Controlled radiation grafting of N-vinyl pyrrolidone into silicone rubber for biomedical applications

by

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INTRODUCTION

The demand for a suitable small caliber vascular prosthesis in cardiovascular coronary bypass replacements is increasing. At present, vascular surgeons rely on the use of autogenous veins for repair of small internal diameter arterial defects. However, the use of these grafts has limitations such as poor quality (varicosis), limited quantity, or inadequate size of the venous graft. Therefore, a readily available synthetic prosthesis would be the most advantageous to patient and surgeon. Commercially available synthetic polymeric prostheses made from Dacron and expanded polytetrafluoroethylene (EPTFE) frequently fail when the internal diameter is less than 8 mm (Lyman et al., 1977). New developments are necessary to improve the properties of the small diameter vascular grafts so that they will resemble those of the natural artery.

The objective of this investigation was to develop a method to control grafting a thin film in the order of 1 micron or less of N-vinylpyrrolidone (NVP) into the surface of microporous vascular prostheses using irradiation. NVP was chosen for grafting since this monomer is known to be a compound producing a hydrophilic hydrogel of of good biocompatibility (Chapiro et al., 1981). A thin film grafting (or impregnation) was desired since it was intended to preserve the mechanical properties of the microporous vascular implant of porosity and compliance.

Controlled microporosity is important to the success of synthetic small diameter prostheses. The pores act as anchoring facilities for the developing neointima. Decreased compliance has also been implicated as one of the causes of long-term occlusion in small internal diameter vascular replacement (White et al., 1983). Grafts with compliance closely matching the elasticity of the native artery were found to have the highest patency rates. Thus, a microporous, compliant, and improved hydrophilicity vascular prosthesis may have potential in cardiovascular applications as small diameter artificial arteries.

To determine the feasibility of the objective of introducing a thin layer of a copolymer of NVP and silicone rubber tubular prosthesis, NVP was grafted into the inner surface of silicone rubber tubing using Cobalt-60 gamma irradiation and subsequently characterized for rim thickness and grafting yield (%). A formulation of 60% NVP/40% methanol was chosen as the monomer-solvent system since it was known to produce significant graft into the surface of silicone rubber tubes (Lee, 1988). To achieve a thin graft layer, grafting was studied using various irradiation doses, especially low irradiation doses such as 25 and 30 KiloRoentgen (Krad). The location and extent of the grafted layer (or grafted front) was determined by staining the grafted tubes with 0.1% acid fuchsin or 0.1% basic fuchsin aqueous dye solutions in which the concentration of methanol was varied from 10% to 100%. In addition, an iodine staining technique was also used to identify the graft depth and different grafted zones throughout the wall of the silicone rubber tube. The graft depth was measured using optical microscopy and verified by scanning electron microscopy.

REVIEW OF LITERATURE

Influence of Porosity on the Patency of Microvascular Prostheses

Porosity is an essential component for long-term function of small internal diameter synthetic microporous vascular prostheses. Porosity is required for extensive healing if it provides luminal blood contact surfaces for ingrowth of periprosthetic tissues. Porosity may be required for transfer of fluid and ions in prostheses even if tissue ingrowth does not occur (Wesolowski et al., 1961).

Pore diameter is known to affect patency rate. Pores must be small enough to limit transprosthetic hemorrhage and to prevent periprosthetic hematoma, but must be large enough to allow tissue ingrowth (Hiratzka et al., 1979). Campbell et al. (1975) studied expanded polytetrafluoroethylene (EPTFE) in dogs, and found 88% patency when the pore size averaged 22 microns or less, compared to 53% when pore size averaged 34 microns or greater. Tizian et al. (1982), in a study of replamineform silicone rubber tubes implanted in the rat abdominal aorta, used 12 microns as the "optimal" pore size, for a pore density of 50%. Their results indicated that an early patency rate of 88% was obtained. This suggests that smaller pore sizes are more desirable than larger pore sizes in terms of periprosthetic tissue ingrowth.

Porosity was also found to correlate with the thickness of the developed neointima since the pores act as anchoring facilities for the developing neointima (Didisheim et al., 1984; Hess et al., 1984). Hess et al. (1984) stated that a continuous lining of vascular graft with a thin neointima is only achieved if the cell invading the prostheses from the anastomotic areas can anchor their cytoplasmic protrusions onto an appropriately inner surface structure. If these anchoring facilities are not provided, (1) the unattached neointima will thicken, interfering with the patency of these microvascular prostheses, or (2) the neointima may fragment, or (3) mural thrombi may constantly strip off and embolize.

Silicone Rubber

Medical-grade silicone rubber is one of the most widely used biomaterials. Typical formulations of this material include the base polymer polydimethylsiloxane (PDMS), a filler such as silica, residues of the crosslinking agent (e.g., an organic peroxide) and various compounds to aid in processing (Braley, 1970). Silicone rubber is very stable with regard to attack by liquids with which they come in contact. The rubber does have an affinity for certain organic solvents such as acetone, chloroform, and toluene which causes it to swell (Noort and Black, 1981). Swelling solvents can also extract leachable components from silicone rubbers. For example, an average weight loss of 1.8% was reported when silicone rubber was washed with a 1:1 mixture of acetone and methanol (Lee, 1988).

Poly(N-vinyl-2-pyrrolidone)

Poly(N-vinyl-2-pyrrolidone) (PNVP), in its uncrosslinked form, is a water-soluble polymer which is physiologically acceptable for use in animal and humans (Siggia, 1957). Because of its strong interaction with water, it can be used for preparing gels which will exhibit high water content (Ratner and Hoffman, 1976).

PNVP gels are also of interest for biomedical applications as this water soluble polymer has had a long history of use in the medical and pharmaceutical fields. One of the most important uses for PNVP solutions has been as a plasma expander (Jenkins et al., 1956). When infused intravenously, PNVP is non-toxic and nonthrombogenic and can be used to maintain circulatory fluid volume in cases of severe injury or trauma. However, at the present time PNVP is no longer used as a plasma expander in humans because it is not metabolized and is not retained in circulation as well as other plasma expanders (e.g., Dextrans) (Ratner and Hoffman, 1976).

Homogeneous PNVP has not often been described in the biomedical literature possibly because high concentrations of crosslinker (5-20%) are needed to produce a material with useful mechanical properties (Ratner and Hoffman, 1976). The difficulties involved in preparing homogeneous PNVP materials make N-vinylpyrrolidone (NVP) an ideal monomer for use in covalent surface grafting systems, especially radiation grafting of NVP onto a suitable trunk polymer.

Radiation Grafting of N-vinylpyrrolidone

Radiation grafting is a useful technique for preparing special products for biomedical applications. Radiation grafted hydrogels on strong supports have offered a unique approach for combining the advantages of the hydrophilic gel interface with the strength of the hydrophobic support material (Ratner and Hoffman, 1976; Chapiro et al., 1980). By using radiation to prepare a grafted hydrogel, the addition of an initiator is not necessary, thereby eliminating one potential source of contamination in the final product.

Radiation grafting of N-vinylpyrrolidone (NVP) into a polymeric support using irradiation has been carried out by many investigators. Table 1 summarizes NVP grafting techniques and investigators.

The earliest application of radiation polymerization techniques to the preparation of materials for biomedical applications was carried out by Yasuda and Refojo (Yasuda and Refojo, 1964). They studied the grafting of vinylpyrrolidone into sheets of polydimethyl siloxane using high-energy electrons. The grafting reaction was promoted by the presence of water, but water decreased the depth of monomer penetration into the sheet. To determine the depth of penetration, the grafted sheet was stained with dyes (such as eosin) which are known to be suitable for staining proteins. The water content of the grafting solution and the radiation dose determined whether the grafting took place on the surface only, or was homogeneous throughout the sheet. The hydrophilicity of the grafted product increased as the amount of N-vinylpyrrolidone (NVP) grafting increased.

TABLE 1. Grafting methods of NVP into silicone rubber

Author(s)	Method
Vale and Greer, 1982	Radiation polymerization was carried out by suspending the strips of silicone rubber (1 x 4 x .05 cm) in Pyrex® test tubes, bubbling nitrogen gas through the solution for 30 minutes to reduce the oxygen content, adding monomer solution of interest and delivering 0.25 Mrad (mega Roentgen absorbed dose) of gamma irradiation from a Cobalt-60 source.
Chapiro et al., 1980	NVP was grafted by the direct radiation method into silicone rubber tubes with inner diameter of 2, 3, and 4 mm and a wall thickness of 1 mm. Prior to grafting, the tubes were extracted for 24 hours in boiling methanol; they were dried in vacuo and kept in a closed vessel. Pyrex® vessel containing silicone rubber tubes, ca. 3 cm long and proper reaction mixtures (NVP, NVP/toluene, NVP/methanol) were sealed under vacuum and exposed for various times to gamma radiation. Irradiation was carried out at 20°C or in an oil-bath at higher temperatures. The dose rate was varied between 14 and 1300 rad per minute.
Ratner and Hoffman, 1975	The Silastic® films were suspended in monomer solutions without removal of air, and irradiated at room temperature using a 20,000 curie Cobalt-60 source. The radiation dose used in all cases was 0.25 Mrad.
Ratner and Hoffman, 1974	The Silastic® films were suspended in monomer-aqueous cupric nitrate solutions without removal of air, and irradiated at room temperature using a 20,000 curie Cobalt-60 source. The radiation dose used in all cases was 0.25 Mrad. Cupric nitrate concentration was varied from 0.001 molar (M) to 0.005 M.
Hoffman et al., 1972	Silicone rubber films (5 mil, type 500-1 non-reinforced Silastic® sheets) 3/4" x 1-1/2" were immersed in the monomer solutions in special reaction vessel, evacuated to remove oxygen, and irradiated at room temperature in a 20,000 curie Cobalt-60 source for 67 minutes to deliver a dose of 0.25 Mrad.

TABLE 1. Continued

Author(s)	Method
Yasuda and Refojo, 1964	The graft copolymerization was carried out in Pyrex® test tubes; the films (1.5 x 10 cm and 0.005 or 0.003" in thickness) and solvent monomer mixtures were degassed by repeating freezing and thawing cycles (three times), and then sealed under vacuum. The amount of the monomer in the sealed tubes was just enough to cover the silicone rubber sheets when the sealed tubes were laid down horizontally. The irradiation was carried out at 25°C using 3 million electron volts (Mev) generated by a Van der Graaf generator. The dose given on each pass was 1.5 Mrad.

In irradiation grafting, it is possible to graft a monomer onto suitable trunk polymer to a desired thickness by varying of experimental conditions such as the monomer concentration, radiation dose, dose rate, type of solvents, pre-swelling time, irradiation temperature, and the use of selective inhibitors. Chapiro et al. (1973) prepared nonionizable, hydrophilic membranes by radiation grafting of NVP into polytetrafluoroethylene films. They found that it was necessary to use aromatic solvent such as pyridine or benzene for the grafting of NVP due to the fact that these solvents have a low free radical G(R*) value. The G(R*) is defined as the number of radicals formed per 100 electron volts (ev) absorbed. The kinetics of the reaction were influenced by the grafting parameters such as temperature, dose, dose rate, and concentration of monomer. The rate of grafting was found highest for monomer concentrations of 60 to 70 percent. Their results also showed that the grafting process was complicated by the high viscosity of the reaction medium due to the "gel effect", and by the fact that the rate of diffusion of monomer into the films may become the controlling factor. The rate of homopolymerization of NVP in benzene and pyridine was reduced possibly because these solvents acted as a "protection barrier" on the monomer by reducing its radiolysis (radical yield) through energy transfer. This effect, coupled with a low $G(R^*)$ value, might have allowed the penetration of monomer into the center of the films before polymerization occurred. The swelling of the resulting membranes in various solvents was also studied. It was found that the equilibrium swelling depended on the composition of the film, but for a given composition, the equilibrium swelling in water also depended on the grafting conditions. In methanol and water, the equilibrium swelling was obtained in less than one minute.

The direct grafting of NVP onto silicone rubber tubes was carried out by the same authors in an effort to find a nontoxic polymer which could be useful in contact with blood for a long period of time (Chapiro et al., 1980). The reaction was carried out in bulk, in methanol, and in toluene solutions. Pyrex® vessels containing silicone rubber tubes (approximately 3 cm long) and the proper reaction mixtures were sealed under vacuum and exposed for various times to gamma radiation. For grafting in bulk, the irradiation of the swollen tubes in an excess of pure NVP monomer resulted in grafting curves which exhibit an auto-accelerated process (high reaction rate at early stage of the grafting process). Plots of the logarithm of weight increase of the tube versus irradiation showed a linear relationship. The resulting straight lines have a slope ("auto-acceleration index") of 2 which means that the conversion (yield) curves were initially proportional to the square of the time. Grafting was accompanied by vigorous homopolymerization, and after some time, the monomer around the tubes was converted to a viscous "gel". At this stage the grafting process suddenly slowed down, due to a lack of supply of monomer to the tube. In the initial auto-accelerated portion of the reaction, the instantaneous rate for grafting between 5-6% was proportional to the 0.85 power of the absorbed dose rate ($I^{.85}$).

Grafting in various solutions (with methanol or toluene as solvent) showed similar trends. However, in methanol solutions the swelling of the silicone rubber tubes was very small, and the grafting did not proceed homogeneously. In contrast, toluene favored the swelling of the samples, and the use of toluene led to more homogeneous grafting conditions. The kinetics of grafting in solution was also changed. Grafting seemed to be retarded when the concentration of NVP in toluene was decreased. Temperature was found to have little effect on the grafting rate. This influence is usually expected for a reaction proceeding in a highly viscous medium where chain termination is likely to become diffusion controlled ("gel effect").

Grafted silicone rubber tubes in 70% solutions of toluene were implanted into the carotid arteries of 6-month-old lambs for periods of 3 and 7 days (Chapiro et al., 1980). Their results showed that for a period of 3 days, a grafting ratio of 24-27% produced a significant improvement of the behavior of the implants. For a period of 7 days, significant improvement of blood compatibility was only observed for samples having a grafting yield in excess of 33%. However, silicone rubber tubes grafted to a level of 33% or more became very stiff in their dry state even though they would swell in water (Chapiro et al., 1981). In order to have a high hydrogel content without altering the bulk properties of the silicone rubber, these researchers carried out the grafting of the tubes in dilute aqueous solutions of NVP. In some cases, the samples were not allowed to swell prior to irradiation. Under these conditions, only the surfaces of the tubes were grafted with NVP (Chapiro et al., 1982). A series of tubes a with surface grafting ratio of approximately 60 percent were obtained in which the thickness of the grafted layer was 100 to 300 microns. In vivo implantation tests in lambs showed significant a improvement in thromboresistance of the silicone rubber tubes grafted with a hydrogel of poly(N-vinylpyrrolidone) (PNVP).

A number of variables affecting the radiation graft polymerization of NVP, and NVP with another monomer into silicone rubber substrates, have been explored by Hoffman, Ratner and coworkers (Hoffman et al., 1972; Ratner and Hoffman, 1974; Khaw et al., 1976). They found that the extent of grafting, the water content, and porosity of the hydrogel can be readily controlled by changes in composition of the grafting solution. The penetration of the hydrogel coating into the support may also be controlled by the use of selected solvents during the grafting step. Ratner and Hoffman (1975) observed that in a system consisting of hydroxyethyl methacrylate (HEMA) and NVP in water, NVP entered into the graft much more rapidly than for that seen using methanolic solvent systems. They believed that in systems containing mostly water, NVP may preferentially partition itself into the silicone rubber phase. On the other hand, in predominantly methanolic systems, the NVP may be more soluble in the external solution. They also observed, however, when NVP was used, the hydrogel can be deposited into the surface rather than as a layer onto the surface. The grafting behavior for a given monomer composition was seen to be highly solvent dependent. By varying the volume percent methanol in the solvent, various levels of graft were achieved. The methanol in this case can be thought of as an inhibitor for the gel formation. At intermediate methanol concentration, there was no gel formed. However, methanol also seemed to be an inhibitor of the polymerization for the system studied. According to Ratner and Hoffman, as the methanol concentration increased beyond a certain point (e.g., $> 60\%$ by volume), a decreasing degree of graft was seen.

The use of a metal salt such as $Cu(NO_3)_2$ or $Fe(NO_3)_3$ in the aqueous monomer solutions permitted more grafting with less homopolymer formation; this resulted in a greater ease of removing ungrafted polymer since the remaining polymer solution was a liquid after irradiation. Ratner and Hoffman (1974) studied radiation grafting systems containing cupric ion, NVP, and other hydrophilic monomers. It was found that such systems, in certain cupric concentration ranges, were capable of producing extremely high levels of graft (a graft level as high as 18 mg/cm^2 was reported) on silicone rubber and other polymers. This was due to complete inhibition of gelation of the homopolymer surrounding the grafted substrate due to the presence of cupric salts, and thus allowed more grafting to occur. The concentration of hydrogel at the surface changed as a function of cupric ion concentration. At higher Cu^{++} concentration, grafting occurred mainly within the silicone rubber matrix while at low concentration grafting took place mainly on the surface. They have postulated that at a certain copper concentration at which grafting could no longer occur on the surface due to complete inhibition of polymerization, grafting might preferentially take place within the silicone rubber where the copper concentration would be expected to be lower. In terms of equilibrium swelling, it has been determined that hydroxyethyl methacrylate (HEMA) monomer does not significantly swell the silicone rubber. NVP monomer, however, will swell silicone rubber to a small degree (~3%). In the presence of NVP, the silicone rubber matrix was assumed to open somewhat to allow further monomer penetration and internal grafting. According to Ratner and Hoffman, the Cu^{++}/NVP system allowed many monomers which would ordinarily graft only with great difficulty to be readily grafted to polymer surfaces. It also allowed control over a number of graft parameters such as graft water content, graft composition, and degree of penetration. However, the use of cupric salts could inhibit grafting in a superficial layer approximately 50 microns from the surface of the polymer (Chapiro and Lamothe, 1983). This suggests that if a thin film grafting on the surface of the trunk polymer is desired, the use of a metal salt such as copper nitrate should be avoided.

