of Dexon and PDS sutures[27–29] and nonabsorbable polymers like celluloses.[36]

There was no apparent effect of T_{irr} on thermal properties, since these properties mainly depend upon the level of crystallinity and crystal sizes and defects. Also, γ irradiation at $T_{irr} < T_g$ of the material would benefit those chain segments located in the amorphous domains most. The crystalline lattice already provides the required cage for radical recombination, irrespective of the relative magnitude of T_{irr} to T_g. As a result, those properties that closely relate to the state of the amorphous chain segments (i.e., broken or intact tie-chain segments) like tensile breaking force benefit most from γ irradiation at $T_{irr} < T_g$ of the material.

Surface Morphology

A significant effect of γ irradiation on the surface morphology of partially hydrolyzed specimens was observed as shown in Figures 5–8. γ irradiation alone, however, did not result in any apparent surface morphologic change in both unhydrolyzed Dexon and Maxon suture fibers and PGA disks. The effect of T_{irr} was also not apparent on Maxon sutures and PGA disks but was observed in Dexon sutures. As compared with the observed significant and striking changes in fiber surface morphology, PGA disks showed no significant changes in surface mor-



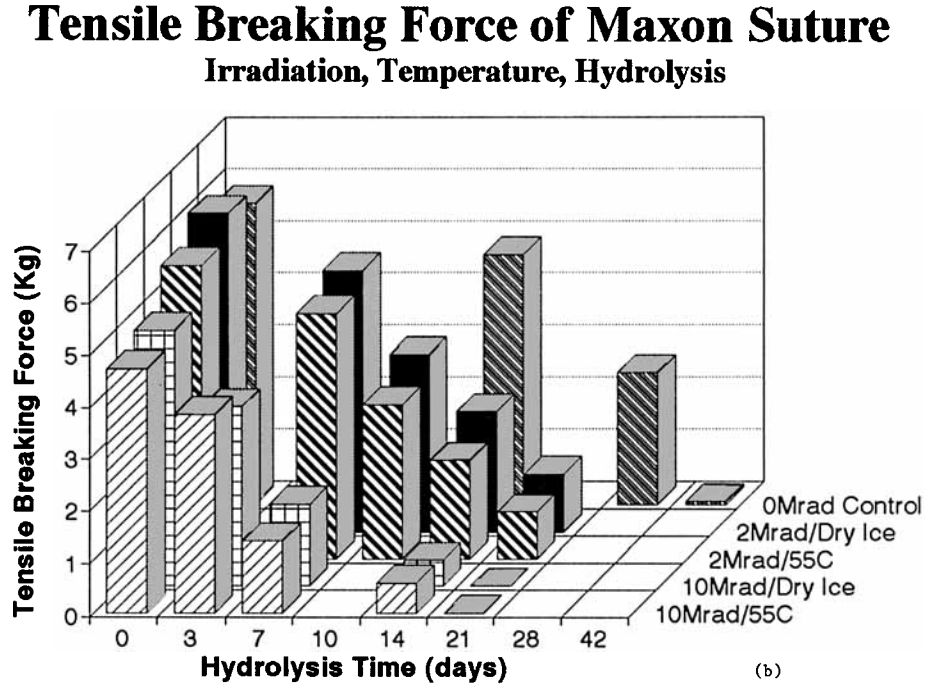


Figure 3 Effect of γ irradiation, irradiation temperature, and hydrolysis time on tensile breaking force (kg) of synthetic absorbable sutures. (a) Dexon suture, (b) Maxon suture.

phology with either γ irradiation or hydrolytic degradation.

In Maxon suture fibers, the most striking features were the formation of both longitudinal and lateral surface cracks and the subsequent removal of concentric outermost skin layers as hydrolysis proceeded. Depending on the dosage level of γ irradiation, either regular or irregular patterns of surface cracks were formed. γ irradiation also accelerated the formation of surface cracks at earlier durations

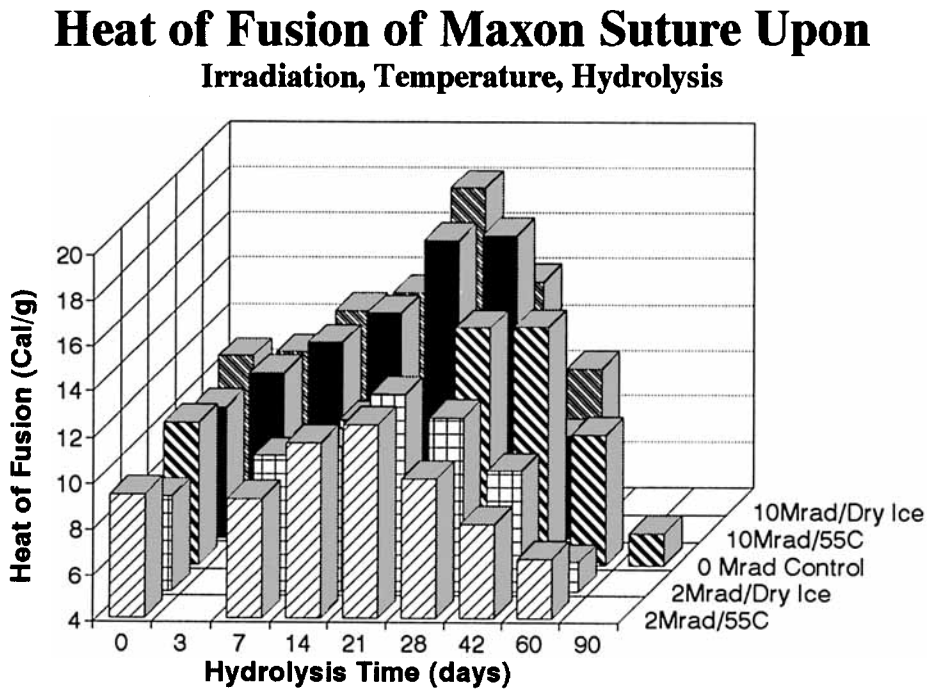


Figure 4 Effect of γ irradiation, irradiation temperature, and hydrolysis time on heat of fusion (cal/g) of Maxon absorbable sutures.

