



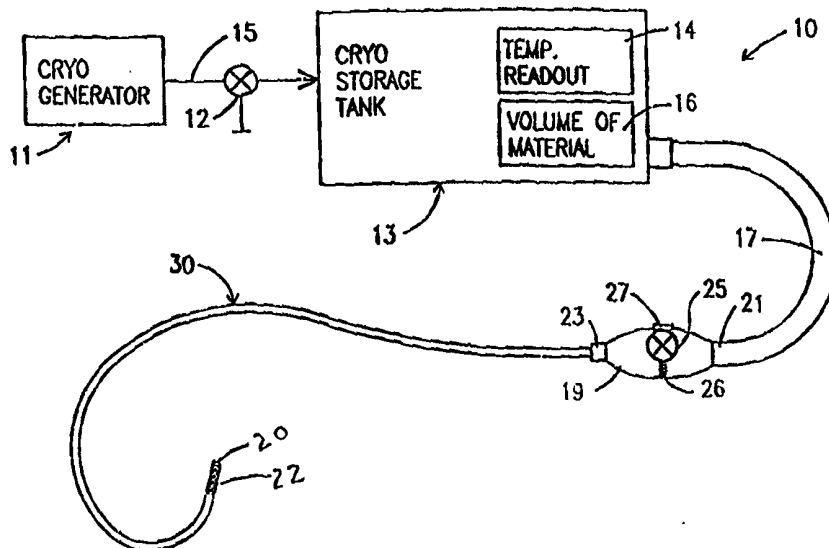
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/15329 (22) International Filing Date: 28 July 1998 (28.07.98) (30) Priority Data: 08/902,020 29 July 1997 (29.07.97) US (71)(72) Applicant and Inventor: JAYARAMAN, Swaminathan [IN/US]; 3415 Misty Meadow Drive, Dallas, TX 75287 (US). (74) Agents: FANUCCI, Allan, A. et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).	(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>	

(54) Title: CRYOTHERAPY METHOD FOR REDUCING TISSUE INJURY AFTER BALLOON ANGIOPLASTY OR STENT IMPLANTATION

(57) Abstract

A cryotherapy method for reducing tissue injury after balloon angioplasty, or stent implantation, contemplates use of a well insulated, low profile catheter (30) designed to transport a low temperature medium such as gas, fluid, or a mixture thereof at a particular temperature over a guide wire (33) to the site of a lesion. The lesion may, or may not have undergone previous procedure for balloon angioplasty, or stent implantation. The cryo-medium is introduced from a well insulated storage chamber (13) having a small nozzle to



which a conduit (15) may be attached to allow conveyance of the fluid to a point of use. A hand held valve (25) is incorporated into the conduit to allow the surgeon to closely control the flow of the cryo-medium to the point of use. The conduit extends downstream of the valve, and is fluidly connected to the catheter that is positioned at the point of the lesion in the body. If desired, antibiotics, anticoagulants, anti-proliferative agents, gene materials, etc. may also be dispersed along the cryo-medium intraluminously. Such additional substances may be mixed with the cryo-medium in the storage chamber before introduction into the catheter. Several alternative catheter structures are contemplated in accordance with the teachings of the present invention.

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**CRYOTHERAPY METHOD FOR REDUCING TISSUE INJURY AFTER
BALLOON ANGIOPLASTY OR STENT IMPLANTATION**

5

BACKGROUND OF THE INVENTION

The present invention relates to a cryotherapy method for reducing tissue injury after balloon angioplasty or stent implantation. One of the well known and well documented causes of failure of angioplasty (use of a balloon
10 inflated within an artery to compress occluding materials against the inner arterial wall) or stent implantation is the mechanism of restenosis. Restenosis is evidenced when the artery re-occludes due to tissue ingrowth and/or elastic recoil of the arterial wall at the site of the prior
15 occlusion.