Blood compatibility of radiation grafted HEMA and NVP/silicone rubber surfaces was evaluated using vena cava ring tests. The tests indicated a greater thromboresistance of the hydrogel grafted surfaces compared to the nongrafted silicone rubber surfaces. However, results of baboon arteriovenous shunt tests and canine renal embolus ring tests did not support the "water content-blood compatibility" relationship which has been suggested for hydrogels (Ratner and Hoffman, 1975). These results indicated that high water content hydrogels tended to cause more damage to the flowing blood than lower water content gels due to significant microembolization (Ratner et al., 1979).

Radiation-induced modification of polyetherurethane tubes using NVP and other hydrophilic monomers (HEMA, acrylamide) using the "preswelling technique" in order to create a more blood compatible polymer surface was investigated by Jansen (1984). With this procedure, graft copolymers with different penetration depths of the graft component in the trunk polymer could be obtained, leading to different surface properties of the grafted substrates. It was found that by varying the preswelling time in monomer or the irradiation dose, the grafting yield and the surface properties could be controlled. Grafting of polyetherurethane tubes with NVP/water-solutions of different concentration resulted in grafted products whose grafting yield (and thus their surface hydrophilicity) depended on the concentration of NVP in the monomer solution. With pure NVP, the highest grafting yield and the highest surface hydrophilicity was observed. However, a great disadvantage of this system is that NVP is a good solvent for polyurethane, so that only grafting with low concentrations of NVP resulted in products with acceptable mechanical properties. It was also found that tubes with grafting yields below 5 mg/cm^2 have almost the same mechanical properties as the ungrafted ones when tested in their water-swollen state.

According to Jansen, the diffusion coefficient of the solvents rules the penetration depth of the graft. Therefore, by using the appropriate solvent (i.e., with a low or a high diffusion coefficient) and by controlling the grafting parameters, it is possible to obtain either surface grafting or bulk grafted substrates (Jansen and Ellinghorst, 1985). They concluded that if grafted substrates with mechanical properties close to those of the trunk polymer are required, grafting yield must be kept as low as possible.

Lee (1988) investigated the radiation grafting of NVP in various solvents (methanol, water, and toluene) into the inside surface of silicone rubber tubes. Only the formulations with high concentration of NVP (60% or greater by volume) in methanol were able to produce significant grafts. The graft concentrations ranging from 0.6 to 19.3 mg/cm^2, and graft thicknesses (graft penetration depth) of 2 to 350 microns were reported.

Graft Polymer Extraction

Graft polymers must be thoroughly extracted as part of their preparation in order to remove unreacted monomer, low molecular weight polymers, and other leachable components which could result in undesirable reactions after implantation if they are still present. The extraction solvents should be poor solvents for the trunk polymer and the grafted hydrogel, but should be good solvents for the unreacted monomer and low molecular weight polymers. Table 2 lists various extraction methods used to remove unreacted NVP from grafted polymers in the post irradiation process.

TABLE 2. Graft polymers extraction methods

Author(s)	Grafting system	Method
Yasuda and Refojo, 1964	NVP into silicone rubber sheets	Washed with distilled water then extracted with water in a Soxhlet extractor for 3 days
Hoffman et al., 1972	NVP into silicone rubber films	Washed for 24 hrs in acetone, 24 hrs in acetone/water (1:1) and 48 hrs in water
Ratner and Hoffman, 1974; 1975	NVP/HEMA into Silastic® films	Rubbed vigorously with a sponge soaked in acetone-water (1:1), agitated for 2 hours in acetone/water (1:1) and stored in water
Chapiro et al., 1973	NVP into polytetrafluoroethylene	24 hrs in distilled water
Chapiro et al., 1980	NVP into silicone rubber	48 hrs in boiling ethanol
Chapiro et al., 1982	NVP into silicone rubber	48 hrs in boiling methanol (MeOH)
Vale and Greer, 1982	NVP/HEMA into silicone rubber sheets	ethanol/water (50/50)
Jansen, 1984	NVP into polyetherurethane	ethanol/water and pure water

Staining of Poly(N-vinylpyrrolidone)

Poly(N-vinylpyrrolidone) (PNVP) tends to bind various substances such as drugs, dye stuffs, etc., just as does serum albumins (Oster and Immergut, 1954). PNVP was found to combine strongly with anionic dyes of the fluorescein family. The binding increases with increasing number and polarizability of the substituted halogens on the dye molecules (Oster, 1952). Similar binding properties have been observed for the native serum albumin (Klotz et al., 1946). Anionic dyes such as acid fuchsin and eosin were found to bind very strongly to proteins (Gurr, 1971). On the other hand, cationic dyes such as basic fuchsin, was used for grading acidic elements of cells and tissues in microscopic specimens of biological (mammalian) materials (Gurr, 1971).

Due to the ability of PNVP to absorb low-molecular weight cosolutes such as dye stuffs, the increase in thickness of the grafted polymer substrate, and the penetration of the grafted front can be visualized by a staining technique. The use of such techniques has been reported in literature (Yasuda and Refojo, 1964; Chapiro et al., 1982). Yasuda and Refojo (1964) used an eosin solution (5 gm eosin in 150 ml. water and 50 ml. 95% ethanol) to determine the percent of penetration based on the thickness of the grafted silicone rubber sheets. The samples were stained in an eosin solution for 15 hours and washed in distilled water for 2 hours before the depth of penetration was measured. Chapiro and Lamothe (1983) used a 0.1% solution of fuchsin in methanol to study the grafted depth of NVP in polyurethane tubes. Cross sections (200-300 microns thick) were immersed in the dye solution for 48 hours, rinsed with methanol, and observations were made. The staining technique is a quick, simple way to characterize the depth of the grafted layers, and it can be carried out in most laboratories.

Poly(N-vinylpyrrolidone)-Iodine

Poly(N-Vinylpyrrolidone) (PNVP) has the ability to bind iodine. The PNVP-Iodine (PNVP-I) resulting from this combination is quite stable to storage since the iodine vapor pressure is reduced essentially to zero, and the PNVP-I "complex" is also quite stable chemically (Siggia, 1957). PNVP-I complex can be prepared by incorporating iodine into PNVP in an aqueous solution of iodine/potassium iodide (e.g., 0.05 molar (M) KI/ 0.002 M I_2) (Eliassaf, 1966) or by simply mixing PNVP with crystalline iodine (Cournoyer and Siggia, 1974). In a nonsolvent preparation, the iodine in the PNVP-I complex probably exists in three forms: iodide, hypoiodide, and iodine (Cournoyer and Siggia, 1974). The formation of the complex is thought to involve the production of iodide and hypoiodide ionic species by iodine hydrolysis, and the association of these ionic species with iodine to give the final stable PNVP-I complex. The hydrolysis of iodine can be written as follows:

$$I_2 + H_2O \rightleftharpoons IO^- + I^- + 2H^+$$

On the other hand, in solution preparations of the complex, when the ionic iodine is already present, the driving force for the hydrolysis is absent and the tri-iodide ions may be the binding species (Eliassaf, 1966).

Since PNVP can interact with molecular iodine, the grafted front of NVP in silicone rubber substrates can be visualized by incorporating iodine into PNVP in a potassium iodide solution, and measuring the penetration using optical microscopy. Eliassaf (1966) studied the interaction of PNVP with iodine in various aqueous potassium iodide/ iodine (KI/I_2) solutions with concentrations varying from 0.05 M to 0.2 M for KI and from 0.0015 to 0.0025 M for I_2. He found that the binding capacity of PNVP for iodine increases with the molecular weight of the polymer. Using this characteristic, various grafting zones throughout the thickness of a polymer substrate can be determined visually. Furthermore, by complexing PNVP with iodine, grafting profiles into a polymer matrix can be studied using an electron microanalyzer. X-rays due to electron beam excitation are emitted by the heavy atoms (iodine) which complex with the NVP groups (Chapiro and Lamothe, 1983). The grafting profiles of NVP in polyurethane tubes were study by Chapiro and Lamothe (1983) using an electron microprobe. Cross sections of the grafted tubes about 200-300 microns thick were immersed in a 1:1 ratio of Lugol solution/acetic acid-sodium acetate solution (Lugol solution: 2 gm KI, 1 gm I_2, and 200 ml. water; acetic acid-sodium acetate : 0.5 mole each in 1 liter of distilled water) for 1 week. The Lugol solution was used because the iodine in this solution is more stable to light. After drying, the grafting profiles were determined using the L-alpha X-rays characteristic of the iodine. The results were then used to determine the graft levels by correlating with X-ray's signal strength with known graft standards (homogeneous grafted samples that were determined by gravimetric analysis and electron microanalyzer).

RADIATION INDUCED GRAFTING

The Direct Radiation Grafting Technique

In this method, the polymer A is irradiated in the presence of a monomer B. Thus, the polymeric radicals generated from polymer A are directly used to initiate the polymerization of monomer B (Chapiro, 1962). Under these conditions, the following reactions take place.

Polymer A, P_A -----> P_A* + $R*$

where P_A* is a macroradical and R* is a radical fragment such as H*, Cl*, or CH_3* for example.

P_A* + monomer B -------> P_A-P_B graft copolymer

R* can extract a hydrogen or other atom from polymer A leading to a fresh site for grafting, and a volatile fragment is released (such as hydrogen). Alternatively, the homopolymer B_n arises from initiation by small fragments of the polymer molecule R* and also by radical resulting from the radiolysis of monomer B:

B -----> R* --+nB---> B_n

Eventually the growing graft or homopolymer chains terminate either by combination or disproportionation (forming two separate polymers).

To optimize the formation of graft copolymer with a minimum of contaminating homopolymer, there are a number of conditions which need to be met. Most importantly, the yield of radicals from the radiolysis (radical yield by radiation) of the polymer must be, as much as possible, in excess of that from the monomer (Chapiro, 1962).

Several methods can be used to minimize the formation of homopolymer:

(a) a free radical inhibitor such as $Cu(NO_3)_2$ or $Fe(NO_3)_3$

could be added to the monomer (Ratner and Hoffman, 1974).

(b) grafting can be carried out with monomer vapor instead of liquid monomer (Takamatsu and Shinohara, 1966).

(c) the concentration of monomer in the grafting solution can be kept to a minimum. For example, the use of monomer swollen polymer A with monomer B is practicable, and is a good method for optimizing grafting (Chapiro, 1962).

An advantage of the direct grafting method is that most monomers act as radiation protectors reducing any degradation of the trunk polymer by the radiation itself (Chapiro, 1962).

Theoretical Considerations in Radiation Grafting

Under irradiation at room temperature, the polymerization observed in most conventional monomers follows the kinetics of the normal free radical process. The rates usually obey the square root law with respect to radiation dose-rate (Grafting rate = $K*I^{0.5}$, where K is a constant and I = dose rate) (Chapiro, 1962). However, a number of specific features result from reaction conditions which prevail in most grafting systems.

The gel effect

Since graft copolymerization usually involves the polymerization of a monomer in a polymeric medium, the initial system (polymer) exhibits a high viscosity which favors the presence of the "gel effect". This effect primarily results from a slowing down of the termination step owing to the lack of mobility of the growing chains (Chapiro, 1962). The features associated with this effect are due to the nonsteady state conditions which then arise in the system; these include auto-accelerated conversion curves, increased molecular weight, and reaction order with respect to the rate of initiation of between 0.5 and 1.0.

Effect of dose rate

In the direct grafting method, the number of branches formed and their lengths are influenced by the dose and dose rate, respectively. The number of radicals formed is determined directly by the size of the dose and G(R*) value, which is the number of radical formed per 100 eV absorbed (Chapiro, 1962). The dose rate, which evidently determines the rate of initiation of polymerization, will therefore affect the kinetic chain length and consequently the length of the grafted branches. The length of the branches also depends on the concentration of monomer, the reaction temperature, and the viscosity of the reaction medium.

Chain transfer

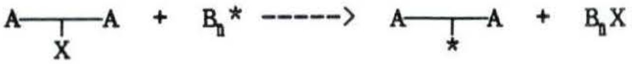
The chain transfer reaction is a very important process in all graft copolymerization. If the monomer or solvent has a high transfer constant (reactivity of free radicals), additional homopolymer will be produced through transfer to monomer or solvent as follow:

$$\underset{\substack{|\\B}}{A\text{---}A} + SX \text{ -----> } \underset{\substack{|\\BX}}{A\text{---}A} + S^* \qquad (1)$$

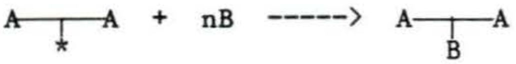
$$S^* + nB \text{ -----> } SB_n \qquad (2)$$

Here SX is the monomer or solvent or any other added substance which transfers readily. It is clear that chain transfer tends to reduce the grafting efficiency.

However, if chain transfer occurs mainly toward the trunk polymer, each polymeric radical will form several grafted branches. This reaction reduces the length of the grafted branches, but does not change the grafting yield (Chapiro, 1962). In most general terms, when a monomer is polymerized in the presence of a polymer, chain transfer to the polymer will take place to some extent and this leads to the formation of some graft copolymer as follows:



$$\underset{X}{A\text{—}\!\text{—}A} + B_n^{*} \text{ -----}> \underset{*}{A\text{—}\!\text{—}A} + B_nX \qquad (3)$$



$$\underset{*}{A\text{—}\!\text{—}A} + nB \text{ -----}> \underset{B}{A\text{—}\!\text{—}A} \qquad (4)$$

The chain transfer process can increase the overall grafting efficiency significantly, particularly when the polymer has a higher transfer constant with respect to the monomer under consideration. Grafting at high temperature tends to favor the chain transfer process in many grafting systems.

The termination step

Due to the high viscosity of the reaction medium in most graft copolymerization reactions, the termination step may become difficult or essentially impossible to occur (Chapiro, 1962). As a result, many growing chains remain unterminated and remain trapped at the end of the grafting process. Such a behavior is expected for all polymerizing systems which exhibit the "gel effect".

The action of the termination step in causing possible crosslinking of the trunk polymer should be mentioned. For example, the termination of the polymerization of monomer B can occur through the combination of two growing chains of polymer A_n linked by a chain of polymer B_n.

For high conversion, such a process could lead to a three-dimensional network in which all chains of A_n are crosslinked by chains of B_n. This would be true if B is a polyfunctional monomer (functionality greater than or equal 2) (Chapiro, 1962).

The diffusion effect

In many grafting systems, the reaction occurs in a polymer A_n swollen to a limited extent with a monomer B. Under this condition, the grafting ratio cannot exceed a limiting value which corresponds to the initial content of monomer B in polymer A_n, since the instantaneous concentration of the monomer tends to drop during the grafting process (Chapiro, 1962).

A higher degree of grafting can be achieved by immersing the polymer A_n in an excess of monomer B. In such a process, the monomer continuously diffuses into the swollen substrate and the reaction can proceed to much higher grafting ratios. However, if the rate of graft polymerization is comparable to, or exceeds, the diffusion rate of the monomer B into polymer A_n, the grafting rate is governed by the diffusion rate of the monomer.

Factors that would cause diffusion to limit grafting rate are the following:

(1) Low intrinsic diffusion constant in the solid polymeric substrate.
(2) Low temperature (causing a decreased diffusion constant).
(3) High intrinsic grafting rate.
(4) High dose rate (causing high grafting rate).

Factors 3 and 4 cause rapid consumption of monomer within the substrate, whereas factors 1 and 2 control the speed with which fresh monomer can get into the trunk polymer.

On the other hand, factors that tend to eliminate the effect of diffusion on grafting rate are the following:

(1) High intrinsic diffusion constant in the solid polymeric substrate.
(2) High temperature (causing an increased diffusion constant).
(3) Low intrinsic grafting rate.
(4) Low dose rate (causing low grafting rate).

Influence of added substances

In radiation grafting, the "gel effect" may either be reduced or enhanced by the addition of appropriate solvents. Chain transfer to the added substance will usually increase the amount of homopolymer formed in the grafting process. In the direct grafting process, homopolymerization can also be initiated by the radiolysis of the added substance. On the other hand, the addition of a metal salt such as $Cu(NO_3)_2$ or $Fe(NO_3)_3$ may reduce homopolymerization without affecting the grafting process too much (Chapiro, 1962).

The influence of solvents on the diffusion effects is much more complex. Generally, a good solvent or swelling solvent will favor the diffusion of monomer into the polymer, while a poor swelling solvent will have little effect on the polymer. The solvent may also dilute the monomer and keep it in the solution, thus reducing the grafting yield.

MATERIALS AND METHODS

The grafting procedures used in this project have been modified from other radiation initiated polymerization procedures reported in literature (Table 1). Grafting of N-vinylpyrrolidone was carried out using the direct radiation method, and mostly in the absence of air.

Using previously reported calibration results for the Iowa State University Cobalt-60 irradiation facility (Lee, 1988), the length of the silicone rubber tubes as well as the center of the radiation field for the Cobalt-60 unit were determined. This was designed to optimize the grafting efficiency for segments of the tubing in terms of repeatability of experiments.

The principal formulation used was 60% NVP/40% methanol (except as otherwise indicated). This formulation was found to produce significant grafting within an acceptable range and looked promising for studies to determine ways to achieve a thin rim (Lee, 1988).

Preparation of Base Polymers

Silicone rubber sheets

Silicone rubber films[1], 1.9 cm x 3.8 cm x 0.01" thick were boiled for three 1-hour periods in 2% aqueous sodium bicarbonate solution in order to clean the surface. They were then rinsed in warm distilled water (3 times), dried briefly (10 minutes) in an oven at temperature about 100 ^{0}C, and subsequently stored in a desiccator over Drierite® ($CaSO_4$) prior to use.

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[1] Silastic®, Type 500-3, Dow Corning Corp., Midland, MI.

Silicone rubber tubes

Eight to nine cm sections of nonreinforced Silastic® tubing[2], 0.125" OD x 0.078" ID x 0.024" wall thickness, were cleaned using an identical cleaning procedure as that for the silicone rubber sheets. They were dried in an oven at temperature of approximately 100°C for about 10 minutes and were stored in a desiccator over Drierite® overnight. Selected samples for grafting were sealed at one end with medical-grade silicone adhesive type A[3] and the sealant allowed to cure at room temperature for at least 24 hours. These tubes were then used for radiation grafting experiments.

Grafting Procedures

Grafting on Silastic® sheets

Prior to irradiation, the initial weight of each silicone rubber sheet (W_S) was determined. An individual silicone rubber sheet was placed inside a Pyrex® test tube (15 cm long). A string was used to keep the silicone rubber sheet in the desired position, which was about 4 cm from the bottom of the test tube (so that the sample would be at the center of the radiation field during irradiation).

