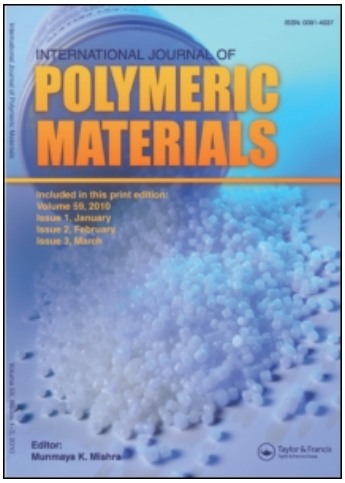

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Vena Cava Occlusion: Balloon Design†

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Various considerations in the development of a natural rubber balloon for vascular occlusion, particularly vena cava occlusion are summarized. The physical properties of the rubber necessary for occlusion are discussed. Since the balloon must remain inflated for at least 4 to 12 weeks after implantation, the balloon should be impermeable to the inflation medium. A measure of the impermeability incorporated in this design is presented. Optimum values for physical properties such as tensile strength, stress and elongation at break are discussed along with the geometric considerations of fixation relative to stress. Results of tests for biological acceptability (such as toxicity and implantability) of the candidate balloon material are included. The occlusion process was studied by investigating the pressure/volume relationships in the unrestricted condition and in restricting tubes of varying compliance resulting in the selection of an appropriate balloon configuration. Experiments indicated that the restricted rupture volume of a balloon (if its unrestricted volume is not exceeded) is determined by the size and compliance of the restricting tube. Pressure–volume data collected while the samples were restricted in cadaver venae cavae are presented. Lastly, *in vitro* testing was done to measure environmental degradation and these effects are described.

INTRODUCTION

For the treatment of certain vascular disorders of the lower extremeties, it is desirable to interrupt blood flow through the inferior vena cava. This is to prevent emboli from migrating to the lungs. Alternate methods to the traditional vena cava ligation technique, include the insertion of an umbrella-shaped caval filter, the Mobin-Uddin Device.[1] An improved method, over that previously proposed, is to implant a balloon inflated with radiopaque contrast medium at the bifurcation of the inferior vena cava and the iliac veins.[2] This balloon would become encapsulated as a permanent implant. The purpose of this paper is to discuss the design criteria for the development of a balloon material for vena

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cava occlusion. Such a discussion is useful, since many elements of this design will be valuable considerations in the development of future materials for the construction of balloons for vascular occlusion and other biomedical applications.

The properties to monitor in the development of such a material are tensile strength, elongation at break, tangent modulus, rupture volume, biological acceptability, encapsulation and rate of contrast media transmission. Values have been determined for these properties and changes in them due to environmental degradation or long term storage have been evaluated. A measure of *in vitro* degradation is a preliminary approximation of the effect of the biological system on the implant.

Permeability studies were undertaken to determine the amount of contrast media which would diffuse through the rubber membrane within 12 weeks after implantation. This parameter was studied to insure that the balloon would not deflate prior to its encapsulation by fibrous tissue which is usually accomplished within 12 weeks from implantation.

Tests were performed on the candidate balloon material to measure biological acceptability. This was an attempt to measure the effect of the implant on the biological system. Also, if any toxic products were produced due to a chemical reaction between the implant and the biological system, the candidate balloon material would fail these tests.

The last areas investigated were the relationship of pressure to volume for balloons of varying chemical composition, shape, and fixation in rigid, stiff and compliant tubes. This study yielded information regarding various geometric considerations for the design of occlusive balloons.

Pressure *vs.* volume curves were generated for balloons inflated with water to rupture, in restricted and unrestricted states. For the restricted conditions, balloons were inflated in rigid tubes, semi-rigid plastic tubes, rubber tubes and tubes of a woven fabric design. Additional pressure-volume curves were prepared for balloons restricted in cadaver venae cavae. Comparisons between the data for synthetic tubes and venae cavae were established, providing a means of routinely monitoring the physical performance of a balloon whose clinical performance had been demonstrated.

EXPERIMENTAL

Physical properties

Using an ASTM D412-68 Type C die, dumbbell test specimens were cut from rubber sheets prepared by a method analogous to that used in the balloon manufacture. Testing was done on an Instron tester at 25.4 cm/min crosshead

speed to measure tensile strength, stress at 300% elongation, stress at 500% elongation and percent elongation at break. Tear strength measurements were made by preparing "trousers-shaped" specimens from the dumbbell samples. Crosshead speed for tear strength measurements was 50.8 cm/min.

Water rupture volume determinations were made at ambient temperature via hand injections. It is felt that these tests better approximate the end use. For this reason, they are employed in characterizing each production lot of balloons. Currently, burst volumes are being monitored for a 12-month duration to determine any aging, storage, and oxidative effects.

Environmental testing was done by immersing dumbbell samples, trousers-shaped test samples or inflated balloon samples in pseudo-extracellular fluid (PECF)[3] at 37°C. Samples were withdrawn from the bath at various time intervals and tested at ambient temperatures. Time of immersion in the environment was related to any change in physical properties of the sample.

Physical properties were measured for samples prepared at various time intervals from the compounding of the latex. This was done to determine the time range when the dipped article would possess optimum physical strengths.

Permeability

Two permeability tests were performed to determine if the contrast media used for inflation would rapidly diffuse through the rubber membrane, prematurely deflating the balloon. In Test 1, the balloon sample is filled with 50cc of radiopaque solution and the external surface of the sample is interfaced with air at ambient temperature. Test 2 is analogous to Test 1 except that each balloon sample is interfaced with 1 liter of PECF at 37°C. Samples of PECF were taken from the test baths at various time intervals and the levels of radiopaque salt that diffused were measured by ultra-violet spectroscopy.