After a balloon angioplasty procedure or stent implantation procedure has been completed, the arterial wall often exhibits damage or inflammation due to the required use of force from inflation of a balloon catheter against the
20 cellular layers of the arterial wall. This ingrowth phenomenon, namely, restenosis, affects the long term success of balloon angioplasties and stent implantations. In the prior art, cryotherapy is a known technique for preserving tissues at reduced temperatures for short periods of time.
25 Cryotherapy has been decisively shown to be effective in tissue preservation, maintenance of tissue function and facilitation of tissue healing processes. Some of the well-defined applications of cryotherapy include the following:

(1) Tissues collected from bovine, pigs and sheep are
30 preserved at reduced temperature so that the elastic membranes or elastin present in the tissues is protected for subsequent applications. Without the use of such temperature reduction, the tissues dry out and lose their original mechanical, physical and chemical properties.

35 (2) During open heart surgery, when the heart is opened to either replace a valve or an underlying diseased coronary artery, the myocardium or the tissues surrounding the heart

are exposed to reduced temperature by dipping them in ice or sub-cooled water while the surgery is underway to preserve them.

(3) During open heart surgery, when the aorta is cross-clamped and blood from the heart is directed into a heart-lung machine, the blood is mixed with cold cardioplegia solution to preserve the cells and other essential components in the blood, an especially critical procedure where surgery is lengthy.

(4) Bovine and other homograft valves that have been preserved in cryo-based solutions and reduced temperature environment have been shown to have superior performance during long term follow-up studies when compared with mechanical bileaflet or single leaflet valves.

(5) In many pain management therapeutic situations, the area or region of acute pain is exposed to reduced temperature fluids or "cold packs" to reduce nerve damage and relieve pain.

The prior art teaches several techniques designed to reduce or eliminate the onset of restenosis. However, Applicant is unaware of any such technique that involves the use of application of reduced temperature within an artery.

One of the most common causes of recurrence of luminal narrowing after balloon angioplasty or stent implantation is the ingrowth of tissue at the site of the previous blockage. When a balloon is inflated at the site of a lesion where the artery is occluded, the lesion is mechanically pushed up by force acting thereon due to inflation of the balloon. Pathology of experiments in pigs and sheep reveals that the balloon inflation causes endothelial injury as well as tissue dislodgement at the site of the lesion. Such an injury is characterized by inner lumen wall cracks that are filled up with blood and some thrombus (clotting material). These cracks may infiltrate into the second and third layers of the vessel wall that are termed adventitia and media primarily composed of collagen, smooth muscle cells and elastic cells that contribute to the compliance of the artery.

When these layers are disrupted due to balloon inflation or stent implantation, compliance response is lost. This results in proliferation of cells as a function of time. Although the proliferation starts immediately after the
5 injury to the arterial wall, maximum proliferation may be observed 6 to 18 months after the initial injury.

Applicant is aware of the following prior art:

United States Patent 5,059,166 to Fischell et al. discloses a technique for reducing the onset of intimal
10 hyperplasia which technique involves the use of irradiation from a radioisotope.

United States Patent 5,213,561 to Weinstein et al. also discloses the use of radioactive material to reduce the incidence of restenosis.

15 United States Patent 5,092,81 to Spears discloses the bonding of a bioprotective material to the arterial wall where angioplasty has been conducted.

United States Patent 5,140,012 to McGovern et al. discloses a method for preventing onset of restenosis after
20 angioplasty which involves administration of pravastatin in combination with an ACE inhibitor.

United States Patent 5,242,397 to Barath et al. discloses prevention or reduction of the incidence of late restenosis through the administration of protein kinase C and
25 tyrosine protein kinase inhibitors.

United States Patent 5,284,869 to Bisaccia et al. discloses a method for preventing restenosis following angioplasty that includes the use of a photophoresis treatment method.

