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(71) Applicant: **NMT MEDICAL, INC.** [US/US]; 27 Wormwood Street, Boston, MA 02210 (US).

(72) Inventors: **RYAN, Carol, A.**; 115 Ashland Street, Melrose, MA 02176 (US). **CARR, Robert, M., Jr.**; 289 Vermont Street, West Roxbury, MA 02132 (US).

(74) Agent: **TURANO, Thomas, A.**; Testa, Hurwitz & Thibeault, LLP, High Street Tower, 125 High Street, Boston, MA 02110-2711 (US).

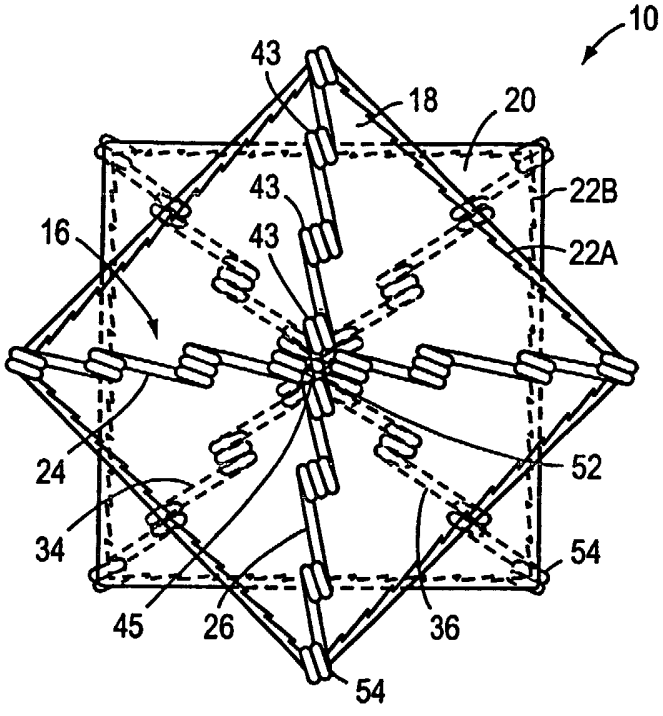
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(54) Title: DEVICE WITH BIOLOGICAL TISSUE SCAFFOLD FOR INTRACARDIAC DEFECT CLOSURE




(57) Abstract: The invention provides an intracardiac occluder (10), which has biological tissue scaffolds as occlusion shells, for the percutaneous transluminal treatment of an intracardiac defect. The intracardiac occluder includes a proximal support structure (24) supporting the proximal occlusion shell (18) and a distal support structure (34) supporting the distal occlusion shell (20). In one embodiment, biological tissue derived from the tunica submucosa layer of the porcine small intestine forms the occlusion shells.

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# DEVICE WITH BIOLOGICAL TISSUE SCAFFOLD FOR INTRACARDIAC DEFECT CLOSURE

## Cross-Reference to Related Application

**[0001]** This application incorporates by reference, and claims priority to and the benefit of, United States provisional application serial number 60/385,274, which was filed June 3, 2002.

## Technical Field

**[0002]** The invention generally relates to devices and related methods for treating intracardiac defects. More particularly, the invention provides an intracardiac occluder with a biological tissue scaffold, and related methods, for the percutaneous closure of intracardiac defects.

## Background

**[0003]** The human heart is divided into four compartments or chambers. The left and right atria are located in the upper portion of the heart and the left and right ventricles are located in the lower portion of the heart. The left and right atria are separated from each other by a muscular wall, the intraatrial septum, while the ventricles are separated by the intraventricular septum.

**[0004]** Either congenitally or by acquisition, abnormal openings, holes, or shunts can occur between the chambers of the heart or the great vessels, causing blood to flow therethrough. Such deformities are usually congenital and originate during fetal life when the heart forms from a folded tube into a four chambered, two unit system. The deformities result from the incomplete formation of the septum, or muscular wall, between the chambers of the heart and can cause significant problems. Ultimately, the deformities add strain on the heart, which may result in heart failure if they are not corrected.

**[0005]** One such deformity or defect, a patent foramen ovale, is a persistent, one-way, usually flap-like opening in the wall between the right atrium and left atrium of the heart. Since left atrial pressure is normally higher than right atrial pressure, the flap typically stays closed. Under certain conditions, however, right atrial pressure exceeds left atrial pressure, creating the possibility for right to left shunting that can allow blood clots to enter the systemic circulation.

This is particularly worrisome to patients who are prone to forming venous thrombus, such as those with deep vein thrombosis or clotting abnormalities.

**[0006]** Nonsurgical (*i.e.,* percutaneous) closure of patent foramen ovales, as well as similar intracardiac defects such as atrial septal defects, ventricular septal defects, and left atrial appendages, is possible using a variety of mechanical closure devices. These devices, which allow patients to avoid the potential side effects often associated with standard anticoagulation therapies, typically consist of a metallic structural framework that is combined with a synthetic scaffold material. The synthetic scaffold material encourages ingrowth and encapsulation of the device. Current devices typically utilize a polyester fabric, expanded polytetrafluoroethylene (ePTFE), Ivalon®, or a metal mesh as the synthetic scaffold material. Such devices suffer, however, from several disadvantages, including thrombus formation, chronic inflammation, and residual leaks.

## Summary of the Invention

**[0007]** The present invention provides a device for occluding intracardiac defects. The device includes a biological tissue scaffold, as opposed to a synthetic scaffold (*e.g.,* a polyester fabric, ePTFE, Ivalon®, or a metal mesh) as presently used by devices known in the art. In a preferred embodiment, the biological tissue scaffold is fabricated from collagen. In one embodiment, a specific type of biological tissue, derived from the tunica submucosa layer of the porcine small intestine, forms the tissue scaffold. As a result of this structure, the aforementioned disadvantages associated with the devices known in the art are minimized or eliminated.

