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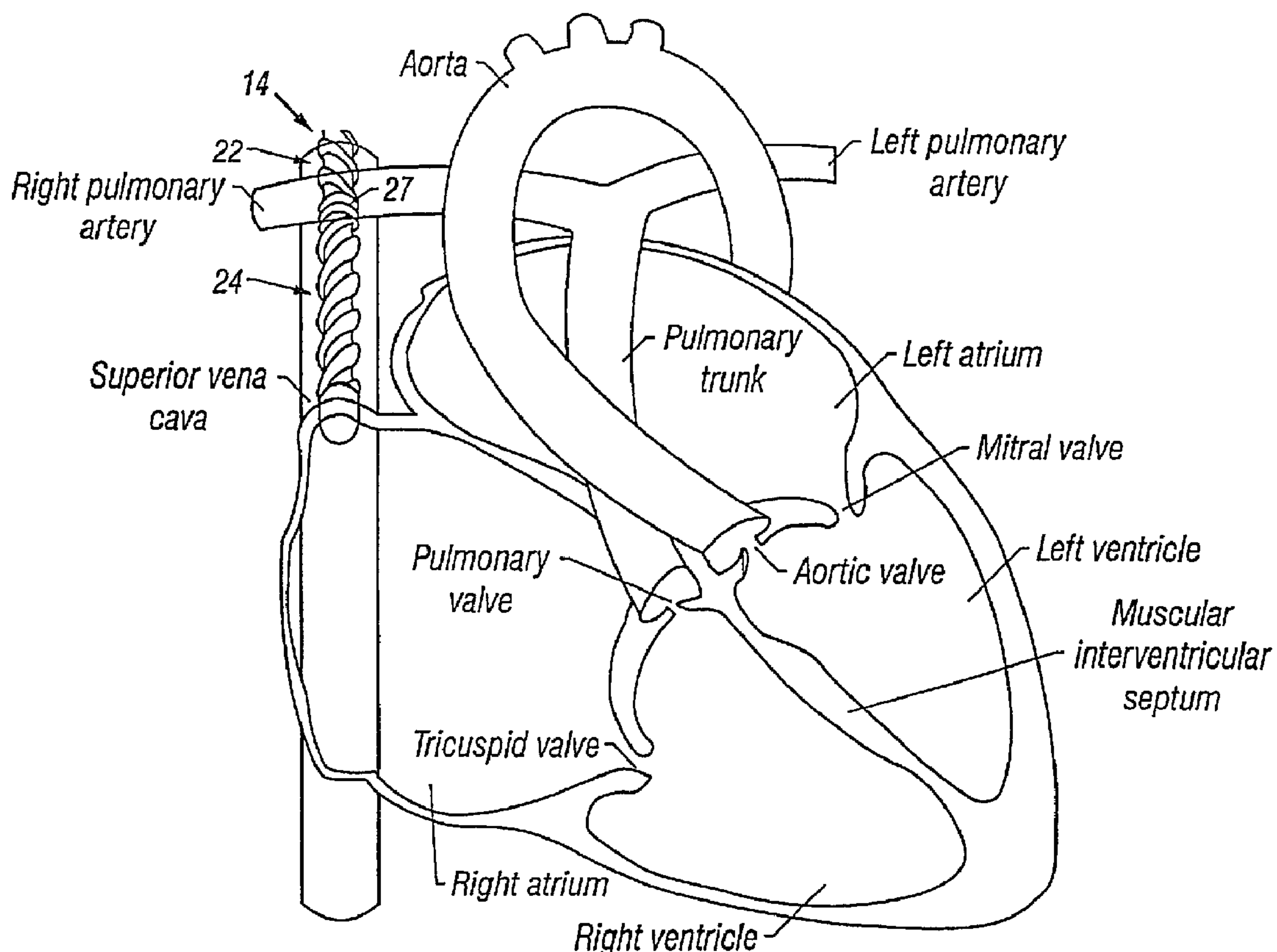
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(54) Title: FEVER REGULATION METHOD AND APPARATUS



(57) Abrégé/Abstract:

A device and method for providing body cooling for treating fever. The cooling device applies cooling to blood flowing in a vein or artery, e.g., the vena cavae, that is then distributed throughout the body.



