Radiation-Grafted Hydrogels for Biomaterial Applications as Studied by the ESCA Technique

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Synopsis

Electron spectroscopy for chemical analysis (ESCA) was used to study the surface composition of several radiation-grafted polymers in both the dry and hydrated (frozen at 160°K) states. Poly(2-hydroxyethyl methacrylate) (HEMA) and polyacrylamide, both hydrophilic polymers, were readily detected in the hydrated or dehydrated states when grafted to polyethylene substrates. For silicone rubber substrates, both grafts were observed on the hydrated surface but were significantly decreased in surface concentration upon dehydration. For grafts on a polyester-urethane, acrylamide was not a major constituent of either the dry or hydrated surface, while HEMA appeared to increase in abundance upon drying. The amount of the hydrophobic poly(ethyl methacrylate) found on the graft surface depended upon the substrate polymer used, but the surface abundance of poly(ethyl methacrylate) was not affected by drying. These results were considered in terms of polar group orientation, polymer chain mobility, substrate permeability, and the limitations of the ESCA technique. The implications of these results with respect to the use of radiation-grafted hydrophilic polymers for biomedical applications are also discussed.

INTRODUCTION

The interface between hydrated, crosslinked hydrophilic polymers (hydrogels) and water has received significantly less study than water–hydrophobic polymer interfaces or water–inorganic solid interfaces. This is perhaps due to the complex nature of the hydrogel interface which probably consists of bulk water, structured and/or bound water, hydrated relatively mobile polymeric chains, and hydrated crosslinked polymeric chains.[1,2] In addition, the interface is not sharp or discrete and the surface area is not readily measurable. Thus, traditional techniques used to investigate surface properties of materials are not generally applicable to hydrogel–aqueous interfaces.

Recent studies on certain crosslinked hydrophilic polymer surfaces have demonstrated significant hysteresis between advancing and receding water contact angles which might be indicative of conformational changes which occur in the polymer between the hydrated and dehydrated conditions.[3] Protein adsorption studies have shown that these surfaces appear to behave in a different manner from conformationally rigid or water-impermeable surfaces, particularly with respect to the absolute amount of protein adsorbed and to protein desorption kinetics.[4–7] Many hydrogels have been found to interact in a passive manner with living tissues and therefore have been extensively studied as biomater-

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ials.[8–10] Thus, their interesting surface properties and potential biomedical applications justify the need for further study of the hydrogel–aqueous interface.

Hydrogels are inherently mechanically weak. To increase their strength, they can be covalently grafted to the surface of polymers that possess more desirable mechanical properties. A grafted hydrogel may have surface properties which reflect both the properties of the hydrogel graft and the hydrophobic substrate. Such polymers have been and are being investigated for biomaterials applications.[10–14] In this study, the surfaces of radiation grafted hydrogels and a radiation grafted hydrophobic polymer on various substrates were examined in the hydrated and dehydrated states by the electron spectroscopy for chemical analysis (ESCA) technique. Uses for ESCA in the analysis of polymeric materials have been reviewed.[15] Extensive changes involving the location of the hydrogel graft with respect to the substrate were found to occur in some systems upon dehydration.

EXPERIMENTAL

Radiation-Grafted Film Preparation

All grafted films were prepared by the mutual irradiation technique. This technique as applied to the preparation of grafted hydrogels has been described in detail elsewhere.[11,12] Briefly, cleaned substrate films were immersed in monomer solutions by evacuating a test tube containing the film to approximately 1 mm Hg and drawing the monomer solution into the test tube. Some samples were further deoxygenated by an N_2 purge. These test tubes were irradiated in a ca. 10,000 Ci cobalt-60 source for a 0.25-Mrad dose at either ambient temperature, or at elevated temperatures by immersion in a Dewar flask of hot water. Grafted films were cleaned of soluble polymer by extensive extraction washings in various solvents and then in water. Films were stored wet, and except where predrying is specifically indicated in the text, were never dehydrated before ESCA analysis. Monomer formulations used are described in Table I along with sources of supply for the various components. Chemicals were reagent grade

TABLE I
Grafting Formulations[a]

	A	B	C	D	E	F	G	H
2-Hydroxyethyl methacrylate[b]	20	16	14	—	—	—	—	—
Acrylamide[c]	—	—	—	20 g	25 g	25 g	—	—
Ethyl methacrylate[d]	—	—	—	—	—	—	20	20
Methanol	40	42	43	—	—	—	76	75
H_2O	40	42	43	—	—	—	4	5
$Cu(NO_3)_2$(0.01*M*) + MES[e] (0.02*M*) (pH = 4.57)	—	—	—	80 ml	—	—	—	—
$Cu(NO_3)_2$ (0.05*M*)	—	—	—	—	75 ml	—	—	—
$Cu(NO_3)_2$ (0.02*M*)	—	—	—	—	—	75 ml	—	—

[a] All quantities in vol-% unless otherwise stated.
[b] High-purity grade generously supplied by Hydromed Sciences, Inc., New Brunswick, N.J.
[c] Eastman Kodak electrophoresis grade.
[d] Polysciences, Inc., purified by distillation.
[e] 2-(N-Morpholino)ethanesulfonic acid, Calbiochem.

TABLE II
Radiation-Grafted Films

Film no.	Substrate polymer	Monomer	Grafting solution[a]	Radiation dose, Mrad	Grafting temperature, °C	mg graft per cm^2	% H_2O in graft
I	Silastic[b]	HEMA[c]	C	0.250	AMB	4.9	27.2
II	Tuftane[d]	HEMA	A	0.250	AMB	6.3	27.2
III	polyethylene[e]	HEMA	A	0.375	~60°C	5.8	25.7
IV	Silastic	AAM[f]	D	0.250	AMB	1.6	64.9
V	Tuftane	AAM	E	0.375	~60°C	7.9	56.5
VI	polyethylene	AAM	F	0.375	~60°C	1.4	38.1
VII	Tuftane	EMA[g]	G	0.375	AMB	6.5	37.6
VIII	Silastic	HEMA	B	0.250	AMB	5.2	30.0
IX	Silastic	EMA	H	0.250	AMB	5.4	7.4

[a] See Table I.
[b] Medical-grade poly(dimethylsiloxane) silicone rubber, Dow Corning Corp.
[c] 2-Hydroxyethyl methacrylate.
[d] Tuftane TF-310 polyester-polyurethane, B.F. Goodrich Co.
[e] Cadillac Plastics Corp.
[f] Acrylamide.
[g] Ethyl methacrylate.

unless otherwise noted. Precise grafting conditions and code designations of each of the grafted films used in these experiments are shown in Table II. The bulk 2-hydroxyethyl methacrylate (HEMA) gel was prepared using a molding technique described elsewhere.[16] The monomer solution for this gel consisted of 10.0 ml HEMA, 0.5 ml tetraethylene glycol dimethacrylate, 3.0 ml ethylene glycol, 2.0 ml H_2O, 1.0 ml $(NH_4)_2S_2O_8$ (40 g/100 ml H_2O), and 1.0 ml $Na_2S_2O_5$ (15 g/100 ml H_2O).

ESCA Measurements

ESCA spectra were taken on a Hewlett-Packard Model 5950B ESCA system. A 0.8-kW monochromatized x-ray beam from an aluminum anode was used for all spectra. An emission from an electron flood gun set to a potential of approximately 2 eV was used to neutralize static charge buildup on the nonconducting polymeric surfaces. All aliphatic carbon 1*s* peaks were assigned a binding energy of 285.0 eV to correct for the energy shift resulting from the electron flood gun.