**[0008]** In one aspect, the invention provides an intracardiac occluder for percutaneous transluminal treatment of an intracardiac defect. The intracardiac occluder includes a proximal support structure supporting a proximal occlusion shell and a distal support structure supporting a distal occlusion shell. The distal support structure is coupled to the proximal support structure and at least one of the occlusion shells includes a biological tissue scaffold.

**[0009]** Various embodiments of this aspect of the invention include the following features. The biological tissue scaffold may be a purified bioengineered type 1 collagen that may be derived from a tunica submucosa layer of a porcine small intestine. Further, in one embodiment, at least one of the support structures includes a corrosion resistant metal. Alternatively, at least one of the support structures includes a bioresorbable polymer or a biodegradable polymer. In yet another embodiment, the proximal support structure includes a plurality of outwardly

extending proximal arms and the distal support structure includes a plurality of outwardly extending distal arms.

**[0010]** In another aspect, the invention provides a method for percutaneous transluminal treatment of an intracardiac defect in a patient. The method includes providing an intracardiac occluder as described above, positioning the intracardiac occluder proximate the intracardiac defect, and engaging the intracardiac defect with the intracardiac occluder to substantially occlude the intracardiac defect.

**[0011]** In one embodiment of this aspect of the invention, the intracardiac defect is engaged by positioning the proximal occlusion shell and the distal occlusion shell on different sides of the intracardiac defect. The intracardiac defect may be, for example, a patent foramen ovale, an atrial septal defect, a ventricular septal defect, or a left atrial appendage.

**[0012]** In yet another aspect, the invention provides a method for making an intracardiac occluder for the percutaneous transluminal treatment of an intracardiac defect. The method includes providing an overall support structure and first and second biological tissue scaffolds. The overall support structure includes a proximal support structure and a distal support structure. The method further includes coupling the first biological tissue scaffold to the proximal support structure and coupling the second biological tissue scaffold to the distal support structure. In various embodiments of this aspect of the invention, the biological tissue scaffolds are sewn, laminated, or glued to the support structures.

**[0013]** The foregoing and other objects, aspects, features, and advantages of the invention will become more apparent from the following description and from the claims.

## Brief Description of the Drawings

**[0014]** In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention.

**[0015]** FIG. 1 is a cutaway view of a heart illustrating an intracardiac defect.

**[0016]** FIG. 2A is a top plan view of an intracardiac occluder according to an illustrative embodiment of the invention.

**[0017]** FIG. 2B is a cross-sectional view of the illustrative intracardiac occluder of FIG. 2A.

**[0018]** FIG. 3A is a top plan view of an intracardiac occluder according to another illustrative embodiment of the invention.

**[0019]** FIG. 3B is a side view of the illustrative intracardiac occluder of FIG. 3A.

**[0020]** FIG. 4 is a perspective view of an intracardiac occluder according to another illustrative embodiment of the invention.

**[0021]** FIGS. 5A-5E illustrate the stages, according to an illustrative embodiment of the invention, for delivering an intracardiac occluder to an anatomical site in the body of a patient.

**[0022]** FIG. 6A illustrates the results from occluding an intracardiac defect with an intracardiac occcluder known in the art, 30-days after delivery of the intracardiac occluder.

**[0023]** FIG. 6B illustrates the results from occluding an intracardiac defect with an intracardiac occluder according to the invention, 30-days after delivery of the intracardiac occluder.

**[0024]** FIG. 7A illustrates the results from occluding an intracardiac defect with an intracardiac occcluder known in the art, 90-days after delivery of the intracardiac occluder.

**[0025]** FIG. 7B illustrates the results from occluding an intracardiac defect with an intracardiac occcluder according to the invention, 90-days after delivery of the intracardiac occluder.

## Detailed Description of the Invention

**[0026]** The present invention provides an intracardiac occluder for the repair of intracardiac defects, such as, for example, a patent foramen ovale, an atrial septal defect, a ventricular septal defect, and left atrial appendages. The intracardiac occluder includes a structural framework and a biological tissue scaffold adhered thereto.

**[0027]** FIG. 1 depicts a cutaway view of a heart 100. The heart 100 includes a septum 104 that divides a right atrium 108 from a left atrium 112. The septum 104 includes a septum primum 116, a septum secundum 120, and an exemplary intracardiac defect 124, which is to be corrected by the intracardiac occluder of the present invention, between the septum primum 116 and the septum secundum 120. Specifically, a patent foramen ovale 124 is shown as an opening through the septum 104. The patent foramen ovale 124 provides an undesirable fluid communication between the right atrium 108 and the left atrium 112. Under certain conditions, a large patent foramen ovale 124 in the septum 104 would allow for the shunting of blood from the right atrium 108 to the left atrium 112. If the patent foramen ovale 124 is not closed or obstructed in some manner, a patient is placed at high risk for an embolic stroke.

**[0028]** FIG. 2A depicts an intracardiac occluder 10 according to an illustrative embodiment of the invention. As shown, the intracardiac occluder 10 includes a proximal occlusion shell 18 (*i.e.*, an occlusion shell that is closest to an operator of the intracardiac occluder 10 (*e.g.*, a

physician)), an opposite distal occlusion shell 20, and an overall support structure 16. The overall support structure 16 includes a proximal support structure 24, for supporting the proximal occlusion shell 18, and a distal support structure 34, for supporting the distal occlusion shell 20. In one embodiment, both the proximal support structure 24 and the distal support structure 34 include outwardly extending arms to support each of their respective occlusion shells 18, 20. As shown in FIG. 2A, for example, the proximal support structure 24 includes four outwardly extending arms 26 and the distal support structure 34 similarly includes four outwardly extending arms 36. In one embodiment, each outwardly extending arm is resiliently biased as a result of including three or more resilient coils 43 radially spaced from a center point 45. Alternatively, other resilient support structures could be used. In one embodiment, the eight arms 26, 36 are mechanically secured together by wire 52. Alternatively, other means, such as, for example, laser welding, may be used to secure the eight arms 26, 36 together. A cross-sectional view of the intracardiac occluder 10 illustrated in FIG. 2A, showing four arms 26, 36, is depicted in FIG. 2B.