30 United States Patent 5,298,018 to Narciso, Jr. discloses administration of a photosensitizer prior to surgical or interventional procedure which is then re-administered after the procedure to maintain the photosensitizer concentration level in the atheromatous plaque and smooth muscle cells in
35 the vicinity of the lesion for a period of about 5-18 days.

United States Patent 5,22,362 to Vincent et al. discloses administration of a green porphyrin to the location of vascular intervention to inhibit the onset of restenosis.

None of the patents discussed above teaches, discloses
5 or suggests the use of a cryo-technique to reduce the onset of restenosis after a balloon angioplasty or stent implantation.

Further, Applicant is aware of an article titled "THE
ROLE OF CRYOTHERAPY FOR AIRWAY COMPLICATIONS AFTER LUNG AND
10 HEART-LUNG TRANSPLANTATION" by Maiwand et al. The article discusses the use of cryotherapy in causing cell lysis of granulation tissue and speculates that such a technique may therefore be effective after lung transplantation for difficult airway problems. This article fails to teach or
15 suggest the use of cryotherapy techniques for reduction of the onset of restenosis within the arterial wall of a patient on whom balloon angioplasty or stent implantation has been completed.

SUMMARY OF THE INVENTION

20 The present invention relates to a cryotherapy method for reducing tissue injury after balloon angioplasty or stent implantation. The present invention includes the following interrelated objects, aspects and features:

(1) The present invention contemplates a well insulated,
25 low profile catheter designed to transport a medium such as gas, fluid or a mixture thereof at a particular temperature over a guide wire to the site of a lesion. The lesion may or may not have undergone previous procedure for balloon angioplasty or stent implantation.

30 (2) The medium is introduced in the following preferred way: air is mixed with freon or helium and is compressed in a chamber to very low temperature between 14°C and -10°C. The medium can also be water, water mixed with saline, or water mixed with suitable coolants that maintain the temperature.
35 From the compression chamber, the cooled fluid is conveyed to a well insulated storage chamber having a small nozzle to which a conduit may be attached to allow conveyance of the

fluid to a point of use. A handheld valve is incorporated into the conduit to allow the surgeon to closely control the flow of the cryo-medium to the point of use. The conduit extends downstream of the valve and is fluidly connected to the catheter that is positioned at the point of the lesion in the body.

(3) Additionally, antibiotics, anticoagulants, antiproliferative agents, gene materials, etc. may also be dispersed along with the cryo-medium intraluminally. Such additional substances may be mixed with the cryo-medium in the storage chamber before introduction into the catheter or concurrently with introduction into the catheter.

(4) These additional substances may also be introduced prior to introduction of the cryo-medium or thereafter.

(5) The procedure for introduction of the cryo-medium and other substance(s) can be applied to all intraluminal, intercranial and endovascular procedures regardless of the size of the lumen of the artery or the vein and regardless of the site on the body where it is located.

(6) Several alternative catheter structures are contemplated in accordance with the teachings of the present invention. These catheter structures are the following:

(a) The catheter may be provided with two lumens, one for introduction over a guide wire and a second lumen having a plurality of holes at the distal end thereof that act as the point of delivery for the cryo-medium and other substance(s). These holes may be provided over an area prescribed based upon the length of the lesion and the diameter of the artery involved.

(b) The catheter may have a triple lumen where one lumen is provided for the guide wire, the second lumen is provided for balloon inflation to center the catheter, and the third lumen is used for delivery of the cryo-medium and other substance(s).

(c) The catheter may have four lumens where three of the lumens perform the functions described in subparagraph (b) above, and the fourth lumen provides an

additional balloon so that there is one balloon upstream of the lesion site and one balloon downstream of the lesion site to isolate the lesion site on both sides with delivery of the cryo-medium occurring therebetween.

5 (d) If desired, the mechanism for delivery of the cryo-medium can comprise a balloon having pores formed in a second layer thereof.