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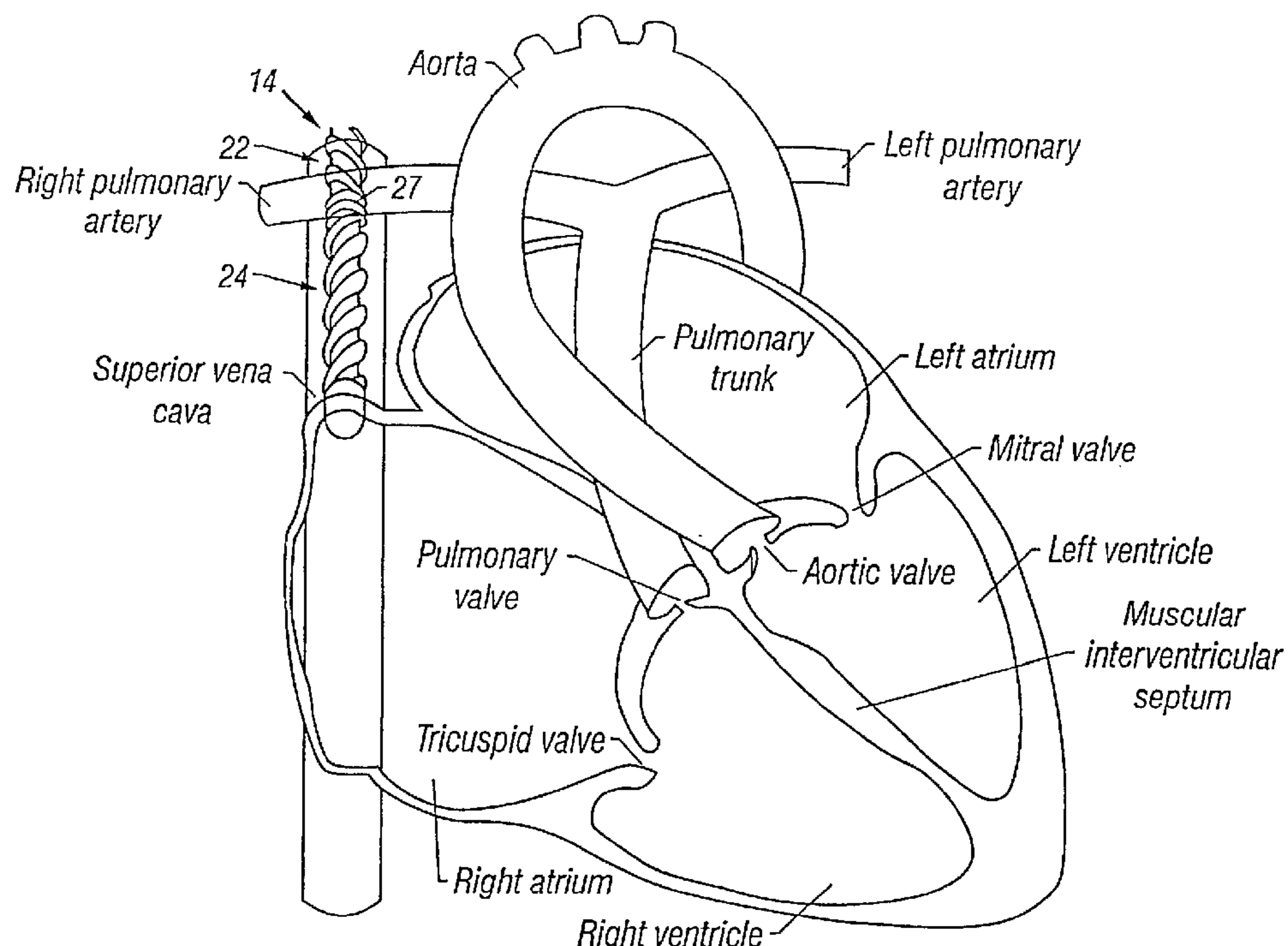
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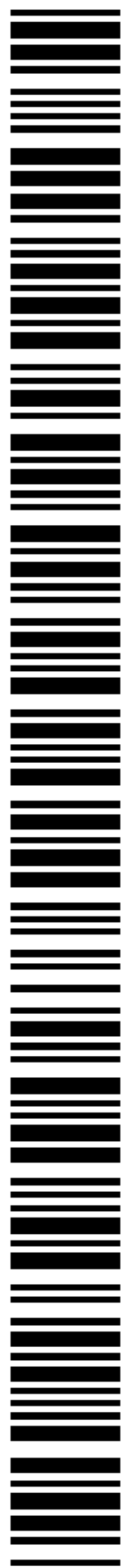
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Fever Regulation Method and Apparatus