Grafted films were placed soaking wet onto the sample stage, rapidly frozen to 160° or 113°K, and then advanced into the sample chamber maintained at ~10^{-8} torr. At these low temperatures, only oxygen was observed in the ESCA spectrum for most samples. Water was volatilized from the surface of the samples by warming *in situ* to ~200°K until a strong carbon spectrum was obtained. This was assumed to be the point at which the surface film of ice was removed from the sample leaving a frozen, hydrated hydrogel surface. After again reducing the temperature, appropriate spectra were taken by scanning over various 20-eV ranges for the elements of interest. By continuously monitoring the vacuum in the sample chamber during this period, it was determined that little or no water was volatilizing from the sample when the temperature was maintained at 160°K.

Samples were also dehydrated *in situ* by raising the temperature to 303°K. When the liberation of water from the sample had ceased as indicated by the vacuum gauges on the ESCA instrument, spectra were taken. In most cases reductions in the size of the oxygen peak were noted after dehydration, which is taken as further evidence that the hydrogels were still hydrated when the spectra were obtained at 160°K. To ensure that the samples were fully dehydrated, spectra on some of the specimens were retaken after remaining in the instrument for 12 hr or longer at pressures of $\leq 10^{-7}$ torr and compared with those taken immediately after the vacuum gauges had indicated that the grafted hydrogels were outgassed.

Normalized ESCA peak intensities which were used for comparing changes in elemental abundance at the surface of the films were obtained by dividing the integrated number of photoelectron counts in the peak area by the number of scans and then dividing again by a relative strength factor based upon calculated electron photoemission cross sections of the various elements for AlK_α excitation. Relative strength factors that were used are carbon 1*s* = 1.000, nitrogen 1*s* = 1.799, oxygen 1*s* = 2.933, and silicon 2*p* = 0.814.[17]

Results are presented in terms of ratios of normalized ESCA peak intensities

TABLE III
Calculated Elemental Ratios Based Upon Polymer Repeat Unit Structural Formulas

Polymer[a]	Elemental ratio[b]				
	C/O	C/Si	O/Si	C/N	O/N
$-(Si(CH_3)_2-O)_n-$ Silastic[c]	2	2	1	—	—
$-(CH_2-CH_2)_n-$ Polyethylene	—	—	—	—	—
$-(CH_2-C(CH_3)(C(=O)OCH_2CH_2OH))_n-$ Poly(HEMA)	2	—	—	—	—
$-(CH_2-CH(C(=O)NH_2))_n-$ Poly ACRYLAMIDE	3	—	—	3	1
$-(CH_2-C(CH_3)(C(=O)OCH_2CH_3))_n-$ Poly(EMA)	3	—	—	—	—

[a] The structural formula for Tuftane is proprietary.

[b] Endgroups and crosslinks were not considered in these calculations.

[c] Contribution of proprietary amounts of silicon dioxide filler is not considered, but ESCA indicates that SiO_2 is not the major constituent on the surface.

which should correspond to the ratio of the elements in the surface region of the materials examined. As a first-order approximation, escape depth variation with electron energy and spectrometer throughput as a function of energy were found to cancel each other out and therefore were not considered in calculating relative abundance of elements. For reference purposes, calculated elemental ratios for most of the polymers observed in this study are listed in Table III.

Additional Grafted Polymer Characterization

The water content in the graft was determined by blotting grafted films (prepared in parallel to those used for ESCA analysis), weighing the wet film, dehydrating the film, and weighing it once again. The water content is expressed as % H_2O in the graft. The procedure for determining water contents has been described in more detail elsewhere.[11,12]

Examination of the graft in the absence of the substrate was performed by dissolving away the substrate. Tuftane substrates were dissolved in dimethylformamide. Silastic substrates were dissolved in NCS tissue solubilizer (Amersham/Searle Corp.). The crosslinked nature of the graft separated from the substrate was ascertained by placing the graft into good solvents for the polymer and observing whether dissolution occurred. Poly(HEMA) graft was placed in methanol, polyacrylamide graft was placed in H_2O, and poly(EMA) graft was placed in toluene in order to determine whether they could be solubilized without breaking covalent bonds.

RESULTS

Elemental ratios for radiation-grafted HEMA films on Silastic, Tuftane, and polyethylene (films I, II, and III, Table II) in the hydrated state (160°K) and dehydrated state (303°K) are shown in Table IV. For the HEMA-grafted Silastic film (I), as the hydrogel is dehydrated, the relative amount of the element silicon at the surface of the film appears to increase. On the other hand, for the HEMA-grafted Tuftane film (II), the relative amount of nitrogen at the surface of the film decreases as the film is dried. As both silicon and nitrogen are present only in the Silastic and Tuftane substrates respectively and not in the graft, opposite effects apparently occurred upon dehydration. In the case of HEMA-grafted Silastic, the substrate signal became stronger upon dehydration, while in the case of the HEMA-grafted Tuftane, the substrate signal became weaker. In order to demonstrate that the elemental ratios observed were not changing owing to a simple temperature dependence, a specimen of HEMA-grafted Silastic (film VIII, Table II) was studied at 200°K (hydrated) and 300°K (dehydrated after overnight pumping in the ESCA unit). Then, the dehydrated sample was recooled to 165°K and again examined (see Table V). The peak intensities and elemental ratios for the dehydrated sample at 300°K and the dehydrated sample at 165°K are almost identical. However, peak intensities for the dehydrated specimen at 165°K and the hydrated specimen at 200°K are significantly different from each other and indicate a strong increase in the abundance of silicon on the surface upon dehydration similar to that noted for film I.

There was poor agreement in the apparent amount of silicon in both the hy-

TABLE IV
Comparison of ESCA Peak Intensities for HEMA Grafted to Silastic, Tuftane, and Polyethylene in the Hydrated (160°K) and Dehydrated (303°K) States

Film	Peak	Normalized ESCA peak intensity		Elemental ratio									
				C/Si		O/Si		C/O		C/N		O/N	
		160°K	303°K	160°K	303°K	160°K	303°K	160°K	303°K	160°K	303°K	160°K	303°K
Silastic + HEMA (film no. I)	C_{1s}	13,775	9,898										
	O_{1s}	5,766	5,099	5.52	1.64	2.31	0.85	2.39	1.94				
	Si_{2p}	2,495	6,020										
Tuftane + HEMA (film no. II)	C_{1s}	13,894	18,486										
	O_{1s}	12,477	6,880					1.11	2.83	5.92	86.60	5.32	30.85
	N_{1s}	2,345	225										
Polyethylene + HEMA (film no. III)	C_{1s}	17,491	21,169										
	O_{1s}	9,608	6,002					1.82	3.53				

TABLE V
Temperature and Hydration Effects on the ESCA Peak Intensities and Elemental Ratios for a HEMA-Grafted Silastic Film (VIII)

Temperature	Peak	Normalized ESCA peak intensity	Elemental ratio C/Si	Elemental ratio O/Si	Elemental ratio C/O
200°K	C_{1s}	1540			
(fully hydrated)	O_{1s}	771	22.0	11.01	2.00
	Si_{2p}	70			
300°K	C_{1s}	2960			
(dehydrated)	O_{1s}	1718	7.42	4.31	1.72
	Si_{2p}	399			
165°K	C_{1s}	3160			
(dehydrated, recooled)	O_{1s}	1793	7.71	4.31	1.76
	Si_{2p}	410			

TABLE VI
Storage and Handling Effects on Elemental Ratios As Determined by ESCA for HEMA-Grafted Silastic Films