of hydrolysis. In 10-Mrad irradiated specimens, for instance, the formation of both longitudinal and lateral surface cracks were observed as early as 14 days hydrolysis, irrespective of T_{irr}; neither 2-Mrad irradiated nor unirradiated Maxon showed any sign of surface cracks at this period of hydrolysis (Fig. 5). The direction of the lateral surface cracks on 10-Mrad irradiated Maxon was always perpendicular to the longitudinal surface cracks which were parallel to the fiber axis. As shown in Figure 6, this characteristic perpendicular nature of the two types of surface cracks associated with highly γ-irradiated and partially hydrolyzed specimens was not found in unirradiated or specimens irradiated at low dosages.

As a result of these longitudinal and lateral surface cracks, portions of the fiber skin started to lift off at 14 days of hydrolysis [Fig. 5(d)] and revealed the interior fibrillar structure underneath. The skin layer was about 8 μm thick, which was about 1.4% of the suture diameter (560 μm). There was no apparent reduction in fiber diameter at 14 days of hydrolysis. At the end of the same hydrolysis period, no apparent changes in surface morphology were found in either 2-Mrad irradiated or unirradiated Maxon sutures. As hydrolysis proceeded to a longer duration (42 days), both 10 Mrad/$-$78°C and 10 Mrad/55°C Maxon fibers retained only 67–68% of their unhydrolyzed fiber diameters. Concurrently, a significant reduction in Maxon suture mass was also observed (Fig. 1) at the end of 42 days of hydrolysis. The observed uniform reduction in the diameter of 10-Mrad irradiated Maxon suture suggests that the hydrolytic degradation of Maxon sutures must proceed through a concentric removal of the outermost layer of the suture as its skin layers peel off from the fiber underneath. As the outermost layer was removed, additional surface cracks would form on the freshly exposed subsurface layer in the same way as with their predecessors. This process of surface crack formation followed by the removal of the outermost skin layer was then repeated throughout the entire hydrolysis period.

There was a subtle but apparent difference between the pattern of surface cracks formed on the deep core and initial skin portions of the fiber. Most of the surface cracks generated on the core Maxon fiber at a later stage of hydrolysis (e.g., 42 days), particularly the one with T_{irr} at $-$78°C, were largely circumferential in nature with no or very few longitudinal cracks. The surface cracks formed on the initial Maxon skin at 14 days hydrolysis, however, occurred about equally in the longitudinal and lateral directions.

In addition to the delayed formation of surface cracks with hydrolysis, unirradiated or lightly ir-