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[2] Dow Corning Corp., Midland, MI, Lot HH127067.

[3] Dow Corning Corp., Midland, MI, Lot HH058742.

The following preparation was performed inside a nitrogen filled bag. N-vinylpyrrolidone (NVP[4]) and methanol liquids were individually deoxygenated by bubbling with nitrogen gas for at least 30 minutes. An appropriate amount of NVP and methanol to produce a 60% NVP/40% methanol formulation by volume was pipetted into a 25 ml flask. The monomer solution was then bubbled with nitrogen for a few more minutes to insure good mixing. The test tube with the silicone rubber sheet was flushed with nitrogen and then the test tube was filled with monomer solution so that the sheet was completely immersed inside the monomer solution (60% NVP/40% methanol). The test tube was again flushed with nitrogen and sealed with Teflon tape on the threads to insure an air-tight fit. All sheet samples were prepared in a similar manner. The test tubes containing the samples were then placed in a nitrogen purged desiccator (containing Drierite®) and transported to the Nuclear Engineering Laboratory for irradiation. Samples were irradiated within 3 to 4 hours after preparation.

Irradiation was performed at room temperature using a 360 Curie Cobalt-60 source at a dose rate of about 241,000 rad/hr. The center of the test tube was positioned at the center of the radiation field of the Cobalt-60 unit (105.1 cm depth). Each sample was given one of the following doses: 50, 150, and 250 Krad.

After irradiation, the sheets were removed from the test tubes and extracted with an ethanol-water (1:1) mixture for 2 hours (3 changes during this period). Subsequently, they were rinsed with distilled water for

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[4] Polysciences, Inc., Warrington, PA, Lot 71411.

24 hours with three changes of water in between. The wet weight (W_w) of the grafted Silastic® sheets was measured by blotting sheets between two pieces of filter paper (Whatman # 1) and then weighing. The sheets were then dried briefly in an oven at 100-110°C for about 5 minutes, and stored in a desiccator over Drierite® overnight before the dry weight (W_d) was determined.

Grafting of silicone rubber tubes

Effect of irradiation dose In this experiment, only one formulation (60% NVP[5]/40% methanol (MeOH)) was used and stock silicone rubber tubes (8-9 cm long) with one end sealed using medical-grade adhesive type A[6] were employed. Prior to filling a silicone rubber tube with monomer, the monomer solution was deoxygenated by bubbling nitrogen gas through it for at least 30 minutes at a rate of approximately 2-3 bubbles per second. At this rate, a minimal amount of solvent was evaporated and the final monomer composition was not affected. An appropriate quantity of monomer solution was introduced into the silicone rubber tube using a syringe having a thin, long needle. The top end of the silicone rubber tube was sealed with a small hemostasis clip (placed at about 0.5 to 1 cm from the top end of the tube). The tubing was then inserted inside a glass tube (8 cm long, 6 mm ID, and 1 mm wall thickness), and the combination of the glass tube and sample was placed into a 15 cm x 1.6 cm Pyrex® test tube, which has a 4 cm high support at the bottom. A clip (alligator type) was used to keep the sample in the center of the test

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[5] Polysciences, Inc., Warrington, PA, Lot 71411.

[6] Dow Corning Corp., Midland, MI, Lot HH058742.

tube. Prior to sealing, the Pyrex® test tube was flushed with nitrogen, and was then sealed with Teflon tape on the threads. All sample preparations were carried out in a nitrogen purged glove bag.

Grafting of samples within the tubes was performed at room temperature in a 360 Ci Cobalt-60 source at a dose rate of 241,000 rad/hr. Each sample was given one of the following doses: 50, 150, and 250 Krad.

After irradiation, grafted samples were removed from the irradiation tubes, both ends of the silicone rubber tube were cut (about 0.75 cm from each end), and the silicone rubber tubes were extracted with ethanol-water (1:1) mixture for 2 hours (3 changes) to remove unreacted monomer and low molecular weight polymers. They were then rinsed in distilled water for 24 hours with three changes during this period. Samples were allowed to dry in a desiccator over Drierite® overnight. The final length of each sample and its weight were determined the next day. An identical length of an ungrafted silicone rubber tube was also extracted with ethanol water (1:1), and it was used to determine the initial weight of a particular sample prior to extraction.

Another set of samples were prepared and irradiated in the same manner, but no effort was made to remove air from either the monomer solution or from inside the irradiation test tube. Post irradiation washing was carried out in a similar fashion. The samples were then dried and stored in a desiccator over Drierite® before any grafting weight was determined.

Effect of solvent composition As before, a similar irradiation grafting experiment was carried out using various formulations in which the concentration of methanol was decreased and water was added as another solvent. Two formulations were studied: (1) 60% NVP[7]/40% water, and (2) 60% NVP/10% methanol/30% water. Formulation 1 was used with samples irradiated at 250 Krad, and formulation 2 was used with samples irradiated at 50 Krad and 250 Krad. Distilled water, NVP, and methanol (MeOH) were individually bubbled with nitrogen for at least 30 minutes under an inert nitrogen atmosphere inside a glove bag. A specific quantity of NVP, water, and methanol to make up a particular formulation was pipetted into a 25 ml flask and mixed. Additional bubbling of the final monomer/solvent(s) solution with nitrogen was continued at a controlled flow rate (2-3 bubbles per second) for a few minutes to assure good mixing. A quantity of a specific formulation was introduced into the silicone rubber tube (stock sample) using a syringe with a thin, long needle, and the sequence of steps of sample preparation was followed as before. Irradiation grafting was performed within 2-3 hours from the time of preparation.

After irradiation, the grafted tubes were removed from the irradiation test tube, both ends of tubes were cut (0.75 cm from each end), and the grafted tubes were extracted with ethanol-water for 2 hours (3 changes during this period). They were then rinsed in distilled water for 24 hours (also 3 changes). The wet weight of the grafted samples was measured by blotting the tubes between two sheets of filter paper

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[7] Polysciences, Inc., Warrington, PA, Lot 71411.

(Whatman # 1) and by passing plugs of filter paper through the lumen using a metal rod, and then weighing the wet samples. The samples were then dried briefly in an oven at temperature of about 100 °C for 5 minutes and stored in a desiccator over Drierite® overnight. The dry weight of each sample was determined the next day.

Grafting at lower doses A series of samples were irradiation grafted using the formulation 60% NVP[8]/40% MeOH. Preparation of samples was done as before and in a nitrogen purged glove bag. Each sample was given one of the following doses: 20, 25, 30, 35, 40, and 45 Krads. To determine the reproducibility of the grafting process, and the uniformity of the radiation field in the Cobalt-60 unit, two sets of samples were irradiated at 25 and 30 Krad, respectively. Each set consisted of 5 silicone rubber tubes, and these tubes were irradiated in sequence. As before, the post irradiation process (extracting, rinsing, etc.) was performed in a similar manner. After the wet weight of each sample was measured, the grafted tubes were dried briefly in an oven at 100-110 °C, and stored in a desiccator (over Drierite®) overnight. Subsequently, the tubes were weighed and the grafted weight of each sample was determined. The initial weight of each sample was taken as the weight of an ungrafted tube with an identical length for which the ungrafted tube was subjected to the ethanol-water (1:1) extraction.

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[8] Polysciences, Inc., Warrington, PA, Lot 71411.

Effect of Irradiation on Polymeric Silicone Rubber

Silicone rubber tubes were prepared and irradiated by the same method used for NVP grafted samples except that they were not filled with any particular monomer solution. Three samples were prepared and each received one of the following doses: 50, 150, and 250 Krad. After irradiation, these irradiated silicone rubber tubes were extracted with ethanol-water (1:1) for two hours, rinsed in distilled water for 24 hours, and dried.

Cross sections of the irradiated silicone rubber tubes about 200 microns thick were obtained using a DSK Microslicer[9] (series 1000). These disk-shaped cross sections were immersed in various 0.1% acid fuchsin and 0.1% basic fuchsin dye solutions (with methanol concentrations of 10, 50, or 100% by volume (methanol/water), respectively) for 48 hours. They were then removed from the dye solutions, rinsed with distilled water, and dried. The ability of irradiated silicone rubber to absorb dyes in various dye solutions was characterized at 100x magnification using a Balplan optical microscope[10]. Nonirradiated silicone rubber which was washed with ethanol-water (1:1) was used as control. Controlled samples were also treated with various dye solutions, and similar observations were made.

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[9] Ted Pella, Inc., Irvine, CA.

[10] Bauch & Lomb, Inc., Rochester, NY.

Equilibrium Swelling of Silicone Rubber in NVP and Solvents

Equilibrium swelling of silicone rubber in NVP and NVP/MeOH

A procedure for change in mass (modified from ASTM D-471-79, 1986) was used to determine the equilibrium swelling of silicone rubber in NVP[11] and 60% NVP/40% methanol (MeOH). Nine cm sections of silicone rubber tubing were boiled in 2% aqueous sodium bicarbonate solution for 2 hours. These tubes were then rinsed in warm distilled water and allowed to dry in a desiccator (over Drierite®) overnight. Three samples (tubes) for each test liquid were used. Each test sample was weighed to the nearest 1 mg using an analytical balance. The tubes were then filled with test liquid and both ends sealed using hemostasis clamps. They were then placed inside a glass jar with stopper for a required length of time (e.g., 1, 2, 3, and 6 hours). After the test had proceeded for the required period, an individual silicone rubber tube was removed from the jar, the liquid drained, and the tube was quickly dipped into acetone to remove excess surface NVP. The tube was then blotted between two sheets of filter paper (Whatman # 1), and plugs of filter paper were passed gently through the lumen to remove excess liquid. Next, the sample was placed inside a pre-weighed Pyrex® test tube, capped and weighed. Samples were weighed at 1, 2, 3, and 6 hours. After weighing, each tube was refilled and returned to the glass jar for the next test period. The process of blotting and weighing was usually done within 30 seconds. Additional tests were carried out at shorter contacting times, such as 15, 30, and 45 minutes for both NVP and 60% NVP/40% MeOH.

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[11] Polysciences, Inc., Warrington, PA., Lot 71411.

Equilibrium swelling of silicone rubber in methanol

Similar equilibrium swelling measurements of silicone rubber were done using methanol as test liquid. The samples were weighed at 1, 2, and 3 hours. Since methanol is a volatile liquid, the experiment was terminated when no weight increase was noted.

Characterization Methods

It was intended to put a thin layer of NVP into the surface of the silicone rubber tubes as a copolymer with the silicone rubber without changing the original mechanical properties of the silicone rubber. Therefore, visual observations were made throughout the irradiation process in terms of monomer/solvent consistency, mechanical stiffness, and color of the irradiated substrates. In this investigation, the monomer/solvent consistency will be referred to as the external polymer solution. The graft water content, graft level (mg/cm^2), and grafting yield were determined gravimetrically. The grafted front of the irradiated substrates was characterized by using optical microscopy, scanning electron microscopy (SEM), and a dye staining technique. Furthermore, a procedure to incorporate iodine into poly(N-vinylpyrrolidone) (PNVP) was also used in parallel with the dyeing process to study the visualization of different grafting zones in the silicone rubber substrates, especially when grafting was carried out at higher doses (e.g., 150 and 250 Krad).

Gravimetric analysis

The water content of the grafted silicone rubber substrates was measured by blotting the substrates between two sheets of Whatman # 1 filter paper, and by gently passing plugs of filter paper through the lumen (in case of a tube), and then weighing immediately. The percent of water in graft was calculated using the relationship:

$$\% \text{ water} = [(W_W - W_d)/(W_W - W_S)] \times 100$$

where W_W is the weight of the wet, grafted substrate; W_d is the weight of the grafted substrate dried in a desiccator over Drierite® for 24 hours; and W_S is the weight of untreated substrate.

The graft level (W_G) is expressed as the weight of the graft per initial area of the substrate. W_G was calculated using the relationship:

$$W_G = (W_d - W_S)/ \text{Area}$$

where Area = final length x original circumference using inside diameter for tubes = (.622 cm) x Length (cm^2); and Area = 1.9 cm x 3.8 cm = 7.22 cm^2 for sheets.

The grafting yield or grafting ratio was determined as follows:

$$G_Y = (W_d - W_S)/W_S \times 100$$

where W_d = weight of dry grafted substrate
W_S = weight of dry ungrafted substrate

Determination of the penetration depth of the graft components

To prepare grafted tubing cross sections for grafting analysis, cork (size # 0) was used as the supporting material. A hole was made in the center of the cork using a 0.125" drill. In all determinations, the cross sections of an individual grafted tube were obtained by fitting a section of interest (e.g., top, middle, or bottom section of the tube) in the center of the drilled cork, gluing the cork on a metal support, and cutting with a microblade of a DSK Microslicer[12] (Series 1000). The cross sections, prepared in this way, had a thickness of about 200 microns. In each case, all cross sections were kept in sequence and placed on a microscope slide. They were then stored in a microscope slide pad.

Light and stereoscopic microscopy analysis The graft depth was measured for the cross sections at 100x magnification using a Balplan microscope[13]. In some cases, measurements were made at five different locations in one cross section to determine the uniformity of the PNVP rim. The inner and outer diameter of the grafted tubing, as well as its wall thickness were measured at 30x magnification using a stereomicroscope[14]. Original dimensions of ungrafted tubing were obtained in a similar manner.

Scanning electron microscopy

Critical point drying Cross sections of tubing about 200 microns thick were taken through a series of acetone-water rinses (30, 50, 70, 80, 90, 95, 100, and 100% v/v%). Each rinse was 15 minutes long. They were then transferred to a Polaron model E3000[15] critical point drying apparatus. The acetone was replaced with liquid carbon dioxide and the samples were critical-point dried.

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[12] Ted Pella, Inc., Irvine, CA.

[13] Bauch & Lomb, Inc., Rochester, NY.

[14] Nikon Corp., Tokyo, Japan.

[15] Polaron Instruments, Inc., Warrington, PA.

Samples were mounted on carbon stubs using double sided adhesive mounting tape or colloidal carbon medium. A Polaron Instrument SEM coating unit (E5100) was used to sputter coat 300 Angstroms of gold onto the cross sectional samples. The samples were observed at 1-20 Kilo electron volts (KeV) using a JEOL-JSM 840 A[16] SEM.

Staining Methods

Dye staining

Comparison of acid fuchsin and basic fuchsin   Various dye solutions of 0.1% acid fuchsin[17] and 0.1% basic fuchsin[18] in 100% methanol, 50% methanol/50% water, and 10% methanol/90% water were used on grafted silicone rubber tubes irradiated at 50, 150, and 250 Krads. Particular sections of dried grafted tubes were immersed in various dye solutions described above for 48 hours. They were then removed, rinsed in distilled water, and dried in a desiccator (over Drierite®) for at least 24 hours before cross sections were cut.

For samples irradiated at 45 Krads and lower doses, only dye solutions with 100% methanol were used in the staining process.

The extent of absorption of acid fuchsin and basic fuchsin, respectively, by NVP grafted samples was tested by treating two cross sections in sequence (non-stained) with either acid or basic fuchsin

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[16] JEOL USA Electron Optics, Peabody, MA.

[17] Fisher Scientific Co., Fair Lawn, NJ, Lot 794846.

[18] Fisher Scientific Co., Fair Lawn, NJ, Lot 792591B.

dye solutions. In other words, two cross sections next to each other were compared; one was treated with acid fuchsin (0.1% in either 100% methanol, 50% methanol/50% water, or 10% methanol/90% water) while the other was treated with basic fuchsin dye solutions in a similar manner.

Photographs of selected cross sections were taken at the following magnifications: 25x, 63x, and 163x. Kodak® Ektachrome®[19] (tungsten 50) professional film was used.

Effect of methanol on the depth of the grafted front   Cross sections about 200 microns thick of irradiated samples which had not absorbed dyes when were treated with dye solutions in which the concentration of methanol was 10 or 50% were then subsequently placed in 100% dye solutions for another 48 hours. After rinsing and drying, the effect of methanol on the penetration depth of NVP was observed at 100x magnification using a Balplan microscope[20].

Iodine methods

Grafted tubes   The PNVP-Iodine complex was formed by immersing disk-shaped cross sections of the irradiated sample about 200 microns thick in aqueous KI/I_2 (0.05 M KI/0.002 M I_2) and reactive Lugol/buffer (1:1) (2 gm KI, 1 gm I_2, and 200 ml distilled water/ 0.5 mole acetic acid and 0.5 mole sodium acetate in 1 liter of distilled water) solutions for various periods of time. The immersion time varied from 2 hours to 1 week. After the designated immersion time, the cross sections were

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[19] Eastman Kodak Co., Rochester, NY.

[20] Bauch & Lomb, Inc., Rochester, NY.

removed, rinsed with distilled water, dried briefly in an oven at 110°C for about 5 minutes, and stored in a desiccator over Drierite® overnight. The grafted depth was then measured at 100x magnification using a Balplan microscope[21]. Photographs of selected cross sections were taken at either 63 or 160x magnification using Kodak® Ektachrome® (tungsten 50) professional film[22].

Grafted sheets Thin strips about 0.3 mm width of homogeneous grafted sheets were immersed in 0.05 M KI/0.002 M I_2, and Lugol/buffer (1:1) solutions for 1 week. They were then removed, rinsed, and dried as before. The colors of the grafted strips were correlated with the graft contents at various irradiation levels. Photographs of the iodine treated strips were also taken using the same type of film (Kodak® Ektachrome®).

Determination of the Required Immersion Time

The time required to achieve a constant rim thickness of grafted samples when treated in various acid and basic dye solutions, and in aqueous KI/I_2, and in Lugol/buffer solutions was determined by immersing nonstained cross sections about 200 microns thick in appropriate solutions for the following periods: 2, 24, 48, 72, 96, 144, and 168 hours. After the designated immersion time, the tubular cross sections were removed, rinsed with water, and then dried in an oven at 110°C for about 5 minutes, and measurements of the rim were made at 100x magnification using a Balplan microscope[21].

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[21] Bauch & Lomb, Inc., Rochester, NY.

[22] Eastman Kodak Co., Rochester, NY.

Subsequently, these tubular cross sections were returned to the original solutions for the next test period.