(e) Alternatively, the delivery mechanism can comprise a simple shaft having a distal tip with an opening or holes thereon that may be closed while the
10 catheter is being introduced into the body but which may be opened by withdrawing a sheath or a similar protective mechanism.

(f) All the delivery mechanism above may
15 incorporate a thermistor or similar temperature recording device which reads the temp and may be displayed onto the unit.

Accordingly, it is a first object of the present invention to provide a cryotherapy method for reducing tissue
20 injury and/or restenosis after balloon angioplasty or stent implantation.

It is a further object of the present invention to provide such a method wherein a cryo-medium is created and stored within a container for later delivery via a catheter.

25 It is a still further object of the present invention to provide such a method wherein other substance(s) may be supplied at the area of a lesion along with a cryo-medium.

It is a yet further object of the present invention to provide such a method wherein a catheter is provided having
30 anywhere from one to four lumens provided to guide the catheter to its place of location, allow inflation of one or more balloons to maintain the catheter end at a desired location, and a plurality of holes to allow dispensing of the cryo-medium.

35 These and other objects, aspects and features of the present invention will be better understood from the

following detailed description of the preferred embodiments when read in conjunction with the appended drawing figures.

BRIEF DESCRIPTION OF THE DRAWINGS

5 Figure 1 shows a schematic representation of the overall system of the present invention.

Figure 2 shows a longitudinal cross-sectional view through a first embodiment of catheter including two lumens.

Figure 3 shows a further side view, partially in cross-
10 section, of the embodiment illustrated in Figure 2.

Figure 4 shows a second embodiment of catheter including three lumens.

Figure 5 shows a third embodiment of catheter including the use of four lumens.

15 Figure 6 shows a fourth embodiment of catheter including a two layered balloon having an inner layer with pores to deliver cryo- medium.

Figure 7 shows a fifth embodiment of catheter having a two layered balloon with the outer layer having pores to
20 deliver cryo- medium.

Figure 8 shows a sixth embodiment of catheter devoid of a balloon but having a series of holes to deliver cryo-medium.

Figure 9 shows the catheter of Figure 8 with a flexible
25 sheath covering the delivery holes, which sheath may be withdrawn to expose the holes and allow cryo-medium delivery.

SPECIFIC DESCRIPTION OF THE PREFERRED EMBODIMENTS

With reference, first, to Figure 1, the overall system
30 of the present invention is generally designated by the reference numeral 10 and is seen to include a cryo-generator 11, a cryo-storage tank 13, a conduit 15 interconnecting the cryo-generator 11 with the cryo-storage tank 13, and an outlet conduit 17 allowing flow of cryo-medium from the
35 storage tank 13 to a handheld controller 19 consisting of an inlet port 21, an outlet port 23, and a valve 25 having a valve actuator 27 that may be manipulated by the user to

allow metering of a flow path through the valve 25 to allow control of flow rate of cryo-medium into the catheter 30. The valve 25 may be of any desired type including one having a spring 26 biasing the valve head to a position of closure so
5 that when the actuator 27 is released, the valve 25 is restored to the closed position. Any suitable valve that will firmly and repeatedly seat to block flow in the contemplated environment, to-wit, that of a cryo-medium having a temperature between -10°C and 4°C may be employed. Such
10 valves are well known to those skilled in the art.

As further seen in Figure 1, the storage tank includes two gauges, a temperature read-out gauge 14 and a volume or a pressure display 16. The volume display 16 may display rate of flow of cryo-medium in any manner well known to those
15 skilled in the art. For example, the flow path of cryo-medium may include a conduit with a restricted orifice and with sensor lines just upstream and downstream of the restricted orifice. The pressure differential on either side of the restricted orifice relates to flow rate in a manner well
20 known to those skilled in the art. Figure 2 shows more details of the catheter 30 also shown in Figure 1. With reference to Figure 2, the catheter 30 includes two lumens, a first lumen 31 provided for insertion therethrough of a guide wire 33 designed to guide movement of the catheter 30
25 to its desired location. The second lumen 35 includes balloon 37 and a plurality of ports 39 in a prescribed pattern and extent designed to dispense cryo-medium to the desired location for the reasons explained herein. The catheter 30 also includes a hub 38 to which the hand held
30 monitor is connected.