**[0029]** FIGS. 3A and 3B depict an intracardiac occluder 10' according to another illustrative embodiment of the invention. An overall support structure 16' forms a clip and includes a proximal support structure 24', for supporting a proximal occlusion shell 18', and a distal support structure 34', for supporting a distal occlusion shell 20'.

**[0030]** An intracardiac occluder 10'' according to yet another illustrative embodiment of the invention is illustrated in FIG. 4. Again, an overall support structure 16'' forms a clip and includes a proximal support structure 24'', for supporting a proximal occlusion shell 18'', and a distal support structure 34'', for supporting a distal occlusion shell 20''.

**[0031]** Alternatively, the overall support structure 16 may assume any shape or configuration to form the proximal support structure 24 and the distal support structure 34.

**[0032]** In one embodiment, the overall support structure 16 is fabricated from a corrosion resistant metal, such as, for example, stainless steel, nitinol, or a nickel-cobalt-chromium-molybdenum alloy (*e.g.,* MP35N). Alternatively, in other embodiments, the overall support structure 16 is fabricated from bioresorbable or biodegradeable polymers.

**[0033]** In accordance with the present invention, the occlusion shells 18, 20, which are attached, as described below, to the proximal support structure 24 and the distal support structure 34, respectively, are made from a biological tissue scaffold. In a preferred embodiment, the tissue scaffold is fabricated from collagen. In one embodiment, a purified (acellular) bioengineered type 1 collagen derived from the tunica submucosa layer of the porcine small

intestine forms the tissue scaffold. More specifically, the tunica submucosa layer, referred to hereinafter as the Intestinal Collagen Layer ("ICL"), is separated or delaminated from the other layers of the porcine small intestine (*i.e.,* the tunica muscularis and the tunica mucosa) by any method known in the art. For example, a Bitterling sausage casing machine is used to perform the separation. Once mechanically separated from the other layers, the ICL is, in one embodiment, chemically cleaned to remove debris and other substances, other than collagen. For example, the ICL is soaked in a buffer solution at 4 degrees Celsius without the use of any detergents, or, alternatively, in a second embodiment, it is soaked with NaOH or trypsin. Other cleaning techniques known to those skilled in the art may also be used. After cleaning, the ICL is decontaminated. Any sterilization system for use with collagen, as known in the art, may be used. For example, a dilute peracetic acid solution, gamma sterilization, or electron-beam sterilization is used to decontaminate the ICL.

**[0034]** Alternatively, collagenous tissue from the fascia lata, pericardium, or dura matter of pigs or other mammalian sources, such as, for example, cows or sheep, may form the tissue scaffold. Additionally, in making the occlusion shells 18, 20, two or more collagen layers may be bonded together and then cross-linked to produce a biocompatible material capable of being remodeled by the host cells.

**[0035]** In one embodiment, the biological tissue scaffold is non-porous and prevents the passage of fluids that are intended to be retained by the implantation of the intracardiac occluder 10. In another embodiment, heparin is ionically or covalently bonded to the biological tissue scaffold to render it non-thrombogenic. In yet other embodiments, proteins or cells are applied to the biological tissue scaffold to render it non-thrombogenic and/or accelerate the healing process. Growth factors may also be applied to the biological tissue scaffold to accelerate the healing process.

**[0036]** Referring again to FIG. 2A, the occlusion shells 18, 20 are, in one embodiment, generally square in shape. Alternatively, the occlusion shells 18, 20 may assume other shapes. The biological tissue scaffold forming the occlusion shells 18, 20 is strong and flexible. The occlusion shells 18, 20 therefore easily attach to the overall support structure 16 and, as explained below, withstand sheath delivery to an anatomical site in the body of a patient. In one embodiment, the occlusion shells 18, 20 are sewn, as at 22A, 22B, with any commonly used suture material (*e.g.,* a polyester suture) that threads through the distal ends 54 of the respective arms 26, 36 of the proximal support structure 24 and the distal support structure 34. Alternatively, the occlusion shells 18, 20 are laminated, glued, or attached by, for example,

hooks or thermal welding to the proximal support structure 24 and the distal support structure 34. In yet another embodiment, the occlusion shells 18, 20 are laminated to the overall support structure 16 and, additionally, to one another, such that the overall support structure 16 is encapsulated entirely within the occlusion shells 18, 20.