Film type	Storage history	Temperature	Peak	Normalized ESCA peak intensity	Elemental ratio C/Si	Elemental ratio O/Si	Elemental ratio C/O
I	never dehydrated;	160°K	C_{1s}	13,775			
	stored approx. 1	(hydrated)	O_{1s}	5,766	5.52	2.31	2.39
	month in H_2O		Si_{2p}	2,495			
	before examina-	303°K	C_{1s}	9,898			
	tion	(dehydrated)	O_{1s}	5,099	1.64	0.85	1.94
			Si_{2p}	6,020			
I	rehydrated	113°K	C_{1s}	2,390			
	immediately	(hydrated)	O_{1s}	2,578	12.45	13.42	0.92
	after the experiment described above;		Si_{2p}	192			
	stored in H_2O	303°K	C_{1s}	11,000			
	approx. 2½	(dehydrated)	O_{1s}	4,841	1.20	0.53	2.27
	months		Si_{2p}	9,140			
VIII	dehydrated after	200°K	C_{1s}	1,540			
	preparation;	(hydrated)	O_{1s}	771	22.00	11.01	2.00
	rehydrated						
	approx. 3 days		Si_{2p}	70			
	before ESCA	300°K	C_{1s}	2,960			
	examination	(dehydrated)	O_{1s}	1,718	7.42	4.31	1.72
	was begun		Si_{2p}	399			

drated and dehydrated states between film I (Table IV) and film VIII (Table V). As these films had different histories with respect to dehydration and rehydration times, a third experiment was done at still another set of conditions to observe the effect on the elemental ratios. This experiment used the same specimen of film I described in Table III which was rehydrated and allowed to soak in H_2O for approximately two months. Data for the three experiments are summarized in Table VI. The rehydrated specimen of film I produced a set of elemental ratios that differed from both the initial film I results and the film VIII

results, but did show the abundance of silicon at the surface to increase significantly relative to C or O upon dehydration of the sample. The differences in elemental ratios between the three experiments can be attributed to either the sensitivity of the hydrogels to dehydration and storage conditions or to differences in the sample placement and performance of the instrument from time to time. However, these similar observations for all three specimens support the conclusion that major changes do occur in the surface of grafted HEMA hydrogels on Silastic upon dehydration.

Further evidence for changes occurring upon dehydration can be obtained by examining the original ESCA spectra. In Figure 1, the C_{1s} spectra for film I (HEMA grafted to Silastic) in the hydrated (165°K) and dehydrated (303°K) states are shown. In the spectrum for the film at 160°K, a number of peaks (partially overlapped) representing carbons present in carboxyl and ester groups and adjacent to hydroxyl groups are seen at higher binding energies from the main aliphatic carbon peak at 285 eV. Upon dehydration these "carbon bound

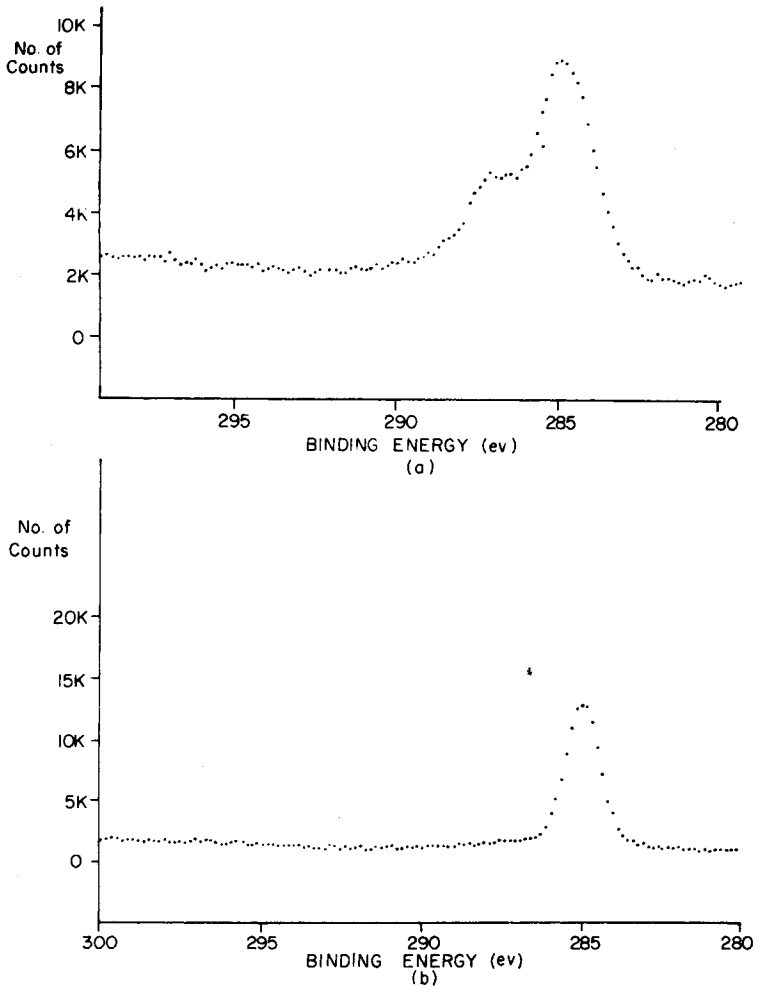

Fig. 1. ESCA C_{1s} spectra for HEMA grafted to silicone rubber (film I): (a) 160°K (hydrated); (b) 303°K (dehydrated).

to oxygen" peaks almost totally disappear. As Silastic produces a C_{1s} spectrum with only one relatively narrow, symmetrical peak at the same binding energy as the HEMA aliphatic carbon peak, the higher binding energy peaks can be taken as indicative of HEMA radiation grafted on the surface. The disappearance of these peaks upon dehydration is consistent with the conclusion that the concentration of HEMA graft at the surface of the Silastic film decreases upon dehydration.

In Figure 2, the C_{1s} spectra for film II (HEMA grafted to Tuftane) in the hydrated and dehydrated states are shown. In the hydrated state, the higher binding energy peaks representative of carbon bound to oxygen are shouldered into the main C_{1s} aliphatic carbon peak and comprise ~25% of the total C_{1s} signal. Upon dehydration, a distinct spectrum is resolved for the higher binding peaks, and these carbon species are found to comprise ~36% of the total carbon spectrum. The C_{1s} ESCA spectrum of cleaned, ungrafted Tuftane film shows only one sharp symmetrical peak. As all the higher binding energy peaks must therefore arise from the HEMA graft, this result also supports the observations described previously on the decrease in the HEMA-grafted Tuftane nitrogen peak intensity upon drying. Both these observations are interpreted as being indicative of an increase in the concentration of graft at the surface of the film in the dry state.

Figure 3 shows the ESCA C_{1s} spectra for film III (HEMA grafted to polyethylene) in the hydrated and dehydrated states. Little change is seen in the clearly resolved higher binding energy peaks or in their relative concentrations between the hydrated and dehydrated states. Untreated polyethylene shows a C_{1s} spectrum consisting of only one symmetrical sharp peak. Thus, for HEMA-grafted polyethylene, the graft appears to be localized on the surface and does not significantly change in surface abundance upon dehydration. The increase in the carbon/oxygen ratio upon dehydration as listed in Table IV could be explained simply by loss of water oxygen upon dehydration.

In order to see if the graft migration effects described for HEMA-grafted hydrogels on Silastic and Tuftane occur with other hydrogel systems, polyacrylamide-grafted films on Silastic, Tuftane, and polyethylene were studied in the hydrated and dehydrated states. Results on relative elemental abundances for these graft hydrogel systems are shown in Table VII. For acrylamide grafted on Silastic (film IV), upon dehydration the abundance of silicon at the surface of the film is seen to substantially increase while the abundance of nitrogen (present only in the graft) is found to decrease below measurable levels. Also, all higher binding energy carbon peaks disappear upon dehydration (see Fig. 4). Acrylamide grafted onto Silastic would appear from these experiments to behave similarly to HEMA grafted to Silastic. To investigate further the total disappearance of the nitrogen peak upon dehydration, the film was argon etched to a depth of ~500 Å in the ESCA unit and reexamined. After this treatment, a moderately strong nitrogen peak was again detected.

