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(54) CRYOTHERAPY CATHETER FOR DETECTING AND TREATING VULNERABLE PLAQUE

KRYOTHERAPIEKATHETER ZUR ERKENNUNG UND BEHANDLUNG VON ABLAGERUNGEN

CATHÉTER DE CRYOTHERAPIE POUR LA DETECTION ET LE TRAITEMENT DE PLAQUES D'ATHEROSCLEROSE VULNERABLES

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(56) References cited:
WO-A-00/27278
US-A- 5 868 735
US-A- 5 868 735
US-A- 5 899 899
US-A- 5 902 299
US-A- 5 902 299

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Description

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates generally to an apparatus for treating blood vessels. More particularly, the present invention provides an apparatus for treating a lesion, and particularly a vulnerable atherosclerotic plaque, within a patient's vasculature to inhibit harmful releases within the vasculature, such as those which may be responsible for strokes or acute coronary syndromes of unstable angina, myocardial infarction, and sudden cardiac death.

[0002] Atherosclerotic plaque is present to some degree in most adults. Plaques can severely limit the blood-flow through a blood vessel by narrowing the open vessel lumen. This narrowing effect or stenosis is often responsible for ischemic heart disease. Fortunately, a number of percutaneous intravascular procedures have been developed for treating atherosclerotic plaque in a patient's vasculature. The most successful of these treatments is percutaneous transluminal angioplasty (PTA). PTA employs a catheter having an expansible distal end, usually in the form of an inflatable balloon, to dilate a stenotic region in the vasculature to restore adequate blood flow beyond the stenosis. Other procedures for opening stenotic regions include directional arthrectomy, laser angioplasty, stents, and the like. Used alone or in combination, these percutaneous intravascular procedures have provided significant benefits for treatment of stenoses caused by plaque.

[0003] While treatments of plaque-induced stenoses have advanced significantly over the last few decades, the morbidity and mortality associated with vascular plaques have remained significant. Recent work suggests that plaque may generally fall into one of two different general types: standard stenotic plaques and vulnerable plaques. Stenotic plaque, which is sometimes referred to as thrombosis-resistant plaque, can generally be treated effectively by the known intravascular lumen opening techniques mentioned above. Although the stenoses they induce may require treatment, these atherosclerotic plaques themselves are often a benign and effectively treatable disease.

[0004] Unfortunately, as plaque matures, narrowing of a blood vessel by a proliferation of smooth muscle cells, matrix synthesis, and lipid accumulation may result in formation of a plaque which is quite different than a standard stenotic plaque. Such atherosclerotic plaque becomes thrombosis-prone, and can be highly dangerous. This thrombosis-prone or vulnerable plaque may be a frequent cause of acute coronary syndromes.

[0005] The characterization of these vulnerable (and potentially life-threatening) plaques is currently under investigation. A number of strategies have been proposed to detect a vulnerable plaque. Proposed strategies include angiography, intravascular ultrasound, angioscopy, magnetic resonance imaging, magnetic resonance diffusion imaging, spectroscopy, infrared spectroscopy, scintigraphy, optical coherence tomography, electron beam computed tomographic scanning, and thermography, all of which have had limited success. In particular, proposed thermography methods detect temperature variations, as vulnerable plaque is typically inflamed and as such gives off more heat than standard stenotic plaque. While current thermography methods show great promise, they continue to suffer from limited temperature sensitivity which may often result in inaccurate detections of vulnerable plaque.

[0006] While the known procedures for treating plaque have gained wide acceptance and shown good efficacy for treatment of standard stenotic plaques, they may be ineffective (and possibly dangerous) when thrombotic conditions are superimposed on atherosclerotic plaques. Specifically, mechanical stresses caused by primary treatments like PTA or stenting may actually trigger release of fluids and/or solids from a vulnerable plaque into the blood stream, thereby potentially causing a coronary thrombotic occlusion.

[0007] For these reasons, it would be desirable to provide an apparatus for the detection and treatment of vulnerable plaque in blood vessels. The apparatus should be suitable for intravascular and intraluminal introduction, preferably via a percutaneous approach. It would be particularly desirable if the new apparatus were able to detect the vulnerable plaque accurately and/or deliver the treatment in a very controlled and safe manner, with minimal deleterious effects on adjacent tissues. Treatment apparatus should further be effective in inhibiting release of the vulnerable plaque with minimum side effects. At least some of these objectives will be met by the invention described herein.

2. Description of the Background Art

[0008] A cryoplasty device and method are described in WO 98/38934. Balloon catheters for intravascular cooling or heating a patient are described in U.S. 5,486,208 and WO 91/05528. A cryosurgical probe with an inflatable bladder for performing intrauterine ablation is described in U.S. 5,501,681. Cryosurgical probes relying on Joule-Thomson cooling are described in U.S. 5,275,595; 5,190,539; 5,147,355; 5,078,713; and 3,901,241. Catheters with heated balloons for post-angioplasty and other treatments are described in U.S. 5,196,024; 5,191,883; 5,151,100; 5,106,360; 5,092,841; 5,041,089; 5,019,075; and 4,754,752. Cryogenic fluid sources are described in U.S. 5,644,502; 5,617,739; and 4,336,691. The following U.S. Patents may also be relevant to the present invention: 5,458,612; 5,545,195; and 5,733,280.

[0009] Thermography is described by Ward Casscells et al. in The Vulnerable Atherosclerotic Plaque: Understanding, Identification, and Modification, chpt. 13, pp. 231-242 (1999); and L. Diamantopoulos et al. at http:

//www.eurekalert.org/releases/ahaati041499.html. The impact of low temperatures on lipid membranes is described by Jack Kruuv in Advances in Molecular and Cell biology, vol. 19, pp. 143-192 (1997); P.J. Quinn in Cryobiology, vol. 22, pp. 128-146 (1985); and Michael J. Taylor, Ph.D. in Biology Of Cell Survival In The Cold, (Harwood Academic Publishers, In Press).

[0010] US 5868735 discloses a catheter having chamber at a distal end and a balloon located around the chamber. This latter receives coding fluid. US5902299 discloses a catheter having a double layer balloon receiving coding fluid.

SUMMARY OF THE INVENTION

[0011] The present invention provides a catheter for detection and cryotherapy treatment of vulnerable plaque within a blood vessel of a patient as disclosed in any one of the claims. The blood vessel may be any blood vessel in the patient's vasculature, including veins, arteries, and particularly coronary arteries. The vessel will typically be partially stenosed, at least in part from vulnerable plaque. In particular, the present invention may inhibit release of retained fluid within the vulnerable plaque so as to inhibit acute coronary syndrome and to help maintain the patency of a body lumen. The present invention may also provide for the treatment of vulnerable plaque in carotid arteries for stroke prevention. Where the patient's vasculature has both the vulnerable plaque and standard stenotic plaque, the treatment techniques described herein may be selectively directed to the vulnerable plaque, optionally without substantial cooling of the standard stenotic plaque. Alternatively , both types of plaque may be treated.

[0012] A method for treating vulnerable plaque of a blood vessel comprises cooling the blood vessel adjacent the vulnerable plaque to a temperature sufficient to inhibit release of retained fluid from within the vulnerable plaque into the blood stream. The cooling treatment will often be directed against all or a portion of a circumferential surface of a lumen of the blood vessel, and will preferably inhibit release of lipid-rich liquid being releasably retained by the vulnerable plaque.

[0013] Cooling of the vessel may be effected by introducing a catheter into a lumen of the blood vessel. A first balloon is positioned within the vessel lumen adjacent the vulnerable plaque. Cryogenic cooling fluid is introduced into the first balloon and exhausted. A second balloon disposed over the first balloon is expanded to radially engage the vessel lumen. Generally, the temperature of an inside surface of the first balloon will be in the range from about -55° C to -75° C and an outside surface of the first balloon will be in the range from about -25° C to -4.5° C. The temperature of an outside surface of the second balloon will be in the range from about 10° C to -40° C, preferably from about 10° C to -20° C, more preferably from about 5° C to -10° C.

[0014] Usually, the temperature at the cell surface of the blood vessel lumen is in the range from about 10° C to -40° C, preferably from about 10° C to -20° C, more preferably from about 5° C to -10° C. The tissue is typically maintained at the desired temperature for a time period in the range from about 15 seconds to 120 seconds, preferably from 30 seconds to 60 seconds. Vulnerable plaque stabilization may be enhanced by repeating cooling in cycles, typically with from about 1 to 3 cycles, with the cycles being repeated at a rate of about one cycle every 120 seconds.

[0015] Surprisingly, cooling temperatures above 0° C can effect a transition of the vulnerable plaque's lipid core from a disordered cystalline state fluid to a ordered crystalline state solid or gel. Thus, vulnerable plaque can be stabilized by cooling the lipid-rich liquid sufficiently to change a state of the lipid-rich liquid, typically to a highly ordered hexagonal lattice at transition temperatures generally in the range from about 10° C to -10° C. Cooling may stabilize the vulnerable plaque while inhibiting necrosis and/or apoptosis of tissue adjacent the lipid-rich liquid, particularly of the tissues defining a cap of cells between the lipid-rich liquid and the lumen of the blood vessel. Cooling may also inhibit inflammation and deterioration of the vulnerable plaque. The cooling treatment may further inhibit rupture of the cap of cells of the vulnerable plaque.