**[0037]** FIGS. 5A-5E depict the stages for delivering the intracardiac occluder 10, according to an illustrative embodiment of the invention, percutaneously to an anatomical site in the body of a patient. Referring to FIG. 5A, a sheath 190 is first inserted into the intracardiac defect 186 as is typically performed by one skilled in the art. The intracardiac occluder 10 is then loaded into the lumen 188 of the sheath 190 and advanced throughout the lumen 188 until positioned at the distal end 192 of the sheath 190. Referring to FIG. 5B, the distal occlusion shell 20 of the intracardiac occluder 10 is released into the distal heart chamber 191 through the distal end 192 of the sheath 190. The distal occlusion shell 20 opens automatically and resiliently. The sheath 190 is then pulled back into the proximal heart chamber 193, as illustrated in FIG. 5C, to seat the distal occlusion shell 20 against the distal wall surface 194 of the intracardiac defect 186. The intracardiac defect 186 is thereby occluded from the distal side. As shown in FIG. 5D, the sheath 190 is then further withdrawn a sufficient distance to allow the proximal occlusion shell 18 to be released from the distal end 192 of the sheath 190. The proximal occlusion shell 18 opens automatically and resiliently to lie against the proximal surface 196 of the intracardiac defect 186, occluding the intracardiac defect 186 from the proximal side. The sheath 190 is then withdrawn from the patient's body, leaving behind the opened intracardiac occluder 10. As shown in FIG. 5E, the occlusion shells 18, 20 are positioned on either side of the intracardiac defect 186 and the intracardiac occluder 10 is permanently implanted within the body of the patient.

**[0038]** FIGS. 6A-6B and 7A-7B depict comparative 30-day and 90-day results, respectively, for the percutaneous closures of interventionally created intracardiac defects in sheep. Specifically, FIGS. 6A and 7A depict the 30-day and 90-day results, respectively, when an exemplary intracardiac occluder known in the art, whose occlusion shells were fabricated from a polyester fabric (*i.e.*, a synthetic scaffold material), is used to occlude the intracardiac defect. FIGS. 6B and 7B depict the 30-day and 90-day results, respectively, when the intracardiac occluder 10 of the instant invention, whose occlusion shells 18, 20 were fabricated from ICL, is used to occlude the intracardiac defect.

**[0039]** As shown, the biological tissue scaffold of the intracardiac occluder 10 of the present invention increases the rate of tissue ingrowth and, consequently, decreases the time needed to

completely close the intracardiac defect. Specifically, referring now to FIG. 7B, the intracardiac occluder 10 of the present invention is barely visible after 90-days. The surrounding tissue ingrowth nearly completely envelopes the intracardiac occluder 10. In comparison, referring now to FIG. 7A, the exemplary intracardiac occluder known in the art is still clearly visible after the same period of time.

**[0040]** As also shown, the intracardiac occluder 10 of the present invention naturally adheres to, and seals completely along, the edge of the intracardiac defect in a manner that is much improved from the exemplary intracardiac occluder known in the art. Additionally, in one embodiment, the biological tissue scaffold of the intracardiac occluder 10 of the present invention is non-porous. As a result, the intracardiac occluder 10 decreases the likelihood of fluid (*e.g.*, blood) leakage through the opening.

**[0041]** Further advantages to the intracardiac occluder 10 of the present invention, in comparison to known intracardiac occluders, include decreased thrombogenicity, quicker endothelialization, superior biocompatibility, minimal foreign body reaction, decreased inmmunological and inflammatory responses, and no fibrosis.

**[0042]** Variations, modifications, and other implementations of what is described herein will occur to those of ordinary skill in the art without departing from the spirit and the scope of the invention as claimed. Accordingly, the invention is to be defined not by the preceding illustrative description but instead by the spirit and scope of the following claims.

**[0043]** What is claimed is:

## Claims

1. An intracardiac occluder for percutaneous transluminal treatment of an intracardiac defect, comprising:

a proximal support structure supporting a proximal occlusion shell; and

a distal support structure, coupled to the proximal support structure, supporting a distal occlusion shell,

wherein at least one of the occlusion shells comprises a biological tissue scaffold.

2. The occluder of claim 1, wherein the biological tissue scaffold comprises a purified bioengineered type 1 collagen.

3. The occluder of claim 2, wherein the purified bioengineered type 1 collagen is derived from a tunica submucosa layer of a porcine small intestine.

4. The occluder of claim 1, wherein at least one of the support structures comprises a corrosion resistant metal.

5. The occluder of claim 1, wherein at least one of the support structures comprises a bioresorbable polymer.

6. The occluder of claim 1, wherein at least one of the support structures comprises a biodegradable polymer.

7. The occluder of claim 1, wherein the proximal support structure comprises a plurality of outwardly extending proximal arms and the distal support structure comprises a plurality of outwardly extending distal arms.

8. A method for percutaneous transluminal treatment of an intracardiac defect in a patient, comprising:

providing an intracardiac occluder, comprising:

a proximal support structure supporting a proximal occlusion shell; and

a distal support structure, coupled to the proximal support structure, supporting a distal occlusion shell,

wherein at least one of the occlusion shells comprises a biological tissue scaffold;

positioning the intracardiac occluder proximate the intracardiac defect; and

engaging the intracardiac defect with the intracardiac occluder to substantially occlude the intracardiac defect.

9. The method of claim 8, wherein engaging the intracardiac defect comprises positioning the proximal occlusion shell and the distal occlusion shell on different sides of the intracardiac defect.

10. The method of claim 8, wherein the intracardiac defect is a patent foramen ovale.

11. The method of claim 8, wherein the intracardiac defect is an atrial septal defect.

12. The method of claim 8, wherein the intracardiac defect is a ventricular septal defect.

13. The method of claim 8, wherein the intracardiac defect is a left atrial appendage.

14. A method for making an intracardiac occluder for percutaneous transluminal treatment of an intracardiac defect, comprising:

providing an overall support structure comprising a proximal support structure and a distal support structure;

providing first and second biological tissue scaffolds;

coupling the first biological tissue scaffold to the proximal support structure; and

coupling the second biological tissue scaffold to the distal support structure.

15. The method of claim 14, wherein coupling the biological tissue scaffolds comprises sewing the biological tissue scaffolds to the support structures.

16. The method of claim 14, wherein coupling the biological tissue scaffolds comprises laminating the biological tissue scaffolds to the support structures.