Biological acceptability

Various tests were performed to determine the effects of the implant on the biological system. Additional tests were run to determine if any toxic products were produced from an interaction between blood-like constituents or drugs used in the procedure. This paper will cover short term tests performed by the Huntingdon Research Center.† Results from long term tests such as long term muscle implant tests, carcinogenesis, and teratogenesis are not available at this time.

For acute toxicity testing, the rubber samples were extracted in sodium chloride injection solution or cottonseed oil for 24 hours at 70°C.[4] Following extraction, mice were injected with the eluate of each extraction. Test injections

†Huntingdon Research Center, Baltimore, Maryland 21204.

were paralleled by appropriate control injections. The mice were observed for seven days.

Short term muscle implant studies were performed by injecting 1mm × 1cm strips of rubber into rabbit paravertebral muscles. Negative control strips[4] were also implanted in each rabbit as control sites. Implant time was 72 hours, after which the animals were sacrificed and macroscopic examination of test and control sites were performed.

Human cell culture toxicity tests were performed by elution[5] and agarose overlay.[6] Cytopathic effects were evaluated microscopically, according to the following scheme:

0 — No cytopathic effect (CPE)
1 + — 25% of cells exhibiting CPE
2 + — 25–50% of cells exhibiting CPE
3 + — 50–75% of cells exhibiting CPE
4 + — 75% of cells exhibiting CPE

Hemolysis testing was performed to determine the blood compatibility of the balloon. Rubber samples were extracted with saline solution for 30 minutes at 37°C. Rabbit blood was added to the extract, centrifuged and light transmission measured in a spectrophotometer at 540 mμ. The percent transmission for the sample was compared to a negative control (no hemolysis) and a positive control (complete hemolysis).

A measure of the extractability of toxic products from the balloon by blood-like constituents was done in PECF at 37°C for four hours. Following the extraction, the eluate was injected into mice which were observed for seven days. Similar tests were done to determine drug compatibility. Samples were extracted for four hours at 37°C in contrast media or a solution of heparin in saline (10 USP units/ml). Tests and control injections were made and the mice observed for seven days.

It should be noted that this list of tests for biological acceptability is not to be considered exhaustive. Additional tests such as sterilizability, including Ethylene Oxide Residue studies, pyrogenicity, and an analysis of heavy metals extraction from the balloon are underway but are not yet completed.

Pressure–volume relationships

In this experiment, pressure values corresponding to various inflation volumes were determined. The apparatus consisted of a test block which housed appropriate pressure gauges for measuring pressure within the system. A stopcock was included at the injection point so that the system could be closed following each increase in volume. Test balloons were connected to the test block via a horizontal tube. Before pressure readings were made, equilibrium was established to insure that the pressure throughout the system was uniform.

RESULTS AND DISCUSSION

Physical properties

The balloon described herein is made from a natural latex formulation without zinc oxide as an accelerator activator.[6,8] Standard dipping techniques and hot air cures are employed. Two unstretched balloon configurations will be discussed.

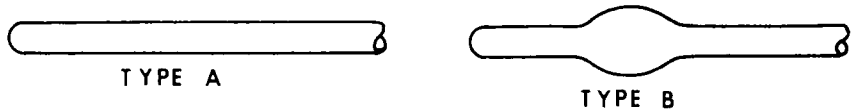

FIGURE 1 Balloon configurations (unstressed).

Figure 1 shows Type A which is a cylindrical balloon affixed at both ends to a rigid plug body. Type B is analogous to Type A except that a spheroidal bulge has been incorporated to increase unrestricted rupture volume.

Physical properties of the latex formulation have been determined via tensile testing of dumbbell and trousers-shaped samples. Values for these properties have been listed in Table I.

TABLE I

	Mean	Std. Dev.
Tensile strength	21,900 *kPa*	1725
Stress at 300%E	1,725 *kPa*	280
Stress at 500%E	3,520 *kPa*	550
Percent elongation at break (%E)	790%	40
Tensile strength	8,800 *N/m*	3500

The range for these values has been demonstrated by measuring physical properties with respect to the age of the latex.

Figures 2 and 3 show computer plots of equations which best fit experimental data for each of these properties *vs.* the age of the latex. Experimental data was fit to Eqs. 1 to 6.

$$y = A + Bx \text{ (linear)} \quad (1)$$
$$y = A\exp Bx \text{ (exponential)} \quad (2)$$
$$y = Ax^B \text{ (power function)} \quad (3)$$
$$y = A + (B/x) \text{ (hyperbolic)} \quad (4)$$
$$y = 1/(A + Bx) \text{ (hyperbolic)} \quad (5)$$
$$y = x/(A + Bx) \text{ (hyperbolic)} \quad (6)$$

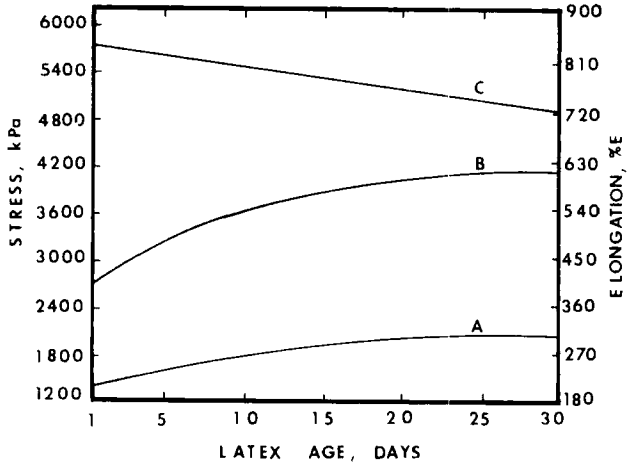

FIGURE 2 Stress and percent elongation at break as functions of age of the latex.