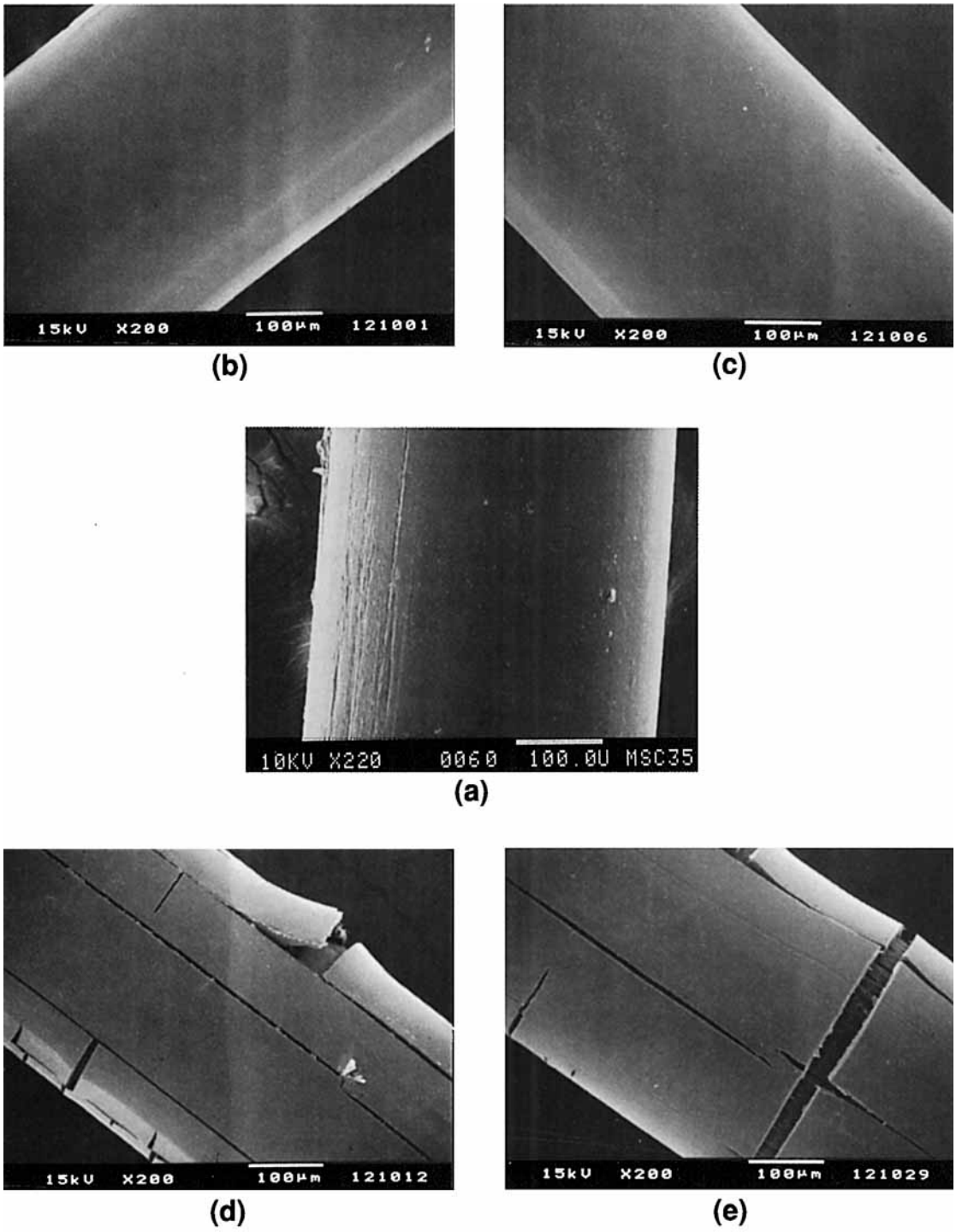


Figure 5 Effect of γ irradiation on the surface morphology of 14-day hydrolyzed Maxon suture fibers. (a) 0 Mrad control, (b) 2 Mrad/−78°C, (c) 2 Mrad/55°C, (d) 10 Mrad/−78°C, (e) 10 Mrad/55°C.

radiated (2-Mrad) Maxon sutures differed from 10-Mrad irradiated ones in the regularity of the cracks. The formation of surface cracks in lightly or unirradiated Maxon was less regular due to the lack of perpendicularity between longitudinal and lateral cracks. As a result, irregularly shaped skin layers peeled off from these lightly γ-irradiated fibers as hydrolysis proceeded [Fig. 6(b) and (c)].

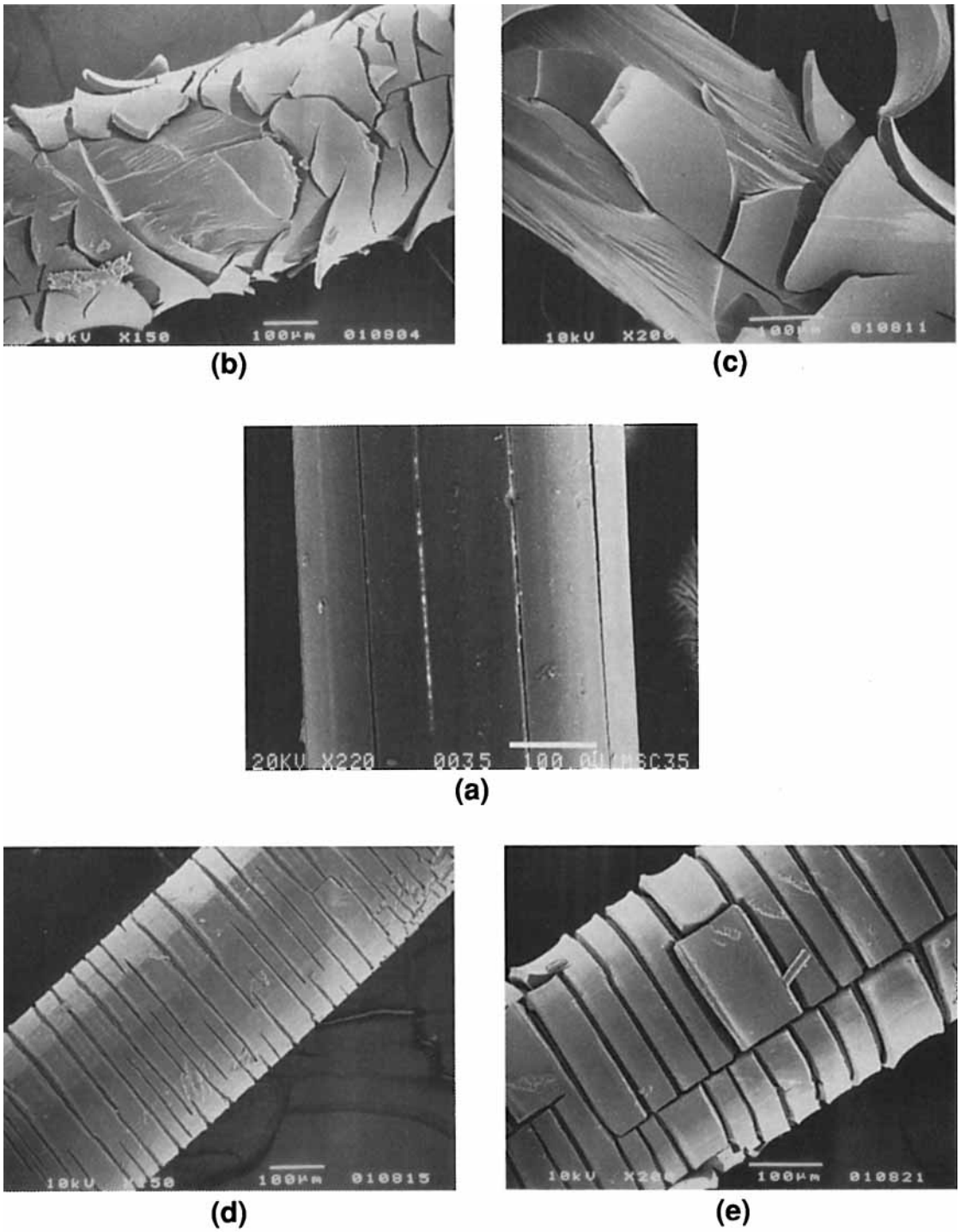


Figure 6 Effect of γ irradiation on the surface morphology of 42-day hydrolyzed Maxon suture fibers. (a) 0 Mrad control, (b) 2 Mrad/−78°C, (c) 2 Mrad/55°C, (d) 10 Mrad/−78°C, (e) 10 Mrad/55°C.