[0016] Cooling the vulnerable plaque to inhibit release of lipid-rich liquid may be combined with additional treatments. For example, one adjunctive method may comprise treating the cooled vulnerable plaque with a primary treatment. Suitable primary treatments may include balloon angioplasty, atherectomy, rotational atherectomy, laser angioplasty, or the like, where the lumen of the treated blood vessel is enlarged to at least partially alleviate a stenotic condition. The primary treatment may also include procedures for controlling restenosis, such as stent placement. In the case of arteries, the primary treatment will be effected shortly before, during, or preferably very shortly after the cooling treatment, preferably within 60 seconds of the cooling treatment, more preferably immediately following the cooling of the lipid-rich liquid to a desired temperature. Alternatively, cooling methods may additionally comprise passivating the vulnerable plaque by reducing a size of the lipid-rich liquid, changing a cellular consistency or composition of the lipid-rich liquid, enhancing a structural integrity of the cap (e.g. increasing a thickness of the cap), modifying a cellular composition or structural properties of the cap, and/or the like by altering the chemistry or life cycle of the vulnerable plaque.

[0017] The catheter of the invention may be used in a method for treating vulnerable plaque of a blood vessel, the vulnerable plaque releasably retaining fluid. The method includes detecting the vulnerable plaque and cooling the blood vessel adjacent the vulnerable plaque to a temperature sufficient to inhibit release of the retained fluid into the blood vessel.

[0018] Also disclosed is a kit for treating vulnerable plaque in a blood vessel. The kit comprises a catheter

according to claim 1 and instructions for use of the catheter. These instructions comprise the step of cooling the blood vessel adjacent the vulnerable plaque to inhibit release of the retained fluid into the blood vessel. Such a kit may include instructions for any of the methods described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019]

Fig. 1A and 1B are cross-sectional views of a blood vessel containing a mature vulnerable plaque.

Fig. 2 illustrates a cross-sectional view of a vulnerable plaque rupture and plaque hemorrhage in the blood vessel.

Fig. 3 illustrates a cross-sectional view of a thrombotic occlusion in the blood vessel.

Fig. 4 illustrates an exploded cross-sectional view of Fig. 1A taken along line 4-4.

Fig. 5 illustrates an exemplary cryotherapy catheter for detecting and treating vulnerable plaque.

Fig. 6 is a cross-sectional view of the catheter taken along line 6-6 in Fig. 5. Fig. 7 is a functional flow diagram illustrating the operation of an automatic fluid shutoff mechanism of the catheter of Fig. 5.

Figs. 8A and 8B illustrate a handle and removable energy pack for use in the cryotherapy catheter of Fig. 5.

Fig. 9 illustrates a block diagram of a circuit which measures a temperature differential of the lumen surface.

Fig. 10A illustrates an alternative catheter for detecting vulnerable plaque. Fig. 10B is a cross-sectional view of the catheter taken along line 10B-10B in Fig. 10A.

Figs. 11A-11C illustrate use of the catheter of Fig. 5 for treatment of vulnerable plaque.

Fig. 12A is a graph illustrating a transition temperature which effects a lipid core transition of the vulnerable plaque.

Fig. 12B illustrates the lipid core transition from a liquid, disordered state to a solid, ordered state.

Fig. 13A and 13B illustrate additional treatments in conjunction with cooling of the vulnerable plaque.

Fig. 14 illustrates a vulnerable plaque treatment kit including the apparatus of Fig. 5 and instructions for use.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

[0020] As used herein, the terms "vulnerable plaque" and "hot plaque" refer to atherosclerotic plaque that is thrombosis-prone. Figs. 1A and 1B illustrate cross-sectional views of a blood vessel 100 containing a mature vulnerable plaque 102 within a lumen 104 of the vessel. The vulnerable plaque 102 generally comprises a necrotic core 106 of soft, lipid-rich, atheromatous gruel and a fibrous, sclerotic cap 108 of a collagen matrix of smooth muscle cells that covers the core 106. The gruel generally comprises a liquid of esterified cholesterol and low density lipoproteins which is releasably retained by the vulnerable plaque 102. Disruption or fissuring of the cap 108 may cause plaque hemorrhage 110 (release of the highly thrombogenic lipid-rich liquid 106 through the ruptured plaque), as seen in Fig. 2. As a result of plaque hemorrhage 110, the highly thrombogenic lipid-rich liquid 106 is exposed to flowing blood of the vessel lumen 104. As illustrated in Fig. 3, release of the thrombogenic liquid may cause a thrombotic occlusion 112 (blood clot) of the entire vessel lumen, which in turn may be lead to life-threatening conditions, such as a stroke or sudden cardiac death.

[0021] Three determinants of vulnerability are illustrated in Fig. 4, which is an exploded cross-sectional view of Fig. 1A taken along line 4-4. Susceptibility of a vulnerable plaque to rupture may be primarily determined from the size 114 and consistency of the atheromatous core (e.g. a larger core increases chances for rupture), the thickness 116 and structural integrity of the sclerotic cap (e.g. a thinner cap increases chances for rupture), and cap inflammation (e.g. macrophage foam cell 118 infiltration weakens the cap cells 120 and increases chances for rupture). Additionally, vulnerable plaque disruption may be triggered by numerous extrinsic stresses imposed on the plaque. For example, fluctuations in intraluminal blood pressure, pulse pressure, heart contraction, vasospasm, and the like may precipitate disruption of a vulnerable plaque. Alternatively, mechanical stresses caused by primary treatments like PTA or stenting may trigger rupture as well.

[0022] Referring now to Figs. 5 and 6, an exemplary cryotherapy catheter 10 (which is more fully described in U.S. Patent 6,514,245) for detecting and treating vulnerable plaque 102 of a blood vessel 100 having a lumen surface 105 (see Fig. 1A) will be described. The catheter 10 comprises a catheter body 12 having a proximal end 14 and a distal end 16 with a cooling fluid supply lumen 18 and an exhaust lumen 20 extending therebetween. A first balloon 22 is disposed near the distal end of the catheter body 12 in fluid communication with the supply and exhaust lumens. A second balloon 24 is disposed over the first balloon 22 with a thermal barrier 26 therebetween.

[0023] The balloons 22, 24 may be an integral extension of the catheter body 12, but such a structure is not required by the present invention. The balloons 22, 24 could be formed from the same or a different material as the catheter body 12 and, in the latter case, attached to the distal end 16 of the catheter body 12 by suitable adhesives, heat welding, or the like. The catheter body 12 may be formed from conventional materials, such as polyethylenes, polyimides, and copolymers and derivatives thereof. The balloons 22, 24 may also be formed from conventional materials used for angioplasty, preferably being inelastic, such as polyethylene terephthalate

(PET), polyethylene, or other medical grade material suitable for constructing a strong non-distensible balloon. Additionally, balloons 22 and 24 could be formed from different material to provide improved protection. For example, the first balloon 22 could be formed from PET to provide strength while the second balloon 24 could be formed from polyethylene to provide durability. The balloons 22, 24 have a length of at least 1 cm each, more preferably in the range from 2 cm to 5 cm each. The balloons 22, 24 will have diameters in the range from 2 mm to 5 mm each in a coronary artery and 2 mm to 10 mm each in a peripheral artery.

[0024] The thermal barrier 26 may comprise a gap maintained between the balloons 22, 24 by a filament. The filament typically comprises a helically wound, braided, woven, or knotted monofilament. The monofilament may be formed from PET or polyethylene napthlate (PEN), and affixed to the first balloon 22 by adhesion bonding, heat welding, fasteners, or the like. The thermal barrier 26 may also comprise a gap maintained between the balloons 22, 24 by a plurality of bumps on an outer surface of the first balloon 22 and/or an inner surface of the second balloon 24. The plurality of bumps may be formed in a variety of ways. For example, the bumps may be intrinsic to the balloon (created during balloon blowing), or the bumps could be created by deforming the material of the balloon wall, by affixing mechanical "dots" to the balloon using adhesion bonding, heat welding, fasteners, or the like. Alternatively, the thermal barrier 26 may comprise a gap maintained between the balloons 22, 24 by a sleeve. The sleeve may be perforated and formed from PET or rubbers such as silicone and polyurathane.

[0025] Hubs 34 and 36 are secured to the proximal end 14 of the catheter body 12. Hub 34 provides a port 38 for connecting a cryogenic fluid source to the fluid supply lumen 18 which is in turn in fluid communication with the inner surface of the first balloon 22. Hub 34 further provides a port 40 for exhausting the cryogenic fluid which travels from balloon 22 in a proximal direction through the exhaust lumen 20. Hub 36 provides a port 42 for a guidewire which extends through a guidewire lumen 44 in the catheter body 12. Typically, the guidewire lumen 44 will extend through the exhaust lumen 20, as shown in Fig. 6. The guidewire lumen 44 may also extend axially outside the exhaust lumen 20 to minimize the occurrence of cryogenic fluid entering the blood stream via the guidewire lumen 44. Optionally, the guidewire lumen 44 may extend outside the inner surface of the first balloon 22 or the guidewire lumen 44 may allow for a guidewire to extend outside both balloons 22, 24. Additionally, a reinforcing coil 46 may extend along the catheter body 12 proximal the first balloon 22. The reinforcing coil 46 may comprise a simple spring having a length typically in the range from 6 cm to 10 cm to prevent the catheter 10 from kinking up inside the blood vessel.