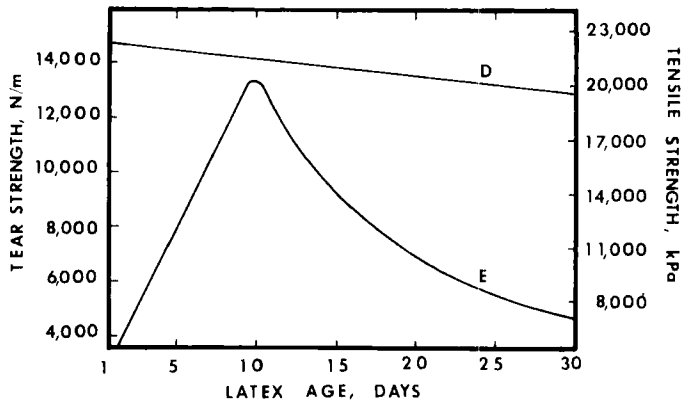

FIGURE 3 Tensile and tear strengths as functions of age of the latex.

Curves A and B represent the best fit for stress at 300% E and stress at 500% E respectively. These curves are of the form of Eq. (3). Curve C is a representation of the computer tracing for percent elongation at break, and is the linear function, Eq. (1). Tensile strength *vs.* age of the latex is represented by Curve D. In this case, a poor fit was obtained due to the wide range of the experimental data. Curve D is a linear function represented by Eq. (1). Curve E depicts the variation of tear strength as a function of the age of the latex. This is a composite of two curves given by Eqs. (1) and (4). Eq. (1) fits the data when the age is less than 10 days and Eq. (4) represents the data for 10 to 28 days after compounding.

TABLE II

Indices of determination

Equation type	Stress at 300%E	Stress at 500%	Tensile strength	%E
1) $y = A + Bx$	0.701	0.776	0.474	0.879
2) $y = Aexp\ Bx$	0.637	0.717	0.492	0.887
3) $y = Ax^B$	0.958	0.961	0.317	0.843
4) $y = A + (B/x)$	0.905	0.842	0.087	0.510
5) $y = 1/(A + Bx)$	0.573	0.655	0.510	0.894
6) $y = x/(A + Bx)$	0.971	0.919	0.100	0.487

	Tear strength	
Equation type	age $\geq$ 10 days	age $\geq$ 10 days
1)	0.839	0.651
2)	0.766	0.582
3)	0.658	0.645
4)	0.451	0.758
5)	0.639	0.471
6)	0.307	0.541

Table II shows the indices of determination obtained for each physical property according to the equation type. For perfect agreement between experimental data and an equation, the index of determination would be 1.000. In this discussion, the representative curve had the highest index of determination or, if several indices were reasonably indistinguishable, the simplest curve was selected.

The purpose of this analysis is to model, as a first approximation, the relationship between physical properties and the age of latex prior to dipping. By studying resulting trends, one can determine the age of the latex when optimum physical properties would be obtained. From Figures 2 and 3, the usable shelf life of the latex was determined to be from five to 21 days after compounding. It has also been shown that during this period the burst volumes are constant within experimental error. The unrestricted rupture volume range for a balloon of Type A in Figure 1 is 140–150 cc. Type B balloons with the same wall thickness as Type A have a rupture volume of 400–500 cc.

In vitro environmental testing of dumbbell and trousers-shaped rubber samples was done in PECF for four weeks. Physical properties were measured at various time intervals and the data indicated that values following four weeks of immersion were equal to those at zero time immersion. A second experiment was performed using balloons of Type A which were inflated with 40 cc of contrast media and immersed in PECF at 37 °C. Forty cc represents 30% of the unrestricted burst volume of Type A balloons. Two concentrations of contrast media were used. For 25% (w/v) contrast media, one sample in PECF

burst nine days after inflation. Four other samples were intact 13 days after inflation when the experiment ended. For the 50% (w/v) contrast media, one sample ruptured 10 days following inflation and all four remaining samples ruptured within 20 days after inflation.

Type B balloons were inflated with 50 cc of the 50% (w/v) contrast media which represents 15% of its total unrestricted burst volume. The first sample of this group ruptured 30 days after immersion in PECF; the second sample ruptured at 40 days. The remaining balloon was intact at 40 days. A second group of Type B balloons was inflated in a tube of woven fabric material to 40% of its restricted rupture volume. No ruptures were observed in this group during 40 days of immersion. A third group of balloons were inflated to 60% of their restricted rupture volume in the woven fabric tube. In this group, two balloons ruptured eight days from the initiation of the test. Two additional samples ruptured 14 days after initiation while the last sample ruptured at 32 days. These experiments demonstrated that Type B balloons when immersed in PECF could be inflated unrestricted to greater volumes than Type A balloons with less possibility of rupture. This is directly related to the larger unrestricted burst volumes for Type B. Further Type B balloons could be safely inflated to 40% of restricted burst volume in a non-extensible tube. In practice, occlusion of a non-extensible tube occurs at volumes less than or equal to 40% of restricted burst volume. Also, since the vena cava is extensible, the restricted rupture volumes that would be expected closely approximate those found in a rubber tube. In a rubber restricting tube, one can inflate a balloon to its unrestricted burst volume for the environment of the test before rupture occurs.

Lastly, it is interesting to note that while the physical property values measured from dumbbell and trousers-shaped samples were unaffected by PECF, the unrestricted balloon samples were affected in some way. That is, additional experiments show that balloons of Types A and B, when inflated with 50 cc of contrast media and exposed to the air at ambient temperature, are intact for three months while samples immersed in PECF at 37°C are intact for at most one month. This implies that the combination of stress and fluid environment greatly change the rubber composition and affect its performance.

Shelf life studies have been conducted for balloon samples by monitoring unrestricted burst values at various time intervals. Balloon samples were covered with opaque polyethylene sheaths and stored in cardboard boxes. Under the storage conditions used, rupture volumes at one year storage are equal to values at zero time of storage.