RESULTS

Grafting Procedures

Grafting on sheets

It was intended to deposit a homogeneous graft throughout the thickness of the silicone rubber film (254 microns thick) so that an iodine staining method could be used to correlate the color change with the graft level for a particular sample (e.g., at an irradiation dose). Results of grafting on silicone rubber films using the formulation 60% NVP/40% MeOH (N_2 purged) are shown in Table 3.

TABLE 3. Results of grafting on silicone rubber sheets using the formulation 60% NVP/40% MeOH (nitrogen purged)

Irradiation dose, Krad	Graft level (mg/cm^2)	Water in graft (%)	Grafting yield (%)	Description of external polymer
50	3.25	46.9	10.3	clear liquid
150	7.17	61.0	22.7	viscous liquid
250	11.3	62.2	35.8	viscous gel

The results show that the grafting yield and graft level depend on the irradiation time (dose) even though the monomer/solvent was allowed to penetrate the substrates for an extended period of time (> 2 hours) before irradiation.

The grafting yield increased with increasing irradiation dose, but grafting seemed to be complicated at higher doses due to the high viscosity of the reaction medium, and that the diffusion of the monomer may become the controlling factor. Grafted silicone rubber sheets at high doses were found to be more rigid in their dry state; however, the surface of the grafted samples were wettable to water and retained their rubbery nature in the wet state.

The thin strips (about 0.3 mm) were treated with a KI/I_2 Lugol buffer solution (1:1) (concentration of I_2 = 0.00054 gm/cm^3) for 1 week. The color of a particular irradiated sample at a particular grafting yield was uniform after 96 hours in iodine solution. The colors were orange-brown, brown, and dark brown for samples irradiated at 50, 150, and 250 Krad, respectively. A uniform color throughout the thickness of the film indicated that homogeneous grafting was achieved.

Grafting on tubes

Effect of irradiation dose

Samples irradiated in the presence of air produced no graft or very little graft (randomly distributed). These results were shown by gravimetric analysis and by the lack of staining when samples were treated with various dye solutions (Table 4).

Tubing irradiated in the absence of air produced significant grafts (Table 4). At graft levels below 5 mg/cm^2, the tubing retained

TABLE 4. Observations on irradiated silicone rubber tubes using the formulation 60% NVP/40% MeOH (in air and nitrogen purged)

Sample description	Description of external polymer	Graft (mg/cm^2)	Stainable
50 Krad, nitrogen	clear liquid	4.23	yes
150 Krad, nitrogen	viscous liquid	5.53	yes
250 Krad, nitrogen	viscous gel	17.8	yes
50 Krad, with air	clear liquid	negligible	no
150 Krad, with air	viscous liquid	no	no
250 Krad, with air	viscous gel	negligible	no

its original flexibility. On the other hand, tubes grafted at 150 and 250 Krad resulted in very stiff materials, even though they were swollen and flexible in water.

The effect of radiation dose on the grafting yield and graft water content for irradiated silicone rubber tubes is shown in Table 5. Graft levels and grafting yields increased as the irradiation dose increased. Grafting at longer irradiation time, such as at 250 Krad, was complicated by the high viscosity of the reaction medium. At this irradiation level, up to a certain point, the monomer could no longer diffuse into the silicone rubber matrix because of the "gel effect", and the monomer grafted onto its own polymer. As a result, the wall thickness of the grafted sample increased. The sample irradiated at 250 Krad showed a thicker wall (635 to 737 microns) than the nongrafted silicone rubber tubing (610 microns); by comparison, the samples irradiated at 50 and 150 Krad showed no significant change in wall thickness.

TABLE 5. Comparison of the effects of radiation dose on radiation grafting into silicone rubber tubes using the formulation 60% NVP/40% MeOH

Irradiation dose, Krad	Graft (mg/cm^2)	Water in graft (%)	Grafting yield (%)
50	4.23	40.2	4.57
150	5.53	62.4	5.92
250	17.8	61.7	19.1

By using silicone tubes with a shorter length (7-8 cm), and by positioning the irradiation tube at the center of the radiation field, grafting for the entire length of tubing was achieved. However, the rim thickness (grafted layer) was not uniform from top to bottom of the tube even though the whole length of the silicone rubber tube was grafted (Table 6). The grafted front is not a linear function of the irradiation dose. The rim thickness increased as the irradiation dose increased; however, it tended to reach a maximum rim thickness, especially when irradiation was carried out at a longer time and the polymerization involved the "gel effect".

TABLE 6. Measurements of grafted depth as a function of position on irradiated silicone rubber tubing prepared using the formulation 60% NVP/40% MeOH (stained using 0.1% acid fuchsin or basic fuchsin in 100% methanol)

	Rim thickness (microns)					
	Acid fuchsin			Basic fuchsin		
Irradiation dose, Krad	Top	Middle	Bottom	Top	Middle	Bottom
50	263	279	438	265	330	457
150	495	432	469	442	535	495
250	445	458	491	356	471	508

Several photographs were taken to demonstrate the nonstained rim depth as shown by the straw color near the edge. Figure 1 shows an ungrafted section of silicone rubber tubing. Figures 2, 3, and 4 show the graft depth of samples irradiated at 50, 150, and 250 Krad, respectively. The 250 Krad sample (Figure 4) shows the surface roughness of the lumen due the to complication of grafting when homopolymerization occurred.

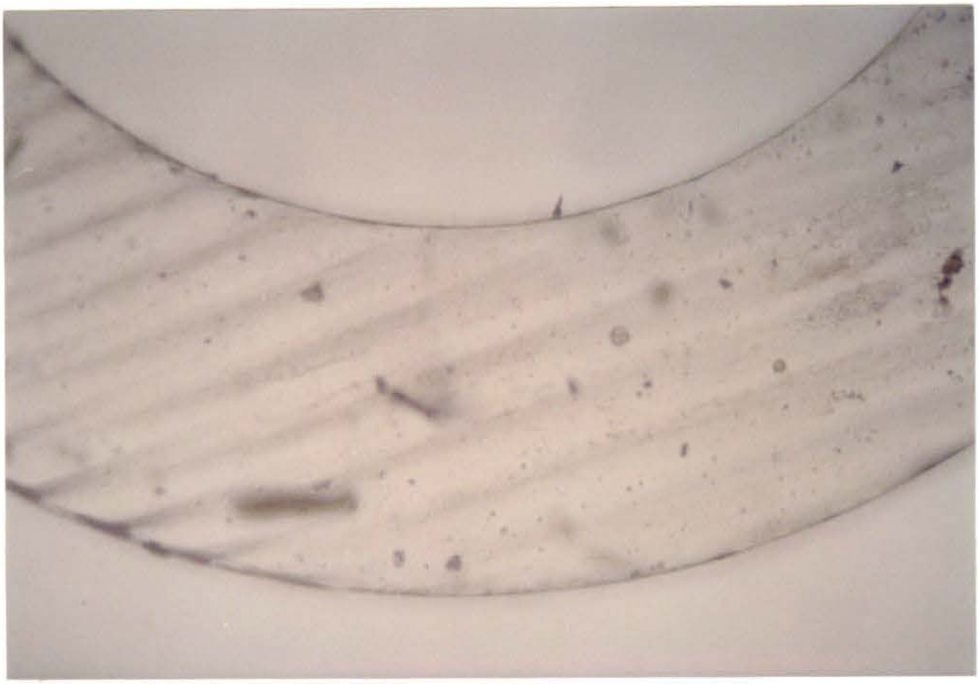

FIGURE 1. Cross section of cleaned, nongrafted silicone rubber (magnification = 69x)

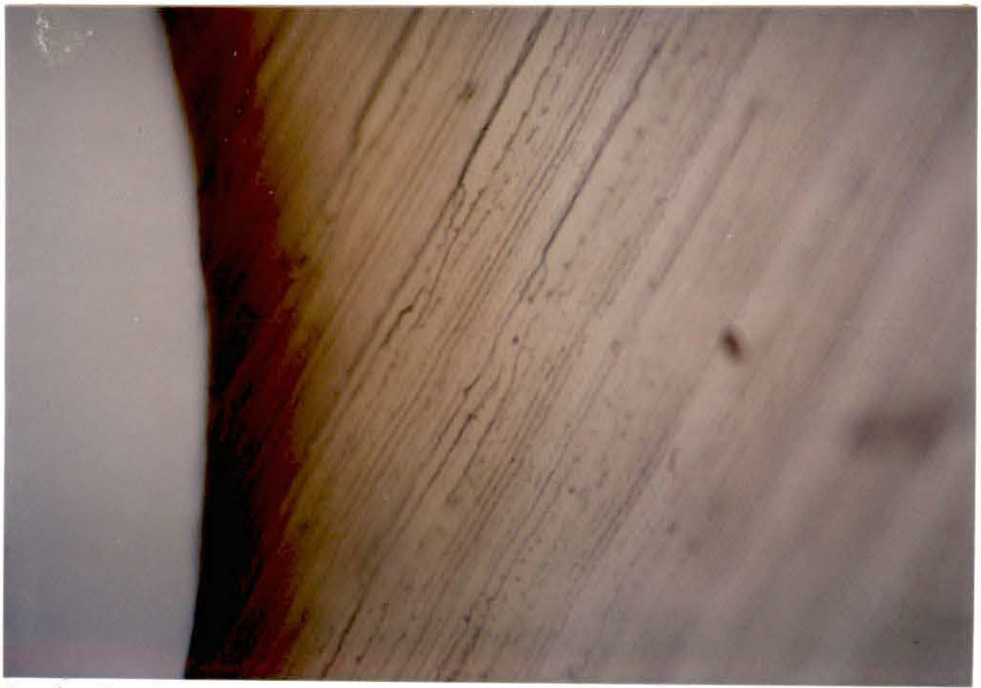

FIGURE 2. Optical microscope photograph of a nonstained cross section from the sample irradiated at 50 Krad using the formulation 60% NVP/40% methanol (magnification = 175x)

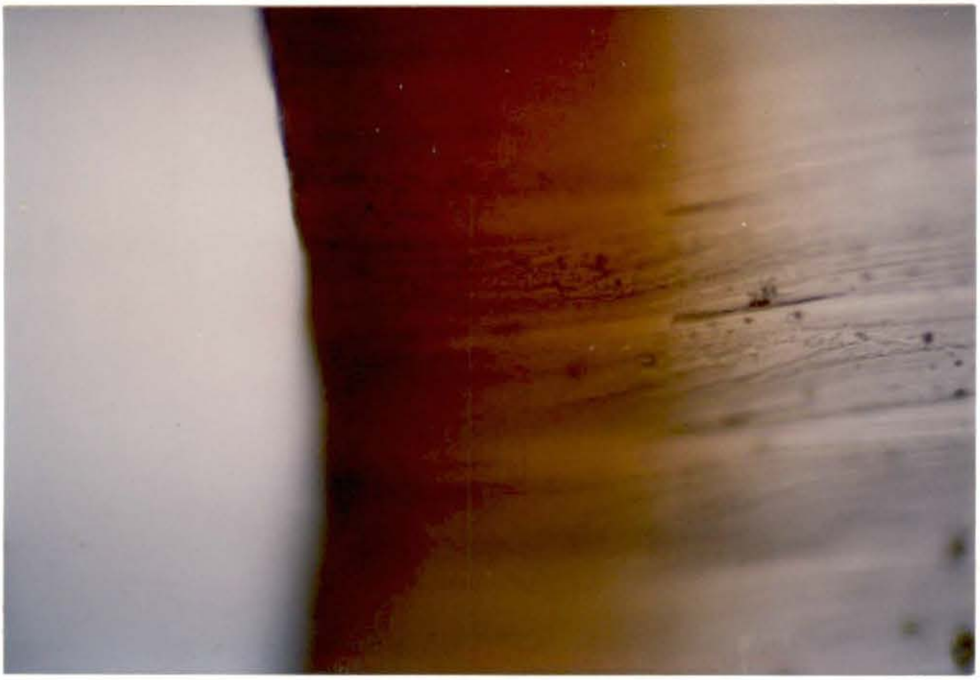

FIGURE 3. Optical microscope photograph of a nonstained cross section from the sample irradiated at 150 Krad using the formulation 60% NVP/40% methanol (magnification = 175x)

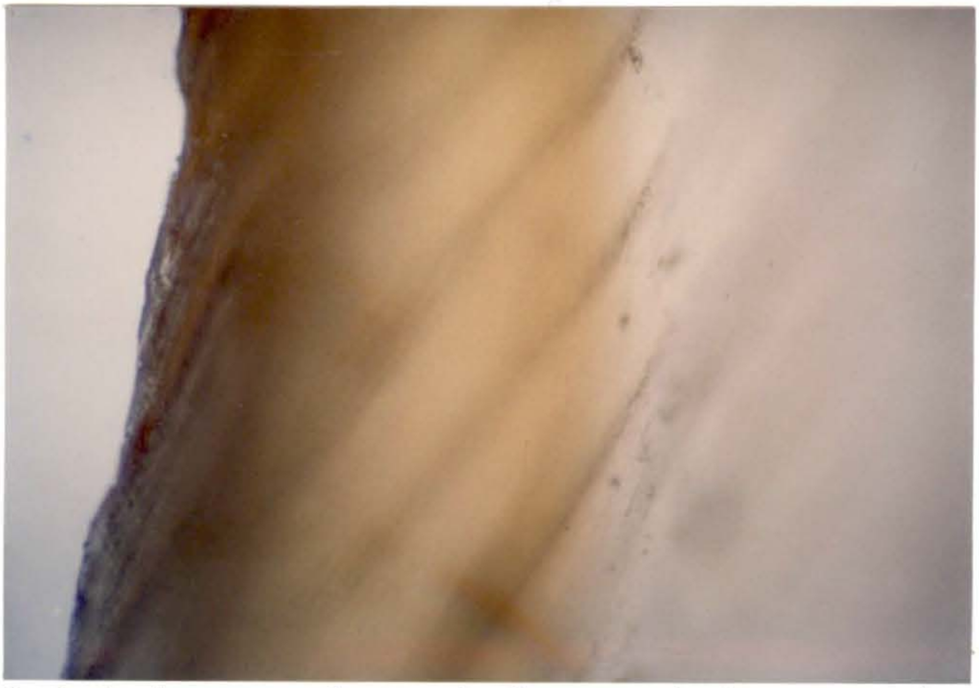

FIGURE 4. Optical microscope photograph of a nonstained cross section from the sample irradiated at 250 Krad using the formulation 60% NVP/40% methanol (magnification = 175x)

Both acid fuchsin and basic fuchsin were able to be used to identify grafted NVP in the silicone rubber matrix; however, basic fuchsin also stained silicone rubber to some extent. This sometimes gave a wrong indication of the location of the grafted front. The rim thickness determination using basic fuchsin in the dyeing technique usually resulted in a thicker rim than that when acid fuchsin was used (Table 6).

The effect of methanol concentration on the measurement of the grafted front is demonstrated in Table 7. The 50 Krad sample could not be stained by dye solutions in which the concentration of methanol was less than 50%. However, cross sections of this sample showed the presence of a rim when they were immersed in 100% methanol-dye solutions for another 48 hours. This indicated that methanol swelled the silicone rubber to some extent and allowed the dye to penetrate the hydrogel-silicone rubber matrix. The thickness of the rim was found to increase with increasing methanol concentration (Table 7). This phenomenon was observed in cross sections obtained within the vicinity of each other. Figures 5-10 demonstrate the effect of methanol on the measurements of the rim (graft depth) for three levels of irradiation (50, 150, and 250 Krad) and three different methanol concentrations (10%, 50%, and 100%) using acid fuchsin or basic fuchsin as the stain.

TABLE 7. Effect of methanol concentration on the measurement of graft depth on irradiated silicone rubber tubing using the formulation 60% NVP/40% methanol (stained using 0.1% acid fuchsin or 0.1% basic fuchsin in 10%, 50%, and 100% methanol)

	Rim thickness (microns)					
	10% methanol		50% methanol		100% methanol	
Irradiation dose, Krad	AF[a]	BF[b]	AF	BF	AF	BF
50	NR[c]	NR	NR	NR	279	330
150	279	330	279	330	432	635
250	305	216	241	356	458	471

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim present.