Figures 3 and 4 show a second embodiment of catheter generally designated by the reference numeral 40 and including three lumens. One lumen 41 includes a port 42 designed to allow insertion of a guide wire (not shown). A
35 second lumen 43 is provided to allow inflation of the balloon 44. A third lumen includes a plurality of holes 45 therein

in a prescribed pattern and extent designed to allow dispensing of cryo-medium at the desired site.

With reference to Figure 5, a further embodiment of catheter designated by the reference numeral 50 includes all of the features of the catheter 50 but with the addition of a further balloon 51 upstream of the site where cryo-medium is to be dispensed. The openings 53, corresponding to the openings 45 in the catheter 40, are provided in a prescribed pattern and extent and the balloon 54 corresponds to the balloon 44 so that the balloons 51 and 54 define, therebetween, an isolated region where the cryo-medium is to be dispensed.

Figure 6 shows a catheter 60 that includes a balloon 61 having an inner layer 63 and an outer layer 65, with the inner layer 63 including openings 64 therethrough. The cryo-medium may be directed into the space 66 between the inner layer 63 and the outer layer 65 so that the cryo-medium may be dispensed within the chamber 67. In this embodiment, dispensing of the cryo-medium within the chamber 67 eliminates direct contact between the cryo-medium and the arterial wall. However, through heat exchange through the inner layer 63 and the outer layer 65 the effect is the same, namely, cooling of the tissues in a desired manner.

Figure 7 shows a catheter 70 having a balloon 71 with an inner layer 73 and an outer layer 75. Openings 74 are formed in the outer layer and cryo-medium may be directed between the layers 73 and 75 in the space 76 defined therebetween to allow cryo-medium to be dispensed therethrough. In this embodiment, as contrasted to the catheter 60 illustrated in Figure 6, the cryo-medium directly contacts the arterial wall.

Figure 8 shows a catheter 80 that is devoid of a balloon but includes a distal end 81 that is closed. On the peripheral walls adjacent the distal end 81 of the catheter 80, a multiplicity of holes 83 are formed in a desired pattern and extent to allow dispensing of cryo-medium through the interior passageway 84 of the catheter 80 and to the

location of the desired site of application thereof. In Figure 9, the catheter 80 is seen to be provided with a flexible, resilient sheath 85 that covers the openings 83 to preclude flow of cryo-medium. The sheath 85 may be withdrawn 5 from covering the openings 83 in a manner well known to those skilled in the art to allow dispensing of cryo-medium, as desired. As explained above, in order to fill the storage tank 13 with cryo-medium, the cryo-generator comprises a compression chamber where air is mixed with freon or helium, 10 or water with suitable agent and is compressed until the temperature falls between the range of 4°C to -10°C. Thereafter, the cryo-medium is conveyed through the conduit 15 by opening of the valve 12 to the storage tank 13 which may be well insulated in a manner well known to those skilled 15 in the art to allow the temperature of the cryo-medium to be maintained substantially constant. The cryo-medium is conveyed in the conduit 17 to the handheld controller 19 which includes the valve 25 and actuator 27. When the operator so desires, the desired catheter, one of the 20 catheters described hereinabove with reference to Figures 2-9, may be affixed to the outlet port 23 of the handheld controller 19 and the operator can operate the actuator 27 to allow a variety of degrees of opening of the valve 25 to allow flow of cryo-medium through the catheter and to the 25 desired location.

If desired, the cryo-medium may be mixed with other substance or substances such as, for example, antibiotics, anticoagulants, antiproliferative agents, gene matter, etc. that may be disbursed at the desired site along with the 30 cryo-medium intraluminally. These substance(s) may be mixed with the cryo-medium in the cryo-generator 11, in the storage tank 13 or downstream of the handheld controller 19 within the catheter.