Permeability

A preliminary evaluation of balloon permeability was accomplished by inflating samples with contrast medium and interfacing them with air at ambient

temperature. The contrast medium used in all permeability studies was a 25% (w/v) aqueous solution of sodium 3,5-diacetamido-2,4,6-triiodobenzoate (Hypaque—25%)† (see Figure 4).

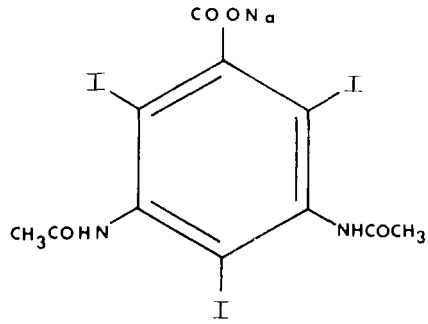

FIGURE 4 Structural formula for radiopaque salt.

Balloon samples tested this way remain impermeable to contrast media for a minimum of 12 weeks. Within eight weeks, the balloon is encapsulated *in vivo*. Thus, a 12-week period of permeability is sufficient for vena cava occlusion.

In vitro permeability studies were done by heating balloon samples to 37°C in PECF, a blood-like constituent. Levels of radiopaque salt which had diffused into the PECF were monitored by U.V. Following an eight-week test period, the levels of radiopaque salt were from 5 to 10 ppm. This experiment further substantiates that these rubber compositions are impermeable to the contrast medium within the period required for encapsulation, since the amount of diffusion of radiopaque salt is about 0.1% of the amount initially in the balloon. It should be noted here that ordinary rubber formulations fail the above permeability tests and that special precautions are required in formulating.

Biological acceptability

Results of acute toxicity tests showed that there was no significant toxicity observed in the test animals following injections of the eluates. This is a short-term test used for preliminary screening of candidate bio-materials.

Short term extractions of the entire device, including the balloon materials, were run in PECF, 25% (w/v) contrast medium, and sodium heparin in saline (10 USP units/c.c.). The eluates from the three extractions were injected into test animals. No significant acute toxicity was noted in any of the test animals.

†Winthrop Laboratories, 90 Park Avenue, New York, N.Y. 10016

Results from these tests indicate that blood-like constituents, such as PECF, do not extract toxic products from the balloon material during a short-term test. Further, the drugs employed during the procedure are compatible with the device.

Short term muscle implant studies indicated that a more severe tissue reaction occurred in test implant sites than at the control sites. Test sites were characterized by moderate muscle fiber necrosis with associated infiltration of polymorphonuclear and mononuclear inflammatory cells. There was also moderate connective proliferation and muscle fiber regeneration.[9]

Cell culture tests by agarose overlay method, indicated that 25–50% of the cells exhibited cytopathic effect, CPE, and the elution method demonstrated the 75% of the cells exhibited CPE. Hemolysis testing of the rubber yielded inconclusive results. The test sample had a percent light transmission of 84% at 540 mμ as compared with a negative control of 94% (no hemolysis) and a positive control of 0.7% (complete hemolysis). The test serum appeared to be turbid not necessarily due to hemolysis but, perhaps, due to an extract from the sample. For vena cava occlusion, the reaction between the bio-system and implant as shown in these tests may be the mechanism or stimulus whereby encapsulation of the balloon is affected. The fibrous tissue encapsulation[2] of the balloon seen in dog venae cavae at two years implantation may be related to the foreign body reaction mechanism. The initiation of this rejection is seen in short term muscle implant studies by the infiltration of polymorphonuclear inflammatory cells. Indeed, foreign body rejection may be employed in this procedure to affect irreversible vena cava occlusion via encapsulation of the balloon. Long term animal testing and additional clinical monitoring will be completed to insure that this mechanism of encapsulation is permanent and reasonably tolerated by the body.

Theoretical pressure–volume relationships

Two observations were made on the failure of constrained balloons. First, the balloons failed at volumes significantly lower than similar unconstrained balloons. Second, the failures appeared to occur at the ends. Based on these observations, the model shown in Figure 5 was proposed.

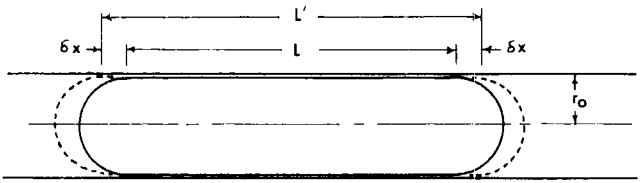

FIGURE 5 Balloon constrained in a rigid tube.

Since there is a non-uniform shear stress along the tube wall, the deformation along L will be non-uniform. However, if σx is sufficiently small, the non-uniformity in this region can be neglected. Furthermore, the end of the balloon is in a state of biaxial deformation. For an incompressible material, one elongation will characterize this deformation. The elongation for the state shown in Figure 5 is:

$$\lambda' = l/l' = (\pi r_o + 2\sigma x)/\pi r_o \tag{7}$$

Eq. (7) is the elongation based on the coordinates of the deformed state as shown by the solid lines of Figure 5. This must be transformed to the coordinates of the undeformed state. For the state of biaxial deformation,

$$\lambda = \lambda' \lambda_1 \tag{8}$$

where λ_1 is the state of deformation from which λ' is measured.