For the acrylamide-grafted Tuftane film (film V), the effect of dehydration on the location of the graft layer cannot be clearly discerned from the data shown in Table VII as there are no unique elemental markers in either the graft or the substrate. However, an examination of the C_{1s} spectra for film V (Fig. 5) in the hydrated and dehydrated states shows little change upon dehydration. A very low abundance of the higher binding energy C_{1s} species is noted in both Figures

TABLE VII

Comparison of ESCA Peak Intensities for Acrylamide Grafted to Silastic, Tuftane, and Polyethylene in the Hydrated (160°K) and Dehydrated (303°K) States

Substrate film	Peak	Normalized ESCA peak intensity		Elemental ratio									
				C/Si		O/Si		C/O		C/N		O/N	
		160°K	303°K	160°K	303°K	160°K	303°K	160°K	303°K	160°K	303°K	160°K	303°K
Silastic (film no. IV)	C_{1s}	7,988	12,461										
	O_{1s}	19,428	5,992	7.70	2.05	18.73	0.99	0.41	2.08	3.41	∞	8.28	∞
	N_{1s}	2,345	0										
	Si_{2p}	1,037	6,068										
Tuftane (film no. V)	C_{1s}	23,550	23,917										
	O_{1s}	4,661	4,087					5.05	5.86	19.94	36.58	3.95	6.59
	N_{1s}	1,181	620										
Polyethylene (film no. VI)	C_{1s}	16,331	19,356										
	N_{1s}	2,627	1,734					2.58	—	6.22	11.16	2.41	—
	O_{1s}	6,319	—										

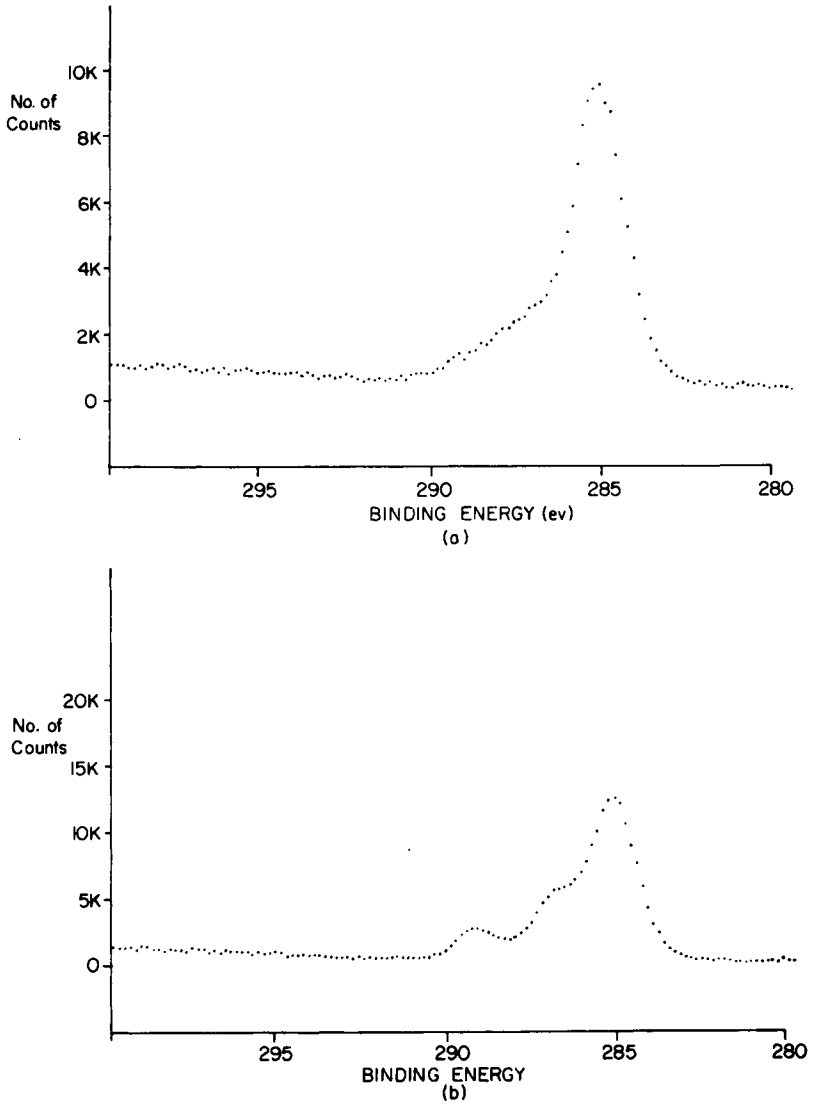

Fig. 2. ESCA C_{1s} spectra for HEMA grafted to Tuftane (film II): (a) 160°K (hydrated); (b) 303°K (dehydrated).

5(a) and 5(b); these species are indicative of the acrylamide graft. Therefore, in this case, the acrylamide graft is apparently localized somewhat within the Tuftane rather than at its surface and does not become more concentrated at the surface upon dehydration.

For the acrylamide grafted to polyethylene (film VI), although the elemental ratios indicate that the fraction of nitrogen at the graft surface decreases upon dehydration to one half its level in the hydrated graft, an examination of the C_{1s} spectra for the hydrated and dehydrated films shows little difference upon dehydration (Fig. 6) with clearly resolved higher binding energy peaks present in both cases. Therefore, a surface-localized graft that does not undergo significant variation in apparent graft location upon dehydration is indicated.

Changes in surface composition upon dehydration were found for both HEMA

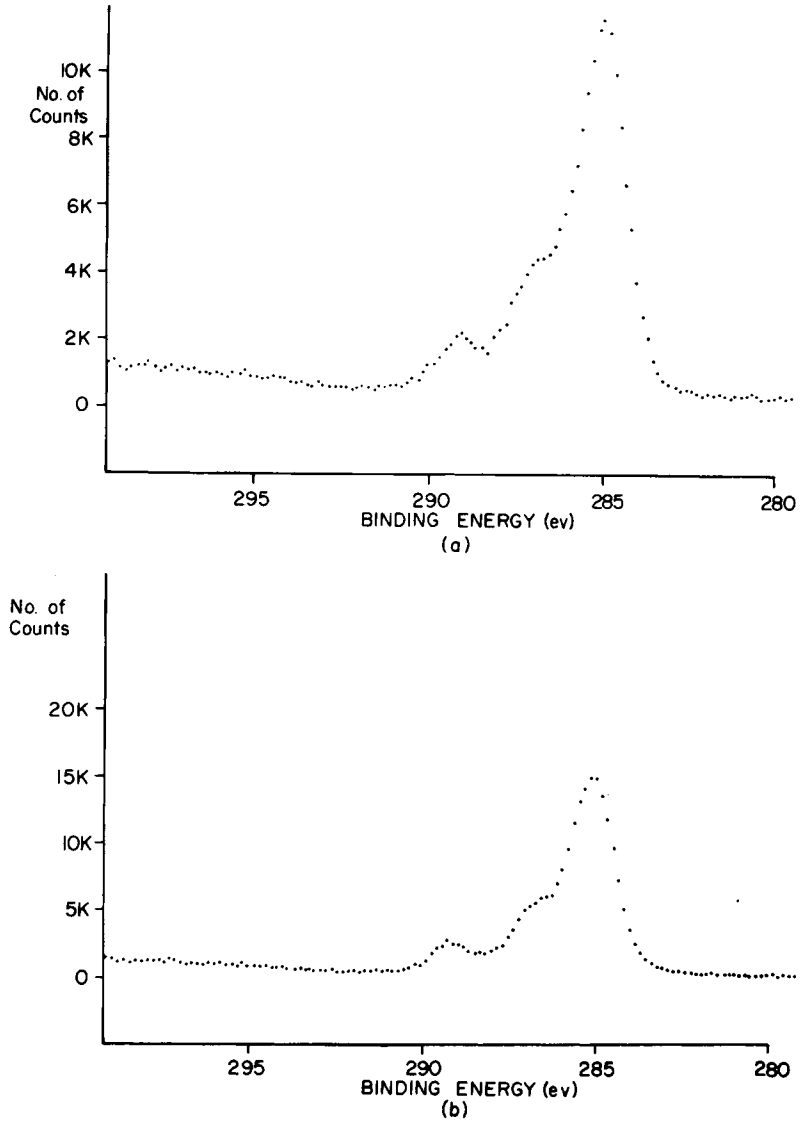

Fig. 3. ESCA C_{1s} spectra for HEMA grafted to polyethylene (film III): (a) 160°K (hydrated); (b) 303°K (dehydrated).