As such, an invention has been disclosed in terms of 35 preferred embodiments that fulfill each and every one of the objects of the invention as set forth hereinabove and provide a new and useful cryotherapy technique for reducing tissue

injury after balloon angioplasty or stent implantation of great novelty and utility.

Of course, various changes, modifications and alterations in the teachings of the present invention may be contemplated by those skilled in the art without departing
5 from the intended spirit and scope thereof.

As such, it is intended that the present invention only be limited by the terms of the appended claims.

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CLAIMS

1. A method of reducing tissue injury, or proliferation within a cardiovascular system after a surgical procedure or an interventional procedure or endovascular

5 procedure at a site therein, including the steps of:

a) providing a quantity of a cryo-medium maintained at a temperature below normal human body temperature in a refillable storage container;

10 b) fluidly connecting said storage container with a catheter;

c) inserting said catheter within a cardiovascular system and conveying said catheter to said site;

15 d) controllably dispensing fluid, gaseous medium, or a mixture thereof from said storage chamber through said catheter and into a cardiovascular system at said site.

2. The method of Claim 1, wherein said providing step includes the step of maintaining said cryo-medium at a temperature between 14°C and -10°C.

20 3. The method of Claim 1, wherein said fluidly connecting step includes the step of interposing a valve between said storage container and catheter.

4. The method of Claim 1, wherein said inserting step further includes the step opening an orifice in a cardiovascular system.

25 5. The method of Claim 1, wherein said conveying step includes the step of guiding said catheter with a guide wire.

6. The method of Claim 3, wherein said dispensing step includes the step of controllably operating said valve.

30 7. The method of Claim 5, wherein said catheter has two lumens, one receiving said guide wire and another conveying said fluid medium.

8. The method of Claim 7, wherein said catheter includes an inflatable balloon for securing said catheter at said site.

35 9. The method of Claim 7, wherein said catheter has two spaced balloons, inflatable upstream and downstream of said site.

10. The method of Claim 8, wherein said balloon has two walls, an outer impervious wall and an inner wall with holes therein, said method including the step of conveying said fluid between said walls and out said holes.

5 11. The method of Claim 8, wherein said balloon has two walls, an inner impervious wall and an outer wall with holes therein, said method including the step of conveying said fluid between said walls and out said holes.

12. The method of Claim 1, wherein said catheter has an
10 inner passageway with a closed distal end and a peripheral wall with holes therein, said method including the step of dispensing said fluid medium through said holes.

13. A method of reducing tissue injury within a cardiovascular system after a surgical procedure at a site
15 therein, including the steps of:

a) providing a quantity of a cryo-fluid medium maintained in a storage container at a temperature between 14°C and -10°C;

b) fluidly connecting said storage container with
20 a catheter via a control valve;

c) inserting said catheter within a cardiovascular system and conveying said catheter to said site while guiding with a guide wire;

d) controllably dispensing fluid medium from said
25 storage chamber through said catheter by operating said control valve and into a cardiovascular system at said site.

14. The method of Claim 13, wherein said inserting step further includes the step opening an orifice in a
30 cardiovascular system.

15. The method of Claim 13, wherein said catheter includes an inflatable balloon for securing said catheter at said site.

16. The method of Claim 13, wherein said catheter has
35 two spaced balloons, inflatable upstream and downstream of said site.

17. The method of Claim 15, wherein said balloon has two walls, an outer impervious wall and an inner wall with holes therein, said method including the step of conveying said fluid between said walls and out said holes.

5 18. The method of Claim 15, wherein said balloon has two walls, an inner impervious wall and an outer wall with holes therein, said method including the step of conveying said fluid between said walls and out said holes.