The peeling off of these skin layers possibly occurs by the following mechanism: As the surface cracks become established, more water is able to penetrate into the suture material via the cracks. The penetrating water molecules follow the path of least resistance and move parallel to the fiber axis along the noncrystalline layer sandwiched between two concentric layers of macrofibrils. This eventually

results in the peeling off of the outermost layer of the fiber. The fiber diameter then becomes progressively smaller with duration of hydrolysis as demonstrated by the Maxon fibers hydrolyzed for 42 days (Fig. 6).

As a result of a combined γ irradiation and hydrolytic degradation, multifilament Dexon sutures exhibited unique, but different, morphologic changes from those of the monofilament Maxon sutures, particularly at the 10-Mrad γ-irradiation dosage level. At the 2-Mrad dosage level, the combined effect of γ irradiation and hydrolysis on Dexon fiber morphology did not appear until 14 days of hydrolysis in which severe multifilament fragments were observed at both irradiation temperatures. This coincided with the previously observed significant weight reduction (about 60% weight loss) and the apparent total loss of tensile breaking force. It was interesting to observe that although more than 50% of the original tensile breaking force was lost in the 2-Mrad irradiated Dexon sutures during the first 7 days of hydrolysis, no apparent change in fiber surface morphology was observed.

As shown in Figure 7, a completely different surface morphology, however, was observed in 10-Mrad irradiated Dexon sutures hydrolyzed for 7 days. Dexon irradiated at a dose of 10 Mrad at 55°C exhibited extremely regular circumferential surface cracks with relatively equal spacing, about 5–8 μm, between adjacent cracks. (No longitudinal surface cracks as in Maxon sutures were observed in Dexon sutures.) This unique surface morphology, however, was far less profound in 10-Mrad Dexon sutures irradiated at −78°C in which random and irregular circumferential cracks were observed. A close examination of fragmented fiber ends of Dexon sutures with this unique surface morphology revealed a skin-core appearance (Fig. 8). The skin layer was about 2 μm thick and snugly wrapped around the core filament underneath but distinctly separated from the core filament by a very small open crack. Some filaments showed concentric removal of the skin layer located at the end of the fiber and subsequent further exposure of the core filaments underneath. It has not been reported in the literature that fibers of these size (14 μm diameter) could have the classic skin-core morphology found only in large monofilament fibers. It is not known why the same surface morphology was not found with 10-Mrad Dexon irradiated at $T_{irr} < T_g$. It is probably due to the high chain segmental mobility at T_{irr} (55°C) > T_g that permits main-chain scission without cage recombination. This characteristic in combination with a high dosage of γ irradiation may equalize uneven sensitivity of fiber surface regions toward hydrolysis and result in the observed extremely regular pattern of circumferential surface cracks.

It is not fully understood why the higher dosage of γ irradiation resulted in a more highly regular pattern of surface cracks in Maxon sutures. Preferential hydrolysis at the sites of the regularly spaced surface cracks may arise from (a) some inherent morphology in the material making it more prone to hydrolysis at these sites or (b) some physical phenomenon which produces a highly regular pattern of cracks.

Inherent morphology in the material responsible for the crack pattern could arise from some surface chemical changes which would make the crack regions more hydrophilic. However, autoxidation, which could produce such changes, could not occur in the vacuum environment used for irradiation. Furthermore, substantial surface chemical changes which should manifest themselves in changes of wettability, were not found in γ-irradiated Maxon sutures.[23] It is also difficult to conceive of any irradiation mechanism which would produce regularly spaced (on the scale of a few microns) sites highly prone to hydrolysis and subsequent crack formation.

A more likely explanation for the crack patterns is a physical phenomenon consisting of a stress relief response of the suture material to the drawing process. That is, the observed surface cracks formed on both Maxon and Dexon sutures and their subsequent layer removal upon simple hydrolysis or a combined γ irradiation and hydrolytic degradation may simply reflect a continual alleviation of internal stresses generated within the suture material by the drawing process. Crack formation occurs by two energetically differing processes, crack initiation and crack propagation. Both crack initiation and crack propagation are aided by a number of previously discussed factors including high dosages of γ irradiation, irradiation above the T_g of the material, longer durations of hydrolysis, and higher degrees of orientation (and consequently higher internal stresses within the material).

Barriers to crack initiation are lowered by the preceding factors. This explains the shorter hydrolysis periods required to induce cracking in the suture materials irradiated at higher dosages. A higher dosage of γ irradiation produced more chain scissions in the initial material, thus facilitating crack formation more easily. The apparent absence of surface cracking in the PGA disks was a consequence of the very low degree of internal stresses in the samples. The PGA disks would have only slight

