

[72] Inventors Edward Emil Schmitt
Norwalk, Conn.;
Rocco Albert Polistina, Port Chester, N.Y.
[21] Appl. No. 852,617
[22] Filed Aug. 25, 1969
[45] Patented Nov. 16, 1971
[73] Assignee American Cyanamid Company
Stamford, Conn.
Continuation-in-part of application Ser. No. 608,086, Jan. 9, 1967, now Patent No. 3,463,158, dated Aug. 26, 1969, and a continuation-in-part of 320,543, Oct. 31, 1963, now Patent No. 3,297,033, dated Jan. 10, 1967. This application Aug. 25, 1969, Ser. No. 852,617

[51] Int. Cl. A61b 17/11
[50] Field of Search 128/334,
335.5; 3/DIG. 1

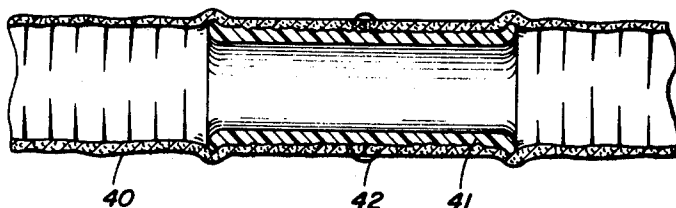
[56] References Cited
UNITED STATES PATENTS
2,127,903 8/1938 Bowen..... 128/334
2,428,918 10/1947 Miller..... 128/334
2,676,945 4/1954 Higgins..... 260/78.3 X
3,155,095 11/1964 Brown..... 128/334
3,297,033 1/1967 Schmitt et al. 128/335.5
3,463,158 8/1969 Schmitt et al. 128/334

Primary Examiner—Dalton L. Truluck
Attorney—Samuel Branch Walker

[54] CYLINDRICAL PROSTHETIC DEVICES OF
POLYGLYCOLIC ACID
6 Claims, 5 Drawing Figs.

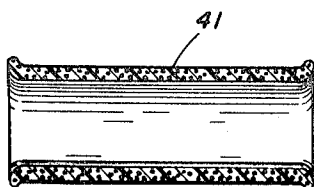
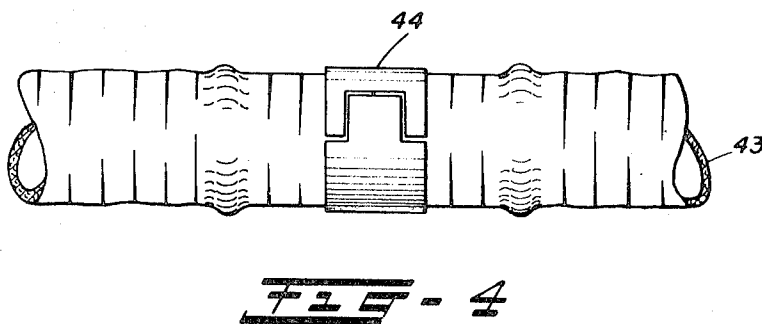
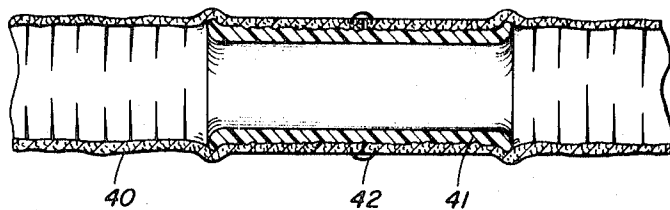
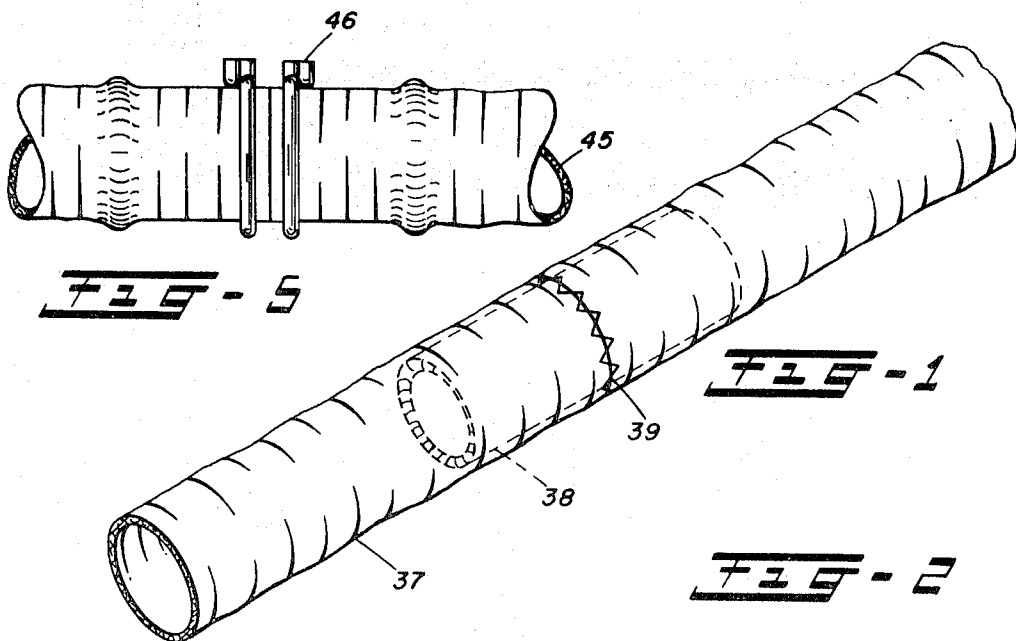
[52] U.S. Cl. 128/334 R,
3/DIG 1