For the initial pressure increment which expands the balloon to fill the tube:

$$\lambda_1 = r_o/R_o \tag{9}$$

R_o is the initial balloon radius. The next small increment yields:

$$\lambda_2 = [1 + 2\sigma x/\pi r_o]\,[r_o/R_o] \tag{10}$$

Note that λ_2 has been transformed to the original coordinates, according to Eq. (8). If each succeeding pressure increment is adjusting so that all σx values are uniform, then

$$\lambda_{n+1} = [1 + 2\sigma x/\pi r_o]^n\,[r_o/R_o] \tag{11}$$

Eq. (11) can be expanded into a binomial series (for small σx). Neglecting all powers of σx greater than the second:

$$\lambda_{n+1} = (r_o/R_o)\,[1 + (2n\sigma x/\pi r_o)\,[1 + (n - 1)\,(\sigma x/\pi r_o)]] \tag{12}$$

However:

$$L = 2(n - 1)\,\sigma x \qquad L' = 2n\sigma x \tag{13}$$

where L' is the length after the deformation. Therefore;

$$\lambda_{n+1} = (r_o/R_o)\,[1 + (L'/\pi r_o)\,[1 + L/2\pi r_o]] \tag{14}$$

As the balloon approaches the bursting point, L and L' become sufficiently close to be assumed equal.

For an unconstrained spherical balloon;

$$\lambda_u = r_u/R_o \tag{15}$$

If the small contribution of the bending stress (due to differences in radius of curvature) is neglected, failure will occur at the equivalent elongations. From Eqs. (14) and (15),

$$r_u = r_o\,[1 + (L'/\pi r_o)\,[1 + L/2\pi r_o]] \tag{16}$$

Once the dimensions have been determined, the equivalent volumes can be computed.

$$V_c = \pi r_o^2 L + 4/3\pi r_o^3 \qquad (17)$$
$$V_u = 4/3\pi r_u^3$$

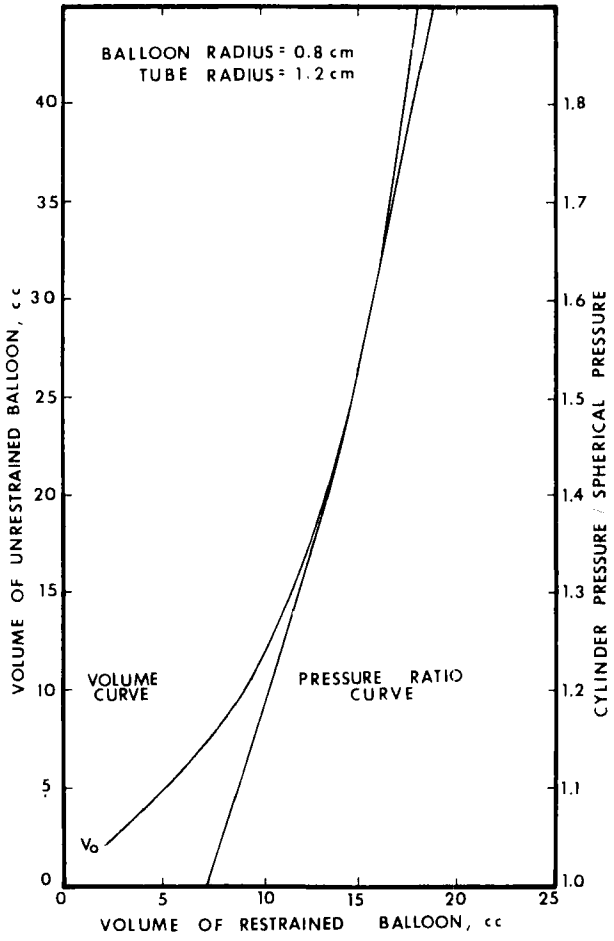

FIGURE 6 Effect of a rigid constraint on spherical balloons.

Figure 6 illustrates a typical case. The initial balloon radius was two-thirds of the tube radius. It can be seen, for this example, that if the unconstrained balloon bursts at 30 cc, then the equivalent volume of the constrained balloon is only 16 cc.

Finally, the pressure required to achieve this volume is greater than that of the unconstrained volume. Using thin wall theory, the ratio of the stresses is:

$$\sigma_u/\sigma_c = p_u r_u t_c / p_c r_o t_u \tag{18}$$

where r_o is the radius of the tube and therefore the radius of the end of the balloon. However, at equivalent wall extensions, the wall stresses and wall thicknesses will be equal. Thus:

$$P_u/P_c = r_o/r_u \tag{19}$$

Using the example parameters chosen before, the resultant curve is shown in Figure 6. At the 30cc unconstrained volume used previously, the unconstrained balloon will require about 1.6 times the pressure to reach the 16cc volume. Therefore, the constrained balloon will appear stiffer and have a lower burst volume than an equivalent unconstrained balloon.

The rigid tube represents an extreme case. If the tube is elastic, r_o will inincrease as the pressure increases. Also, the length of contact, L will not increase as rapidly. This will result in the constrained volume approaching the unconstrained value, as can be seen from Eqs. (16) and (17). The rate at which r_o will increase depends upon the pressure–volume relationship of the tube and its comparison with the pressure–volume relationship of the balloon. For the case of a vena cava constraining a latex balloon, this will be a complex problem since both have non-linear pressure–volume relationships.

The actual shape of the balloon will also modify these results. The method of fastening the balloon to a catheter will result in a region with a smaller radius of curvature or even a negative radius. Non-uniform thickness (increasing toward the end) will, obviously, change these results. The simplest method to achieve greater burst volumes is to design a balloon which will expand in a more uniform manner when constrained. Such a design will modify the basic assumptions made in Eq. (7).

Experimental pressure–volume relationships

Measurements of internal balloon pressure were made with respect to inflation volume. These data were evaluated with regards to Eqs. (1) to (6). In general, Eqs. (2) and (5) were good approximations while in some cases, Eq. (1) was also an acceptable approximation. For purposes of comparison, it was necessary to select one curve type to evaluate effects of size and compliance of restricting tube, balloon shape and latex formulation on the pressure–volume relationship. Figures 7 to 13 represent computer tracings fit to experimental data. In each case, the curve selected as the best fit was one of the family of curves represented by Eq. (2), the exponential function. The four groups of balloons evaluated in these experiments are the following:

Group I—Type A, unstressed balloon I.D. is 5.8 mm High Modulus Formula.