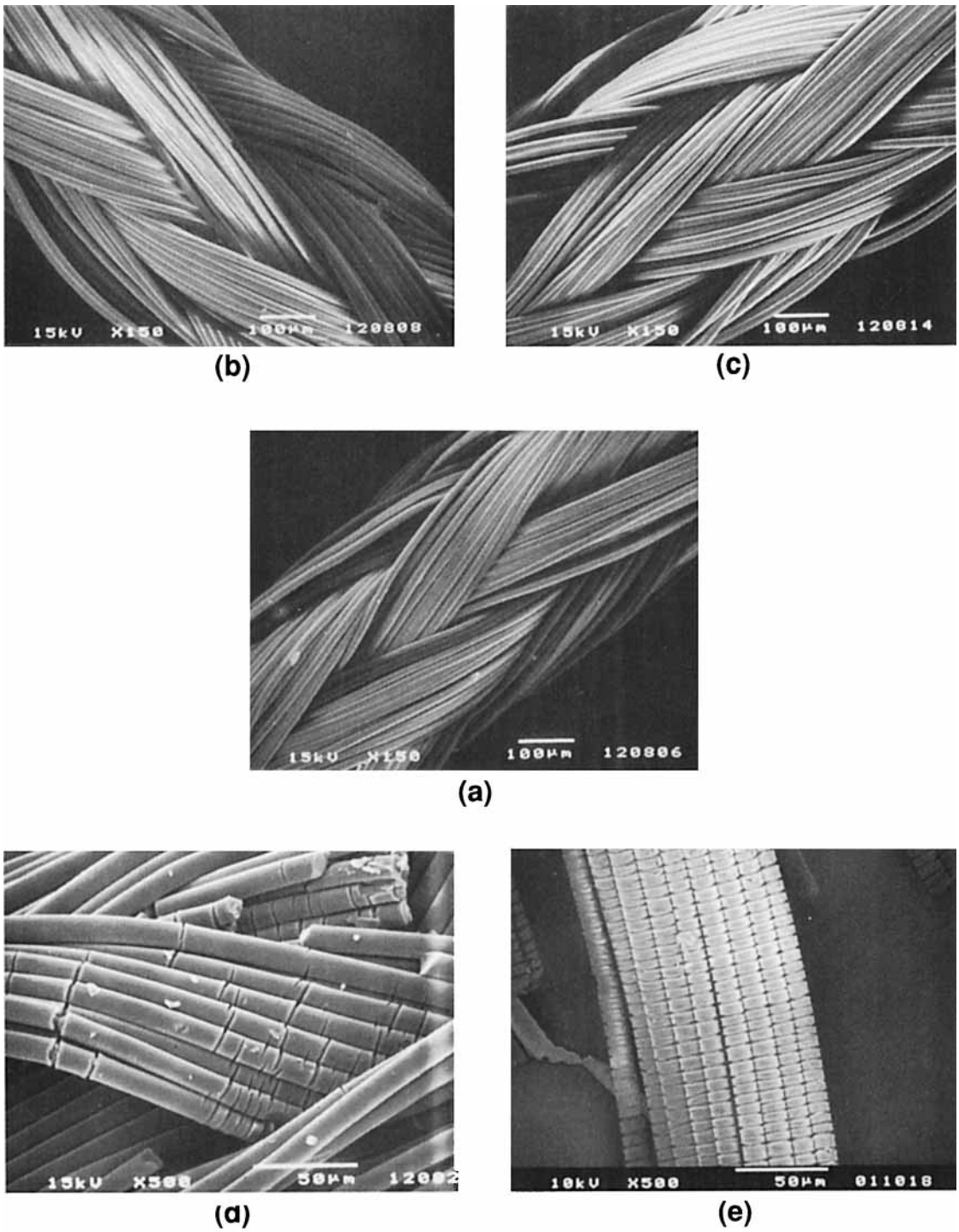
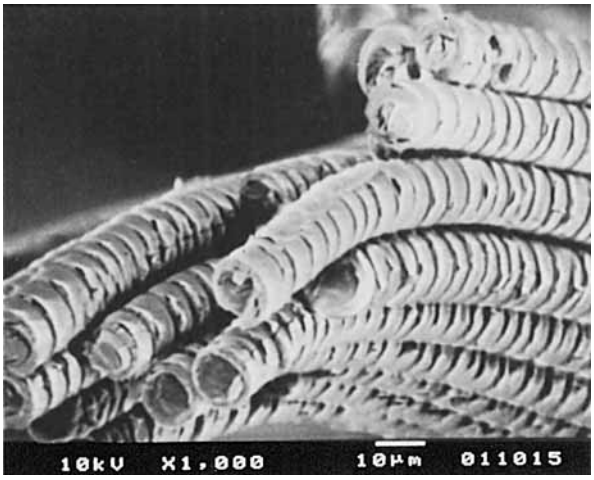


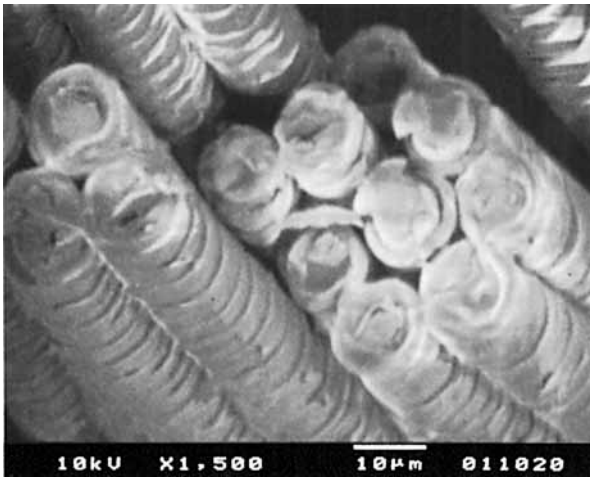
Figure 7 Effect of γ irradiation on the surface morphology of 7-day hydrolyzed Dexon suture fibers. (a) 2 Mrad/−78°C, (b) 2 Mrad/55°C, (c) 10 Mrad/−78°C, (d) 10 Mrad/55°C.

biaxial orientation, if any, resulting from their formation by injection molding. Thus, the extent of internal stresses in the disks was very low in comparison to that generated in the highly drawn suture fibers.