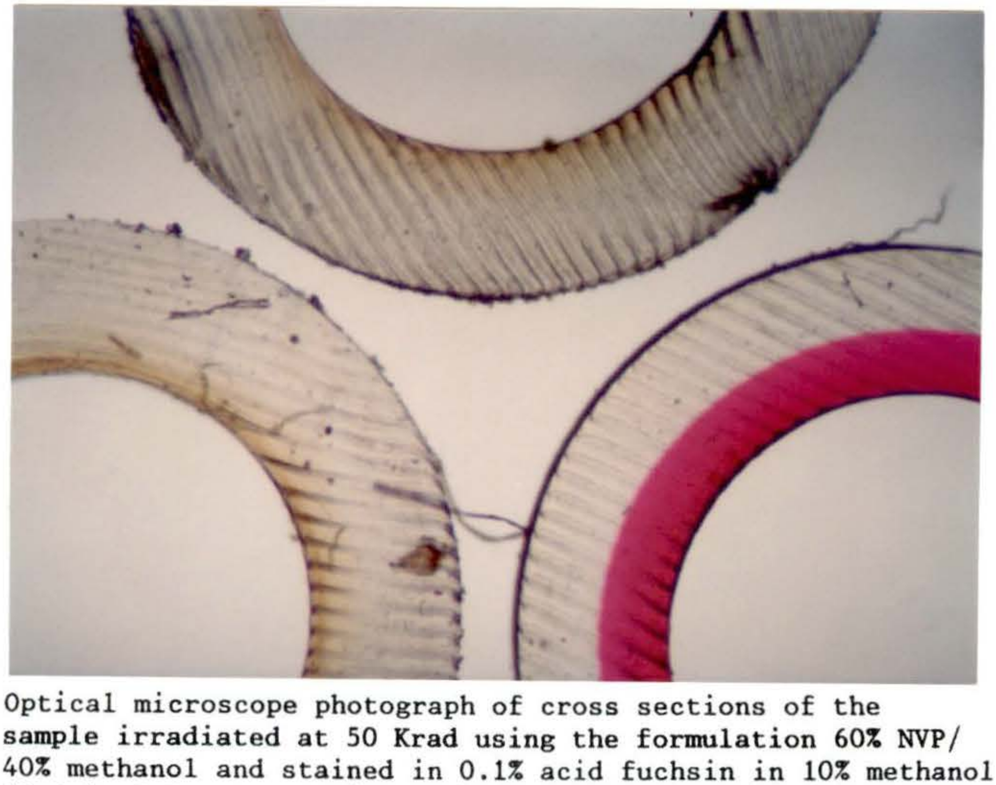

FIGURE 5. Optical microscope photograph of cross sections of the sample irradiated at 50 Krad using the formulation 60% NVP/ 40% methanol and stained in 0.1% acid fuchsin in 10% methanol (left), 50% methanol (center), and 100% methanol (right) (magnification = 32x)

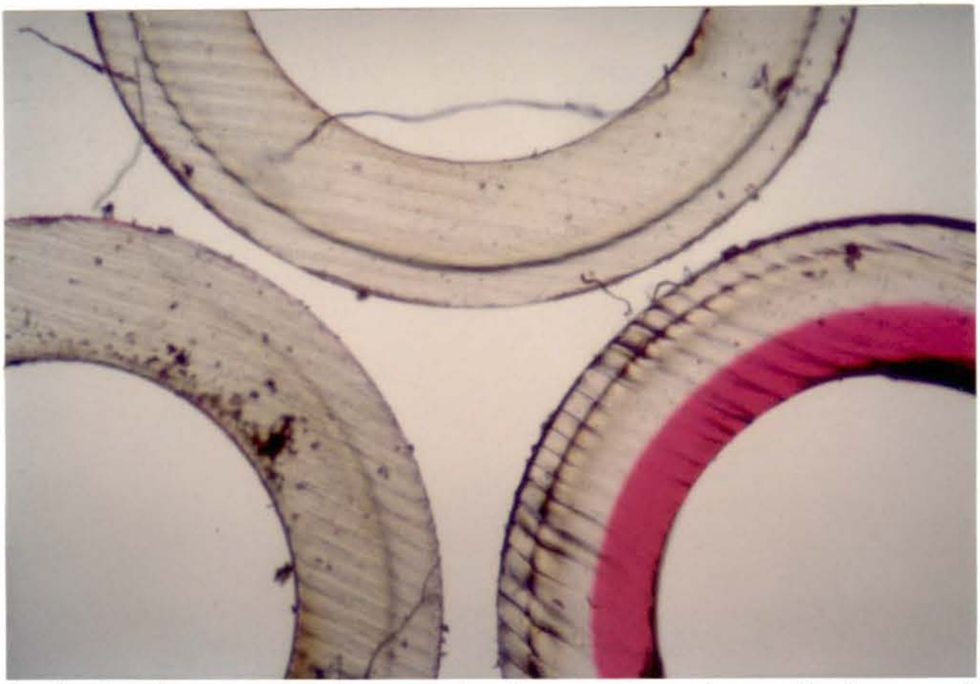

FIGURE 6. Optical microscope photograph of cross sections of the sample irradiated at 50 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% basic fuchsin in 10% MeOH (left), 50% MeOH (center), and 100% MeOH (right) (magnification = 32x)

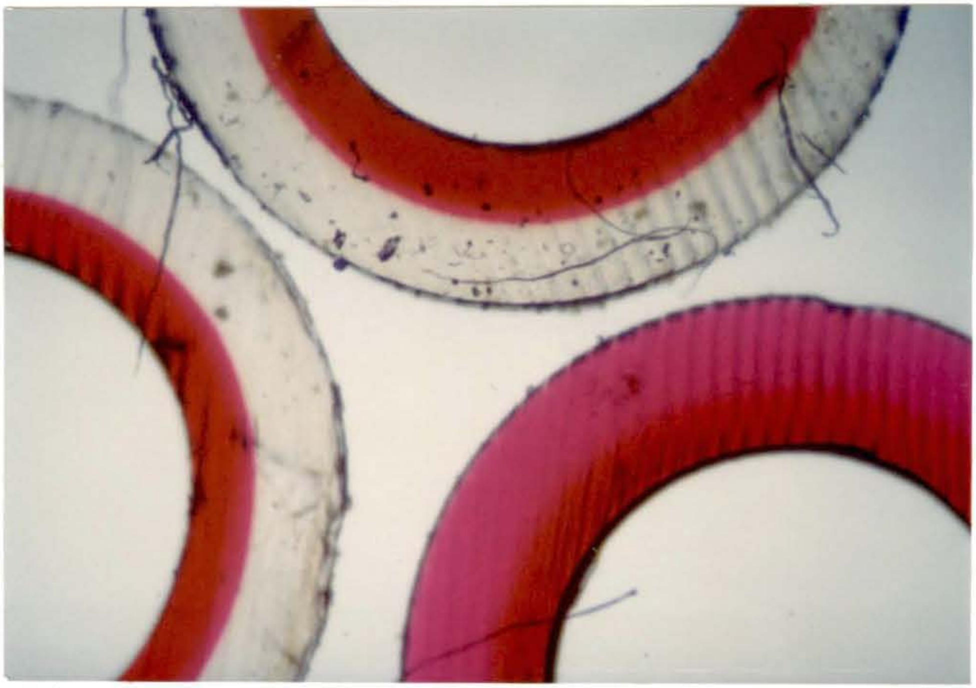

FIGURE 7. Optical microscope photograph of cross sections of the sample irradiated at 150 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% acid fuchsin in 10% MeOH (left), 50% MeOH (center), and 100% MeOH (right) (magnification = 32x)

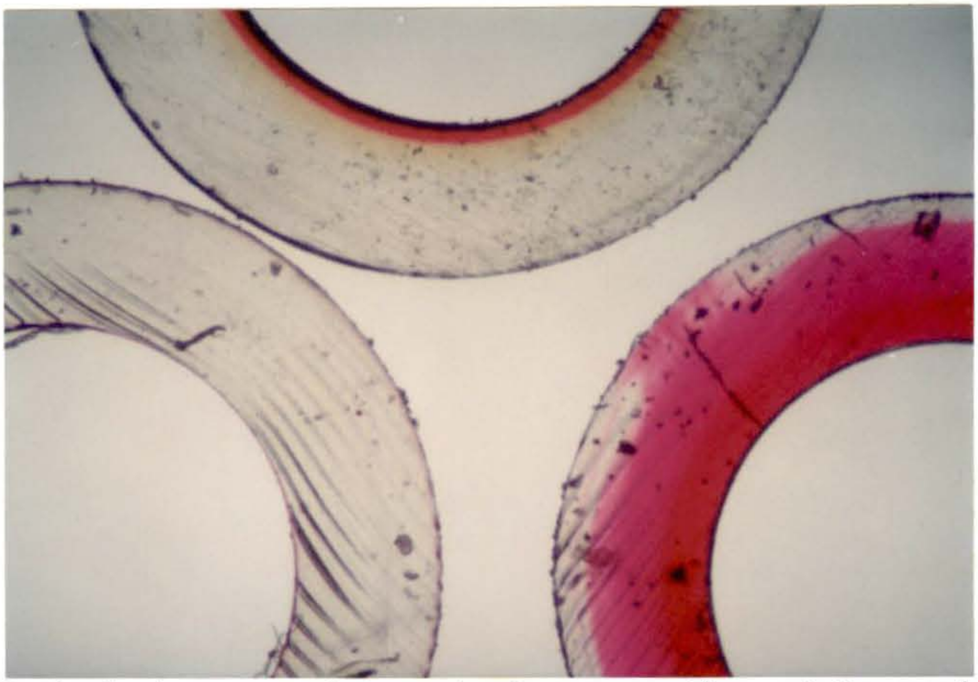

FIGURE 8. Optical microscope photograph of cross sections of the sample irradiated at 150 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% basic fuchsin in 10% MeOH (left), 50% MeOH (center), and 100% (right) (magnification = 32x)

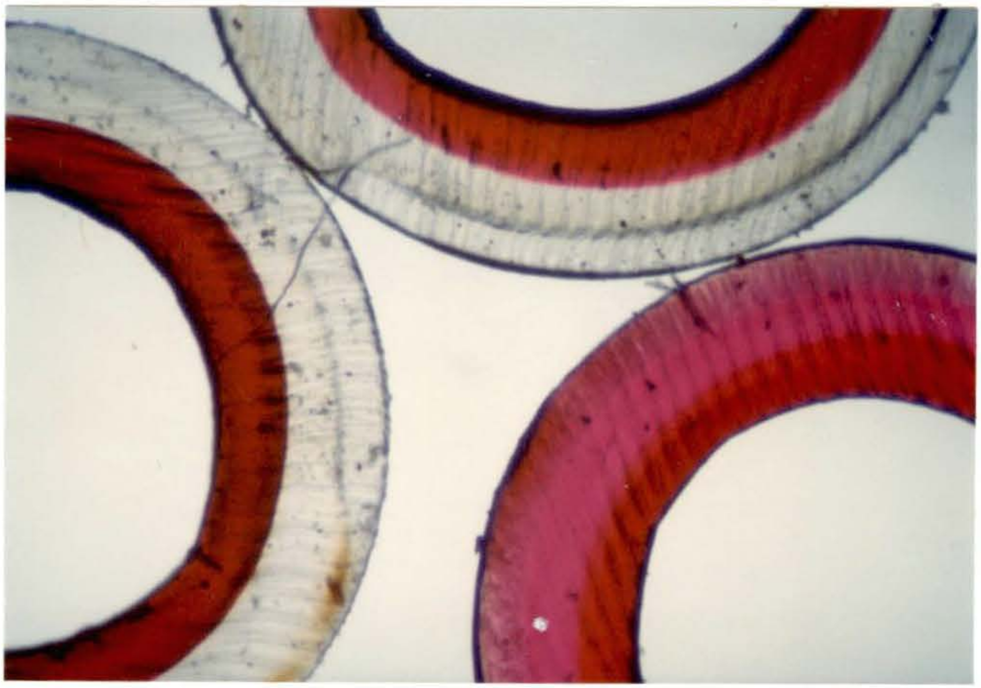

FIGURE 9. Optical microscope photograph of cross sections of the sample irradiated at 250 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% acid fuchsin in 10% MeOH (left), 50% MeOH (center), and 100% MeOH (right) (magnification = 32x)

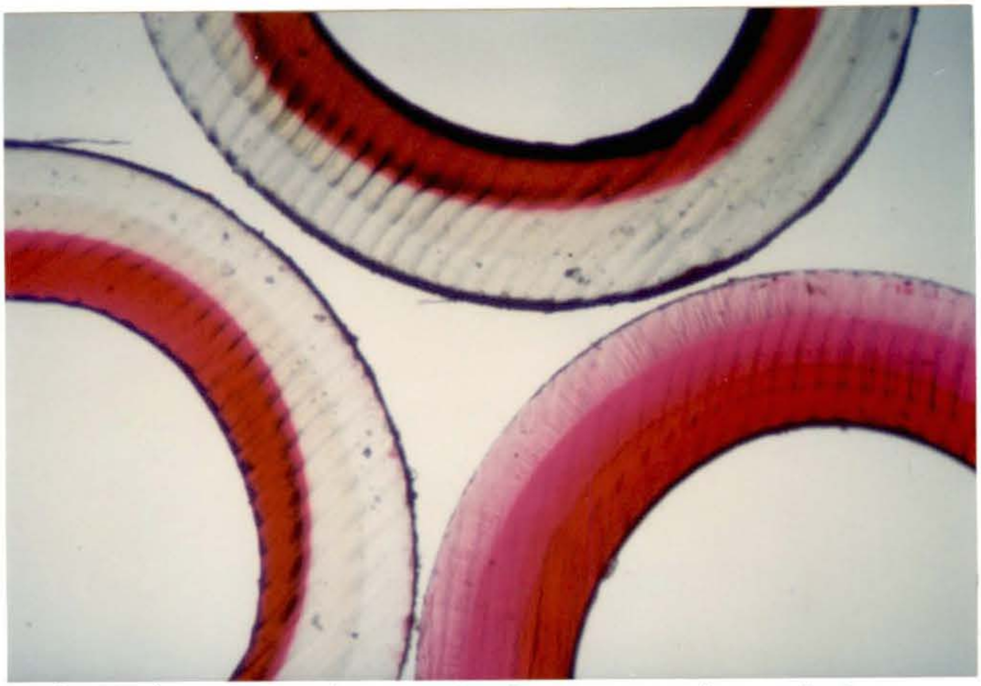

FIGURE 10. Optical microscope photograph of cross sections of the sample irradiated at 250 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% basic fuchsin in 10% MeOH (left), 50% (center), and 100% MeOH (right) (magnification = 32x)

Staining of cross sections ca. 200 microns thick of irradiated samples using 0.05 M KI/0.002 M I_2 and Lugol/buffer (1:1) (KI/I_2 in (aqueous acetic acid-sodium acetate medium) solutions produces rims with rim thicknesses comparable to the results obtained when samples were treated with 0.1% acid fuchsin or 0.1% basic fuchsin in 100% methanol (Table 8). Results for the 250 Krad sample could not be compared due to a nonuniform wall thickness resulted from homopolymerization. Iodine bound to the polyvinylpyrrolidone (PNVP) very strongly, and the binding increased markedly with molecular weight of the polymer. This was evidenced by the fact that a brown or a dark brown rim can be seen within 5 minutes when cross sections of samples irradiated at 150 Krad and 250 Krad were treated with KI/I_2 solution or reactive Lugol/buffer solution. It took a longer time for a rim to develop for samples irradiated at lower radiation doses. However, in order for a rim to fully develop, the cross sections must be immersed in the solutions for at least 96 hours or more.

TABLE 8. Comparison of graft depths resulting from the dye staining technique and iodine staining technique for irradiated silicone rubber tubes using the formulation 60% NVP/40% MeOH

	Rim thickness (microns)			
	100% methanol 0.1% dye			Lugol/buffer (1:1)
Irradiation dose, Krad	AF[a]	BF[b]	0.05 M KI/0.002 M I_2 aqueous solution	aqueous solution
50	254	279	241	254
150	381	432	381	381
250	483	584	521	660

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

The iodine staining technique was able to reveal different grafting zones across a wall thickness (Figures 11-16). Normally, a dark brown rim indicated a region of heavy grafting, and a light brown rim corresponded to a light grafting region. This general trend was observed in most samples that were irradiated at 50 Krad and above. The 150 Krad sample had only one dark brown rim. This could be due to the time of irradiation and the polymerization process in which diffusion is the controlling factor, especially when the reaction medium become viscous in the late stage of the irradiation process.

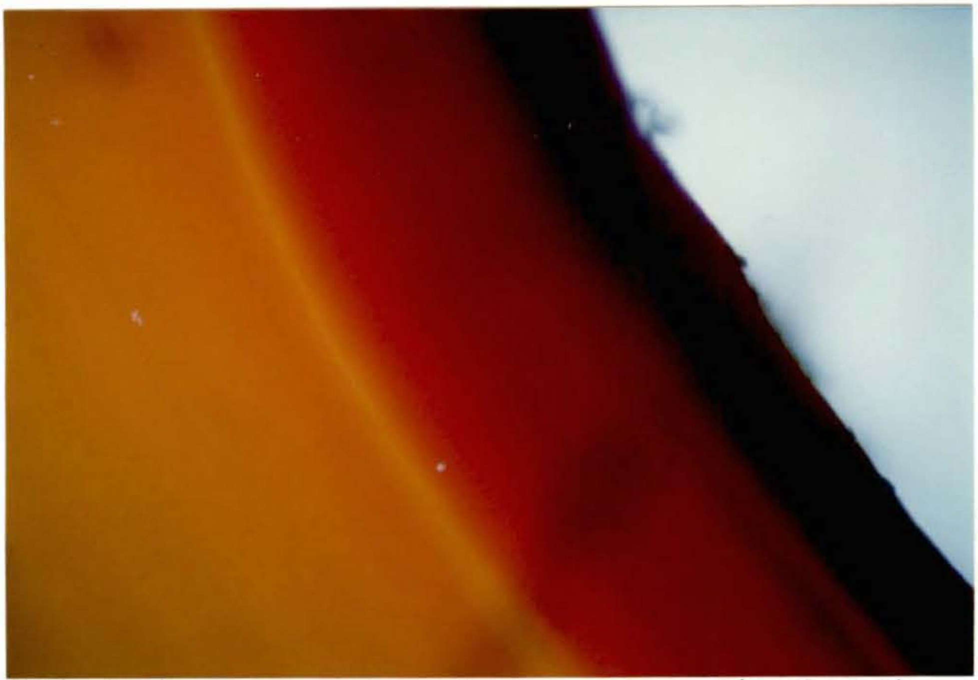

FIGURE 11. Optical microscope photograph of a cross section from the sample irradiated at 50 Krad using the formulation 60% NVP/ 40% MeOH and stained in 0.05 M KI/0.002 M I_2 aqueous solution (magnification = 175x)

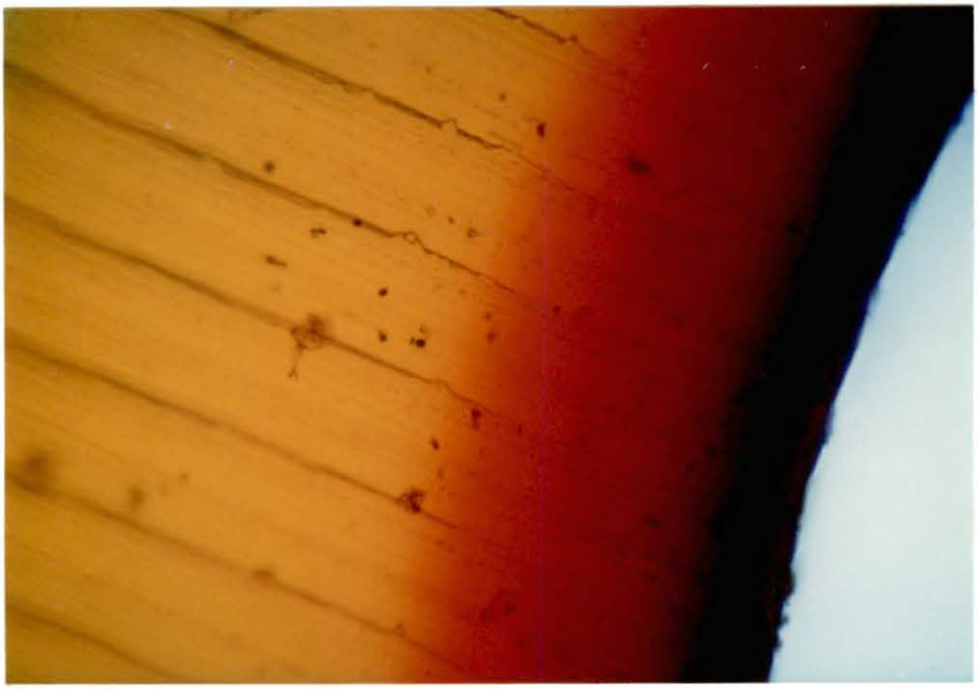

FIGURE 12. Optical microscope photograph of a cross section from the sample irradiated at 50 Krad using the formulation 60% NVP/ 40% MeOH and stained in reactive Lugol/buffer (1:1) solution (magnification = 175x)