17. The method of claim 14, wherein coupling the biological tissue scaffolds comprises gluing the biological tissue scaffolds to the support structures.

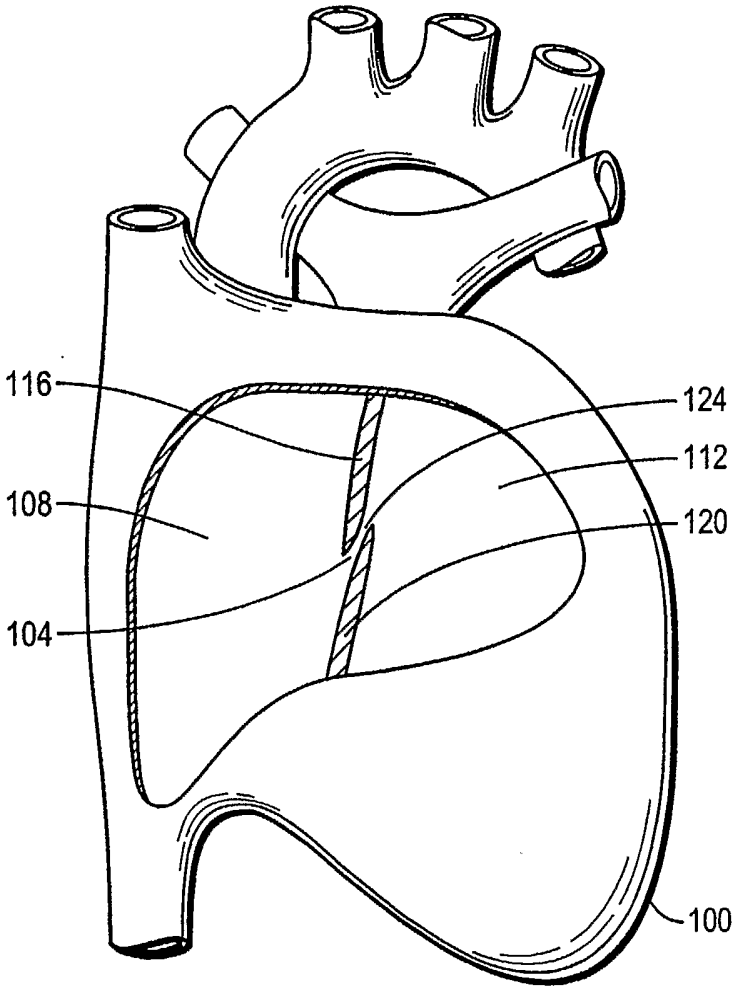



FIG. 1

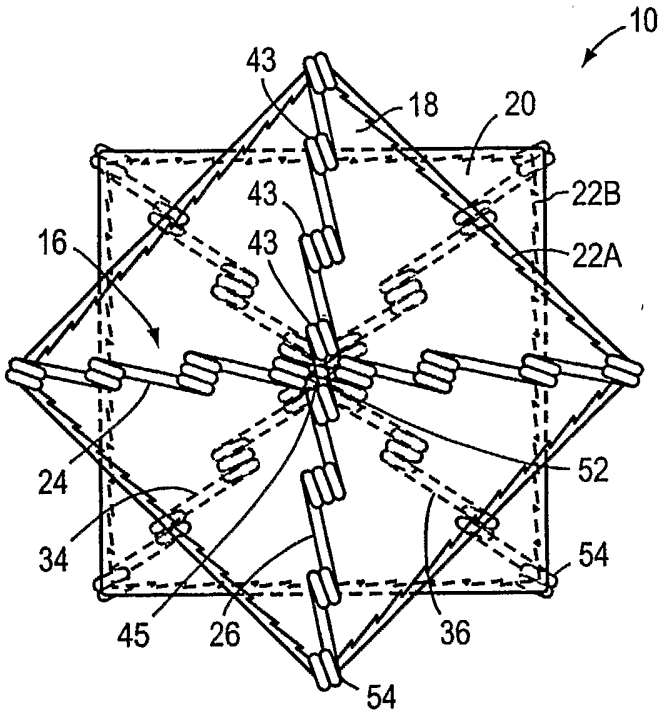

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FIG. 2A

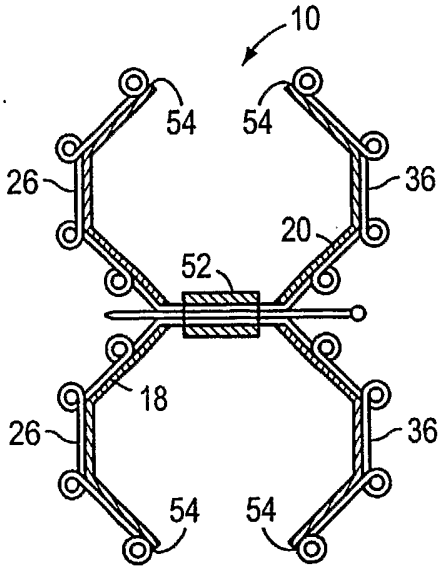

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FIG. 2B

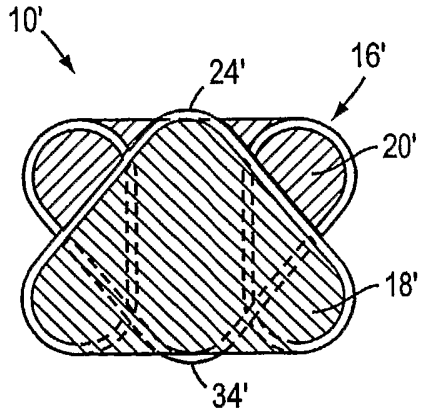



FIG. 3A