Barriers to crack propagation are also lowered by the aforementioned factors. A propagating crack produces two crack faces with high surface energy. This surface energy is minimized, when possible, by the formation of unidirectional, regular cracks of



(a)



(b)

Figure 8 Skin-core morphology of fragmented fiber ends of 10 Mrad Dexon sutures at T_{irr} = 55°C and 7 days hydrolysis.

lower surface area than that of jagged, irregular cracks. High degrees of chain scission, induced, for example, by higher radiation dosages, facilitate the propagation of more regular cracks. This would explain the highly regular circumferential and lateral cracks induced in the highly irradiated (10 Mrad) Dexon suture.

The apparent equal spacing of the cracks in the highly irradiated samples may also be a consequence of the internal stress relief behavior of the material during hydrolysis. Surface energy is minimized by minimizing the amount of exposed area of crack faces. This exposed crack face area is in turn minimized by reducing the number of cracks to that sufficient to lower a given amount of internal stresses over a given hydrolysis period. If one assumes that some minimum number of surface cracks of the suture material is needed to relieve internal stresses within a given subsection of surface, the number of surface cracks over all of the suture surface area is minimized when the cracks are equidistant, or nearly so, from one another. The high degrees of chain scission in the more highly irradiated samples would tend to favor this phenomenon.

FTIR Spectra

Internal reflection absorption spectra for the unirradiated (control) PGA disks are shown in Figure 9 spanning from the unhydrolyzed state to 21 days of hydrolysis. Prominent changes in the absorption spectra with progressive hydrolysis included the appearance of a band at 1613 cm^{-1}, loss of intensity in two C–O stretching frequencies peaking at 1142 and 1077 cm^{-1}, and the loss of intensity of four bands, 850, 753, 713, and 560 cm^{-1}, associated with the amorphous phase of the material.[30]

The band at 1613 cm^{-1} may be assigned to an asymmetric CO_2^- stretching frequency[37] occurring as a result of progressive hydrolytic chain scission of the PGA disks. The progressive hydrolysis would result in more $—COO^-$ chain ends and thus was reflected in an increase in band intensity with hydrolysis time. The corresponding symmetric stretching frequency for the carboxylic acid salt, believed to appear between 1360 and 1450 cm^{-1}, displayed much weaker intensity in the infrared and was not discernible in these spectra.

Unlike in the various series of irradiated PGA disks (Figs. 10–13), the 1613 cm^{-1} band of the unirradiated PGA disks reached a maximum intensity at 7 days and subsequently diminished at 21 days to an intensity similar to that at 2 days. This band was also resolvable at an earlier hydrolysis time (at 2 days) in the unirradiated samples than in any of the irradiated samples (which required 7 days of hydrolysis). The earlier appearance of the carboxylic acid salt in the unirradiated samples may imply greater stability in these samples of chain fragments containing $—COO^{-1}$ end groups. That is to say, irradiation of the PGA disks prior to hydrolysis may lead to the earlier formation of shorter, more mobile and soluble chain fragments which are more easily removed from the bulk sample during the early stages of hydrolysis. This argument was consistent with the previously described intrinsic viscosity data

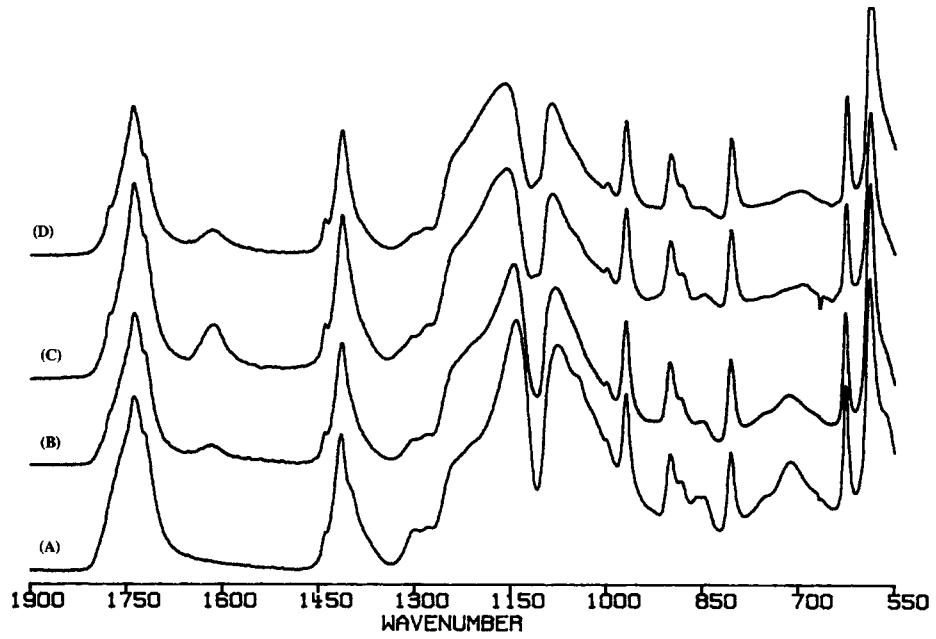


Figure 9 FTIR spectra of unirradiated PGA disks as a function of hydrolysis time (days). (A) 0 day, (B) 55 h, (C) 7 days, (D) 21 days.

in which more than 50% of the original $[\eta]$ of the unhydrolyzed PGA disks was lost due to γ irradiation [(Fig. 2(b)]. At longer periods of hydrolysis (21 days), the intensities of the 1613 cm^{-1} band were similar for irradiated and unirradiated samples. This indicates that at the more advanced stages of hydrolysis the formation and removal rates of fragments containing acid salt end groups are relatively equal for the two types of samples. Comparison of only the irradiated samples at the same hydrolysis