and acrylamide hydrogels grafted to Silastic. Therefore, a structurally related monomer, ethyl methacrylate (EMA), which is hydrophobic rather than hydrophilic, was studied to determine whether changes in graft abundance upon dehydration could occur for hydrophobic graft polymers. EMA was grafted to Silastic, stored in water, and examined wet and dry. The water content of 7.4% for this hydrophobic graft reported in Table II (film IX) is believed to be related more to water trapped within pores in the graft than to true water of hydration, since upon drying and rehydration the percent H_2O in the graft decreased to near zero.[18] The data in Table VIII indicate that no significant changes in surface elemental ratios occur for this film upon dehydration. The C_{1s} ESCA spectra for film IX (Fig. 7) show little change between the spectrum taken at 160°K and

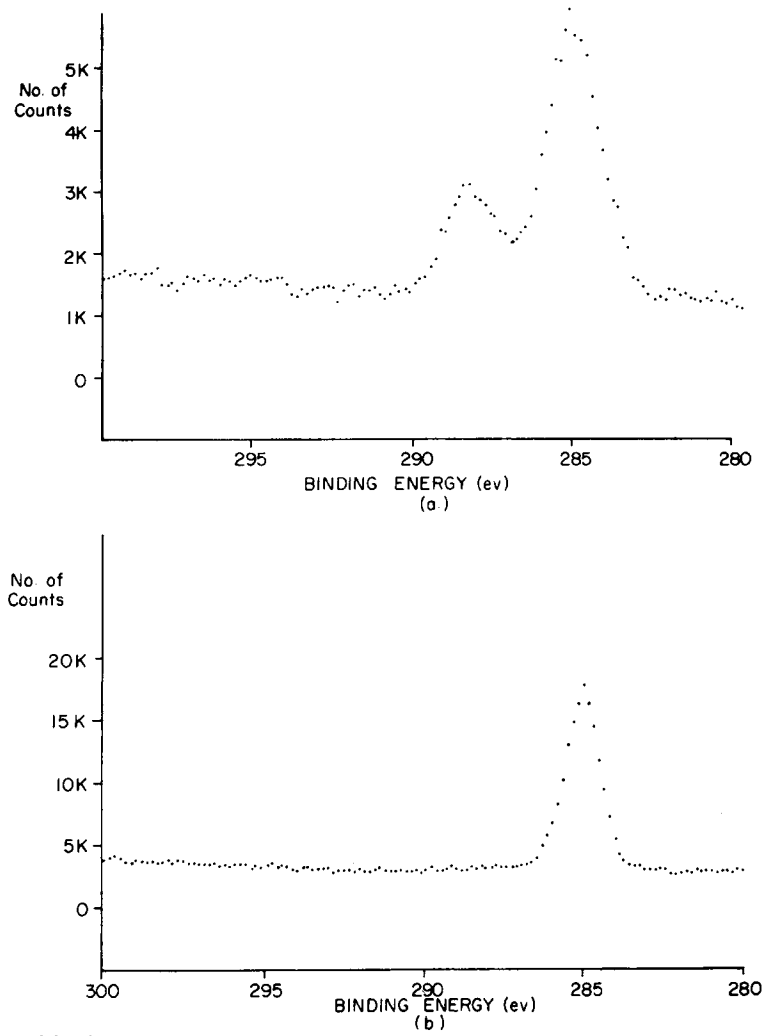

Fig. 4. ESCA C_{1s} spectra for acrylamide grafted to silicone rubber (film IV): (a) 160°K (hydrated); (b) 303°K (dehydrated).

that taken at ambient temperature. Also, as there is a relatively low abundance of the higher binding energy carbon species indicative of the ester group in EMA, the graft can be assumed to be distributed more within the film rather than on the surface. A film prepared by grafting EMA to Tuftane (film VII) was examined in only the dry (303°K) state. For this film, no nitrogen was detected, and the C_{1s} spectrum showed a well-resolved region at higher binding energies, indicating the presence of carbons bound in ester and carboxyl groups (Fig. 8). Thus, unlike the EMA graft on Silastic, EMA grafted to Tuftane apparently covers the surface rather penetrating into the substrate.

In order to determine whether surface composition changes upon dehydration were unique only to hydrogels grafted to various substrates, a sample of a poly-(HEMA) crosslinked gel was examined in the hydrated and dehydrated states. Upon dehydration, the carbon/oxygen ratio for this material went from 0.59 to 2.35, which is consistent with water oxygen loss upon dehydration. The C_{1s} spectrum for this bulk gel may have also changed upon dehydration (Fig. 9).

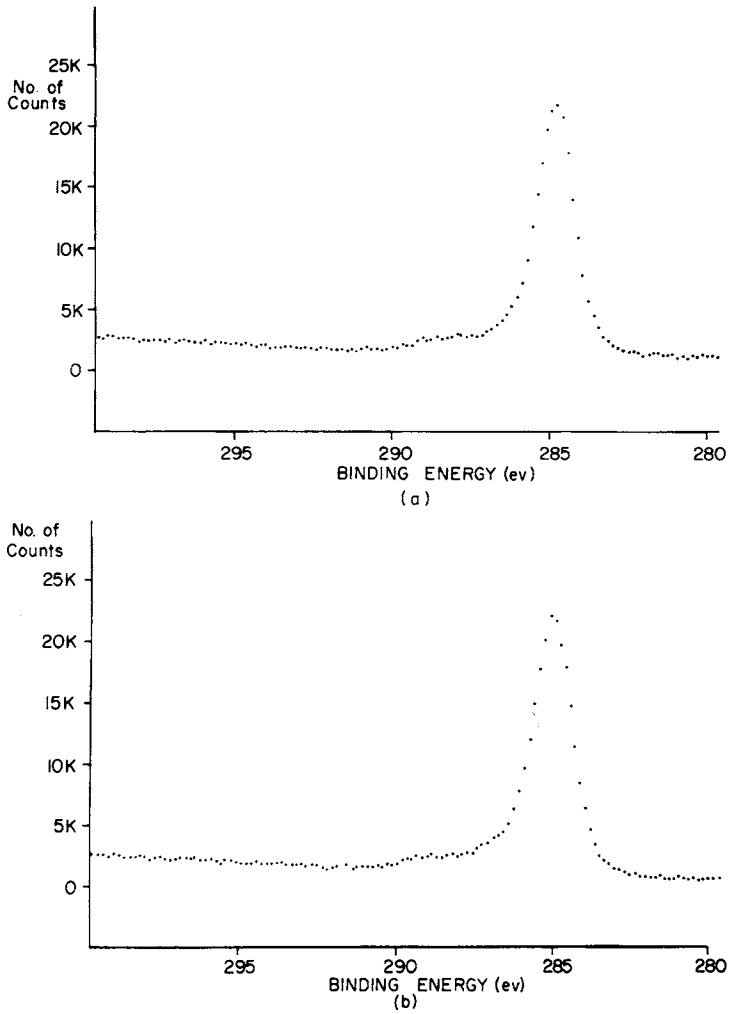

Fig. 5. ESCA C_{1s} spectra for acrylamide grafted to Tuftane (film V): (a) 160°K (hydrated; (b) 303°K (dehydrated).