[0026] The cryotherapy catheter 10 in Fig. 5 additionally illustrates a safety mechanism that monitors the containment of the first and second balloons 22, 24. The first balloon 22 defines a volume in fluid communication with the supply and exhaust lumens. A fluid shutoff is coupled to a cryogenic fluid supply with the supply lumen 18. The second balloon 24 is disposed over the first balloon 22 with a vacuum space 52 therebetween. The vacuum space 52 is coupled to the fluid shutoff so as to inhibit flow of cryogenic fluid into the first balloon 22 in response to a change in the vacuum space 52.

[0027] Fig. 7 illustrates a functional flow diagram of the automatic fluid shutoff mechanism 54. The fluid shutoff 54 typically comprises a vacuum switch 56 connected to a shutoff valve 58 by a circuit, the circuit being powered by a battery 60. The switch 56 may remain closed only when a predetermined level of vacuum space 52 is detected in the second balloon 24. The closed switch 56 allows the shutoff valve 58, in fluid communication with the cryogenic fluid supply 62, to be open. Alternatively, the circuit may be arranged so that the switch 56 is open only when the predetermined vacuum space 52 is present, with the shutoff valve 58 being open when the switch is open. The vacuum space 52 is reduced when either the first balloon 22 is punctured, allowing cryogenic fluid to enter the vacuum space 52, or the second balloon 24 is punctured, allowing blood to enter the vacuum space 52. In addition to monitoring the containment of both balloons 22, 24, in the event of a failure, the vacuum switch 56 will be triggered to prevent the delivery of additional cryogenic fluid from the fluid supply 62 into the supply lumen 18. The second balloon 24 also acts to contain any cryogenic fluid that may have escaped the first balloon 22.

[0028] The vacuum space 52 may be provided by a simple fixed vacuum chamber 64 coupled to the vacuum space 52 by a vacuum lumen 66 of the body 12 via a vacuum port 68 (See Fig. 5). In the exemplary embodiment, a positive displacement pump (ideally being similar to a syringe) is disposed within handle 74 and may be actuated by actuator 75, as seen in Fig. 8A. The vacuum space 52 should comprise a small volume of vacuum in the range from 1 mL to 100 mL, preferably 10 mL or less, as a smaller vacuum space 52 facilitates detection of a change in the amount of vacuum when a small amount of fluid leakage occurs. The cryogenic fluid supply 62 and battery 60 for powering the circuit may be packaged together in an energy pack 70, as seen in Fig 8B. The energy pack 70 is detachable from a proximal handle 74 of the catheter body and disposable. A plurality of separate replaceable energy packs 70 allow for multiple cryogenic cooling cycles. Additionally, an audio alert or buzzer 76 may be located on the handle 74, with the buzzer providing an audio warning unless the handle is maintained sufficiently upright to allow flow from the fluid supply 62. The cryotherapy catheter may additionally comprise a hypsometer 72 coupled to the volume by a thermistor, thermocouple, or the like located in the first balloon 22 or handle to determine the pressure and/or temperature of fluid in the first balloon 22. The hypsom-

eter allows for accurate real time measurements of variables (pressure, temperature) that effect the efficacy and safety of cryotherapy treatments.

[0029] The dual balloon cryotherapy catheter 10 in Fig. 5 also illustrates a temperature sensing mechanism that provides for thermographic detection of vulnerable plaque. A plurality of temperature sensors 78 are affixed to the second balloon 24 so as to provide direct temperature measurements of the lumen surface 105 (see Fig. 1A). The temperature sensors 78 may comprise a plurality of up to 20 thermocouples or thermistors and may be capable of detecting temperature differences greater than 0.1 °C. The temperature sensors 78 may be secured to the second balloon 24 at a series of axial and circumferential locations. The plurality of temperature sensors 78 may be affixed by adhesion bonding, heat welding, fasteners, or the like to an outer surface of the second balloon 24, as shown in Fig. 5, or may be alternatively affixed to an inner surface of the second balloon 24. Temperature sensor wires 80 may be secured along the length of the catheter shaft 12 within a thin sleeve 82 formed from PET or rubbers such as silicone and polyurathane, or in the latter case the wires 80 may be threaded through the vacuum lumen 66. A connector 84 at the proximal end 14 of the catheter 10 may also be provided to connect the temperature sensor wires 80 to a temperature readout device for temperature mapping along the lumen surface. Additionally, a circuit 77 may be attached to the connector 84 for measuring a temperature differential ΔT along the lumen surface from temperature measurement T1 and T2 sensed by the temperature sensors 78, as illustrated in the block diagram of Fig. 9. An indicator which is triggered above a threshold temperature differential may also be located on the connector for alerting purposes.

[0030] Detection of vulnerable plaque may be carried out by introducing the cryotherapy catheter 10 into a lumen 104 of the blood vessel 100 over a guidewire. The first balloon 22 is positioned within the blood vessel lumen 104 adjacent a plaque. The first balloon 22 is inflated so that the plurality of temperature sensors 78 affixed to the second balloon 24 (which expands upon inflation) thermally couple a surface of the vessel lumen. A temperature differential along the lumen surface 105 is sensed with the sensors. Inflation of balloon 22 may be effected by a gas, such as carbon dioxide, nitrous oxide, or the like, at a pressure in the range from about 5 psi to 50 psi. The balloon 22 will typically be inflated for a time period in the range from 10 to 120 seconds. The balloon catheter may sense for a temperature differential in a static position or as it moving along the lumen surface. Advantageously, temperature sensors 78 thermally engage the lumen surface to allow for direct temperature measurements to be made at specific locations along the lumen surface. This increased temperature sensitivity may in turn lead to improved temperature mapping and accurate vulnerable plaque detections. Cryotherapy catheter 10 may then be used for treating the detected vulnerable plaque as described in more detail below with reference to Figs. 11A-11C.

[0031] An alternative catheter 10' for detecting a vulnerable plaque of a blood vessel having a lumen surface is illustrated in Figs. 10A and 10B. Detection catheter 10' comprises a catheter body 12 having a proximal end 14 and a distal end 16 with a supply lumen 88 and an exhaust lumen 88 extending therebetween. A balloon 86 is disposed on the distal end of the catheter body 12. Balloon 86 has an inner surface in fluid communication with the supply lumen and exhaust lumen. A plurality of temperature sensors 78 are affixed to an outer surface of the balloon 86 so as to provide direct temperature measurements of the lumen surface 105 (see Fig. 1A).

[0032] Detection of vulnerable plaque may be carried out by introducing the detection catheter 10' into a lumen 104 of the blood vessel 100 over a guidewire. The balloon 86 is positioned within the vessel lumen adjacent a plaque. The balloon 86 is inflated so that a plurality of temperature sensors 78 affixed to the balloon thermally couple a surface of the vessel lumen. A temperature differential along the lumen surface is sensed with the sensors. Balloon 86 is generally inflatable with standard inflation media, such as contrast, saline, or the like. An inflation media supply and/or exhaust port 90 is connected to the supply and/or exhaust lumen 88 which is in turn in fluid communication with the inner surface of balloon 86. Balloon 86 will typically be inflated for a time period in the range from 10 to 120 seconds. The balloon catheter may sense for a temperature differential in a static position or as it moving along the lumen surface.

[0033] Referring now to Figs. 11A through 11C, use of cryotherapy catheter 10 of Fig. 5 for treatment of vulnerable plaque 102 will be described. As illustrated in Fig. 11 A and 11B, catheter 10 will be introduced into a lumen 104 of the blood vessel 100 over a guidewire GW. The first balloon 22 is positioned within the blood vessel lumen 104 adjacent the vulnerable plaque 102. Cryogenic cooling fluid is introduced into the first balloon 22 (in which it often vaporizes) and exhausted. The second balloon 24 expands to radially engage the vessel wall, as illustrated by Fig. 11C. The vaporized fluid serves both to inflate balloon 22 (and expand balloon 24) and to cool the exterior surface of the balloons 22, 24. The blood vessel 100 adjacent the vulnerable plaque 102 is cooled to a temperature sufficient to inhibit release of retained fluid 106 from within the vulnerable plaque 102 into the blood vessel 100. The cooling treatment will be directed at all or a portion of a circumferential surface the vessel lumen. Preferably cooling will inhibit release of lipid-rich liquid being releasably retained by the vulnerable plaque by stabilizing the lipid-rich liquid 106 to a lipid-rich solid or gel 106' (which is described in more detail in Figs. 12A-12B below). Heat transfer will also be inhibited between the first and second balloons 22, 24 by the thermal barrier 26 so as to limit cooling of the vulnerable plaque to a desired temperature profile. Additionally, containment of the first and second balloons 22, 24 will be monitored

during cooling by the fluid shutoff mechanism (see Fig. 7).

[0034] Suitable cryogenic fluids will preferably be non-toxic and may include liquid nitrous oxide, liquid carbon dioxide, cooled saline and the like. The cryogenic fluid will flow through the supply lumen 18 as a liquid at an elevated pressure and will vaporize at a lower pressure within the first balloon 22. For nitrous oxide, a delivery pressure within the supply lumen 18 will typically be in the range from 600 psi to 1000 psi at a temperature below the associated boiling point. After vaporization, the nitrous oxide gas within the first balloon 22 near its center will have a pressure typically in the range from 15 psi to 100 psi. Preferably, the nitrous oxide gas will have a pressure in the range from 50 psi to 100 psi in a peripheral artery and a range from about 15 psi to 45 psi in a coronary artery.