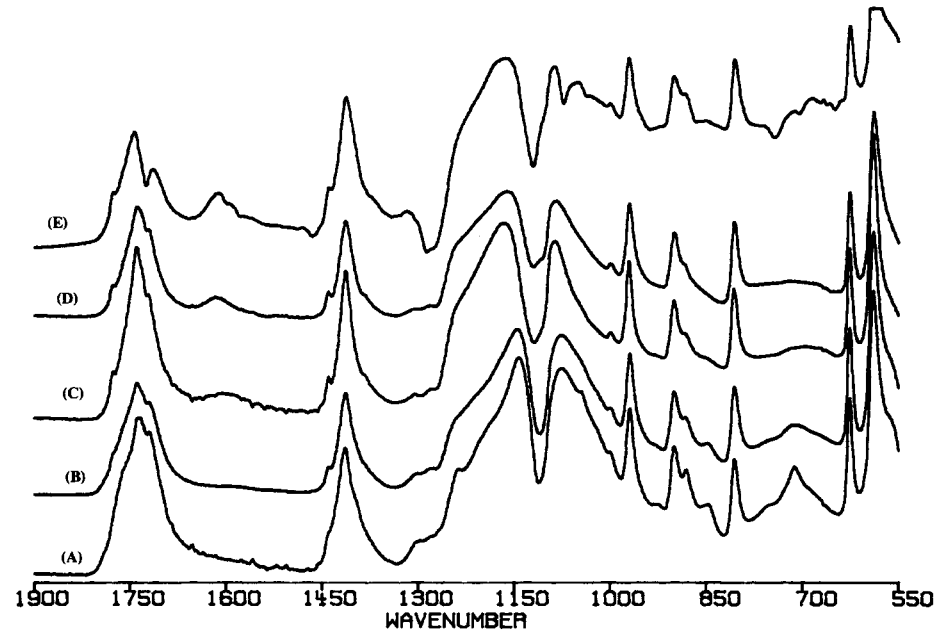


Figure 10 FTIR spectra of 2 Mrad and dry ice temperature irradiated PGA disks as a function of hydrolysis time (days). (A) 0 day, (B) 2 days, (C) 7 days, (D) 21 days, (E) 28 days.

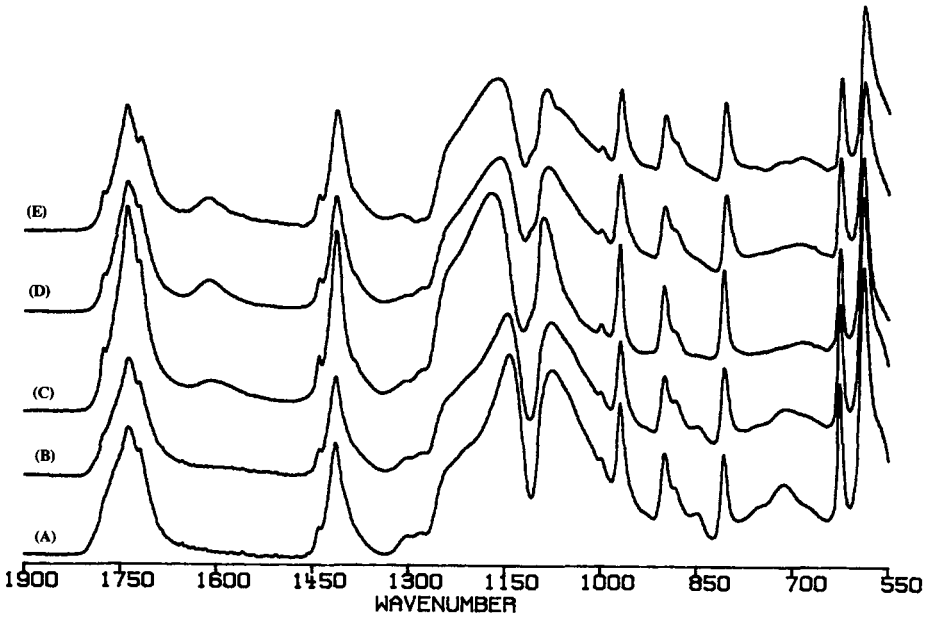


Figure 11 FTIR spectra of 2 Mrad and 55°C irradiated PGA disks as a function of hydrolysis time (days). (A) 0 day, (B) 2 days, (C) 7 days, (D) 21 days, (E) 28 days.

times show no marked differences in the 1613 cm^{-1} band with varying either the radiation dosage or T_{irr} of the samples.

As shown in Figure 9, the four bands at 850, 753, 713, and 560 cm^{-1} associated with the amorphous regions of the PGA disks all exhibited progressive losses of intensity with hydrolysis. However, the amorphous bands in the irradiated samples displayed faster losses in intensity. This was consistent with the observed faster loss of tensile breaking strength (which is mainly derived from tie chains in amorphous domains) in irradiated suture materials described earlier.

Peaks associated with the crystalline phase included those at 972, 901, 806, 627, and 590 cm^{-1}. There was little change in the intensities or band-