Group II—Type A, unstressed balloon I.D. is 5.8 mm Low Modulus Formula.

Group III—Type A, unstressed balloon I.D. is 7.6 mm High Modulus Formula.

Group IV—Type B, High Modulus Formula.

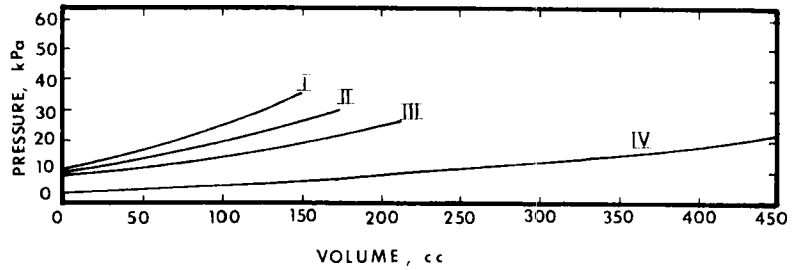

FIGURE 7 Pressure as a function of volume for balloons in the unrestrained condition.

Figure 7 represents pressure as a function of inflation volume for the four balloons in the unrestricted state. Each curve is labeled according to the balloon type it represents.

From a comparison of the four curves, two trends become apparent. First, rupture volume is increased greater by increasing unstressed balloon shape as in Curves III and IV than by decreasing modulus as in Curve II. Secondly, as rupture volume increases, the rate of change of pressure with respect to inflation volume or slope decreases. In general, rupture occurs at a lower pressure as rupture volume increases, indicating that a failure at large volumes occurs predominantly due to the "r" component of Eq. (20).

$$\sigma = pr/t \tag{20}$$

where σ = stress
p = pressure
r = existing radius
t = existing thickness

Figure 8 depicts the curves for balloon samples of Group I restricted in four woven fabric tubes varying in internal diameter from 17.2 mm for Curve F to 31.2 mm for Curve J. This figure shows that rupture volume restricted in a non-extensible tube is less than that unrestricted. Further, restricted rupture volume

is dependent upon the restricting tube's compliancy and internal diameter. Apparent balloon stiffness increases. These changes are in accordance with the theoretical predictions.

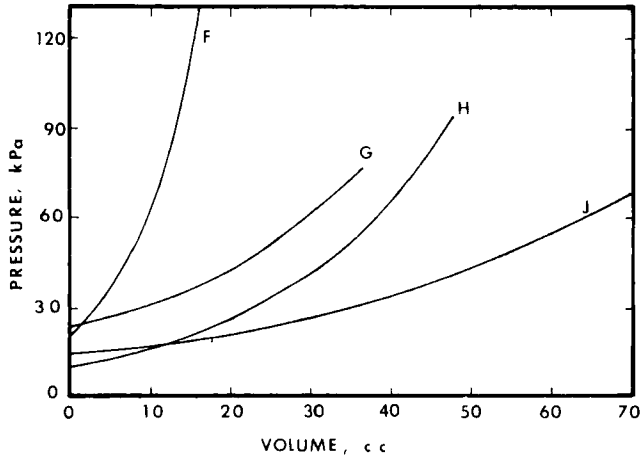

FIGURE 8 Pressure as a function of volume for Group I balloons restrained in four woven fabric tubes.

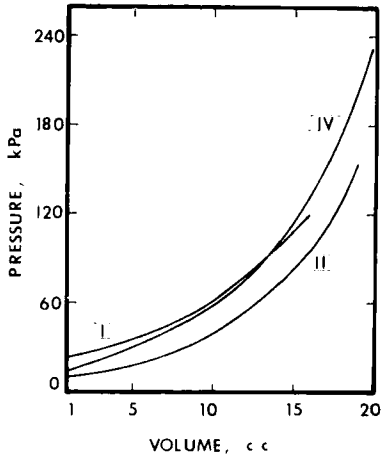

FIGURE 9 Pressure as a function of volume for balloons restrained in a 17.2 mm I.D. woven fabric tube.

Figure 9 compares the curves generated for balloons of Groups I, II and IV restricted in a woven fabric tube with an internal diameter (I.D.) of 17.2 mm. Curves I and IV are nearly indistinguishable for volumes less than

15 cc. Group I balloons have slightly lower restricted rupture volumes than Group IV, but this difference in rupture volumes is not termed significant. Group II as represented by Curve II has a rupture volume equal to that of Curves I and IV while the slope of the curve at various points is slightly less than that of Curves I and IV.

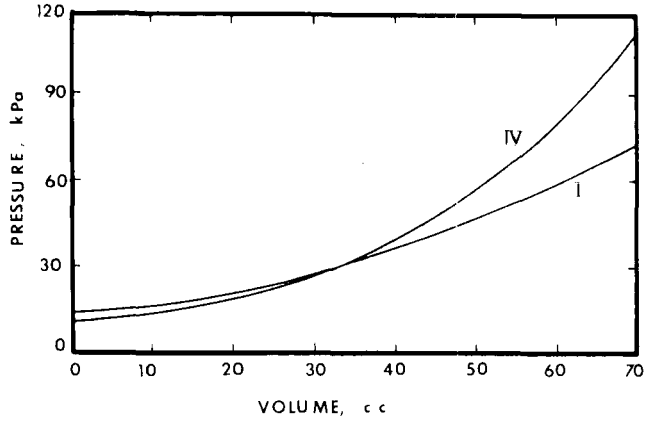

FIGURE 10 Pressure as a function of volume for balloons restrained in a 31.2 mm I.D. woven fabric tube.