[0035] Generally, the temperature of an inside surface of the first balloon will be in the range from about -55° C to -75° C and an outside surface of the first balloon will be in the range from about -25° C to -45° C. The temperature of an outside surface of the second balloon will be in the range from about 10° C to -40° C, preferably from about 10° C to -20° C, more preferably from about 5° C to -10° C. This will provide a desired treatment temperature in a range from about 10° C to -40° C, preferably from about 10° C to -20° C, more preferably from about 5° C to -10° C. The tissue is typically maintained at the desired temperature for a time period in the range from about 15 to 120 seconds, preferably being from 30 to 60 seconds. Vulnerable plaque stabilization may be enhanced by repeating cooling in cycles, typically with from about 1 to 3 cycles, with the cycles being repeated at a rate of about one cycle every 120 seconds.

[0036] In some instances, cooling of the vessel may be limited to inhibiting necrosis and/or apoptosis of tissue adjacent the lipid-rich liquid, particularly of the tissues defining a cap of cells 108 between the lipid-rich liquid 106 and the lumen of the blood vessel 104 (see Fig. 1A). Apoptosis or cell necrosis may be undesirable if it weakens the cap of cells as cap weakening may likely incite rupture of the vulnerable plaque and release of the lipid-rich liquid. Thus, the present invention may inhibit release of the retained fluid into the blood vessel without affecting the viability of the cap cells 108 and other cells which line the body lumen.

[0037] In other applications, cooling of the vessel at lower temperatures may be desirable to provide for apoptosis and/or programmed cell death stimulation of inflamatory cells (e.g. macrophages 118, see Fig. 4) in the vulnerable plaque 102. Apoptosis may be desirable as the presence of such inflamatory cells may trigger cap weakening or erosion which in turn may lead to vulnerable plaque release of the lipid-rich liquid. Cooling at temperatures in the range from about 0° C to -15° C may inhibit inflammation and deterioration of the vulnerable plaque, particularly of the tissues defining the cap of cells 108. Alternatively, it may be beneficial to provide for necrosis in the cap cells 108 at cooling temperatures below about -20° C. Cap necrosis may stimulate cellular proliferation and thickening of the cap which in turn may inhibit cap rupture.

[0038] Referring now to Figs. 12A and 12B, transition of the vulnerable plaque's lipid-rich liquid core 106 will be described. Fig. 12A illustrates the transition temperature which effects a lipid core transition. The main transition point 122 occurs at some point between the transition temperature range of 10° C to -10° C. At this transition point 122, the lipid core may undergo a phase change from a disordered crystalline state fluid 106 to a ordered crystalline state solid or gel 106', as shown in Fig. 12B. Thus, vulnerable plaque can be stabilized by cooling the lipid-rich liquid core 106 sufficiently to change its state, typically from a disordered lipid to a highly ordered hexagonal lattice. Advantageously, a transition temperature above -5° C also inhibits necrosis and/or apoptosis of tissue adjacent the lipid-rich liquid 106, particularly of the cap 108.

[0039] With reference now to Figs. 13A and 13B, additional treatments in conjunction with cooling of the vulnerable plaque will be illustrated. Fig. 13A illustrates a cross section of a blood vessel 100 that has been cooled so that the vulnerable plaque has been stabilized to lipid-rich solid/gel 106'. A stent 124 has been placed within the vessel lumen while the plaque is stabilized to provide a long-term restraint of lipid-rich fluid 106, and possibly to provide a structural scaffolding for healthy endothelial cells via tissue ingrowth. The stent may also alleviate plaque-induced stenosis and to improve the patency of the lumen. Other suitable primary treatments of the stabilized plaque may include balloon angioplasty, atherectomy, rotational atherectomy, laser angioplasty, or the like, where the lumen of the treated blood vessel is enlarged to at least partially alleviate a stenotic condition. In the case of arteries, the primary treatment will be effected shortly before, during, or preferably very shortly after the cooling treatment, preferably within 60 seconds of the cooling treatment, more preferably immediately following the cooling of the lipid-rich liquid to a desired temperature. In some instances, cooling may effect passivation of the vulnerable plaque, possibly reducing a size of the lipid-rich liquid 106", as illustrated in Fig. 13B, or modifying a cellular consistency or composition of the lipid-rich liquid, and/or the like by altering the chemistry or life cycle of the vulnerable plaque. Passivation may also include enhancing a structural integrity of cap 108 (e.g. increasing the thickness, strength, elasticity, or hardness of the cap), modifying a cellular composition or property of the cap, and/or the like via scar formation or alteration of the chemistry of the vulnerable plaque.

[0040] A kit 126 including a catheter 10 and instructions for use 128 is illustrated in Fig. 14. Catheter 10 may comprise the dual balloon catheter of Fig. 5, as illustrated in Fig. 14, or a catheter having a proximal end, a distal end, and a cooling member near its distal end. Instructions for use 128 may describe any of the associated method steps set forth above for detection and/or treat-

ment of vulnerable plaque. Instructions for use 128 will often be printed, optionally appearing at least in part on a sterile package 130 for balloon catheter 10. In alternative embodiments, instructions for use 128 may comprise a machine readable code, digital or analog data graphically illustrating or demonstrating the use of balloon catheter 10 to detect and/or treat vulnerable plaque. Still further alternatives are possible, including printing of the instructions for use on packaging 132 of kit 126, and the like.

[0041] While the above is a complete description of the preferred embodiments of the invention, various alternatives, modifications, and equivalents will be obvious to those of skill in the art. Hence, the above description should not be taken as limiting the scope of the invention which is defined by the appended claims.

Claims

1. A cryotherapy catheter (10) for detecting and treating vulnerable plaque of a blood vessel having a lumen surface, said catheter comprising:

a catheter body (12) having a proximal end and a distal end with a cooling fluid supply lumen (18) and an exhaust lumen (20) extending therebetween;
a first balloon (22) disposed at the distal end of the catheter body, the first balloon having an inner surface in fluid communication with the supply lumen and exhaust lumen **characterized in that** the catheter further comprises:

a second balloon (24) disposed over the first balloon with a thermal barrier (26) therebetween; and
a plurality of temperature sensors (80) affixed to the second balloon so as to provide temperature measurements of the lumen surface,
wherein the thermal barrier (26) comprises a gap maintained between the balloons (22, 24) by an element selected in the group consisting of

- a filament;
- a plurality of bumps on an outer surface of the first balloon (22) and/or an inner surface of the second balloon (24);
- a perforated sleeve.

2. A cryotherapy catheter as in claim 1, wherein the filament comprises a helically wound, braided, woven, or knotted monofilament.

3. A cryotherapy catheter as in claim 2, wherein the monofilament is formed from PET or polyethylene napthlate (PEN), and affixed to the first balloon 22 by adhesion bonding, or heat welding, or fasteners.

4. A cryotherapy catheter as in claim 1, wherein the plurality of bumps are intrinsic to the balloon, or the bumps have been created by deforming the material of the balloon wall, or by affixing mechanical dots to the balloon.

5. A cryotherapy catheter as in claim 1, wherein the sleeve is formed from PET or rubbers such as silicone and polyurathane.

6. A cryotherapy catheter as in claim 1, wherein the plurality of temperature sensors (78) are affixed to an outer surface of the second balloon.

7. A cryotherapy catheter as in claim 6, wherein the plurality of temperature sensors (78) provide direct temperature measurements of the lumen surface.

8. A cryotherapy catheter as in claim 1, wherein the plurality of temperature sensors (78) are affixed to an inner surface of the second balloon.

9. A cryotherapy catheter as in claim 1, wherein the plurality of temperature sensors (78) comprise thermocouples or thermistors.

10. A cryotherapy catheter as in claim 1, wherein the plurality of temperature sensors (78) are affixed circumferentially about the second balloon.

11. A cryotherapy catheter as in claim 1, further comprising a connector (84) to a temperature readout device on the proximal end of the catheter.

12. A cryotherapy catheter as in claim 1, comprising hubs (34 and 36) secured to the proximal end (14) of the catheter body (12).

13. A cryotherapy catheter as in claim 12, wherein one hub (34) provides a port (38) for connecting a cryogenic fluid source to the fluid supply lumen (18) which is in turn in fluid communication with the inner surface of the first balloon (22), said hub (34) further providing a port (40) for exhausting the cryogenic fluid which travels from balloon (22) in a proximal direction through the exhaust lumen (20).

14. A cryotherapy catheter as in claim 12, wherein one hub (36) provides a port (42) for a guidewire which extends through a guidewire lumen (44) in the catheter body (12).