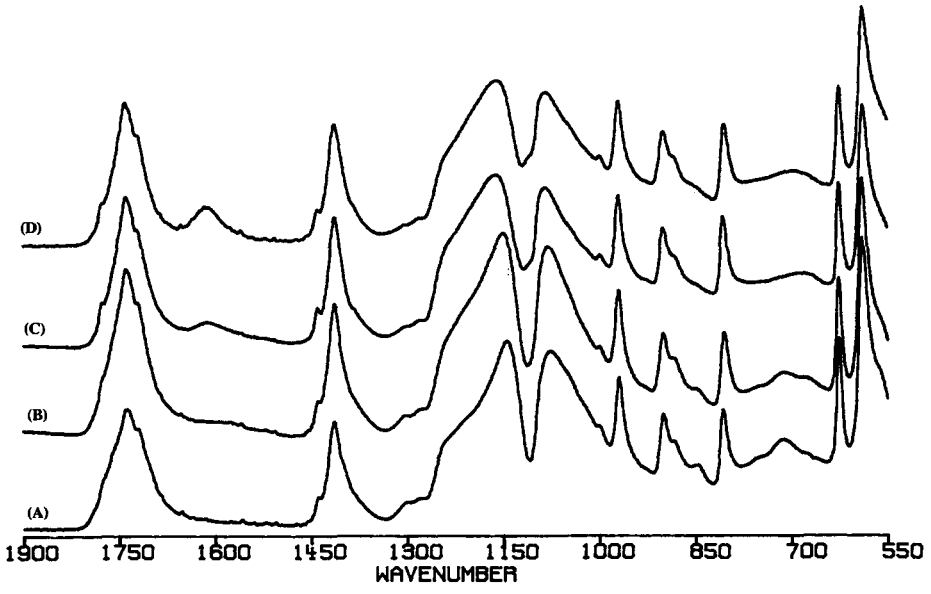


Figure 12 FTIR spectra of 20 Mrad and dry ice temperature irradiated PGA disks as a function of hydrolysis time (days). (A) 0 day, (B) 2 days, (C) 7 days, (D) 21 days.

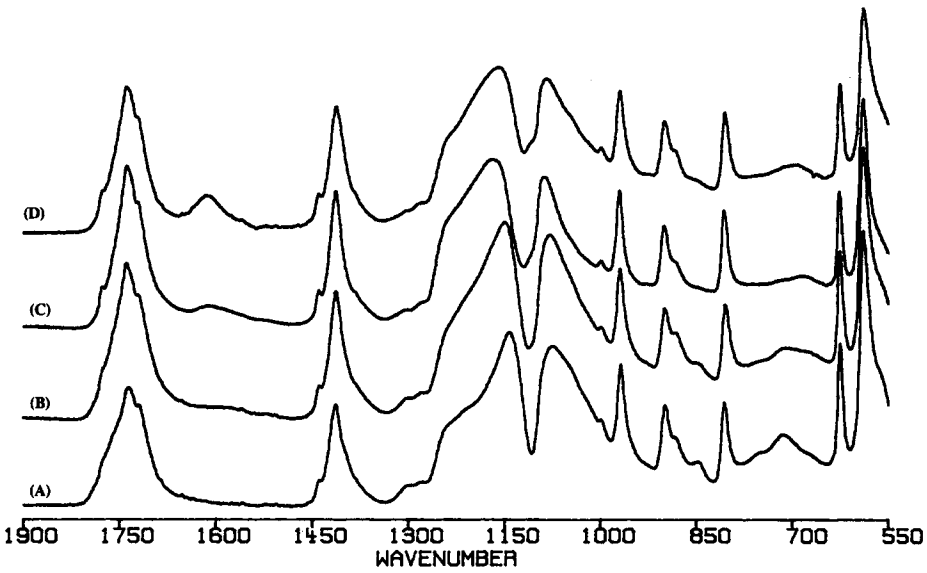


Figure 13 FTIR spectra of 20 Mrad and 55°C irradiated PGA disks as a function of hydrolysis time (days). (A) 0 day, (B) 2 days, (C) 7 days, (D) 21 days.

shapes of these crystalline peaks with hydrolysis and regardless of any prior irradiation. Any weight losses through 21 days of hydrolysis in the PGA disks were predominantly associated with the losses from amorphous domains.

A comparison of the relative intensities of the amorphous 713 cm^{-1} band in all of the spectra showed pronounced differences in morphology arising solely from differences in irradiation dosages or temperature. In the unhydrolyzed (0 day) samples, the intensity of this band was nearly equal for the unirradiated PGA disk and for the PGA disk irradiated with a dosage of 2 Mrad at −78°C. Raising the irradiation temperature to 55°C, however, led to a pronounced decrease in intensity of this band for the unhydrolyzed sample. The decrease in intensity of the amorphous 713 cm^{-1} band was even more dramatic when the radiation dosage was increased to 20 Mrad. At this much higher dosage, the effects of irradiation well above T_g or well below T_g were apparently overwhelmed as the unhydrolyzed 20 Mrad/−78°C and 20 Mrad/55°C samples displayed nearly equal intensities for the 713 cm^{-1} band. In agreement with earlier discussions, these losses in intensity of amorphous infrared bands could be attributed to various levels, depending upon the dosage and T_{irr}, of irradiation-induced destruction in the amorphous domains.

Two broad intense peaks at 1142 and 1077 cm^{-1} can be assigned to C—O stretching modes in the ester groups and oxymethylene groups, respectively. These two peaks appeared to be associated mainly with ester and oxymethylene groups originating in the amorphous domains. Hydrolysis caused both of these C—O stretching modes to substantially decrease in intensity. Furthermore, the peaks shifted to higher frequencies (1160 and 1088 cm^{-1}) that may have been more reflective of the C—O vibrations associated with groups in the crystalline domains. (The substantial frequency difference between the crystalline and amorphous ester C—O stretching modes may be due to repulsion of neighboring side groups in the crystalline unit cell. That is to say, neighboring pendant oxygen atoms in carbonyl groups increase the restoring force of the C=O contribution to the C—O mode. This leads to a larger force constant, and hence a higher frequency, of the crystalline C—O stretching mode. Notice that, consistent with this mechanism, the oxymethylene C—O stretching mode displays a smaller frequency difference between the crystalline and amorphous states.) The losses in intensity of the "amorphous" C—O stretching modes appeared to be slightly greater after 21 days for the irradiated samples than for the unirradiated control sample. Unlike in the case of the amorphous 713 cm^{-1} band, it was difficult to detect any pronounced differences in these C—O stretching modes arising from variations in radiation dosage or temperature.

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