ABSTRACT: Polyhydroxyacetic ester, also called polyglycolic acid (PGA), has surgically useful mechanical properties as a solid prosthesis, such as reinforcing pins, screws, plates, or cylinders. On implantation, in living mammalian tissue, the polyglycolic acid is absorbed, and replaced by living tissue.



PATENTED NOV 16 1971

3,620,218



INVENTORS,
EDWARD EMIL SCHMITT
ROCCO ALBERT POLISTINA
BY

Samuel Brank & Alter

ATTORNEY

CYLINDRICAL PROSTHETIC DEVICES OF POLYGLYCOLIC ACID

CROSS-REFERENCES

This application is a continuation-in-part of application Ser. No. 608,086, Jan. 9, 1967 now U.S. Pat. No. 3,463,158, Aug. 26, 1969, "Polyglycolic acid Prosthetic Devices" and Ser. No. 320,543, filed Oct. 31, 1963 now U.S. Pat. No. 3,297,033, Jan. 10, 1967, "Surgical Sutures."

FIELD OF INVENTION

This invention relates to absorbable surgical structural elements of polyhydroxyacetic ester hereafter called polyglycolic acid (PGA).

PRIOR ART

The use of submucosal tissue and ribbons therefrom internally is described in such patents as U.S. Pat. No. 2,167,251, Rogers, "Surgical Tape of Submucosa Tissue," July 25, 1939, U.S. Pat. No. 2,143,910, Didusch, "Ribbon Gut and Method of Using the Same," Jan. 17, 1939, and U.S. Pat. No. 2,127,903, Bowen, "Tube for Surgical Purposes and Method of Preparing and Using the Same," Aug. 23, 1938.

U.S. Pat. No. 3,155,095, A. M. Brown "Anastomosis Method and Means" shows an internal and external absorbable coupling for the joining of vascular vessels.

SUMMARY

Definitions in the textile trades are frequently somewhat ambiguous. For purposes of the present application, certain terms are defined:

A "filament" is a single, long, thin flexible structure of a nonabsorbable or absorbable material. It may be continuous or staple.

"Staple" is used to designate a group of shorter filaments which are usually twisted together to form a longer continuous thread.

An absorbable filament is one which is absorbed, that is digested or dissolved, in living mammalian tissue.

A "thread" is a plurality of filaments, either continuous or staple, twisted together.

A "strand" is a plurality of filaments or threads twisted, plaited, braided, or laid parallel to form a unit for further construction into a fabric, or used per se, or a monofilament of such size as to be woven or used independently.

A "solid prosthetic device" is a thin solid sheet, or plate, or tube, which may be split, or bar, or nail, or screw, or pin or other solid shape which has inherent mechanical strength in compression, bending and shear to act as a solid discrete surgical reinforcing element, and has at least one dimension greater than 2 millimeters, and which may have a dimension as great as about 200 millimeters, or as required, to fit into or adjacent to and furnish mechanical support and reinforcement to a bone, or bones, or gland, or organ, for support during a healing process.

The size and shape of the prosthetic devices, or protheses, is controlled by usage. For example, in the human body, in the case of a bone fracture, a pin is used to reinforce a bone, and is of such a size as to be a tight driving fit into a central portion of the bone, or a hole drilled into a bone. Such a pin can be from about 1/16-inch diameter and 3/4-inch length for finger bones, or for children, up to 1 1/4-inch diameter and 6-inch length to reinforce the femur, or thigh bone of large adult humans, or even larger for valuable race-horses or other mammals.