5 CROSS REFERENCE TO RELATED APPLICATIONS

This is a continuation-in-part patent application of U. S. Provisional Patent Application Serial No. 60/246,620, filed 11/7/00, entitled "Fever Regulation Method and Apparatus" and of U. S. Patent Application Serial No. 09/566,531, filed 5/8/00, entitled "Method of Making Selective Organ Cooling Catheter", which is a
10 continuation of U.S. Patent Application Serial No. 09/103,342, filed on 06/23/98, entitled "Selective Organ Cooling Catheter and Method of Using the Same", now issued U.S. Patent No. 6,096,068. This is also a continuation-in-part patent application of U. S. Patent Application Serial No. 09/586,000, filed 6/2/00, entitled "Method for Determining the Effective Thermal Mass of a Body or Organ Using a Cooling
15 Catheter"; the entirety of all of the above applications being incorporated by reference herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

20 Not Applicable

BACKGROUND OF THE INVENTION

Field of the Invention - The present invention relates generally to the lowering and control of the temperature of the human body. More particularly, the invention
25 relates to a method and intravascular apparatus for cooling the whole body, especially during periods of fever.

Background Information - Organs in the human body, such as the brain, kidney and heart, are maintained at a constant temperature of approximately 37° C.
30 Hypothermia can be clinically defined as a core body temperature of 35° C or less. Hypothermia is sometimes characterized further according to its severity. A body core temperature in the range of 33° C to 35° C is described as mild hypothermia. A body

temperature of 28° C to 32° C is described as moderate hypothermia. A body core temperature in the range of 24° C to 28° C is described as severe hypothermia.

Hypothermia is uniquely effective in reducing brain injury caused by a variety of neurological insults and may eventually play an important role in emergency brain resuscitation. Experimental evidence has demonstrated that cerebral cooling improves outcome after global ischemia, focal ischemia, or traumatic brain injury. For this reason, hypothermia may be induced in order to reduce the effect of certain bodily injuries to the brain as well as other organs.

Cerebral hypothermia has traditionally been accomplished through whole body cooling to create a condition of total body hypothermia in the range of 20° C to 30° C. The currently-employed techniques and devices used to cause total body hypothermia lead to various side effects. In addition to the undesirable side effects, present methods of administering total body hypothermia are cumbersome.

Catheters have been developed which are inserted into the bloodstream of the patient in order to induce total body hypothermia. For example, U.S. Patent No. 3,425,419 to Dato describes a method and apparatus of lowering and raising the temperature of the human body. Dato induces moderate hypothermia in a patient using a rigid metallic catheter. The catheter has an inner passageway through which a fluid, such as water, can be circulated. The catheter is inserted through the femoral vein and then through the inferior vena cava as far as the right atrium and the superior vena cava. The Dato catheter has an elongated cylindrical shape and is constructed from stainless steel. By way of example, Dato suggests the use of a catheter approximately 70 cm in length and approximately 6 mm in diameter. Thus, the Dato device cools along the length of a very elongated device. Use of the Dato device is highly cumbersome due to its size and lack of flexibility.

U.S. Patent No. 5,837,003 to Ginsburg also discloses a method and apparatus for controlling a patient's body temperature. In this technique, a flexible catheter is inserted into the femoral artery or vein or the jugular vein. The catheter may be in the form of a balloon to allow an enhanced surface area for heat transfer. A thermally conductive metal foil may be used as part of a heat-absorbing surface. This device fails to disclose or teach use of any ability to enhance heat transfer. In addition, the disclosed device fails to disclose temperature regulation.

An ailment particular susceptible to treatment by cooling, either selective or whole body, is fever or hyperthermia. There is a growing awareness of the dangers associated with fever. Many patients, especially after surgery and/or in the intensive care unit, suffer from fever. For example, it is estimated that 90% of patients in neurointensive care units suffering from sub-arachnoid hemorrhage have a fever. Further, 60% of patients in neurointensive care units suffering from intra-cranial hemorrhage have a fever. 80% of patients in neurointensive care units suffering from traumatic brain injury have a fever. These patients are typically treated with Tylenol, cooling blankets, or other such methods. These methods are not believed to be very effective; moreover, they are difficult to control.

Therefore, a practical method and apparatus that lowers and controls the temperature of the human body satisfies a long-felt need.

SUMMARY OF THE INVENTION

In one aspect, the apparatus of the present invention can include a heat transfer element that can be used to apply cooling to the blood flowing in a large vein feeding the heart.

The heat transfer element, by way of example only, includes first and second elongated, articulated segments, each segment having a mixing-inducing exterior surface. A flexible joint can connect the first and second elongated segments. An inner lumen may be disposed within the first and second elongated segments and is capable of transporting a pressurized working fluid to a distal end of the first elongated segment. In addition, the first and second elongated segments may have a mixing-inducing interior surface for inducing mixing within the pressurized working fluid. The mixing-inducing exterior surface may be adapted to induce mixing within a blood flow when placed within an artery or vein. In one embodiment, the flexible joint includes a bellows section that also allows for axial compression of the heat transfer element as well as for enhanced flexibility. In alternative embodiments, the bellows section may be replaced with flexible tubing such as small cylindrical polymer connecting tubes.