Comparison of these spectra is complicated by the poor resolution of the low-temperature spectrum (presumably due to uneven surface charging). However, both show the presence of higher binding energy species indicative of the ester and hydroxyl groups in HEMA.

DISCUSSION

ESCA—Technical Considerations

Significant changes were noted between the hydrated and dehydrated states in the ESCA spectra of some radiation-grafted hydrogels. As the ESCA technique can readily yield artifactual results, relevant variables such as sample positioning within the instrument and surface roughness have been considered with respect to their possible effect on this study. Hydrophilic polymeric gels undergo shrinkage upon dehydration, and therefore movement of the sample would be expected to occur between spectra taken at 160° and 303°K even though the sample within the specimen chamber was never handled. Also, surface

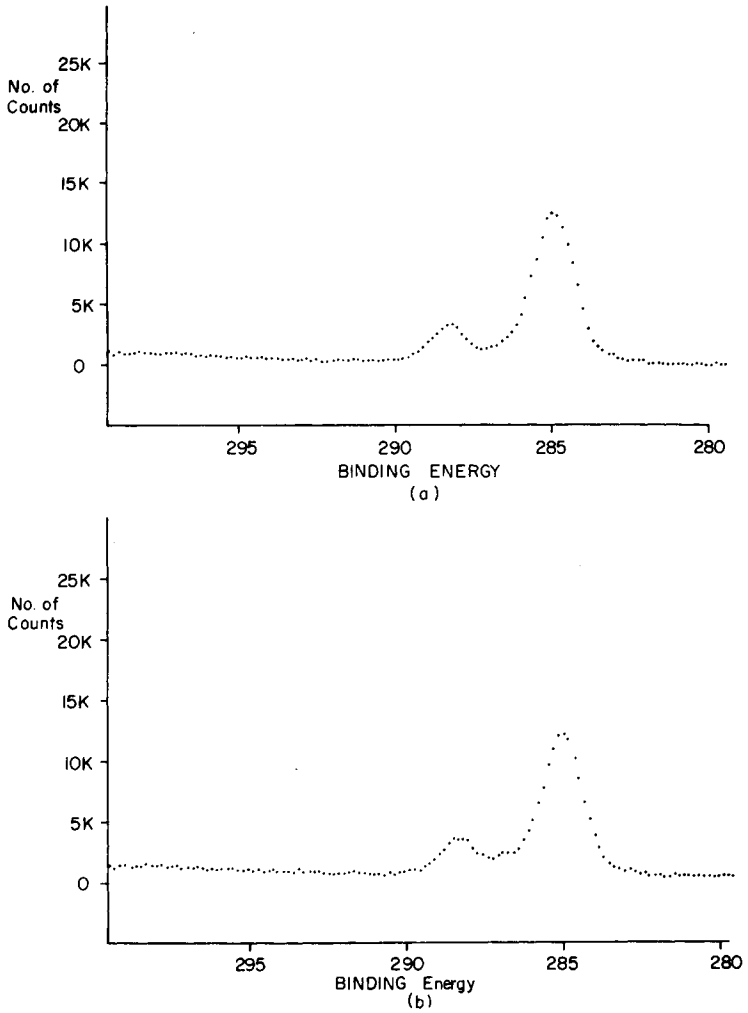

Fig. 6. ESCA C_{1s} spectra for acrylamide grafted to polyethylene (film VI): (a) 160°K (hydrated); (b) 303°K (dehydrated).

roughness probably undergoes some variation during the dehydration process.

Since these changes in the polymer specimens were anticipated, the following protocols were adhered to in considering the ESCA data. All deductions about grafted hydrogel surface composition were based upon ratios of peak intensities (the relative elemental composition of each sample) rather than absolute numbers of counts. Also, the only effects that were considered to be of significance were those involving very large changes in elemental ratios (generally threefold changes or greater). In many cases, a given element which was present in large quantities in the hydrated sample was seen to disappear completely (within the limits of sensitivity of the instrument) upon dehydration. Such extreme changes in elemental abundance cannot be accounted for by positional variation within the instrument or roughness changes during analysis. Finally, the presence or absence of the peaks for various "carbon bound to oxygen" species in the C_{1s} spectra always corresponded in a direction consistent with observed changes in the ele-

TABLE VIII
ESCA Peak Intensities and Elemental Ratios for an EMA-Grafted Silastic Film (IX) in the Hydrated and Dehydrated States

Temperature	Peak	Normalized ESCA peak intensity	Elemental ratio C/Si	O/Si	C/O
160°K (hydrated)	C_{1s}	1460			
	O_{1s}	866	7.12	4.22	1.69
	Si_{2p}	205			
Ambient (dehydrated)	C_{1s}	1440			
	O_{1s}	839	6.13	3.57	1.72
	Si_{2p}	235			

mental ratios. Based upon these arguments, the graft alterations which are observed to occur upon dehydration were considered to be real effects and not artifacts of the ESCA technique.

Graft Structure

The large variations in the abundance of the graft at the surface of grafted hydrogels on Silastic and Tuftane upon dehydration were unexpected. Two models can be proposed to explain the observed decrease in the concentration of hydrogel graft at the surface of Silastic upon dehydration. These are illustrated schematically in Figure 10. The hydrated graft polymers were found to have a significant quantity of the hydrogel at the surface intermixed with silicone polymer chains. Upon dehydration, more of the silicone polymer and less of the hydrogel graft is observed in the ESCA spectra. This could be explained by graft chains penetrating into the silicone rubber (path a–b–d, Fig. 10) or clustering together on the surface (path a–c–e, Fig. 10). Only the graft penetration model is consistent with the complete loss of graft signal seen for the dehydrated acrylamide hydrogel on Silastic. A decrease (but not disappearance) of the graft signal might be consistent with either model suggested in Figure 10 (i.e., path a–b vs path a–c–e).

In order for the element nitrogen to become completely "invisible" (i.e., less than 100 ppm at the surface, the approximate sensitivity limit of the HP 5950B ESCA unit as used in the experiments) upon dehydration of the acrylamide-grafted hydrogel on Silastic (film IV), the graft would have to penetrate into the substrate at least 40–50 Å (the estimated escape distance for nitrogen photoelectrons in an organic matrix). That the graft probably did penetrate into the substrate was demonstrated by finding the element nitrogen present in the bulk of the film after argon etching ~500 Å from its surface. By solubilizing the Silastic or polyurethane substrate polymer from the graft, it has been found that the acrylamide and HEMA radiation grafts are most probably crosslinked hydrogels while the EMA graft is an uncrosslinked polymer. It is difficult to postulate a mechanism whereby a crosslinked polymer (i.e., the HEMA or acrylamide hydrogel) could penetrate into another crosslinked polymer (Silastic) through a distance of 50 Å. This suggests that the graft may consist of a crosslinked hydrogel network interpenetrated with the silicone rubber matrix plus long, relatively linear hydrogel chains tethered to the hydrogel network which might