The support may be in part directive of growth, as for example in nerve tissue, which grows slowly, and as a result has regeneration impaired by the more rapid growth of scar tissue which can block the growth of the nerve tissue. With a wraparound sheath of PGA sheet, or a split or solid tube used to support, place, hold and protect; regeneration of nerve tissue and function is greatly aided. Other factors may inhibit

regeneration of nerve tissue or function, but with the exclusion of scar tissue, such other factors may be separately treated. PGA is particularly useful in splicing nerves because PGA is completely dissolved in tissue and leaves minimal or no residual scar tissue from the PGA.

For different purposes and in different types of tissue the rate of absorption may vary but in general an absorbable prosthesis should have as high a portion of its original strength as possible for at least 3 days, and sometimes as much as 15 days or more, and preferably should be completely absorbed by muscular tissue within from 45 to 90 days or more depending on the mass of the cross section. The rate of absorption in other tissues may vary even more.

In common with many biological systems, the requirements are not absolute and the rate of absorption as well as the short-term strength requirement varies from patient to patient and at different locations within the body, as well as with the thickness of the section of PGA.

The PGA may be formed as tubes or sheets for surgical repair and may also be spun as thin filaments and woven or felted to form absorbable sponges or absorbable gauze, or used in conjunction with other compressive structures as prosthetic devices within the body of a human or animal where it is desirable that the structure have short term strength, but be absorbable. The useful embodiments include tubes, including branched tubes or Tees, for artery, vein or intestinal repair, nerve splicing, tendon splicing, sheets for tying up and supporting damaged kidney, liver and other intestinal organs, protecting damaged surface areas such as abrasions, particularly major abrasions, or areas where the skin and underlying tissues are damaged or surgically removed.

The medical uses of PGA include, but are not necessarily limited to:

A. Pure PGA

1. Solid Products, molded or machined

- a. Orthopedic pins, clamps, screws and plates
- b. Clips (e.g., for vena cava)
- c. Staples
- d. Hooks, buttons and snaps
- e. Bone substitute (e.g., mandible prosthesis)
- f. Needles
- g. Nonpermanent intrauterine devices (antispermicide)
- h. Temporary draining or testing tubes or capillaries
- i. Surgical instruments
- j. Vascular implants or supports
- k. Vertebral discs
- l. Extracorporeal tubing for kidney and heart-lung machines

2. Fibrillar Products, knitted or woven, including velours

- a. Burn dressings
- b. Hernia patches
- c. Absorbent paper or swabs
- d. Medicated dressings
- e. Facial substitutes
- f. Gauze, fabric, sheet, felt or sponge for liver hemostasis
- g. Gauze bandages
- h. Dental packs

3. Miscellaneous

- a. Flake or powder for burns or abrasions
- b. Foam as absorbable prosthesis
- c. Substitute for wire in fixations
- d. Film spray for prosthetic devices

B. PGA in Combination with other Products

b 1. Solid Products, molded or machined

- a. Slowly digestible ion-exchange resin
- b. Slowly digestible drug release device (pill, pellet)
- c. Reinforced bone pins, needles, etc.

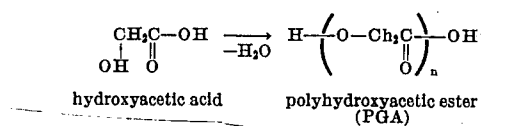
2. Fibrillar Products

- a. Arterial graft or substitutes
- b. Bandages for skin surfaces
- c. Burn dressings (in combination with other polymeric films.)

The synthetic character and hence predictable formability and consistency in characteristics obtainable from a controlled process are highly desirable.

The most convenient method of sterilizing PGA prostheses is by heat under such conditions that any micro-organisms or deleterious materials are rendered inactive. A second common method is to sterilize using a gaseous sterilizing agent such as ethylene oxide. Other methods of sterilizing include radiation by X-rays, gamma rays, neutrons, electrons, etc., or high-intensity ultrasonic vibrational energy or combinations of these methods. The present materials have such physical characteristics that they may be sterilized by any of these methods.

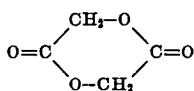
PGA can be considered as essentially a product of polymerization of glycolic acid, that is hydroxyacetic acid, which in simplified form is shown by the equation:



Preferably n is such that the molecular weight is in the range of about 10,000 or more. Above 500,000 the polymer is difficult to mold.