10 19. The method of Claim 13, wherein said catheter has an inner passageway with a closed distal end and a peripheral wall with holes therein, said method including the step of dispensing said fluid medium through said holes.

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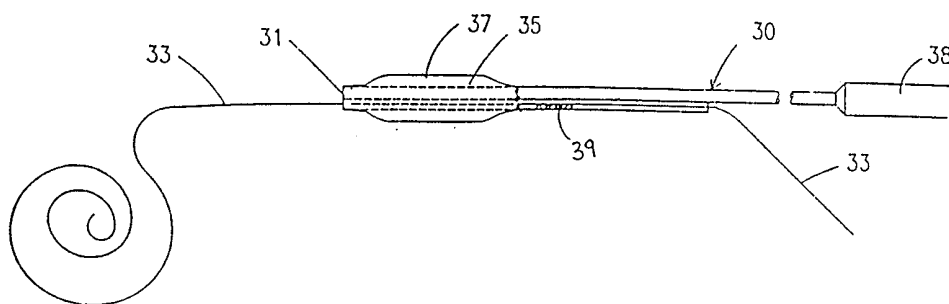
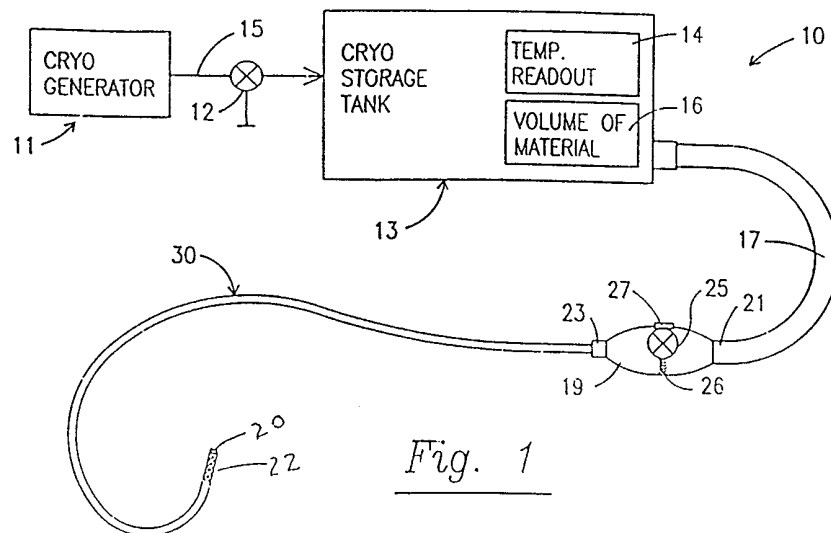
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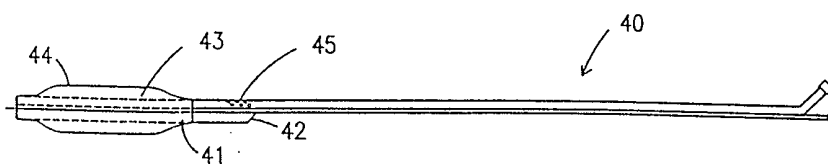