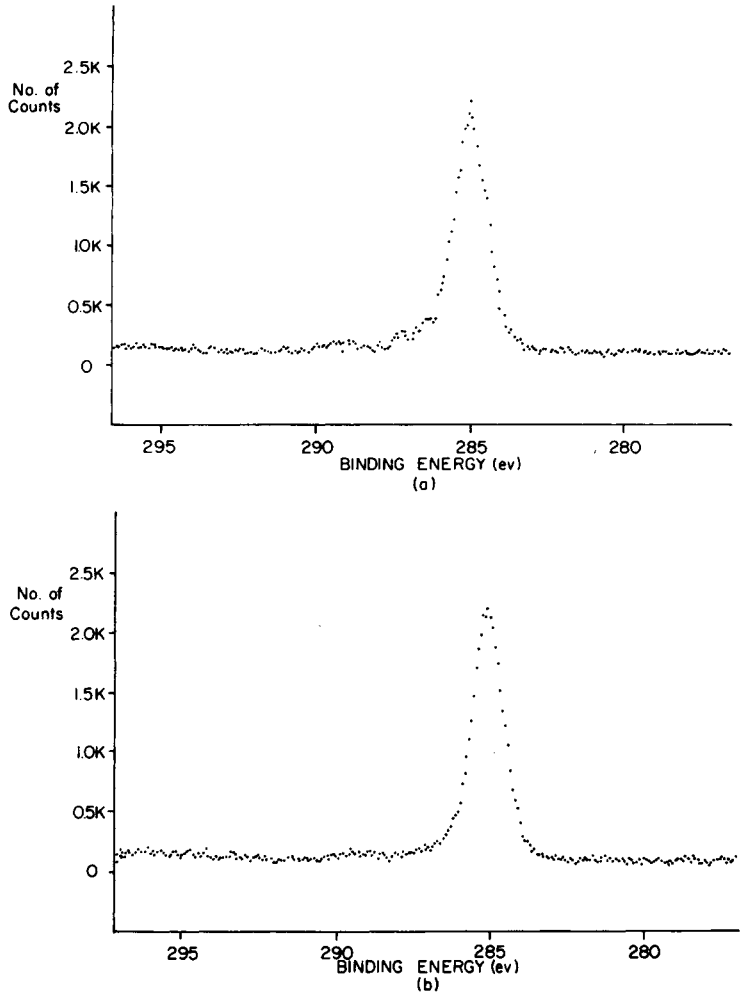

Fig. 7. ESCA C_{1s} spectra for EMA grafted to silicone rubber (film IX): (a) 160°K (hydrated); (b) ambient temperature (dehydrated).

extend to the surface of the graft polymer in the hydrated state and collapse into the silicone rubber matrix upon dehydration.

Based upon observed contact angle hysteresis, Holly and Refojo have hypothesized that in the hydrated state polar groups on poly(HEMA) crosslinked gels are hydrogen bonded to water and are facing outward at the hydrogel surface, while in the dehydrated state the polar groups are intramolecularly hydrogen bonded and the backbone methyl groups are pointing outward from the surface.[3] A similar suggestion was also proposed by Hoffman and Harris.[19] This reversible change in the chain configuration might account at most for a 5–10 Å translational or rotational movement of the polar components of the HEMA molecule. ESCA results with the HEMA bulk gel support this model in that the C/O ratio for the bulk HEMA gel in the dehydrated state was found to be 2.35, as opposed to the expected value of 2.0. If the backbone methyl groups were pointing outward and the polar groups were oriented inward, a carbon enrichment at the surface would be expected. It is not certain whether ESCA as used in these ex-

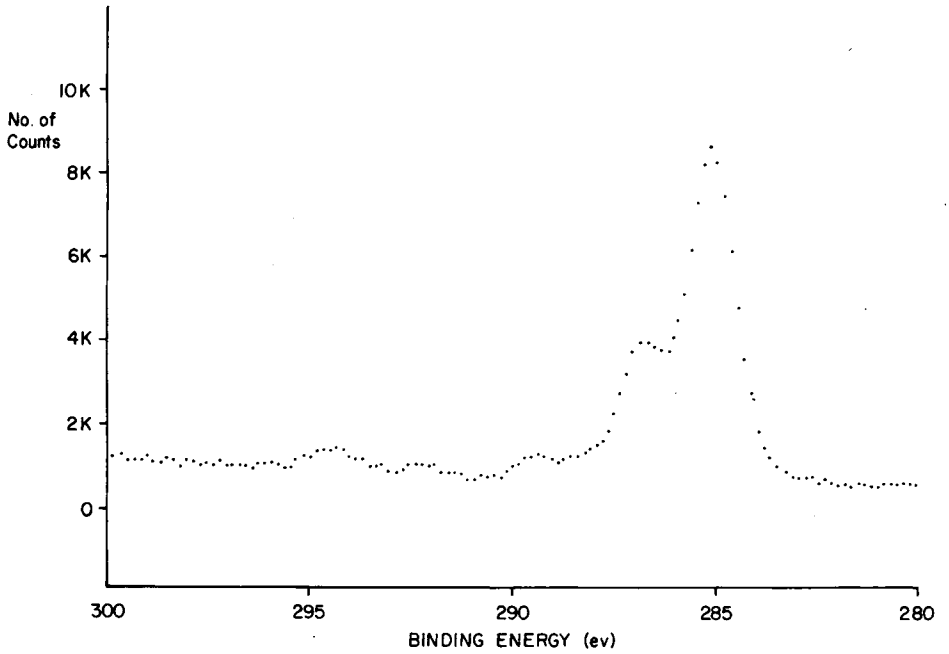

Fig. 8. ESCA C_{1s} spectrum for EMA grafted to Tuftane (film VII): ambient temperature (dehydrated).

periments has sufficient precision to detect chain orientation effects. However, these data do agree in direction, if not in order of magnitude, with what might be expected if such orientation effects were detected. Although it seems that this chain orientation mechanism could explain at least part of the observed effect with the grafted polymers, particularly with respect to changes in higher binding energy carbon peaks in the C_{1s} ESCA spectra, an additional effect must simultaneously be taking place to account for the ~40–50 Å changes that are taking place with some of the polymer systems examined.

It is enlightening to consider the graft penetration effects observed in these experiments in terms of the known properties of the substrate polymers. All grafts were found to cover incompletely the surface of the silicone rubber, which is a polymer highly permeable to many molecules due to its high chain flexibility.[20,21] On the other hand, all grafts were found to dominate the surface composition of the polyethylene substrates. Polyethylene has a significant fraction of its chains tied up in relatively impermeable crystalline regions. Also, the solvents used in the radiation grafting would not be expected to swell the polyethylene enough to allow appreciable graft penetration. The Tuftane polyurethane films would be expected to have a permeability somewhere between polyethylene and silicone rubber to the grafting solvents that were used. For the Tuftane samples, some of the grafts were seen to be covering the surface, while others were apparently interpenetrated with the substrate matrix. The changes noted in these experiments in terms of relative abundance of graft at the surface are summarized in Table IX for the various materials examined.