In these molecular weight ranges the polymer has a melt viscosity at 245° C. of between about 400 and about 27,000 poises. Because the PGA is from a synthetic and controllable source, with the controlled molecular weight and controlled small percentage of comonomer, the absorbability, stiffness, and other characteristics can be modified.

Among several methods by which PGA can be prepared, one preferred route involves the polymerization of glycolide,



the cyclic dimeric condensation product formed by dehydrating hydroxyacetic acid. During polymerization of glycolide, the ring is broken and straight-chain polymerization occurs.

Small quantities of other materials may be present in the chain, as for example, d,l-lactic acid, its optically active forms, homologs, and analogs. In general plasticizers tend to interfere with crystallinity, orientation, etc. and weaken the prosthesis but are useful for sponges and films. Other substances may be present, such as dyes, antibiotics, antiseptics, anaesthetics, and antioxidants. Surfaces can be coated with a silicone, beeswax, and the like to modify handling or absorption rate.

The polymerization of glycolide occurs by heating with or without a catalyst, or may be induced by radiation such as X-rays, gamma rays, electron beams, etc. Polymers may also be obtained by condensing glycolic acid or chloroacetic acid with or without a catalyst under a variety of conditions. Good moldable objects or fibers are most readily obtained when the melt viscosity at 245° C. is about 400 to about 27,000 poises.

Polyhydroxyacetic esters have been described in U.S. Pat. No. 2,668,162, Lowe, "Preparation of High Molecular Weight Polyhydroxyacetic Ester," and U.S. Pat. No. 2,676,945, Higgins, "Condensation Polymers of Hydroxyacetic Acid."

The processes described in the above two patents can be used for producing PGA from which prostheses may be made. Additives such as triphenylphosphite or Santo-Nox, a disulfide aromatic phenol, can be added as color stabilizers.

DRAWINGS

FIG. 1 shows a spliced artery having an internal sleeve with slightly tapered ends, with a sewn splice.

FIG. 2 is a cross section of a spliced artery having an internal sleeve with expanded ends.

FIG. 3 shows a prosthetic sleeve formed of a unitary coupling of solid polyglycolic acid with slightly expanding ends to aid in holding a blood vessel about the sleeve.

FIG. 4, shows the sleeve of FIG. 12 in use in which an external spring clip of solid polyglycolic acid holds the ends of the blood vessel together.

FIG. 5 shows the sleeve of FIG. 12 in which two expandable annular clips are used to hold the ends of the blood vessel approximated.

PGA for the construction of the prostheses shown in the drawings can be produced as set forth in the following examples, in which parts are by weight, unless otherwise clearly indicated.

EXAMPLE 1

One hundred parts of recrystallized glycolide (melting point 85.0 to 85.5° C.) are intimately mixed with 0.02 part of methoxyacetic acid, 0.03 part of phenoldisulfide (Santo-Nox), and 0.03 part antimony trifluoride. Separate glass tubes are each charged with approximately 20 grams of the mixture, deoxygenated by repeated evacuation and argon purging, then sealed under vacuum and heated to 185° to 190° C. for 4 ½ hours. On cooling a white opaque tough PGA is produced in a 97.5 percent yield with a melt viscosity at 245° C. of 5,000 poises. The polymer is reheated and spun into filaments at a temperature of about 230° C. at a speed of about 150 feet per minute. The filaments produced are cooled, then drawn at about 55° C. When drawn to 5 times the original length a strong tough filament is produced. The dry filaments are in condition for use.

EXAMPLE 2

The polymer of the preceding example is formed into a plurality of smaller filaments, seven of which are twisted into a polyfilamentary strand, which is sterilized and used following the techniques of examples 1.

Because it is a synthetic polymer the methods of forming are more versatile than in starting with naturally occurring materials.

EXAMPLE 3

Into a suitable reaction vessel there is charged 400 parts of a commercial glycolic acid which is then heated from room temperature to about 200° C. over a period of about 4 hours. When the pot temperature has reached 185° C., the pressure of the system is reduced from atmospheric pressure to 15 mm. of Hg, causing the water of condensation and/or esterification to distill off. The residue is allowed to cool and is pulverized into about 280 parts of a powder which is then added in small increments to a suitable pyrolysis chamber maintained at a temperature of about 250°-285° C. at a pressure of less than 15 mm. of Hg. The distillate which weighed about 238 parts is dissolved in a minimum amount of hot ethyl acetate, and after decolorizing and purifying with active carbon, the distillate is recrystallized from the above solution to provide 160 parts of product having a melting point of about 82.5°-84.0° C. The infrared spectrum confirms that the product is substantially pure glycolide.