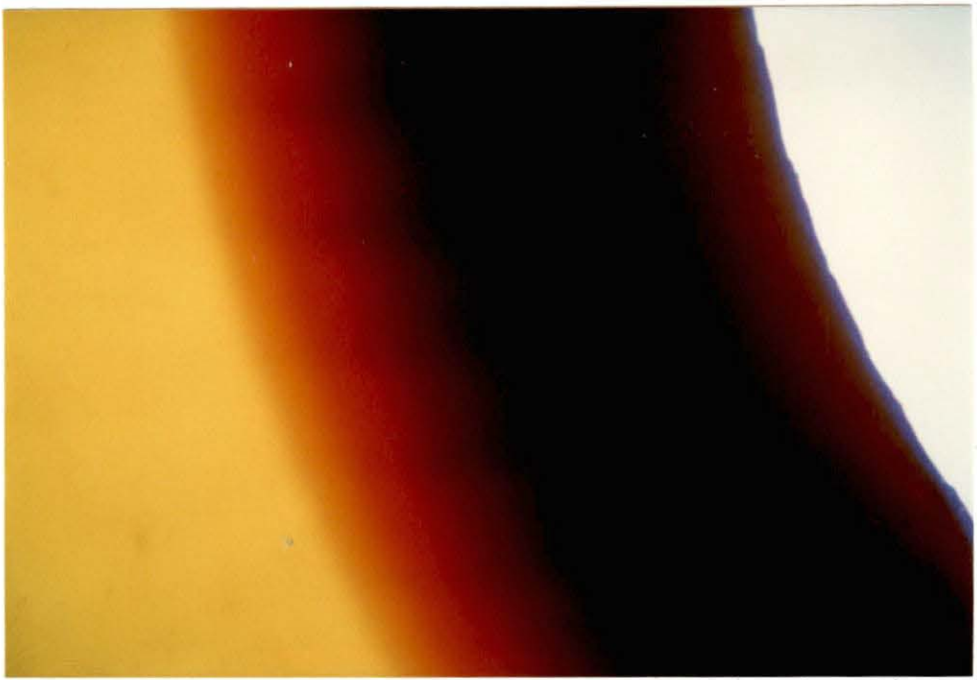

FIGURE 13. Optical microscope photograph of a cross section from the sample irradiated at 150 Krad using the formulation 60% NVP/40% MeOH and stained in 0.05 M KI/0.002 M I_2 aqueous solution (magnification = 175x)

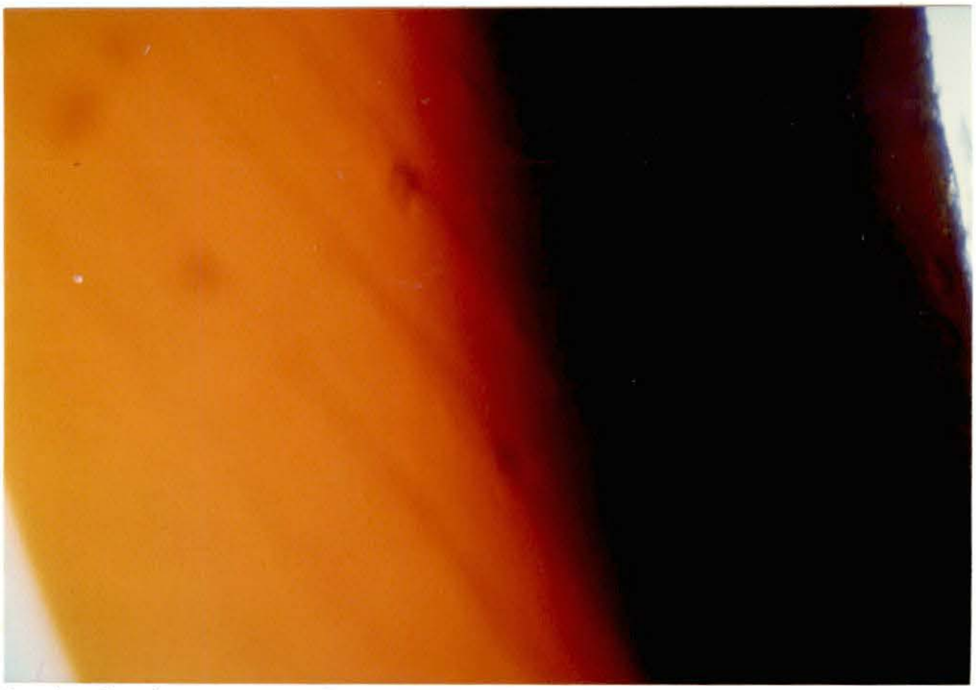

FIGURE 14. Optical microscope photograph of a cross section from the sample irradiated at 150 Krad using the formulation 60% NVP/40% MeOH and stained in Lugol/buffer (1:1) solution (magnification = 175x)

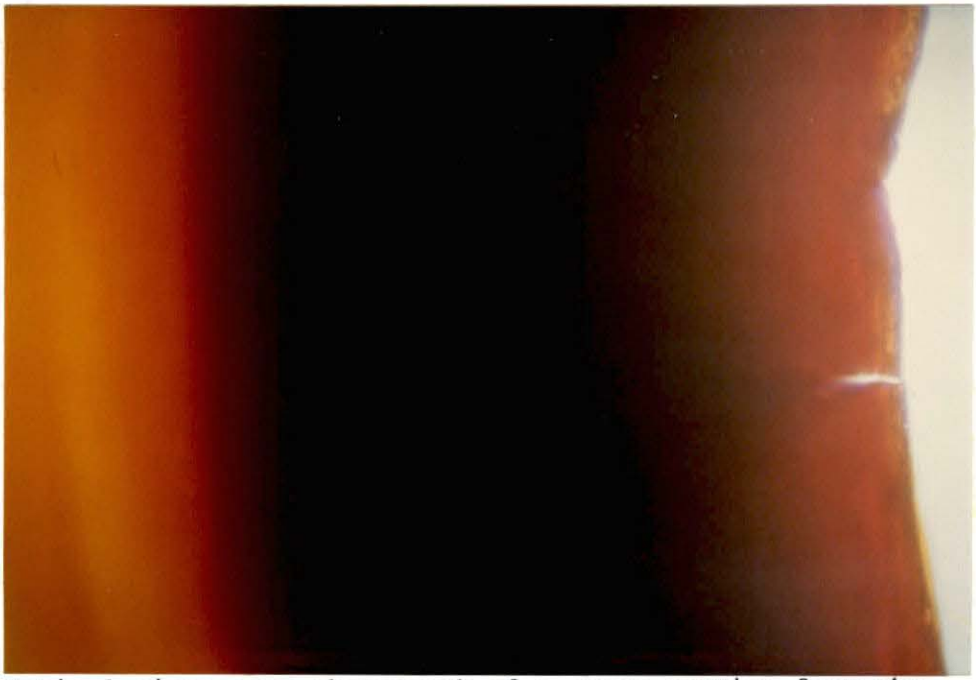

FIGURE 15. Optical microscope photograph of a cross section from the sample irradiated at 250 Krad using the formulation 60% NVP/40% MeOH and stained in 0.05 M KI/0.002 M I_2 aqueous solution (magnification = 175x)

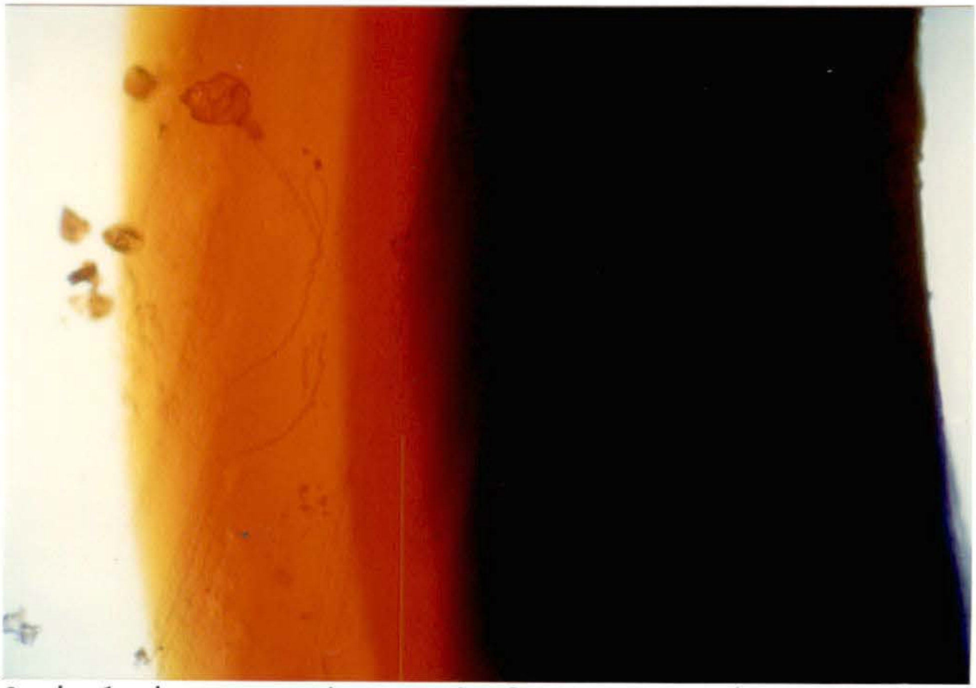

FIGURE 16. Optical microscope photograph of a cross section from the sample irradiated at 250 Krad using the formulation 60% NVP/40% MeOH and stained in Lugol/buffer (1:1) solution (magnification = 175x)

The reactive Lugol/buffer (1:1) solution stained PNVP to a better degree as compared to the KI/I_2 (0.05 M KI/0.002 M I_2).

Effect of solvent composition The water solvent formulations which contained high concentrations of water, or just water alone, produced no graft and a high degree of homopolymerization, even when the samples were irradiated at low irradiation doses. This was shown by results of gravimetric analysis and by a lack of staining (Table 9). Homopolymerization occurred in these systems since water is not a swelling agent of the silicone rubber. Accordingly, in these particular systems, water behaves as the controlling agent of the swelling of the polymer and as an accelerator for the polymerization of vinylpyrrolidone. The homopolymerized plug formed when irradiation was carried out at 250 Krad could not be removed by the post-irradiation cleaning in ethanol/water. However, it could be removed after it was dried, since the plug did not adhere to the wall of the tubing.

Table 9. Observations on irradiated silicone tubing prepared using formulations containing water as the solvent

Formulation	Irradiation dose, Krad	Solvent consistency	Graft, mg/cm^2	Stainable
60% NVP/40% water	250	plugged	none	no
60% NVP/30% water/10% MeOH	250	plugged	none	no
60% NVP/30% water/10% MeOH	50	clear gel	none	no

Grafting at lower doses   Irradiation grafting of silicone rubber tubes using the formulation 60% NVP/40% methanol at lower doses, such as 25 and 30 Krad, resulted in much thinner rims as compared to the results obtained for samples irradiated at 35 Krad or more. However, reproducibility for samples irradiation grafted at the same dose and on the same day could not be achieved (Table 10). This could be due to a nonuniform irradiation field. Attempts to copolymerize a graft using a lower dose, such as 20 Krad, had no success in that no measurable rim was produced (Table 10).

All samples that were irradiated at low irradiation doses (45 Krad or less) retained their natural rubbery state. The monomer solution after irradiation was a clear liquid, and was easily removed or extracted with ethanol/water. There was no increase in wall thickness for all samples. Acid fuchsin (0.1%) and basic fuchsin (0.1%) in 100% methanol, and KI/I_2-buffer solution were able to stain the hydrogel effectively for rims as small as 8 microns in thickness. However, a longer immersion time was required (> 72 hours) for the rim to develop when either acid or basic fuchsin was used.

The general trend observed for rim thicknesses was that the top part of the tube always had a thinner rim relative to the middle part and bottom part for each irradiated sample. Although the irradiation tube was positioned at the center of the irradiation field, a uniform grafting could not be achieved for any particular sample (Table 10). This could be due to the unavailability of the monomer to the upper part of the sample as a function of irradiation time, as well as due to a nonuniform irradiation field.

TABLE 10. Measurements on irradiated silicone tubing prepared using the formulation 60% NVP/40% methanol (irradiation grafted at low doses, and stained using 0.1% acid fuchsin or 0.1% basic fuchsin in 100% methanol, and in aqueous Lugol/buffer solution)

	Rim thickness (microns)								
	100% methanol (0.1% dye)						Lugol/buffer (1:1)		
	Acid fuchsin			Basic fuchsin					
Irradiation dose, Krad	T[a]	M[b]	B[c]	T	M	B	T	M	B
20	NR[d]	NR	NR	NR	NR	NR	NR	NR	NR
25	51	51	51	38	51	64	38	51	64
25	38	76	51	25	76	38	38	38	38
25	51	51	64	50	51	64	51	114	64
25	25	76	76	38	76	51	38	76	76
25	25	25	38	25	38	38	38	38	38
30	8	13	13	8	13	13	13	13	13
30	25	51	38	25	51	38	25	51	38
30	51	114	76	51	127	76	51	127	76
30	38	102	76	64	102	89	64	102	76
30	25	64	25	25	76	38	38	76	38
35	178	203	292	254	254	279	203	330	254
40	304	229	317	330	381	330	330	381	330
45	305	330	305	318	330	318	343	394	317

[a] T: top portion of the tube; sample usually not in contact with monomer at the end of an irradiation.

[b] M: middle portion of the tube; sample in contact with monomer at the end of an irradiation.

[c] B: bottom portion of the tube; sample in contact with monomer at the end of an irradiation.

[d] NR: no rim was observed.

Samples that were irradiated at 25 and 30 Krad possessed the thickest rim at the middle portion of the tube. The average rim thicknesses for these samples were 63.5 and 73.7 microns, respectively.

There were significant variations between samples irradiated at the same irradiation dose (e.g., 25 and 30 Krad) in terms of graft level, percent graft, and graft water content (Table 11). There were no correlations between graft level and graft water content. However, samples with extremely low graft levels exhibited very high graft water content (Table 11).

TABLE 11. Results of grafting on silicone rubber tubes at low irradiation doses using the formulation 60% NVP/40% methanol

Irradiation dose, Krad	Graft level (mg/cm^2)	Water in graft (%)	Grafting yield (%)	Description of external polymer
20[a]	-	-	-	clear liquid
25	0.60	46.3	0.64	clear liquid
25	0.22	50.0	0.23	clear liquid
25	0.67	51.3	0.71	clear liquid
25	0.58	47.4	0.62	clear liquid
25	0.11	80.8	0.11	clear liquid
30	0.06	89.3	0.06	clear liquid
30	0.57	49.1	0.61	clear liquid
30	1.06	53.8	1.13	clear liquid
30	0.86	56.4	0.91	clear liquid
30	0.90	43.5	0.96	clear liquid
35	1.81	61.3	1.92	clear liquid
40	2.76	57.5	2.93	clear liquid
45	2.98	59.7	3.18	clear liquid

[a] Grafting was not achieved at this irradiation level.

Several photographs and scanning electron micrographs were taken of the samples irradiated at 25 and 30 Krad. Figures 17 and 18 show the rim depth for a sample irradiated at 25 Krad and stained with 0.1% acid fuchsin and 0.1% basic fuchsin in 100% methanol, respectively. Figures 19 and 20 show the rim depth for a 30 Krads sample stained in a similar way. Figures 21 and 22 exhibit the rim depth stained by using the iodine technique (Lugol/buffer solution) for the 25 and 30 Krad samples, respectively. Figure 23 is a scanning electron microscope photograph showing the material textural differences between the grafted (left) and nongrafted (right) regions. Figure 24 is a high magnification scanning electron micrograph emphasizing the region of the poly(N-vinylpyrrolidone) (PNVP) rim.

The color of the grafted rim when compared visually with the colors of homogeneous grafted sheets (Figures 25 and 26) indicated that a surface grafting ratio of between 10 and 22% was achieved.