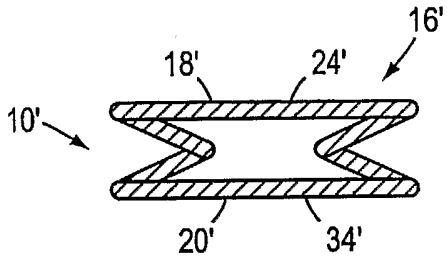



FIG. 3B

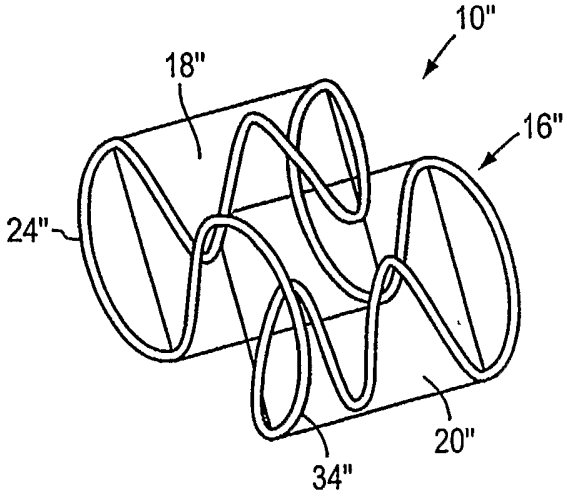



FIG. 4

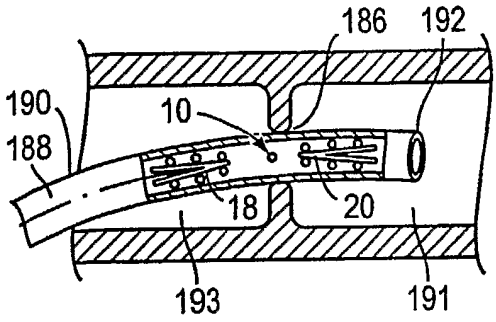



FIG. 5A

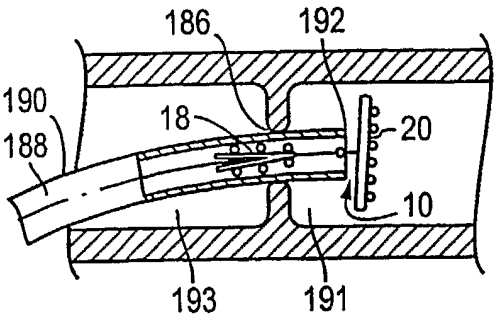



FIG. 5B

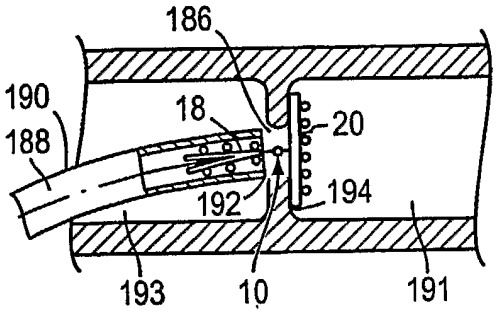



FIG. 5C

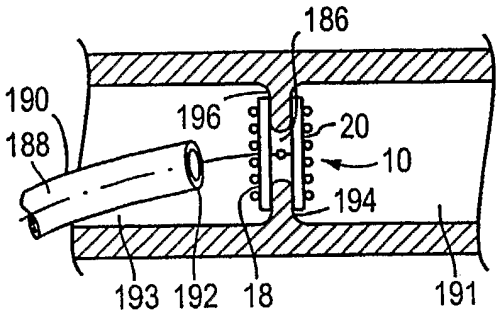



FIG. 5D

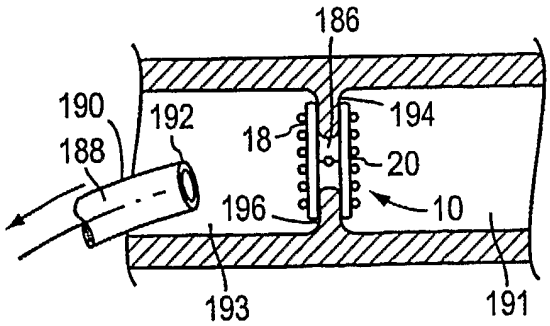



FIG. 5E

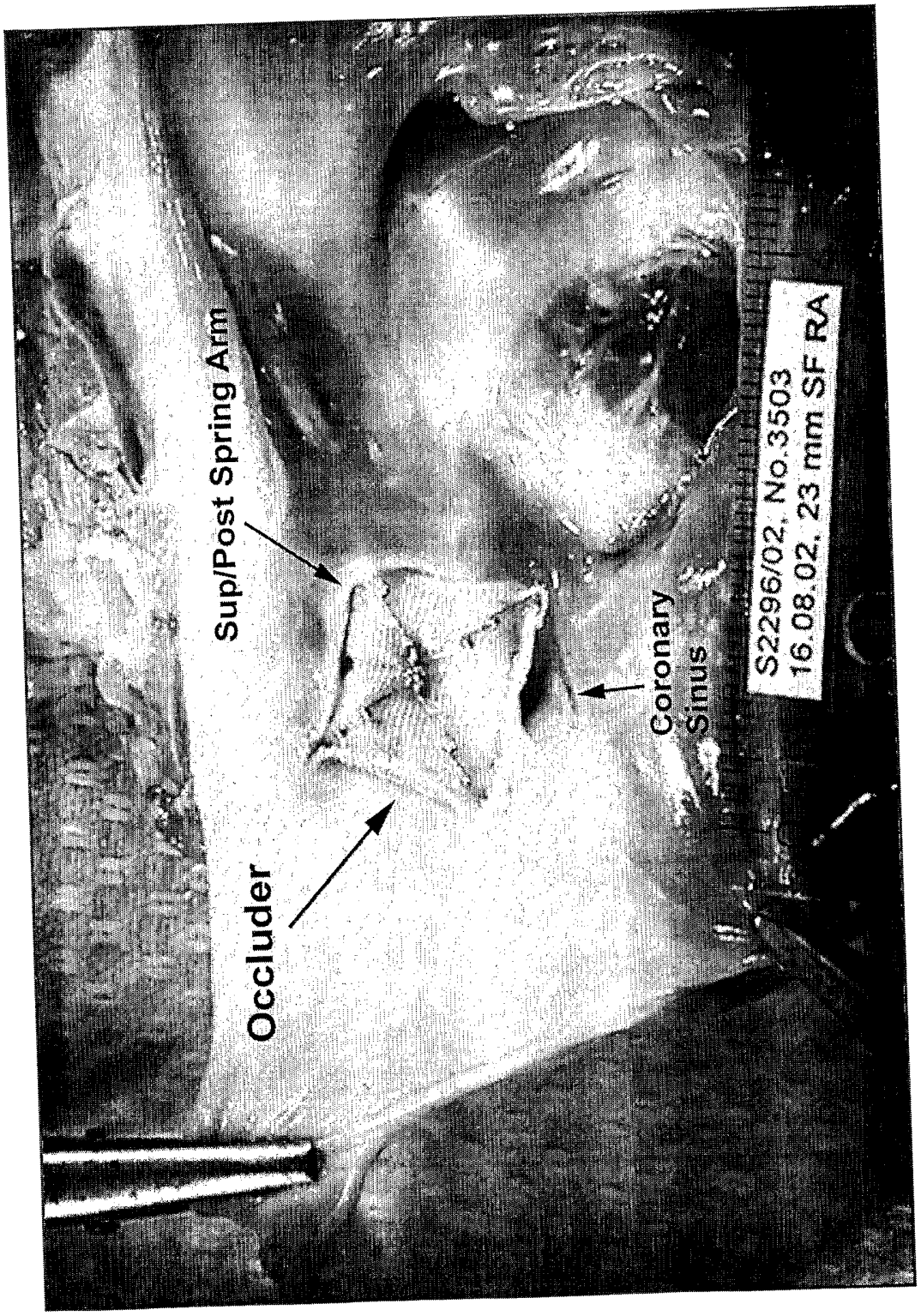

Occluder
Sup/Post Spring Arm
Coronary Sinus
S2296/02, No.3503
16.08.02, 23 mm SF RA