The glycolide thus prepared is polymerized in the presence of an alcohol free of nonbenzenoid unsaturation and free of any reactive groups other than alcoholic hydroxy groups and in the presence of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$.

A heavy walled glass tube having a bore of about three-tenth inch and sealed at one end is charged with 3 parts of the substantially pure glycolide composition, 0.04 part of a 0.1 percent ether solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (about 0.0013 percent of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ based on the weight of the substantially pure glycolide composition), 0.0166 part of lauryl alcohol (0.346 mole percent based on the moles of the substantially pure glycolide composition), and a magnetic steel ball five thirty-

second inch in diameter. The tube is evacuated and purged with argon. The tube is evacuated again to a vacuum of less than 1 mm. of Hg and the top is sealed. The reaction tube is placed in a vertical position in a closed glass chamber throughout which dimethyl phthalate is refluxed at 222° C. The boiling point of the dimethyl phthalate is controlled by decreasing the pressure of the system. At periodic intervals after melting, the viscosity of the reaction mixture is measured by raising the steel ball by means of a magnet and measuring the rate of the fall of the ball in sec./in. Ninety minutes after the melt is first achieved, the ball drop time is 550 sec./in. or about 7,200 poises, and after 120 minutes, the ball drop time is 580 sec./in. or about 7,600 poises.

The PGA thus produced is spun into 0.002-inch diameter fibers and used to form strands.

Additional PGA, similarly produced is used to form sheets, or tubes. These are wrapped around nerves, traumatically severed, to protect such nerves from invasive scar tissue growth, while the nerve is regenerating.

Also the PGA so produced is fabricated into the prosthetic devices shown in the drawings. The PGA may be moulded or machined or extruded to a desired configuration.

In FIG. 1 is shown an artery 37 which is joined together over a tapered end PGA tube 38 which forms a stent about which the ends of the artery wall are joined by a suture splice 39. The tapered end is easier to insert in the artery.

In FIG. 2 the artery walls 40 are joined together over a flared end PGA tube 41 and the ends are joined by a suture splice 42.

FIG. 3 shows the flared end PGA tube 41.

In FIG. 4 is shown a blood vessel 43, the ends of which are each separately placed over the end of a flared PGA tube and which blood vessel is held in place with the ends adjacent to permit healing by a PGA spring clip 44. PGA, such as produced in the above example 3, shows an Izod impact strength of 0.14 ft.-lbs. per inch width or greater. It may be heated and formed into a desired shape which shape is retained on cooling, and by shaping as a flat spring clip, can be used to hold together the walls of a blood vessel 43 until natural regeneration takes place.

In FIG. 5 is shown a similar splice of a blood vessel 45 but in which the ends are held together by an annular clip 46 of molded PGA. Such annular clips are well known for the attachment of radiator hoses to radiators in automobiles and the attachment of other flexible tubing to connectors. By a suitable choice of diameter and shape, as is well known in the industry, the radial compression at all points about the periphery may be caused to be approximately uniform and within a desired range. This is important in the splicing of blood vessels as it is desired to hold the blood vessel in position during regeneration, but yet not hold the vessels so tightly that necrosis sets in because of an impaired blood supply to the vessel walls.

While disclosed primarily for blood vessels, or vascular vessels, because jointure of such vessels is of greatest interest at present, obviously the same techniques and hollow splice cylinders can be used on any of a variety of vessels in the body of man or animals. Such tubes include fallopian tubes, spermatic ducts, bile ducts, ureters, sinus tubes, eustachian tubes, tear ducts, or for absorbable drain tubes in body cavities, or where a splice or jointure is required in any body tube. The size of the hollow cylinder is preferably such that the lumen, or internal diameter is about that of the tube being joined. The ends of the cylinder are conveniently tapered, so that the ends are readily insertable in the body tube, and for blood vessels so that a minimum of tubulence is induced in flowing blood, and hence thrombus formation is minimized. The PGA cylinder appears to be essentially nonthrombogenic.

The splice PGA cylinder normally is of uniform diameter, as usually the ends of the vessel to be spliced are the same. The diameters may be made different to join vessels of different sizes as may occur where a splice is to be made between vessels not normally joined. T or Y-joints can be formed by mold-

ing or machining, with the various openings of a desired size, with the PGA prostheses to be completely covered by the vessel walls. As the PGA prostheses is absorbed, the vessel walls must grow together without defects.