Patentansprüche

1. Cryotherapiekatheter (10) zum Detektieren und Behandeln von anfälligem Plaque eines Blutgefäßes, das eine Lumenoberfläche hat, wobei der Katheter umfasst:

   einen Katheterkörper (12), der ein proximales Ende und ein distales Ende aufweist, mit einem Kühlfluidzuführungslumen (18) und einem Auslasslumen (20), die sich dazwischen erstrecken;
   einen ersten Ballon (22), der an dem distalen Ende des Katheterkörpers angebracht ist, wobei der erste Ballon eine innere Oberfläche hat, die in Fluidverbindung mit dem Zuführungslumen und dem Auslasslumen steht, **gekennzeichnet dadurch, dass** der Katheter weiter umfasst:

      einen zweiten Ballon (24), der über dem ersten Ballon angebracht ist, mit einer thermischen Barriere (26) dazwischen; und
      eine Vielzahl von Temperatursensoren (80), die an dem zweiten Ballon angebracht sind, um Temperaturmessungen der Lumenoberfläche zu liefern,
      wobei die thermische Barriere (26) einen Spalt umfasst, der zwischen den Ballons (22, 24) durch ein Element aufrechterhalten wird ausgewählt aus der Gruppe bestehend aus

         - einem Filament;
         - einer Vielzahl von Erhebungen auf einer äußeren Oberfläche des ersten Ballons (22) und/oder einer inneren Oberfläche des zweiten Ballons (24);
         - einer perforierten Hülle.

2. Cryotherapiekatheter gemäß Anspruch 1, wobei das Filament ein wendelförmig gewundenes, geflochtenes, gewebtes oder geknotetes Monofilament umfasst.

3. Cryotherapiekatheter gemäß Anspruch 2, wobei das Monofilament aus PET oder Polyethylennaphthalat (PEN) gebildet ist, und befestigt an dem ersten Ballon (22) durch Kleben oder Hitzeschweißen oder Halterungen.

4. Cryotherapiekatheter gemäß Anspruch 1, wobei die Vielzahl von Erhebungen dem Ballon innewohnend sind, oder wobei die Erhebungen durch Deformieren des Materials der Ballonwand erzeugt worden sind, oder durch Befestigen von mechanischen Punkten an dem Ballon.

5. Cryotherapiekatheter gemäß Anspruch 1, wobei die Hülle aus PET gebildet ist oder Gummis, wie Silikon und Polyurethan.

6. Cryotherapiekatheter gemäß Anspruch 1, wobei die Vielzahl von Temperatursensoren (78) an eine äußere Oberfläche des zweiten Ballons befestigt sind.

7. Cryotherapiekatheter gemäß Anspruch 6, wobei die Vielzahl von Temperatursensoren (78) direkte Temperaturmessungen der Lumenoberfläche liefern.

8. Cryotherapiekatheter gemäß Anspruch 1, wobei die Vielzahl von Temperatursensoren (78) an einer innere Oberfläche des zweiten Ballons befestigt sind.

9. Cryotherapiekatheter gemäß Anspruch 1, wobei die Vielzahl von Temperatursensoren (78) Thermokoppler oder Thermistoren umfassen.

10. Cryotherapiekatheter gemäß Anspruch 1, wobei die Vielzahl von Temperatursensoren (78) entlang des Umfangs um den zweiten Ballon befestigt sind.

11. Cryotherapiekatheter gemäß Anspruch 1, weiter umfassend ein Verbindungselement (84) zu einer Temperaturauslesevorrichtung an dem proximalen Ende des Katheters.

12. Cryotherapiekatheter gemäß Anspruch 1, der Muffen (34 und 36) umfasst, die an dem proximalen Ende (14) des Katheterkörpers (12) fixiert sind.

13. Cryotherapiekatheter gemäß Anspruch 12, wobei eine Muffe (34) einen Anschluss (38) zum Verbinden einer Quelle cryogenischen Fluids an das Fluidzuführungslumen (18), welches wiederum in Fluidverbindung mit der inneren Oberfläche des ersten Ballons (22) ist, wobei der Hub (34) weiter einen Anschluss (40) zum Auslassen des cryogenischen Fluids, die vom Ballon (22) in eine proximale Richtung durch das Auslasslumen (20) wandert, zur Verfügung stellt.

14. Cryotherapiekatheter gemäß Anspruch 12, wobei eine Muffe (36) einen Anschluss (42) für einen Führungsdraht zur Verfügung stellt, welcher sich durch ein Führungsdrahtlumen (44) im Katheterkörper (12) erstreckt.

Revendications

1. Cathéter de cryothérapie (10) pour détecter et traiter des plaques d'athérosclérose vulnérable d'un vaisseau sanguin ayant une surface de lumière, ledit cathéter comportant :

   un corps de cathéter (12) ayant une extrémité proximale et une extrémité distale avec une lu-

mière d'alimentation en fluide de refroidissement (18) et une lumière d'évacuation (20) s'étendant entre celles-ci ;
un premier ballon (22) disposé à l'extrémité distale du corps de cathéter, le premier ballon ayant une surface interne en communication de fluide avec la lumière d'alimentation et la lumière d'évacuation, **caractérisé en ce que** le cathéter comporte de plus :

un second ballon (24) disposé par dessus le premier ballon avec une barrière thermique (26) entre eux ; et
une pluralité de capteurs (80) de température fixés au second ballon de façon à fournir des mesures de température de la surface de lumière,
dans lequel la barrière thermique (26) comporte un espace maintenu entre les ballons (22, 24) par un élément sélectionné dans le groupe consistant en :

- un filament ;
- une pluralité de bossage sur une surface externe du premier ballon (22) et/ou une surface interne du second ballon (24) ;
- un manchon perforé.

2. Cathéter de cryothérapie selon la revendication 1, **caractérisé en ce que** le filament comporte un monofilament enroulé en hélice, tressé, tissé ou tricoté.

3. Cathéter de cryothérapie selon la revendication 2, **caractérisé en ce que** le monofilament est formé de polyéthylène téréphtalate (PET) ou de polyéthylène naphtalate (PEN), et est fixé au premier ballon (22) par des liaisons de collage, ou par soudage à chaud, ou par des fixations.

4. Cathéter de cryothérapie selon la revendication 1, dans lequel la pluralité de bossages sont intrinsèques au ballon, ou les bossages ont été créés en déformant le matériau de la paroi du ballon, ou par fixation de points mécaniques du ballon.

5. Cathéter de cryothérapie selon la revendication 1, **caractérisé en ce que** le manchon est formé de PET ou de caoutchoucs tels que le silicone et le polyuréthane.

6. Cathéter de cryothérapie selon la revendication 1, **caractérisé en ce que** la pluralité de capteurs (78) de température sont fixés à une surface externe du second ballon.

7. Cathéter de cryothérapie selon la revendication 6, **caractérisé en ce que** la pluralité de capteurs (78) de température fournissent des mesures directes de température de la surface de lumière.

8. Cathéter de cryothérapie selon la revendication 1, **caractérisé en ce que** la pluralité de capteurs (78) de température sont fixés à une surface interne du second ballon.

9. Cathéter de cryothérapie selon la revendication 1, **caractérisé en ce que** la pluralité de capteurs (78) de température comportent des thermocouples ou des thermistors.

10. Cathéter de cryothérapie selon la revendication 1, **caractérisé en ce que** la pluralité de capteurs (78) de température sont fixés circonférentiellement autour du second ballon.

11. Cathéter de cryothérapie selon la revendication 1, comportant de plus un connecteur (84) à un dispositif de lecture de température sur l'extrémité proximale du cathéter.

12. Cathéter de cryothérapie selon la revendication 1, comportant des moyeux (34, 36) fixés à l'extrémité proximale (14) du corps de cathéter (12).

13. Cathéter de cryothérapie selon la revendication 12, dans lequel un moyeu (34) fournit un port (38) pour connecter une source de fluide cryogénique à la lumière (18) d'alimentation en fluide qui est à son tour en communication de fluide avec la surface interne du premier ballon (22), ledit moyeu (34) fournissant de plus un port (40) pour évacuer le fluide cryogénique qui circule depuis le ballon (22) dans une direction proximale à travers la lumière d'évacuation (20).

14. Cathéter de cryothérapie selon la revendication 12, dans lequel un moyeu (36) fournit un port (42) pour un fil de guidage qui s'étend à travers une lumière (44) de fil de guidage dans le corps de cathéter (12).