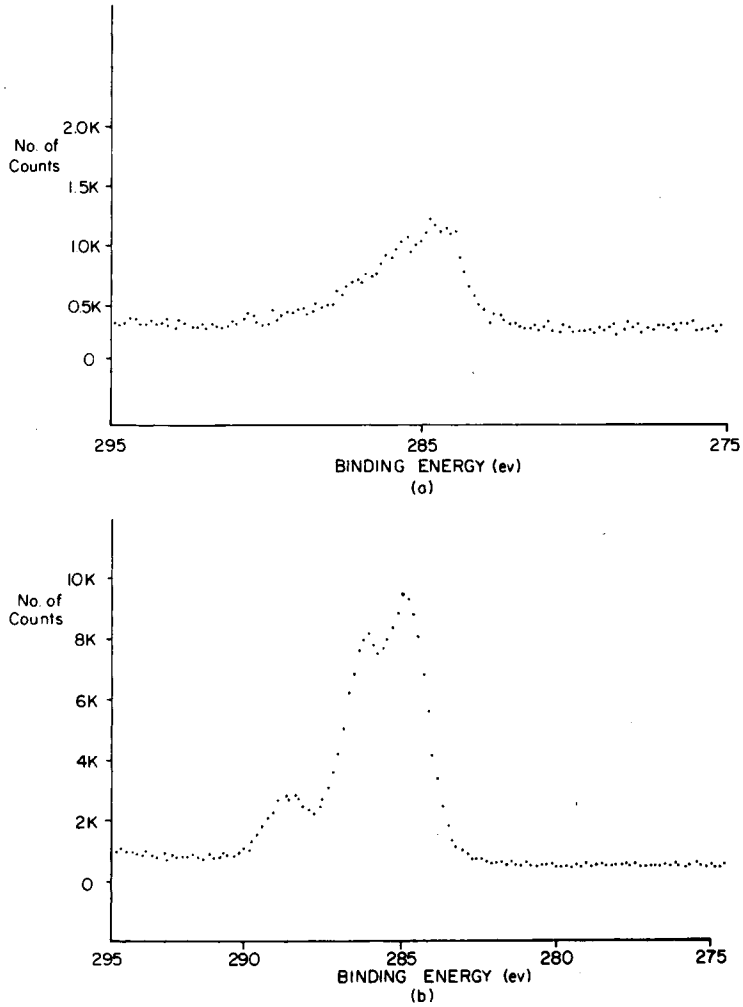

Fig. 9. ESCA C_{1s} spectra for a bulk poly(HEMA)-crosslinked gel: (a) 113°K (hydrated); (b) ambient temperature (dehydrated).

Polyurethane Grafts

Polyurethane polymers and hydrogel-grafted polyurethanes have shown considerable promise as materials for use in medical applications.[22,23] In an ESCA study of polyether-urethanes designed for biomedical applications, Lyman et al.[24] found that for solvent-cast films of these polymers, the side of the film facing the air during preparation differed appreciably from the side of the film in contact with the glass casting surface. This was attributed to different fractions of hard and soft segments exposed at the two sides. The C_{1s} spectra for these polyether-urethanes showed a large peak attributed to aliphatic carbons and carbons bound to nitrogen and a smaller complex peak at a higher binding energy, shouldered into the aliphatic carbon peak, representing the various carbons bound to oxygen. In the experiments reported in this work, only one symmetric peak was seen in the C_{1s} spectrum for Tuftane. A number of explanations are possible for this since the precise structure of the polyester-urethane Tuftane polymer was not know to us. Large aliphatic segments incorporated

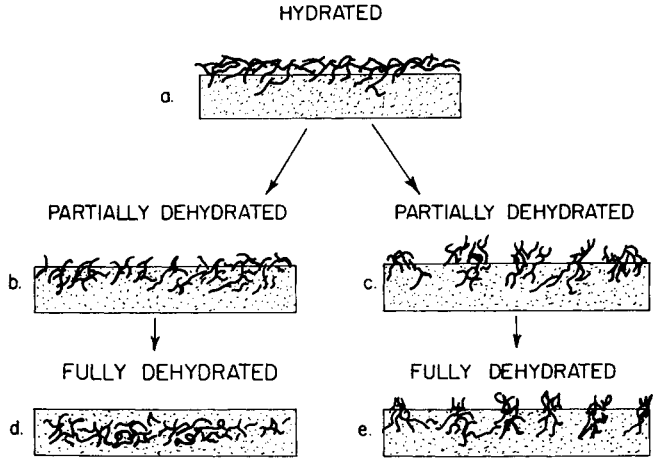

Fig. 10. Schematic representation of models to explain the surface depletion of graft upon dehydration for hydrogels grafted to silicone rubber. Pathway a–b–d: hydrogel graft withdraws below the silicone rubber surface. Pathway a–c–e: hydrogel graft clusters on the surface exposing the silicone rubber substrate.

TABLE IX
Location of Graft[a] for Various Radiation-Grafted Films as Determined by ESCA

Monomer	Silastic		Tuftane		Polyethylene	
	Hydrated	Dehydrated	Hydrated	Dehydrated	Hydrated	Dehydrated
HEMA	S[b]	I[c]	I	S	S	S
Acrylamide	S	I	I	I	S	S
EMA	I	I	—	S	—	—

[a] As determined by the presence of peaks representative of carbon species bound to oxygen.
[b] S = Surface (bulk of the graft located at the surface of the film).
[c] I = Internal (bulk of the graft located 50 Å or more beneath the surface of the film).

into the chain structure and diluting the concentration of carbon atoms bound to oxygen would tend to reduce the intensity of higher binding energy C_{1s} subpeaks. Also, orientation effects similar to those proposed for HEMA gels could be directing the aliphatic structures outward and the polar groups inward into an intermolecularly hydrogen bonded state. Finally, the domain structure of the polymer might be such as to concentrate hard (hydrophobic) segments nearer to the surface. In a survey study of other commercially available polyurethanes, Renathane (Renal Systems Inc., Minneapolis, Minn.) also produced only one symmetric peak in the C_{1s} ESCA spectrum while Pellethane 2363-80A (Upjohn, Inc.) and Tygothane C-210A (Norton Tubing and Molded Products Inc.) showed more complex multiple peak spectra in the C_{1s} region.[25]

Polyurethanes are generally more hydrophilic materials than either silicone rubber or polyethylene. Tuftane will pick up 1.3% H_2O by weight upon equilibration in water. The hydration behavior of this substrate polymer could also be explored further by the ESCA technique in order to help understand the changes occurring in hydrogel grafts on this polymer in the hydrated and dehydrated states.

Biomedical Implications

Certain implications with respect to the use of these radiation-grafted hydrogel materials for biomedical applications can be drawn from this work. If a grafted hydrogel material were implanted in the dehydrated state with the intention of allowing it to swell to equilibrium *in situ,* the organism might initially interact with a very different type of surface from that which was originally intended for the particular application. This is of importance as it has been hypothesized that events which occur in the first few seconds (e.g., protein adsorption) when a foreign material is placed in contact with the body may determine the long-term success or failure of the implant.[26,27] Applications have been described for hydrophilic implants which are inserted *in vivo* in the dehydrated state.[28,29]

It would be of practical value to determine whether hydrogels rehydrate completely reversibly with respect to their surface character and at what rate such rehydration occurs. At the present time, hydrogel devices intended for biomedical applications (e.g., contact lenses, tubing) are shipped in a hydrated state often presenting significant problems with packaging. If rapid reversible hydration with respect to the surface structure could be demonstrated, it would be feasible to package and ship such devices in the dehydrated state. Although evidence for reversible hydration could not be obtained from the present study, ESCA would appear to be an ideal technique for obtaining this information.

CONCLUSIONS

ESCA analyses of the surfaces of radiation-grafted hydrogels have indicated that major changes occur upon dehydration which alter the location of the graft with respect to the surface. These changes can manifest themselves as an increase or decrease in the abundance of the graft within ~50 Å of the surface depending upon the nature of the hydrogel and substrate. Although ESCA elemental ratios must be used cautiously in describing graft distribution because of possible surface orientation of polar groups and intermixing of graft and substrate, in cases where the complete absence or presence of an expected element is observed, positive conclusions can be made as to the location of the graft with respect to the substrate surface regions. The permeability of the substrate to the monomers and/or grafting solvents would appear to be an important variable with respect to the changes that occur in the graft location upon dehydration. Implantation *in vivo* of a dry, radiation-grafted hydrogel should be approached with caution because of the major surface structural differences observed between the hydrated and dehydrated materials.

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