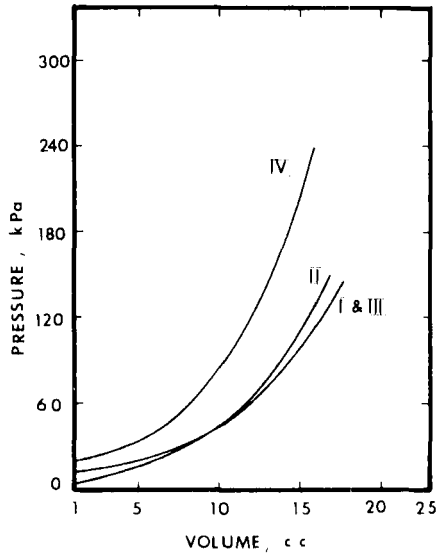

FIGURE 11 Pressure as a function of volume for balloons restrained in a 17.2 mm I.D. semi-rigid tube.

Figures 10 to 13 indicate that, in general, internal balloon pressures for Groups I and IV are equal at low inflation volumes. However, at higher volumes near rupture, pressure changes associated with incremental volume changes are greater for Group IV balloons than for Group I. An exception to this trend is seen in Figure 12, for occlusion in a 38.1 mm semi-rigid tube, which depicts similar curves for Group I and IV balloons. Since the rupture volumes in both cases are nearly equivalent, the greater pressure differential normally found for Group IV balloons indicate that the balloon is inflating more in diameter than in length. As the balloon expands and contacts the rigid or partially extensible wall, the force on the balloon increases causing a rise in internal pressure. Group III balloons exhibit a relationship of pressure to volume which is similar to that for Group I balloons. In conclusion, for Groups I, III and IV, little change in rupture volume was noted. Also, the slopes at various points of the curves are equal except at high inflation volumes where Group IV values are greater than those obtained for Groups I and III.

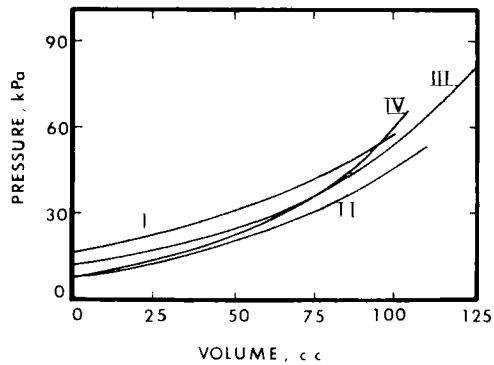

FIGURE 12 Pressure as a function of volume for balloons restrained in a 38 mm I.D. semi-rigid tube.

Comparisons of curves for Groups I and II in Figures 9, 11, and 12 demonstrate the effects of decreasing the modulus of the latex formulation. The rupture volume is equivalent for Group I and II balloons. Also, the rate of change in pressure with respect to changes in inflation volumes is less for Group II balloons than Group I except in the 17.2 mm I.D. semi-rigid tube, Figure 11. This trend is expected since the slope of the pressure–volume curve is analogous to modulus, the slope of the stress–strain curve.

Figures 11 and 12 do not depict the trends which are evident in the remaining data. It is felt that this disagreement is not due to experimental error but rather with experimental insensitivity for occlusion in an extensible tube. In general, it would be convenient to monitor internal balloon pressures as a function of inflation volumes for production lots of balloons to insure reproducibility. It has

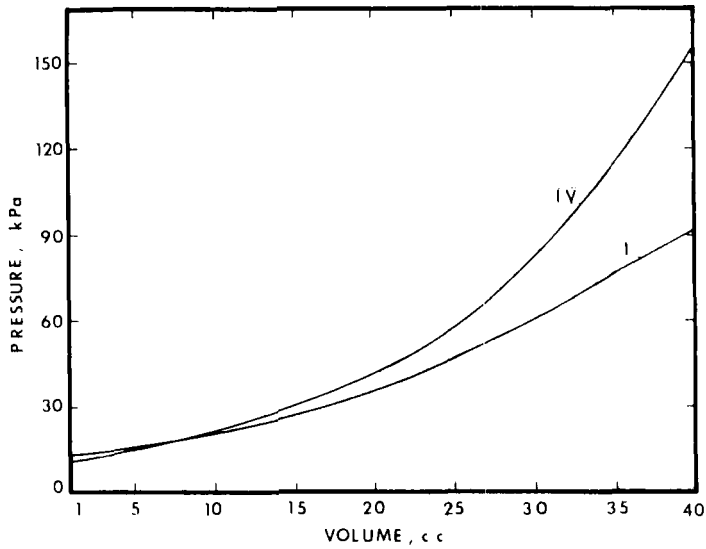

FIGURE 13 Pressure as a function of volume for balloons restrained in a 25.4 mm I.D. rigid tube.

been shown that in rigid or stiff textile tubes changes in shape or latex formulation produce variations in this relationship. Since occlusion in an extensible tube is insensitive due to the expansion of the restricting tube itself, characterization of balloon samples via pressure and volume measurements should be done in rigid or at least stiff tubes.

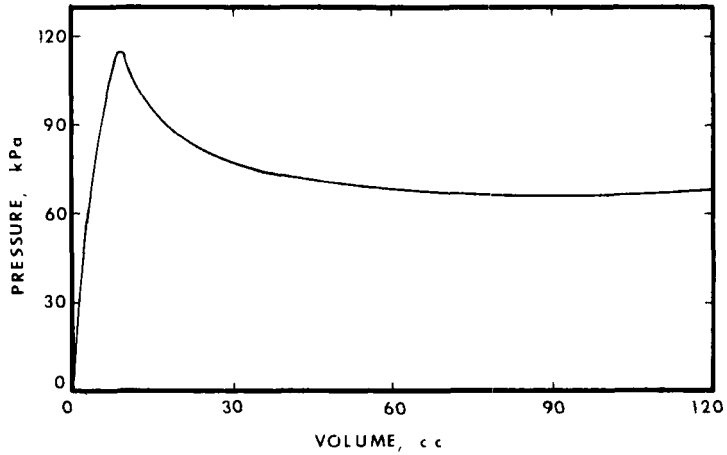

FIGURE 14 Pressure as a function of volume for a balloon restrained in a 9.5 mm I.D. rubber tube.