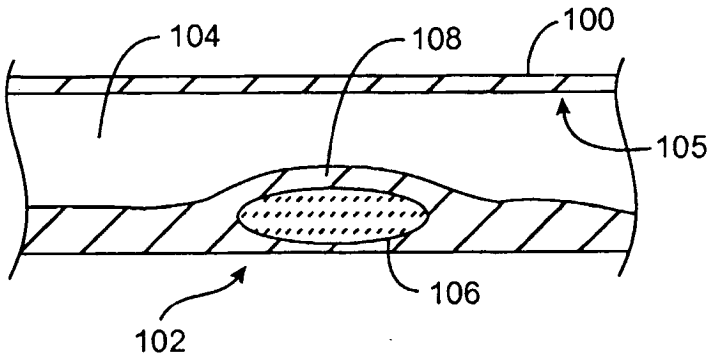


FIG. 1A

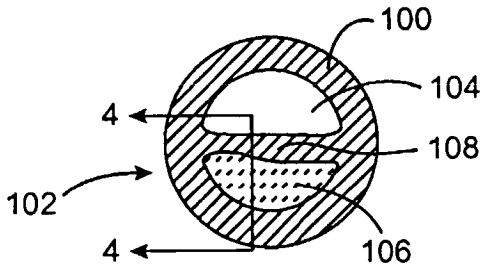


FIG. 1B

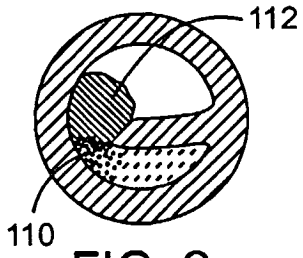


FIG. 2

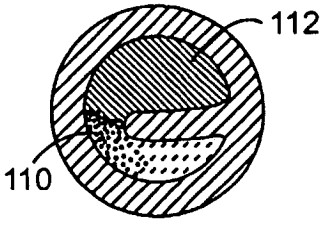


FIG. 3

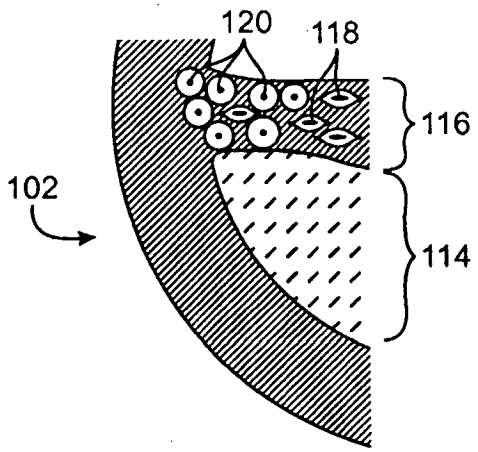


FIG. 4

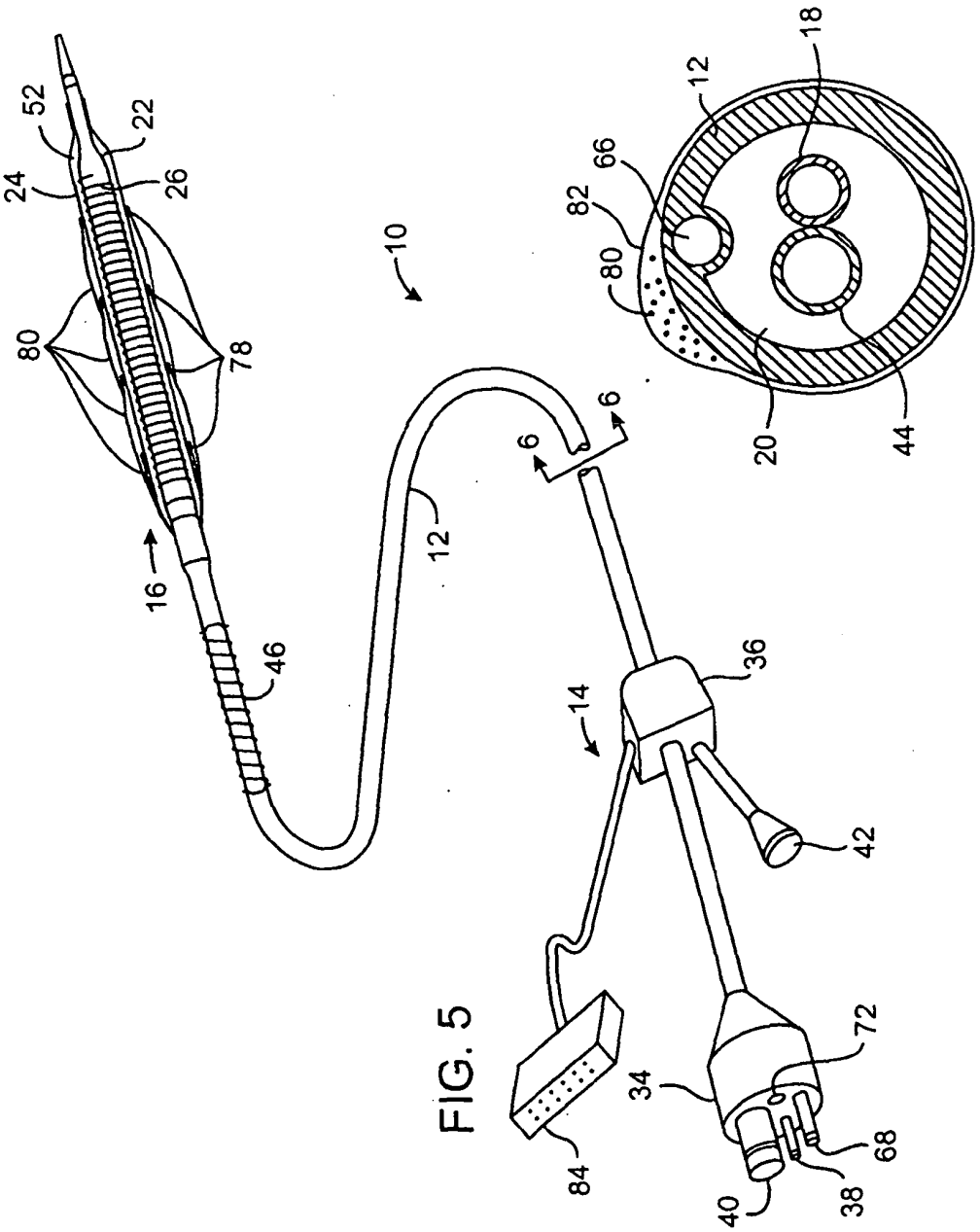

52
22
24
26
80
78
10
16
46
12
6
6
14
36
42
72
34
68
84
40
38

FIG. 5

18
12
66
82
80
20
44

FIG. 6

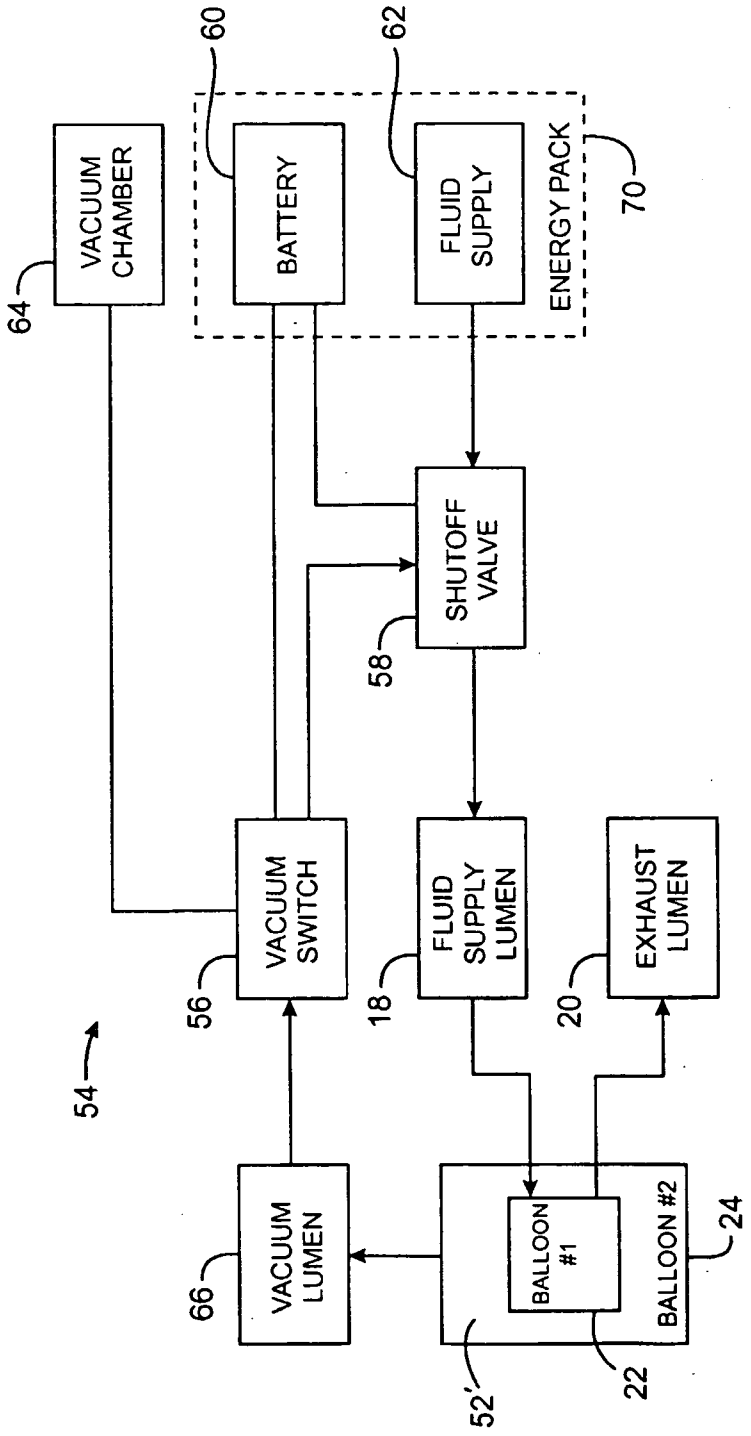

VACUUM CHAMBER
64
BATTERY
60
FLUID SUPPLY
62
ENERGY PACK
70
SHUTOFF VALVE
58
VACUUM SWITCH
56
FLUID SUPPLY LUMEN
18
EXHAUST LUMEN
20
54
VACUUM LUMEN
66
BALLOON #1
BALLOON #2
24
22
52'