FIG. 6A

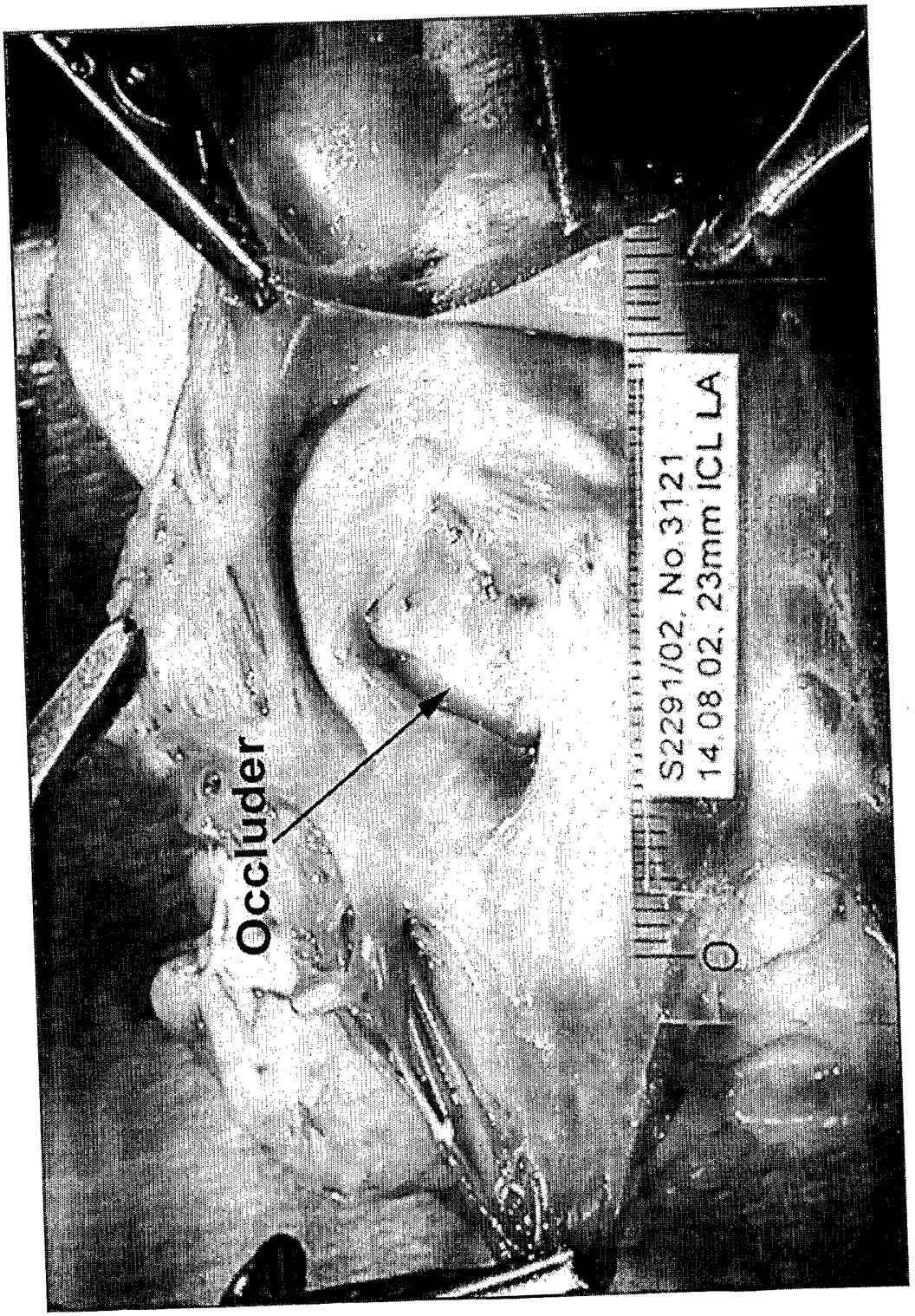



FIG. 6B

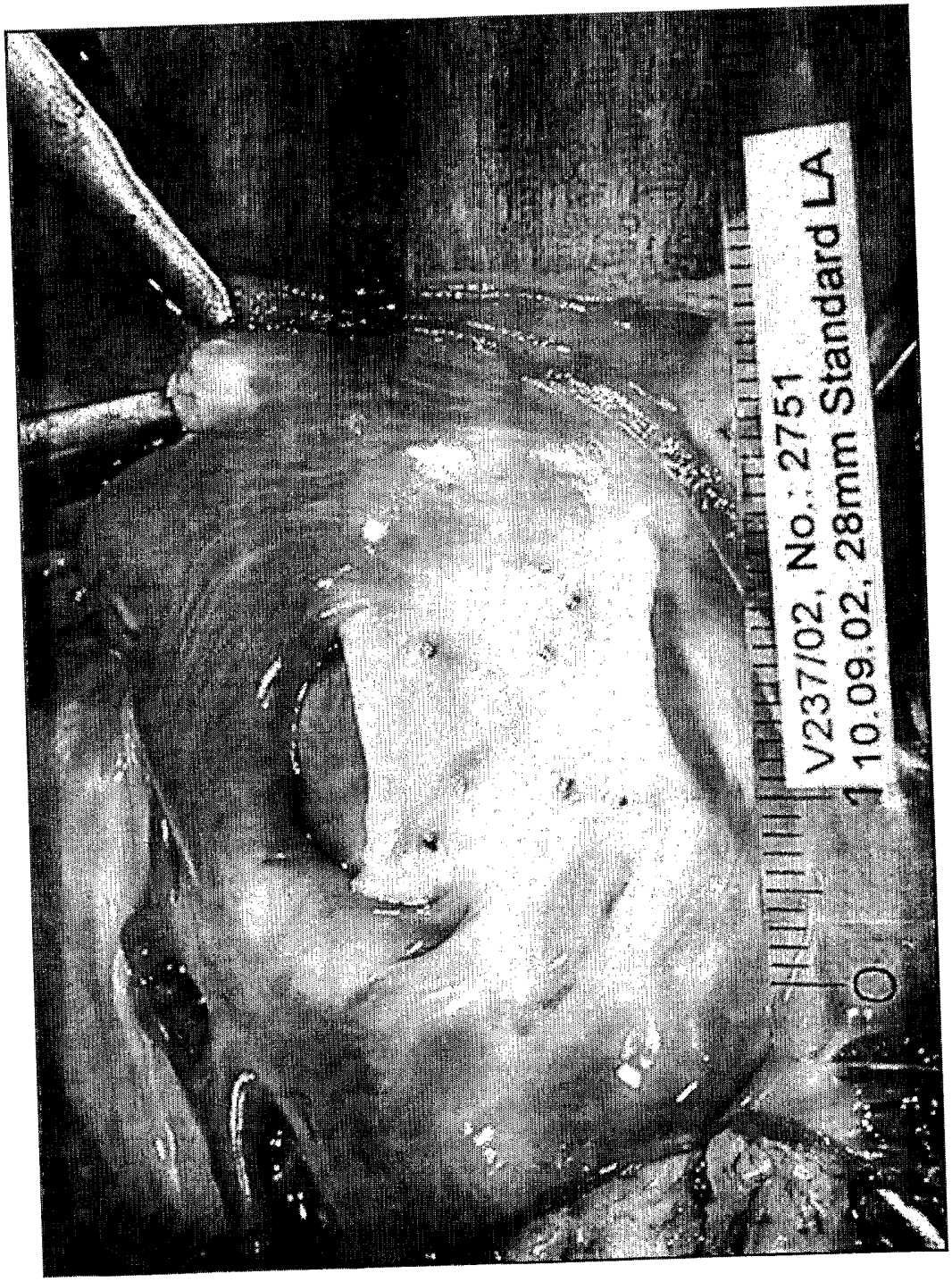



FIG. 7A




FIG. 7B

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/17390

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61B 17/08
US CL : 606/213

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 606/213, 76, 77, 215, 217

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | US 6,346,074 B1 (ROTH) 12 February 2002 (12.02.2002), see entire document. | 1, 3, 4, 7, 8, 10-12, and 14 |
| A | US 2001/0037129 A1 (THILL), 01 November 2001 (01.11.2001), see entire document. | |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 22 September 2003 (22.09.2003) | 06 OCT 2003 |
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703)305-3230 | Authorized officer<br>Bradford C Pantuck<br>Telephone No. (703) 308-1148 |

Form PCT/ISA/210 (second sheet) (July 1998)

# INTERNATIONAL SEARCH REPORT

PCT/US03/17390

**Continuation of Item 4 of the first sheet:**
Title exceeds prescribed limit. Rename the invention "DEVICE WITH BIOLOGICAL TISSUE SCAFFOLD FOR INTRACARDIAC DEFECT CLOSURE".