Figures 14 and 15 are the pressure-volume relationships for Group I balloons restricted in a rubber tube and in a cadaver vena cava. Both curves are composites of Eqs. (3) and (4) fit to experimental data.

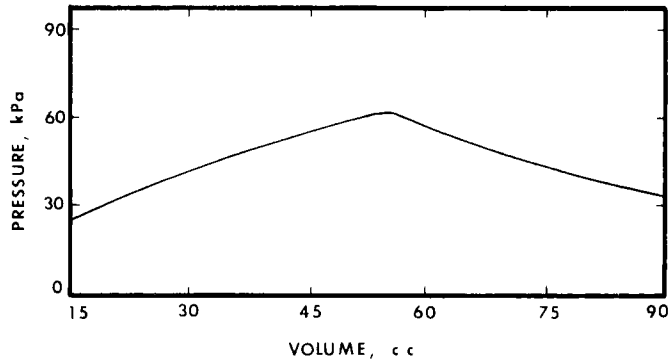

FIGURE 15 Pressure as a function of volume for a balloon restrained in a 19 mm I.D. cadaver vena cava.

Some general trends in the two curves are common, indicating that occlusion in a rubber tube is more analogous to vena cava occlusion than the other tubes tested. This result is to be expected. However, in terms of characterizing the pressure to volume relationship for a balloon, the simpler curves obtained in rigid tubes are more convenient. For these two curves, balloon pressure increases to a maximum until the restricting tube expands causing pressure to decline. Pressure values level off to a constant until balloon rupture occurs. Rupture volume in a rubber tube with a 9.5 mm I.D. is 120 cc which is 80% of the unrestricted rupture volume. In the cadaver vena cava with a 19 mm I.D., the rupture volume is 83 cc which is 55% of the unrestrained rupture volume.

The final consideration in this balloon development was the evaluation of the strength of occlusion. This was done by estimating forces acting on the implant causing it to migrate to the heart. Migration to the lower extremities was not considered since the inflated balloon diameter is too large to permit migration through the iliac veins. Theoretical calculated forces acting to cause migration were compared to the experimentally measured force which resists migration. The force acting to move the balloon is exerted by the blood. This force can be calculated as:

$$F_m = pA \tag{21}$$

where: F_m is the force to cause migration
p is the blood pressure in the vena cava
A is the vena cava cross sectional area

The forces opposing migration are the weight of the implant, F_w, and the frictional forces between the vena cava wall and the balloon surface, F. The experimentally measured force required to cause balloon migration is the sum of F_w and F. For the calculations, vena cava pressure is assumed to be 50 mm of *Hg*. This value is 10 times the maximum pressure normally experienced in the vena cava. It required a force of 4.45N to 8.9N to dislodge the balloons placed in the cadaver venae cavae.

Even though the assumed pressure value is exceedingly high, the calculated force working to cause migration is about one-half the measured force which resist migration.

TABLE III

Vena cava I.D.	Balloon group	Calculated force to cause migration	Volume of occlusion	Measured force of migration
1.9 cm	I	2.2N	12cc	4.1N
1.9 cm	I	2.2N	15cc	6.7N
1.9 cm	I	2.2N	12cc	3.9N
1.9 cm	I	2.2N	15cc	5.8N
1.9 cm	IV	2.2N	24cc	5.3N
2.54 cm	IV	3.6N	15cc	6.7N
2.54 cm	IV	3.6N	10cc	3.2N
2.54 cm	IV	3.6N	15cc	4.9N

Table 3 lists calculated forces and experimentally measured forces. Comparison of these two sets of values indicates that occlusion has been affected with little possibility of migration and at inflation volumes which are less than 30% of the rupture volume when restricted in the vena cava. Further, at these inflation volumes, balloon failure is not imminent.

SUMMARY AND CONCLUSIONS

Various characteristics of vena cava occlusion balloons have been discussed. Physical properties of the latex formulation have been presented. Effects of the *in vitro* environment on these properties have been demonstrated. Further, permeability of the balloon material to the inflation medium has been shown to be negligible, such that balloon deflation due to diffusion of contrast medium is not a realistic concern. Short term biologic tests have been performed showing that the balloon rubber is not acutely toxic. Long-term tests will be conducted to insure that short-term tissue reaction, which affects balloon encapsulation, is part of the foreign body reaction mechanism

Internal balloon pressures were monitored as a function of inflation volume. By studying the relationship of pressure to volume in synthetic tubes, a means to insure reproducibility in manufacturing techniques was established. This data combined with studies with cadaver venae cavae demonstrate the safety of fixation, balloon strength, its adaptability to varying venae cavae I.D. and efficacy. In addition, these studies aided in improvements of balloon configuration. Type A and Type B balloon configurations were studied. Type B balloons were able to occlude larger I.D. restricting tubes than Type A with less danger of balloon failure. This is related to the greater unrestricted rupture volume of Type B. Lastly, the forces acting on the implant causing it to migrate were discussed and compared with experimental findings of forces acting to resist migration. The conclusion was made that the balloon implant was secure at low inflation volumes and the danger of migration to the heart was negligible.

Previous studies[2] have demonstrated the feasibility of using a balloon for long-term occlusion of the vena cava. Our study has highlighted tests necessary for designing a balloon with proper characteristics for this difficult application. As illustrated, the correct formulation to insure retention of the radiopaque medium must be carefully chosen. Also, if the balloon is to have sufficient tensile strength for the application, an appropriate geometric shape in conjunction with a suitable formulation is needed. Once these parameters are determined, short and long term biological tests (for toxicity, permeability and strength retention) and shelf life studies must be carried out. Finally, once the design is complete, manufacturing parameters must be defined and sufficient quality assurance tests designed to insure repeatability.

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