Fig. 3

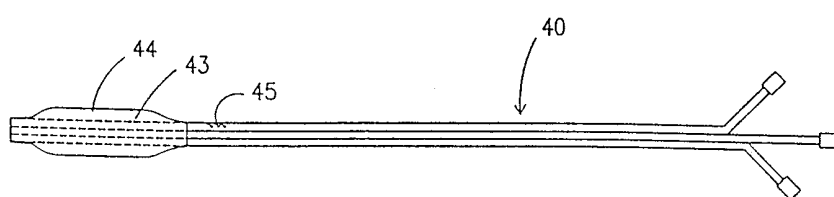


Fig. 4

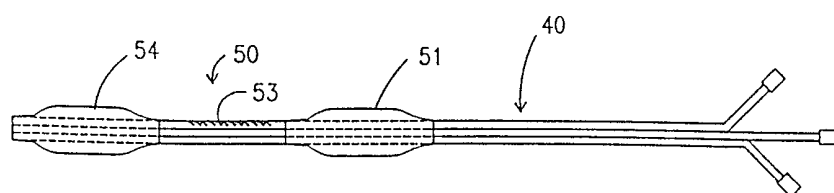


Fig. 5

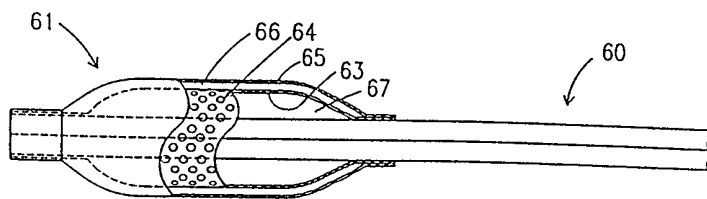


Fig. 6

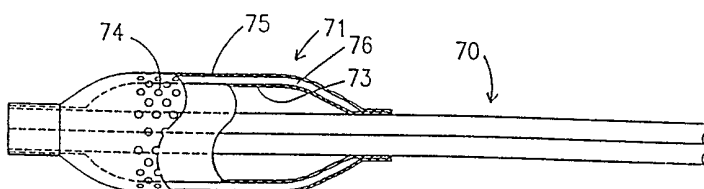


Fig. 7

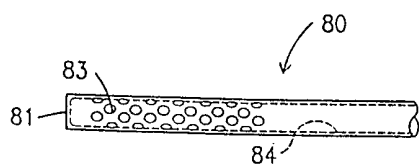


Fig. 8

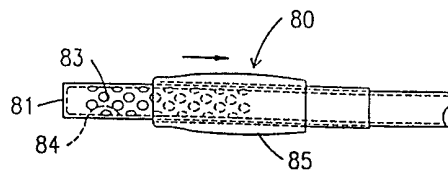


Fig. 9

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/15329

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61B 17/36

US CL : 604/53, 101, 113; 606 20-26

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. : 606/20-26; 604/53, 101, 113

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

NONE

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

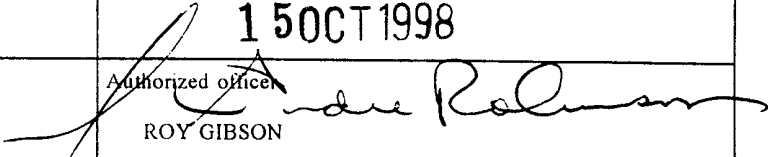
NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,108,390 A (POTOCKY ET AL.) 28 APRIL 1992, ENTIRE DOCUMENT.	1, 3, 4, 6
Y,P	US 5,741,248 A (STERN ET AL.) 21 APRIL 1998, ENTIRE DOCUMENT.	2, 13-16, 18, 19
Y	US 5,624,392 A (SAAB) 29 APRIL 1997, ENTIRE DOCUMENT.	5, 7, 8, 11, 13-16, 18, 19
Y,P	US 5,674,198 A (LEONE) 07 OCTOBER 1997, ENTIRE DOCUMENT.	9
Y	US 5,569,184 A (CROCKER ET AL.) 29 OCTOBER 1996, ENTIRE DOCUMENT.	11
Y	US 4,292,976 A (BANKA) 06 NOVEMBER 1981, ENTIRE DOCUMENT.	12

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

* Special categories of cited documents:	*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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
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Date of the actual completion of the international search	Date of mailing of the international search report
10 SEPTEMBER 1998	15 OCT 1998
Name and mailing address of the ISA US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3590	Authorized officer  ROY GIBSON Telephone No. (703) 308-3520

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/15329

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,334,181 A (RUBINSKY et al.) 02 August 1994, entire document.	1-19
A	US 5,452,582 A (LONGWORTH) 26 September 1995, entire document.	1-19