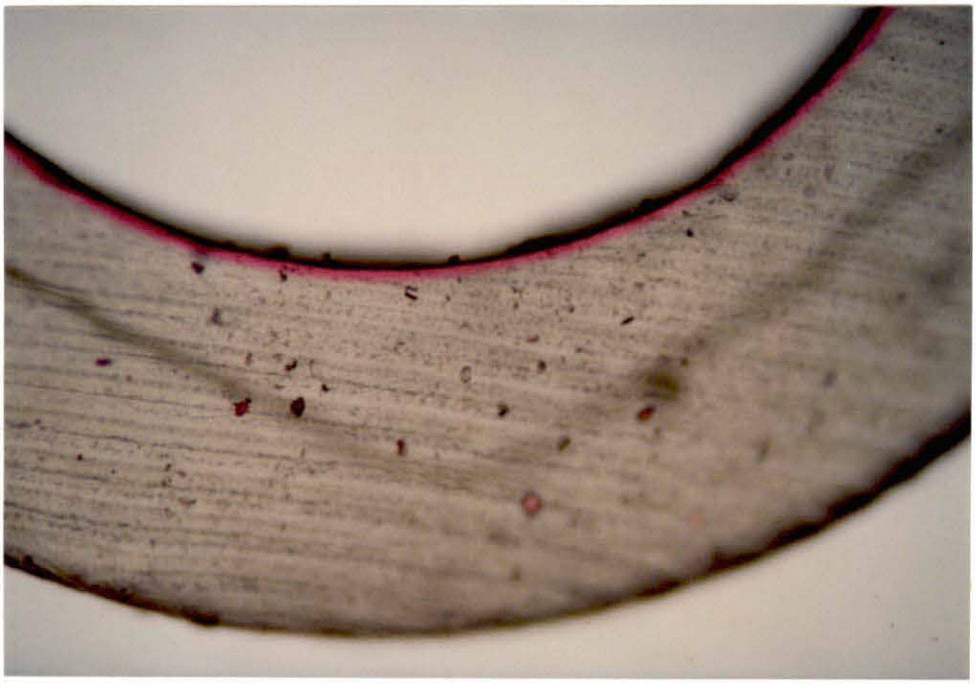

FIGURE 17. Optical microscope photograph of a cross section from the sample irradiated at 25 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% acid fuchsin in 100% MeOH (magnification = 69x)

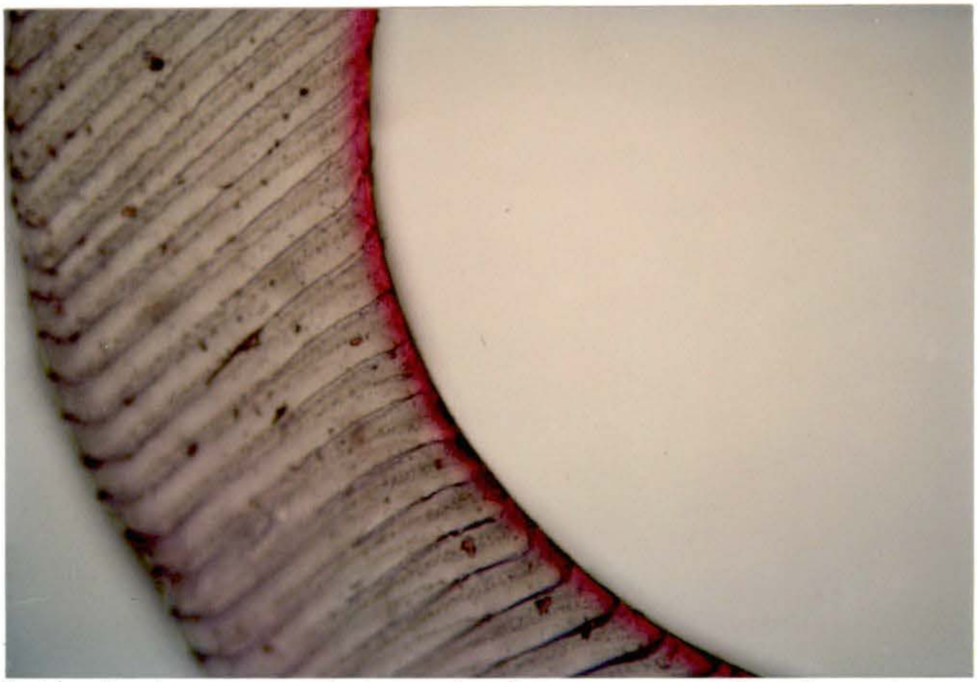

FIGURE 18. Optical microscope photograph of a cross section from the sample irradiated at 25 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% basic fuchsin in 100% MeOH (magnification = 69x)

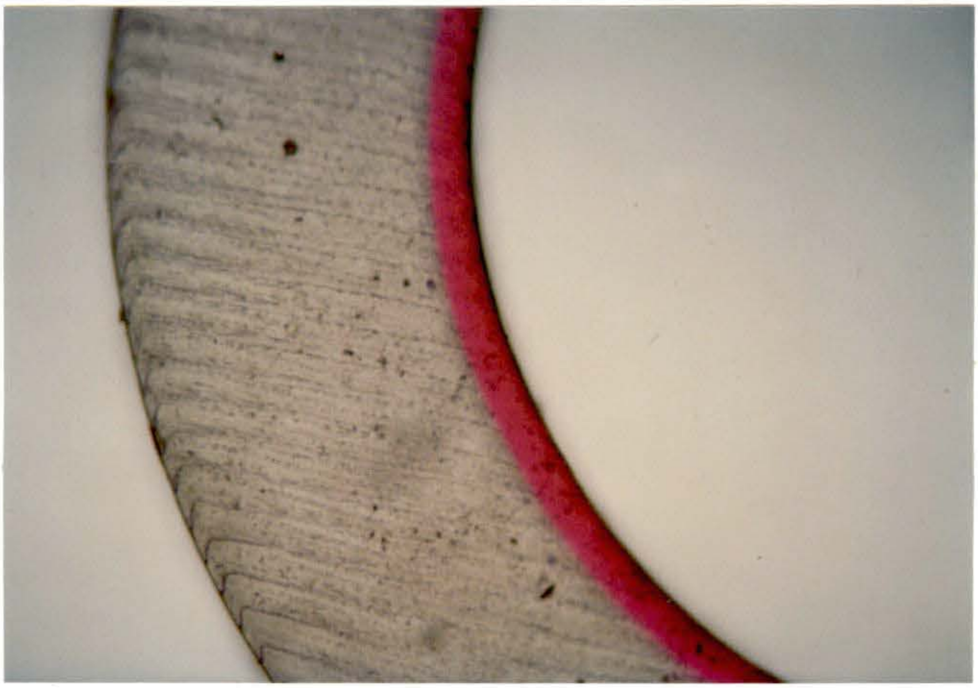

FIGURE 19. Optical microscope photograph of a cross section from the sample irradiated at 30 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% acid fuchsin in 100% MeOH (magnification = 69x)

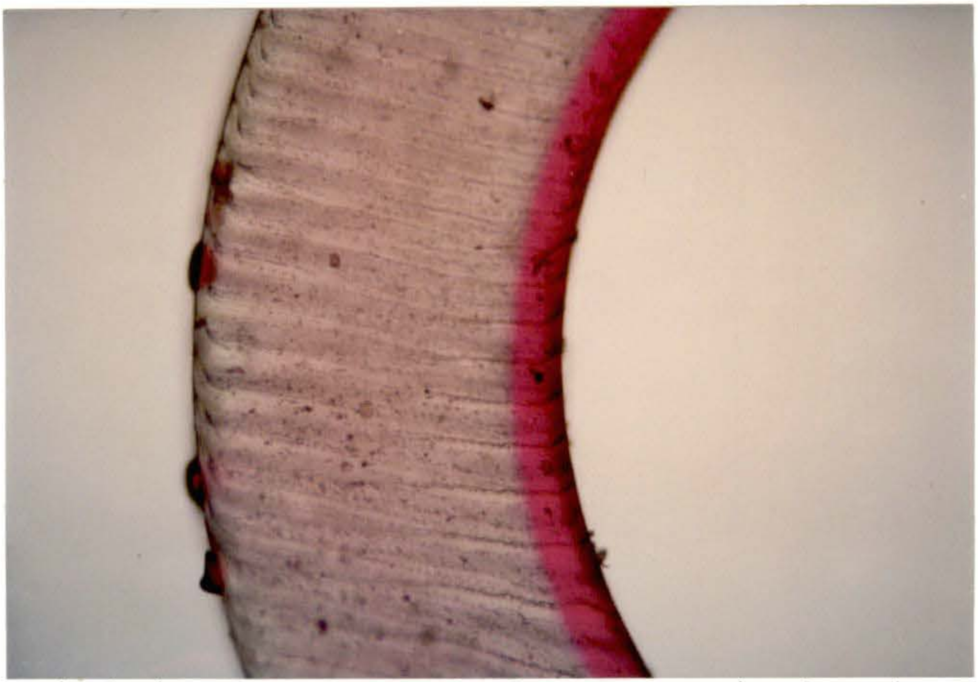

FIGURE 20. Optical microscope photograph of a cross section from the sample irradiated at 30 Krad using the formulation 60% NVP/40% MeOH and stained in 0.1% basic fuchsin in 100% MeOH (magnification = 69x)

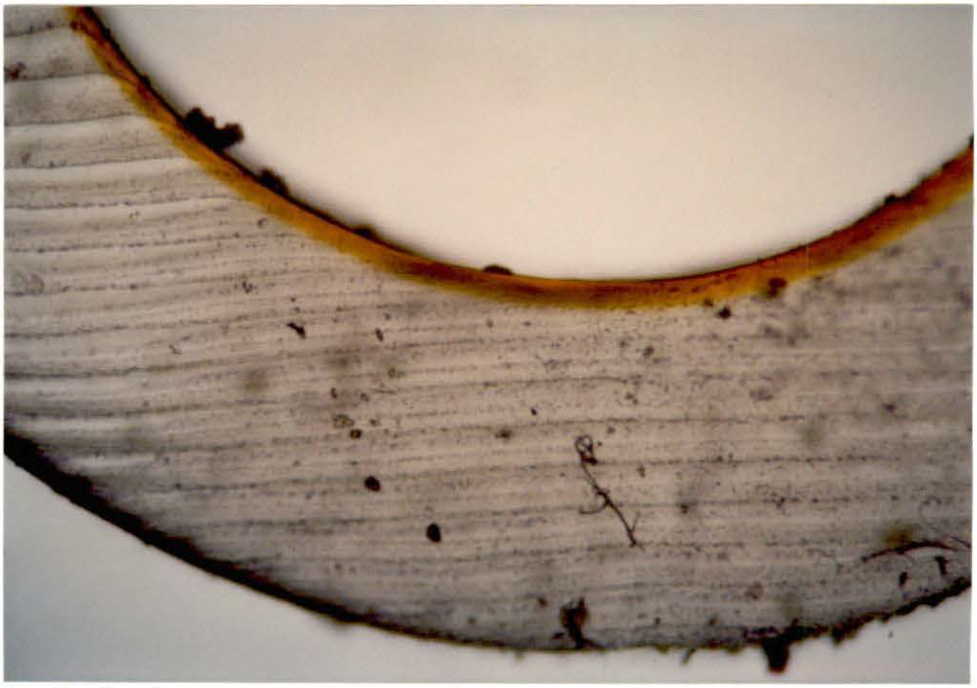

FIGURE 21. Optical microscope photograph of a cross section from the sample irradiated at 25 Krad using the formulation 60% NVP/40% MeOH and stained in reactive Lugol/buffer (1:1) solution (magnification = 69x)

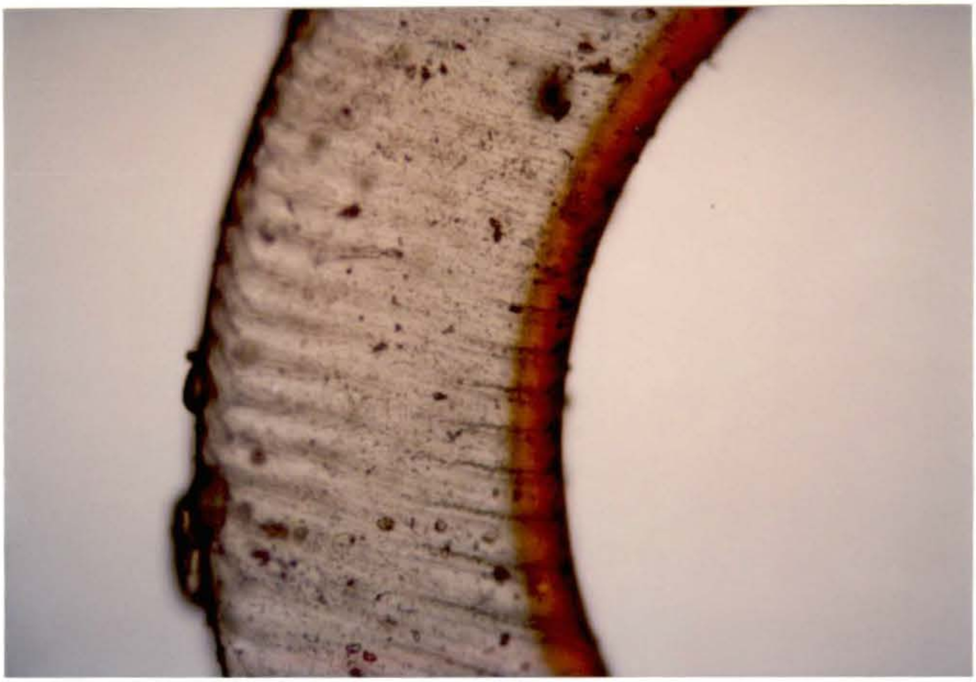

FIGURE 22. Optical microscope photograph of a cross section from the sample irradiated at 30 Krad using the formulation 60% NVP/40% MeOH and stained in reactive Lugol/buffer (1:1) solution (magnification = 69x)

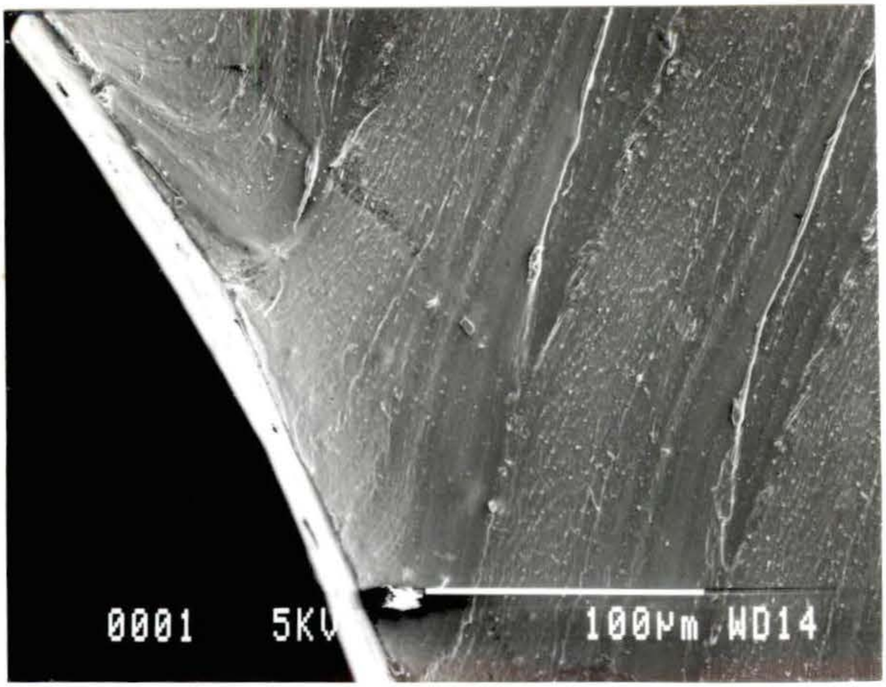

FIGURE 23. Scanning electron micrograph of a nonstained cross section from the sample irradiated at 25 Krad using the formulation 60% NVP/40% MeOH (magnification = 370x). Note the white NVP rim (left side; 13 microns thick)

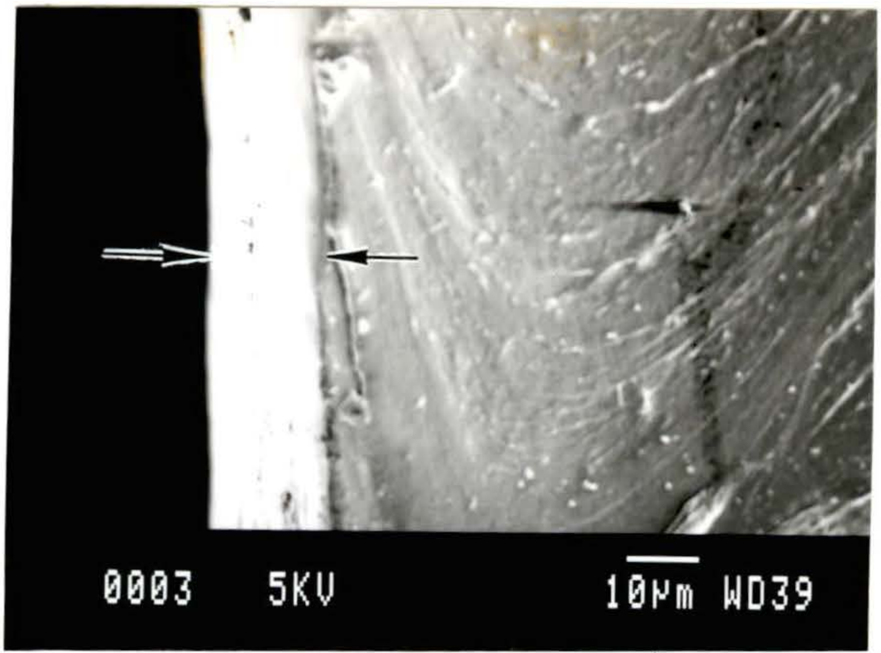

FIGURE 24. Scanning electron micrograph of a nonstained cross section from the sample irradiated at 25 Krad using the formulation 60% NVP/40% MeOH (magnification = 950x). Note the white NVP rim (between arrows; 13 microns thick)

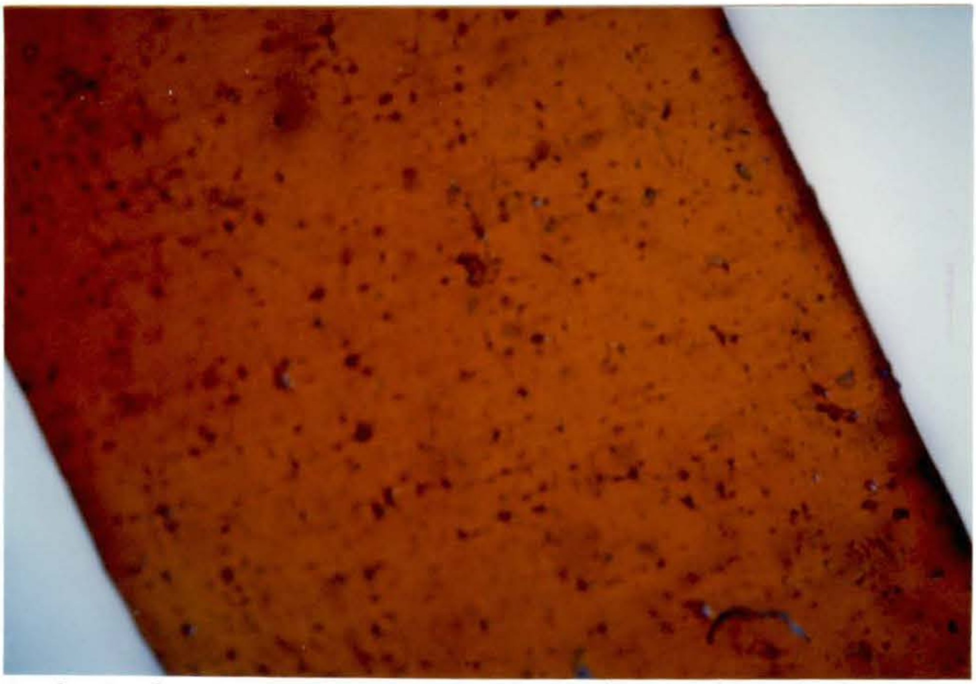

FIGURE 25. Optical microscope photograph of a thin section of the homogeneous grafted film with grafting yield of 10.3% using the formulation 60% NVP/40% MeOH and stained in Lugol/buffer (1:1) solution for 1 week (dose level = 50 Krad) (magnification = 69x)

FIGURE 26. Optical microscope photograph of a thin section of the homogeneous grafted film with grafting yield of 22.7% using the formulation 60% NVP/40% MeOH and stained in Lugol/buffer (1:1) solution for 1 week (dose level = 150 Krad) (magnification = 69x)

Effect of Irradiation on Polymeric Silicone Rubber

Irradiation had little or no effect on the silicone rubber in terms of dye absorption (Table 12). It seemed that swelling solvents such as methanol played a more important role in opening up some passages, and allowing the dye to absorb into the silicone rubber matrix. Furthermore, the absorption of dye is also dependent on the nature of the substrate and the dye itself. Basic fuchsin stained silicone rubber to a small degree regardless of the characteristics of the silicone rubber. On the other hand, acid fuchsin did not stain silicone rubber.