Also because of the tremendous strength of the solid PGA, a surgical needle can be formed on the end of a PGA suture by either fusing the PGA of the suture, or molding additional PGA onto the suture end, the needle being bent and pointed as may be surgically preferred for a specific surgical procedure. The ends or edges of monocomponent or bicomponent fabrics containing PGA may be rendered rigid by moulding such edges, with or without additional solid PGA to a desired configuration. It is often easier to insert and retain a flexible fabric prosthetic tube if the end of the tube is of a size and shape to be inserted into the severed end of a vessel.

The drawings above are illustrative only of embodiment of the present invention in which various prosthetic devices are incorporated into the human body to aid impaired functions of natural elements. From the above drawings and descriptions, it will be obvious to those skilled in the art that many other modifications may be adapted for particular injuries or ills to which the flesh is heir.

The finding that polyglycolic acid, abbreviated PGA, is absorbable in living tissue, and has marked mechanical strength, as a fiber or solid, including sheet, and hence can be used as an element in, or as, a surgical prosthesis, is most unexpected and unpredictable.

Following the method set forth in the American Society for Testing and Materials, 1969 Books of Standards, Part 27, Plastics—General Methods of Testing, Nomenclature, ASTM, 1916 Race St., Philadelphia, Pa. 19103, May 1969, procedure 709-66 at page 303 to 310, (procedure B); a flexure strength of about 40,000 pounds per square inch and a flexure modulus of 1.2 to 1.4×10⁸ pounds per square inch is developed by the solid bars of PGA. For an unfilled plastic these values are spectacularly high. It is even more remarkable that such high-strength values are developed by a polymer that is absorbable by living mammalian tissue.

Catgut, or regenerated collagen has in the past been used for tissue emplacement, but with collagen, as the collagen is absorbed, a fibrotic tract replaces the collagen, so that in effect scar tissue remains at the site of the emplaced collagen for many years, in many instances for life. Some patients are allergic to collagen. PGA is not a protein, has no amino acids, and has given no evidence of allergic reactions in thousands of implants. With the present PGA prostheses, the PGA is completely absorbed, and a minimal or no trace of the inserted matter remains after a comparatively short period. This complete absorption, without residual fibrotic tissue, is unique, and an important contribution to surgery.

We claim:

1. An absorbable prosthesis for the anastomosis of vessels in the tissue of a living mammal consisting essentially of a hollow cylinder of polyglycolic acid, having an inner diameter approximately the same as the inner diameter of the subject vessel, and a smooth outer surface of a diameter which is insertable in said vessel when stretched, whereby one end of a vessel from traumatic or surgical severance may be emplaced over each end of said cylinder, and fixedly positioned thereon, said cylinder being open to and permitting the flow of body fluids, and being absorbable by living mammalian tissue within a few weeks.

2. The absorbable prosthesis of claim 1 in cooperative configuration with at least one circular cooperative clamp, whereby in assembled relationship, with a vascular vessel end on each end of said cylinder, the vascular vessel ends are uniformly positioned and retained on said cylinder, tightly enough to avoid substantial slippage, and loosely enough to permit circulation into the vessel ends, and hence avoid necrosis.

3. The absorbable prosthesis of claim 2 in which the said cooperative clamp is a single split ring, with inward tension sufficient to hold the ends of said vascular vessels, when positioned over said vessels in place over said hollow cylinder.

7

8

4. The absorbable prosthesis of claim 2 having two circularly bent rod clamps, said clamps having radii of curvature such that the vascular vessels are held against the hollow cylinder with approximately uniform pressure, around the periphery of said cylinder sufficiently tight to retain the vascular vessels during regeneration, but loosely enough to avoid necrosis.

5. A method of anastomizing two vessels in living mammalian tissue comprising inserting one end of a hollow cylinder of polyglycolic acid having an inner diameter of ap-

proximately the inner diameter of one of the vessels in the end of each of the vessels, so that the ends of the vessels abut, and fastening the ends of the vessels in abutting relationship over said cylinder of polyglycolic acid, said cylinder being open to and permitting the flow of body fluids, and being absorbed by said living mammalian tissue within a few weeks.

6. The method of claim 5 in which the ends of the vessels are fastened in abutting relationship by suturing the ends together.

* * * * *

15

20

25

30

35

40

45

50

55

60

65

70

75