FIG. 7

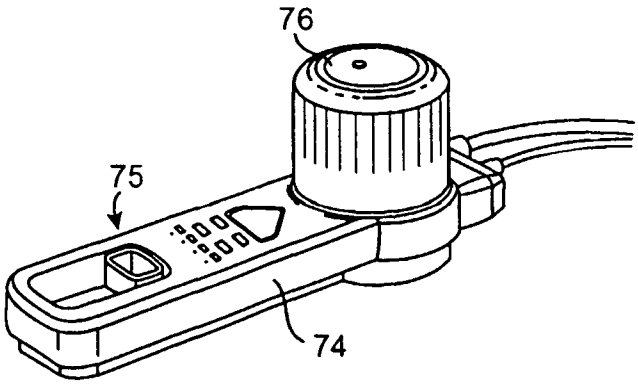


FIG. 8A

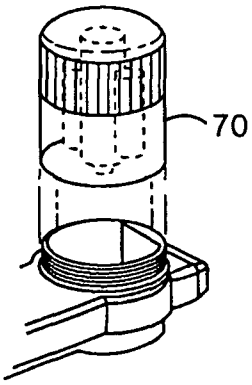


FIG. 8B

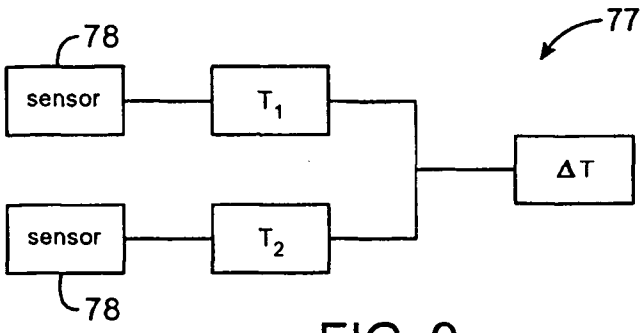
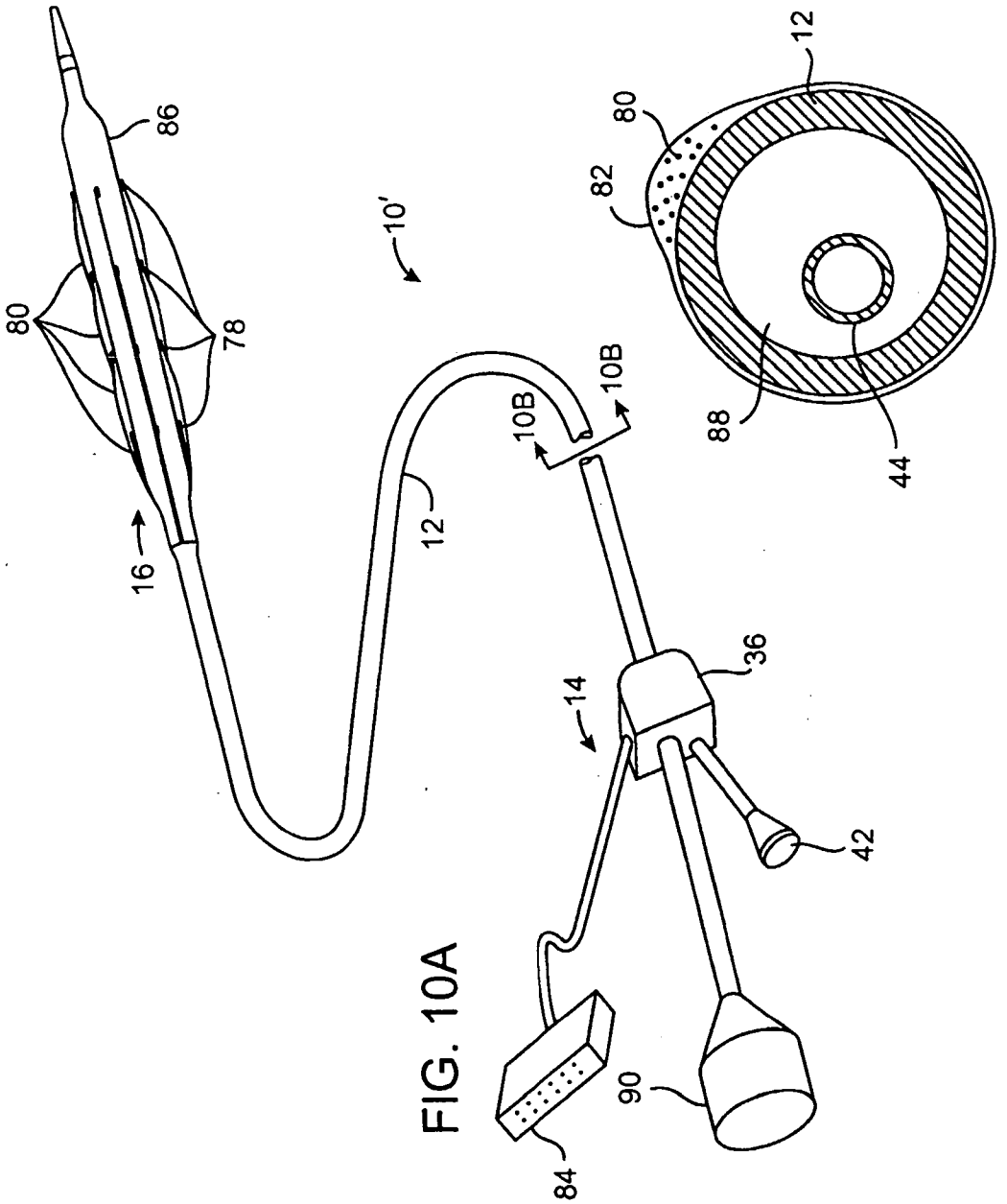