TABLE 12. Absorption of dyes on irradiated and nonirradiated silicone rubber

Description/solution	Observation
Irradiated SiR[a], 50 Krad, .1% AF[b], 10% MeOH	no dye absorbed
Irradiated SiR, 50 Krad, .1% AF, 50% MeOH	no dye absorbed
Irradiated SiR, 50 Krad, .1% AF, 100% MeOH	no dye absorbed
Irradiated SiR, 50 Krad, .1% BF[c], 10% MeOH	light pink color
Irradiated SiR, 50 Krad, .1% BF, 50% MeOH	light pink color
Irradiated SiR, 50 Krad, .1% BF, 100 MeOH	light pink color
Irradiated SiR, 150 Krad, .1% AF, 10% MeOH	no dye absorbed
Irradiated SiR, 150 Krad, .1% AF, 50% MeOH	no dye absorbed
Irradiated SiR, 150 Krad, .1% AF, 100% MeOH	no dye absorbed
Irradiated SiR, 150 Krad, .1% BF, 10% MeOH	light pink color
Irradiated SiR, 150 Krad, .1% BF, 50% MeOH	light pink color
Irradiated SiR, 150 Krad, .1% BF, 100% MeOH	light pink color
Irradiated SiR, 250 Krad, .1% AF, 10% MeOH	no dye absorbed
Irradiated SiR, 250 Krad, .1% AF, 50% MeOH	no dye absorbed
Irradiated SiR, 250 Krad, .1% AF, 100% MeOH	no dye absorbed
Irradiated SiR, 250 Krad, .1% BF, 10% MeOH	light pink color
Irradiated SiR, 250 Krad, .1% BF, 50% MeOH	light pink color
Irradiated SiR, 250 Krad, .1% BF, 100% MeOH	light pink color
Nonirradiated SiR, .1% AF, 10% MeOH	no dye absorbed
Nonirradiated SiR, .1% AF, 50% MeOH	no dye absorbed
Nonirradiated SiR, .1% AF, 100% MeOH	no dye absorbed
Nonirradiated SiR, .1% BF, 10% MeOH	light pink color
Nonirradiated SiR, .1% BF, 50% MeOH	light pink color
Nonirradiated SiR, .1% BF, 100% MeOH	light pink color

[a] SiR: silicone rubber.

[b] AF: acid fuchsin.

[c] BF: basic fuchsin.

Equilibrium Swelling of Silicone Rubber in NVP and Solvents

Equilibrium swelling of silicone rubber in NVP and NVP/MeOH

The absorption of NVP and 60% NVP/40% methanol into silicone rubber tubing was found to be about 3.5% and 3.85%, respectively. The absorption of 60% NVP/40% methanol (MeOH) into silicone rubber was slightly higher than NVP alone possibly due to the presence of methanol. In a methanolic system, a longer time may be required to reach equilibrium swelling as compared to the NVP system (Table 13). It was found that the silicone rubber tubes saturated with either NVP or 60% NVP/40% MeOH within 2 to 3 hours of continuous liquid contact. This was shown by the presence of small liquid beads on the outer surface of the tubes, as well as by weight stabilization.

TABLE 13. Equilibrium swelling of silicone rubber tubing in NVP and in 60% NVP/40% methanol

	Percent swelling (%)						
Liquid(s)	0.25 hr	0.5 hr	0.75 hr	1 hr	2 hr	3 hr	6 hr
NVP	2.81	3.35	3.43	3.47	3.74	3.48	3.81
60% NVP/40% MeOH	2.82	2.91	2.55	3.57	3.84	3.85	3.86

Equilibrium swelling of silicone rubber in methanol

Methanol was found to swell silicone rubber to a very small degree. The equilibrium swelling of silicone rubber in methanol was about 0.4%.

Determination of the Required Immersion Time

In various dye solutions of 0.1% acid fuchsin and 0.1% basic fuchsin, it took at least 72 hours to achieve a constant rim thickness. The sample irradiated at 50 Krad could not be stained in dye solutions in which the concentration of methanol was less than 50%. This was observed throughout the various duration test periods. In KI/I_2 and in Lugol/buffer solutions, a full rim developed after 96 hours of immersion. The results for various test periods are given in Tables 14 to 20.

TABLE 14. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, and 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 2 hours)

	Rim thickness (microns)							
	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (.0005 gm I_2/cm^3)	Lugol-buffer solution
Irradiation dose, Krad	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	NR	203	241	76	76
150	292	267	241	330	381	355	343	356
250	330	343	318	368	483	483	559	559

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

TABLE 15. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, and 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 24 hours)

	Rim thickness (microns)							
Irradiation dose, Krad	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (0.0005 gm I_2/cm^3)	Lugol-buffer solution
	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	76	254	254	76	102
150	292	267	343	330	381	406	381	368
250	343	381	432	483	483	559	509	610

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

TABLE 16. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, and 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 48 hours)

	Rim thickness (microns)							
Irradiation dose, Krad	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (0.0005 gm I_2/cm^3)	Lugol-buffer solution
	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	76	254	279	102	102
150	305	305	305	330	406	394	381	368
250	381	381	432	559	483	559	521	610

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

TABLE 17. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, and 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 72 hours)

	Rim thickness (microns)							
	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (0.0005 gm I_2/cm^3)	Lugol-buffer solution
Irradiation dose, Krad	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	102	254	279	229	152
150	305	305	305	330	381	432	381	368
250	381	381	432	559	483	584	521	660

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

TABLE 18. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, and 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 96 hours)

	Rim thickness (microns)							
	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (0.0005 gm I_2/cm^3)	Lugol buffer solution
Irradiation dose, Krad	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	102	254	279	241	254
150	305	305	305	330	381	432	381	381
250	381	381	432	559	483	584	521	660

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

TABLE 19. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, and 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 144 hours)

	Rim thickness (microns)							
Irradiation dose, Krad	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (0.0005 gm I_2/cm^3)	Lugol-buffer solution
	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	102	254	279	241	254
150	305	305	305	330	381	432	381	381
250	381	381	432	559	483	584	521	660

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

TABLE 20. Measurements of rim thickness as a function of time stained in various dye solutions (0.1% acid fuchsin or 0.1% basic fuchsin in 10, 50, 100% methanol), KI/I_2 solution, and in Lugol-buffer solution (immersion time = 168 hours)

	Rim thickness (microns)							
Irradiation dose, Krad	10% MeOH		50% MeOH		100% MeOH		KI/I_2 (0.0005 gm I_2/cm^3)	Lugol-buffer solution
	AF[a]	BF[b]	AF	BF	AF	BF		
50	NR[c]	NR	NR	102	254	279	241	254
150	305	305	305	330	381	432	381	381
250	381	381	432	559	584	584	521	660

[a] AF: acid fuchsin.

[b] BF: basic fuchsin.

[c] NR: no rim observed.

DISCUSSION

It was determined that irradiation grafting of N-vinylpyrrolidone (NVP) into the inner surface of silicone rubber tubes using the formulation 60% NVP/40% methanol, and employing low irradiation doses, such as 25 and 30 Krad resulted in lower graft concentrations (graft levels) and thinner graft rims as compared to the results obtained for samples that were irradiated at 35 krad or more. The average rim thicknesses for the 25 Krad and 30 Krad samples are 65 and 73 microns, respectively. For our objective, to achieve a thin grafting layer in the order of one micron or less, these rim thicknesses would be undesirable. For microporous prostheses with optimum pore size in the order of 18 to 25 microns (White et al., 1981), a grafted layer of one micron or more may significantly alter the mechanical properties of these highly favorable porous structure vascular prostheses. The presence of a thicker rim was probably due to the fact that the monomer solution was allowed to contact the silicone rubber tubes for an extended period of time before irradiation. In all experiments, the inner surface of the tube was allowed to contact the monomer solution for at least one hour before irradiation was performed.

The grafting levels and graft depths for samples that were irradiated on the same day, and at the same irradiation dose (e.g., 25 and 30 Krad) were highly variable. The difference in graft depth was as high as 50%, and the difference in graft level was estimated to be about 94%. These differences could be attributed to the following factors: (1) contamination due to the presence of oxygen in the solution, even though this effect was minimized by bubbling the solution with nitrogen for at least 30 minutes and under a nitrogen atmosphere inside a glove bag, plus the samples were sealed from air prior to irradiation, (2) a nonuniform irradiation field, and (3) the grafted tubing material is silicone rubber which is highly permeable to oxygen. Oxygen is known to destroy radicals, and as a result, the grafting yield decreases. This effect was observed by Chapiro (1962), and by Ratner and Hoffman (1974).

There was no correlation between graft depth and graft level. Samples with relative high graft levels but with relative thin graft rims were observed (see Tables 10 and 11). This suggests that a more concentrated graft was formed.

The average grafting ratios for samples that were irradiated at 25 and 30 Krad were 0.5 and 0.7%, respectively. These results are comparable to the grafting ratios reported by Chapiro and Lamothe (1983). At approximately 30 Krad, they were able to obtain an overall grafting ratio of 1% with a surface grafting ratio of between 5 and 21%. Our overall grafting ratio (0.7%) at 30 Krad was in the same range as theirs and could be higher, since in our case only the inner surface of the tube was grafted, whereas in their samples both the inner and outer surfaces were grafted. The surface grafting ratio for samples that were irradiated at 25 and 30 Krad was estimated to be between 10 and 22% (also see Figures 21-22 and 25-26). This is somewhat lower than the grafting ratio of 33% or more suggested by Chapiro et al. (1980) for significant improvement in thromboresistance. However, this ratio is again comparable to their results (5-21%) given the same irradiation dose (30 Krad). The surface grafting ratio for samples that were irradiated at 50 Krad and above was estimated to be as high as 35%, but these samples were usually stiff and not useful for our purpose.

Acid fuchsin or basic fuchsin can be used to stain poly(N-vinylpyrrolidone) (PNVP); however, the nature of the dye and the methanol concentration in the dye solutions can influence the measurements of the grafted front. Basic fuchsin which is a cationic dye, tends to stain silicone rubber to some degree. This sometimes resulted in a wrong indication of the location of the grafted front, and as a result, the graft thickness obtained was almost always thicker than that of acid fuchsin which is an anionic dye. Anionic dyes of the fluorescein family are known to bind strongly to PNVP (Oster and Immergut, 1954). The binding increases markedly with molecular weight, especially in the molecular weight range of 1000 to 10,000 (Oster, 1952). Acid fuchsin was found to bind with PNVP better as compared to basic fuchsin, and it did not stain silicone rubber as in the case of basic fuchsin. Samples that were irradiated at 50 Krad or less were able to resist stain in dye solutions in which the methanol concentration was less than 50%. This was presumably due to the fact that the binding capacity of PNVP for dyes increases with the molecular weight of the polymer. Perhaps at low irradiation doses, only the low molecular weight polymers were formed and they were not be able to bind the dyes due to a lack of binding sites. In 100% methanol dye solutions (acid or basic fuchsin), the methanol may swell the silicone rubber-hydrogel matrix to a small degree and allow dyes to penetrate into the PNVP. The concentration of methanol was determined to influence the measurements of the grafted front, since it was found that irradiation had no effect on the capability of the silicone rubber to absorb dyes.

The iodine technique can also be used to stain PNVP and identify the grafted front or different grafted zones since the binding capacity of PNVP for iodine is also a function of the molecular weight of the polymer. Grafted depths obtained using the iodine technique and optical microscopy are comparable to those obtained using acid or basic fuchsin in 100% methanol when analyzed in a similar manner. The results of graft depths obtained by using the iodine technique seemed to correlate well with those obtained using acid fuchsin in 100% methanol, especially for the 50 and 150 Krad samples.

In various 0.1% acid fuchsin and 0.1% basic fuchsin dye solutions, the time required for the grafted front to fully develop was at least 72 hours. This interval of time was significantly longer than 48 hours reported by Chapiro and Lamothe (1983). The immersion time was found to be a crucial factor which influences the measurements of the grafted front.

In iodine solutions, a period of 96 hours is required to achieve a constant grafted rim.

Both optical microscopy and scanning electron microscopy can be used to identify and measure the grafted front of NVP into silicone rubber. The results of measurements obtained using these techniques usually agreed with each other.

Water is a poor solvent for silicone rubber since it would not wet or swell silicone rubber, and it would seem to be an ideal solvent to achieve a thin film grafting; however, water also promotes the polymerization of NVP. Replacing the methanol in the formulation 60% NVP/40% methanol with water and irradiating at 50 and 250 Krad resulted mostly in the homopolymer of PNVP.

The equilibrium swellings of NVP and 60% NVP/40% methanol into silicone rubber are 3.5% and 3.85%, respectively. The equilibrium swelling of NVP alone is slightly higher than those reported by Chapiro et al. (1980), 3%, Ratner and Hoffman (1974), 3%, and Yasuda and Refojo (1964), 1.7%. The difference is presumably due to the differences in the nature of the silicone rubber (e.g., sheet, tubing, filler content, etc.). The equilibrium swelling of 60% NVP/40% methanol was higher than that of NVP alone possibly due to the combined swelling of NVP and methanol. Methanol swelled silicone rubber to a small extent, about 0.4%.

A uniform grafting was not achieved in this investigation because of the following factors: (1) a nonuniform irradiation field, and (2) a lack of availability of monomer to the upper region of the tube as a function of irradiation time, since the level of the monomer solution in the tube dropped as the monomer was consumed during the irradiation process. Due to the unavailability of the monomer at the upper region of the tube, the grafted depth at this part is almost always smaller relative to the grafted fronts at the middle and the bottom of the tube.

A most desirable property of the grafting system is a nongelling (liquid) external polymer. Such a system could allow the rapid, reproducible preparation of evenly grafted substrate. Furthermore, a clear liquid external polymer solution after irradiation can easily be removed by a simple solvent mixture such as water/ethanol. The formulation 60% NVP/40% methanol used in this project was a clear liquid when used for irradiation grafting at doses of 50 Krad or less. On the other hand, it was a clear viscous gel when grafting was carried out at 150 and 250 Krad. For microporous prostheses, it would be important to have only a clear liquid for removal from among the pores after irradiation in which NVP would bond within the silicone rubber surface ($<$ 1 micron in thickness).

CONCLUSIONS

Irradiation grafting using the formulation 60% NVP/40% methanol and several irradiation doses, especially low doses such as 25 and 30 Krad was carried out in an effort to develop a method to graft a thin film of NVP (in the order of less than 1 micron) into silicone rubber tubing. The thinnest graft depth achieved in this investigation was within a range of 8 to 13 microns. The graft levels obtained for low irradiation dose samples were from 0.06 mg/cm^2 to 1.06 mg/cm^2. However, these results could not be reproduced. Factors that contributed to the inability to reproduce the results could be oxygen contamination due to the method of sample preparations, as well as the presence of a nonuniform irradiation field.

In order to achieve a uniform grafting from the top to the bottom of the silicone rubber tubing, the whole length of the silicone rubber tube must have equal access to the monomer solution, and a uniform irradiation field must be used.

The grafting method can be optimized and the sources of error such as oxygen contamination can be minimized if the monomer is circulated through the tubing instead of being filled and clamped. This should help to decrease the oxygen contamination, increase the chance of a uniform grafting, and prevent the formation of homopolymer.

A poor solvent such as water can limit the penetration of NVP into silicone rubber, but water also promotes homopolymerization of NVP and therefore should be avoided.

Higher concentrations of methanol (> 40%) in the monomer solution may be able to keep the NVP in the solution and limit the grafting to a relatively thin film.

The graft depths obtained using either the Lugol/buffer (1:1) solution or the KI/I_2 solution in the staining technique were comparable to each other. These results also correlated well with graft depths obtained using acid fuchsin (Tables 17-20).

Acid fuchsin should be used for staining PNVP since it is more compatible to PNVP than basic fuchsin in terms of the nature of the dye (anionic dye).

Iodine technique can also be used to identify the graft depth, and application of the technique verified the results obtained from the dye staining technique.

Although the desired grafting thickness (< 1 micron) was not obtained, this investigation showed that the graft depth is a function of irradiation dose for the grafting system used. If a thin graft layer is required, lower irradiation doses (as low as 25 Krad or less) must be used. Furthermore, the contacting time between the monomer solution and the silicone rubber tubing must be minimized as much as possible since the equilibrium swellings of NVP and 60% NVP/40% methanol in silicone rubber tubing were found to reach a constant level within one hour. The results of this investigation also indicated that irradiation grafting using high irradiation doses above 35 Krad for the chosen system (60% NVP/40% methanol) was not a method of choice, since thicker graft depth (> 200 microns) always resulted. Electron irradiation may provide a more uniform irradiation field compared with the Cobalt-60 irradiation method.

Even though this investigation did not identify a clear method which could be used to graft a thin layer (< 1 micron) of NVP into silicone rubber using Cobalt-60 gamma irradiation, it has established a direction for further research and development in that a more stable irradiation field is required. Also, several dye stain characteristics for NVP have been developed in sufficient detail to be applied with confidence.

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