FIG. 9


86
80
78
16
10'
12
10B
10B
14
36
42
90
84
FIG. 10A
12
80
82
88
44
FIG. 10B

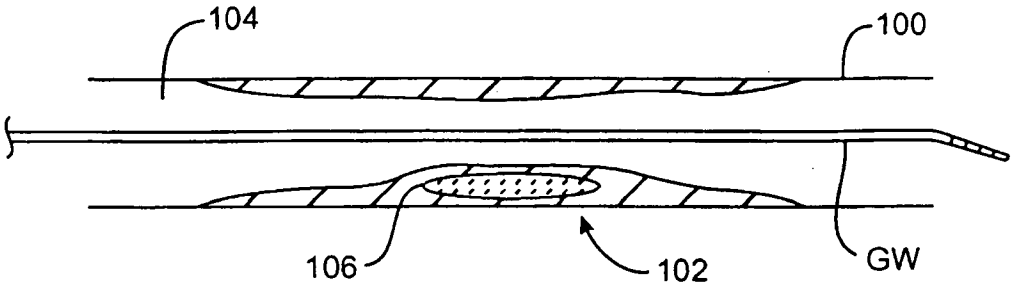


FIG. 11A

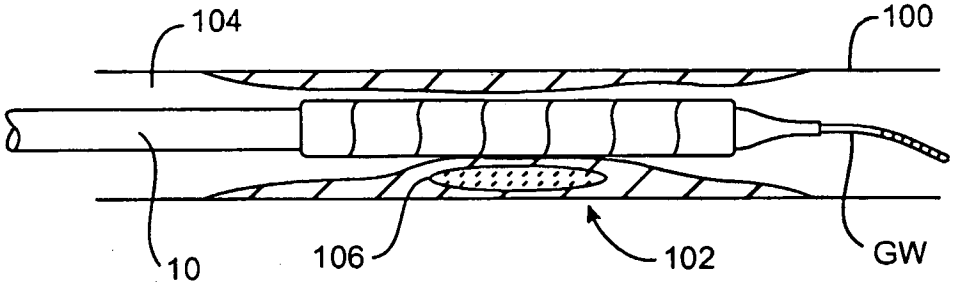


FIG. 11B

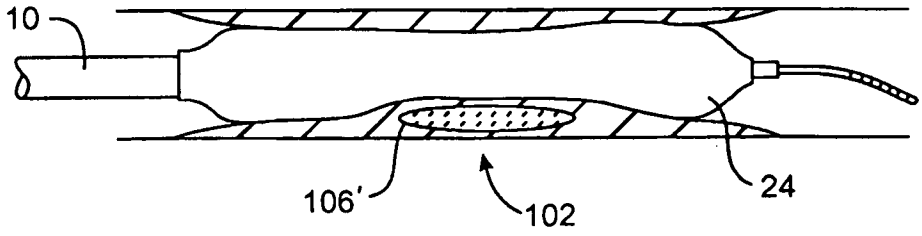


FIG. 11C

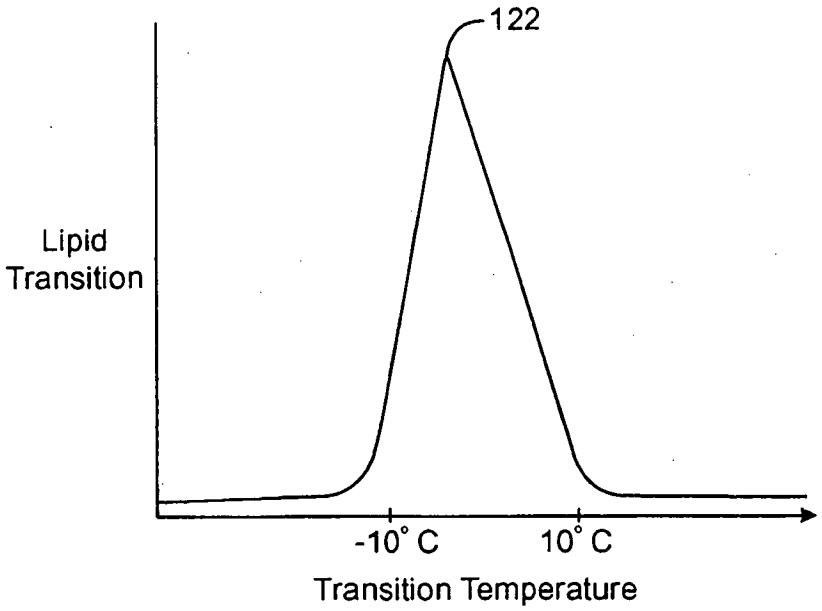


FIG. 12A

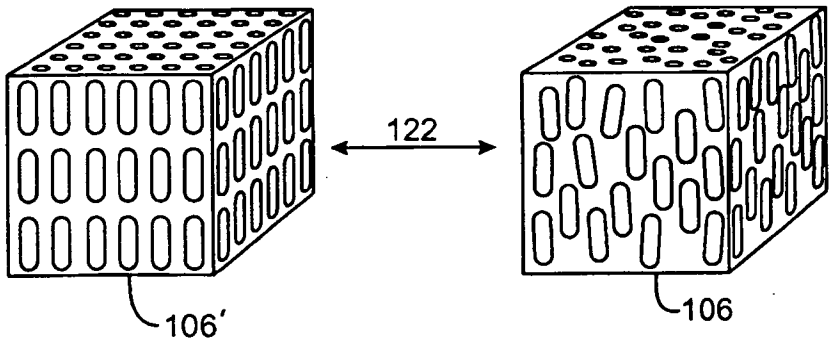


FIG. 12B

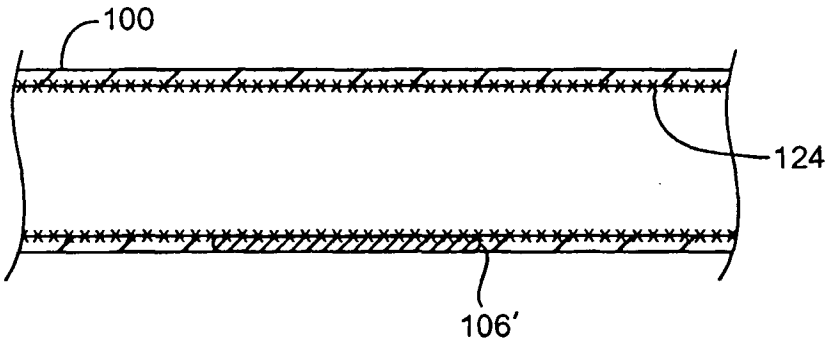


FIG. 13A

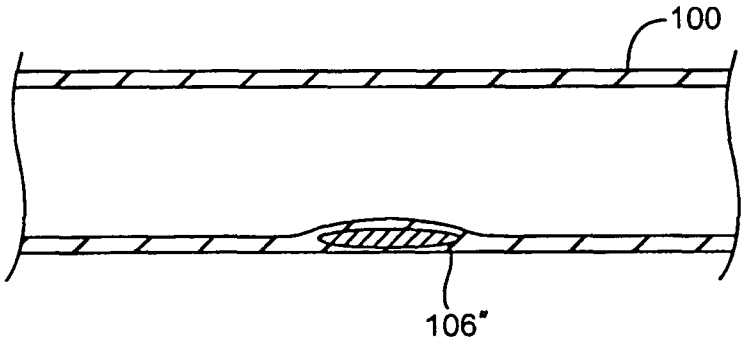


FIG. 13B

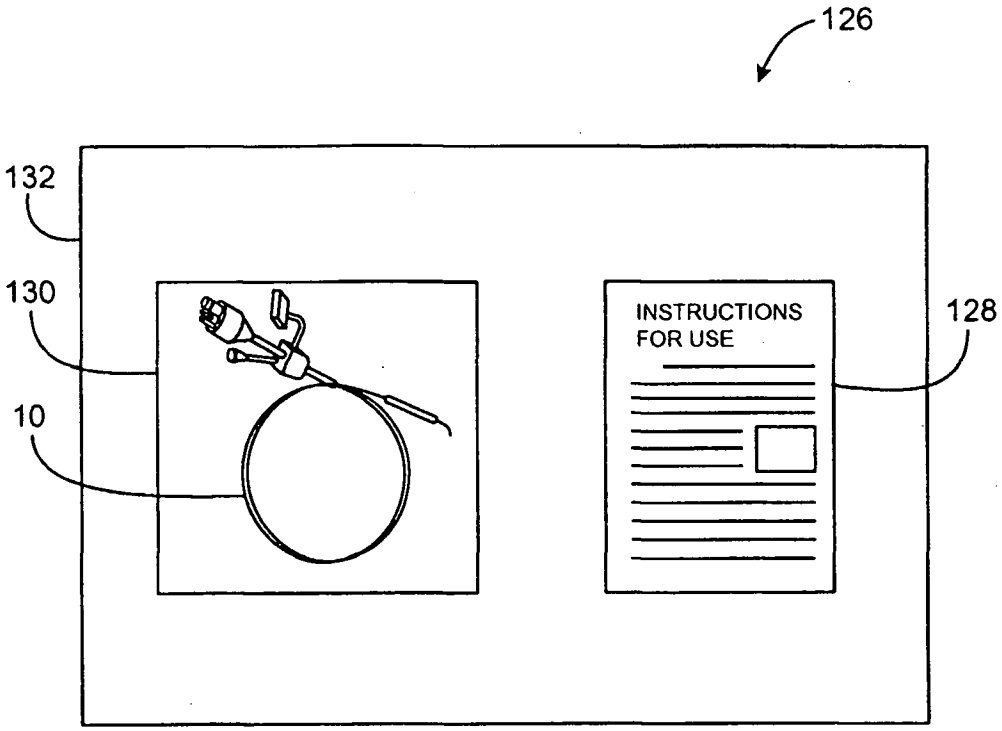


FIG. 14

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- WO 9838934 A **[0008]**
- US 5486208 A **[0008]**
- WO 9105528 A **[0008]**
- US 5501681 A **[0008]**
- US 5275595 A **[0008]**
- US 5190539 A **[0008]**
- US 5147355 A **[0008]**
- US 5078713 A **[0008]**
- US 3901241 A **[0008]**
- US 5196024 A **[0008]**
- US 5191883 A **[0008]**
- US 5151100 A **[0008]**
- US 5106360 A **[0008]**
- US 5092841 A **[0008]**
- US 5041089 A **[0008]**
- US 5019075 A **[0008]**
- US 4754752 A **[0008]**
- US 5644502 A **[0008]**
- US 5617739 A **[0008]**
- US 4336691 A **[0008]**
- US 5458612 A **[0008]**
- US 5545195 A **[0008]**
- US 5733280 A **[0008]**
- US 5868735 A **[0010]**
- US 5902299 A **[0010]**
- US 6514245 B **[0022]**

Non-patent literature cited in the description

- **Ward Casscells et al.** The Vulnerable Atherosclerotic Plaque: Understanding, Identification, and Modification. 1999, 231-242 **[0009]**
- **Jack Kruuv.** *Advances in Molecular and Cell biology,* 1997, vol. 19, 143-192 **[0009]**
- **P.J. Quinn.** *Cryobiology,* 1985, vol. 22, 128-146 **[0009]**
- **Michael J. Taylor.** Ph.D. in Biology Of Cell Survival In The Cold. Harwood Academic Publishers, In Press **[0009]**

专利名称(译)	用于检测和治疗易损斑块的冷冻方法		
公开(公告)号	EP1311201A4	公开(公告)日	2009-09-09
申请号	EP2001968016	申请日	2001-08-17
[标]申请(专利权)人(译)	CRYOVASCULAR SYST		
申请(专利权)人(译)	CRYOVASCULAR系统公司.		
当前申请(专利权)人(译)	CRYOVASCULAR系统公司.		
[标]发明人	JOYE JAMES TATSUTANI KRISTINE		
发明人	JOYE, JAMES TATSUTANI, KRISTINE		
IPC分类号	A61B18/02 A61B5/00 A61B17/00 A61B17/22 A61B18/18		
CPC分类号	A61B5/01 A61B5/6853 A61B18/02 A61B2017/00101 A61B2017/22001 A61B2017/22002 A61B2017/22051 A61B2018/0022 A61B2018/0212 A61B2018/0262		
代理机构(译)	WORK，伊利亚		
优先权	09/641462 2000-08-18 US		
其他公开文献	EP1311201A1 EP1311201B1		
外部链接	Espacenet		

摘要(译)

方法，设备和试剂盒检测和/或治疗血管的易损斑块。 可以在装有热气体的气球上沿着温度传感器沿着管腔表面感测温度差。 治疗方法包括对易损斑块进行受控和安全的低温冷却，以抑制易损斑块内滞留液的释放，从而抑制急性冠状动脉综合征并帮助维持体腔通畅。