In one embodiment, the mixing-inducing exterior surfaces of the heat transfer element include one or more helical grooves and ridges. Adjacent segments of the heat

transfer element can be oppositely spiraled to increase mixing. For instance, the first elongated heat transfer segment may include one or more helical ridges having a counter-clockwise twist, while the second elongated heat transfer segment includes one or more helical ridges having a clockwise twist. Alternatively, of course, the first
5 elongated heat transfer segment may include one or more clockwise helical ridges, and the second elongated heat transfer segment may include one or more counter-clockwise helical ridges. The first and second elongated, articulated segments may be formed from highly conductive materials such as metals, thin polymers, or doped polymers.

10 The heat transfer device may also have a supply catheter with an inner catheter lumen coupled to the inner lumen within the first and second elongated heat transfer segments. A working fluid supply configured to dispense the pressurized working fluid may be coupled to the inner catheter lumen or alternatively to the supply catheter. The working fluid supply may be configured to produce the pressurized
15 working fluid at a temperature of about 0°C and at a pressure below about 5 atmospheres of pressure.

In yet another alternative embodiment, the heat transfer device may have three or more elongated, articulated, heat transfer segments each having a mixing-inducing exterior surface, with additional flexible joints connecting the additional elongated
20 heat transfer segments. In one such embodiment, by way of example only, the first and third elongated heat transfer segments may include clockwise helical ridges, and the second elongated heat transfer segment may include one or more counter-clockwise helical ridges. Alternatively, of course, the first and third elongated heat transfer segments may include counter-clockwise helical ridges, and the second elongated heat
25 transfer segment may include one or more clockwise helical ridges.

The mixing-inducing exterior surface of the heat transfer element may optionally include a surface coating or treatment to inhibit clot formation. A surface coating may also be used to provide a degree of lubricity to the heat transfer element and its associated catheter.

30 The present invention is also directed to a method of treating fever in the body by inserting a flexible cooling element into a vein that is in pressure communication with the heart, *e.g.*, the femoral or iliac veins, the superior or inferior vena cavae or

both. The vena cavae may be accessed via known techniques from the jugular vein or from the subclavian or femoral veins, for example. The heat transfer element in one or both vena cavae may then cool virtually all the blood being returned to the heart. The cooled blood enters the right atrium at which point the same is pumped through the right ventricle and into the pulmonary artery to the lungs where the same is oxygenated. Due to the heat capacity of the lungs, the blood does not appreciably warm during oxygenation. The cooled blood is returned to the heart and pumped to the entire body via the aorta. Thus, cooled blood may be delivered indirectly to a chosen organ such as the brain. This indirect cooling is especially effective as high blood flow organs such as the heart and brain are preferentially supplied blood by the vasculature.

A warming blanket or other warming device may be applied to portions of the body to provide comfort to the patient and to inhibit thermoregulatory responses such as vasoconstriction. Thermoregulatory drugs may also be so provided for this reason.

The method further includes circulating a working fluid through the flexible, conductive cooling element in order to lower the temperature of the blood in the vena cava. The flexible, conductive heat transfer element preferably absorbs more than about 100 or 300 Watts of heat.

The method may also include inducing mixing within the free stream blood flow within the vena cava. It is noted that a degree of turbulence or mixing is generally present within the vena cava anyway. The step of circulating may include inducing mixing in the flow of the working fluid through the flexible heat transfer element. The pressure of the working fluid may be maintained below about 5 atmospheres of pressure.

The present invention also envisions a method for lowering a fever in the body of a patient which includes introducing a catheter, with a cooling element, into a vena cava supplying the heart, the catheter having a diameter of about 18 mm or less, inducing mixing in blood flowing over the cooling element, and lowering the temperature of the cooling element to remove heat from the blood to cool the blood. In one embodiment, the cooling step removes at least about 50 Watts of heat from the blood. The mixing induced may result in a Nusselt number enhancement of the flow of between about 5 and 80.

Advantages of the invention are numerous. Patients can be provided with an efficient method of reducing fever that does not suffer from the deleterious consequences of the prior art. The procedure can be administered safely and easily. Numerous cardiac and neural settings can benefit by the hypothermic therapy. Other
5 advantages will be understood from the following.

The novel features of this invention, as well as the invention itself, will be best understood from the attached drawings, taken along with the following description, in which similar reference characters refer to similar parts, and in which:

10 BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an elevation view of one embodiment of a heat transfer element according to the invention;

Figure 2 is a longitudinal section view of the heat transfer element of Figure 1;

Figure 3 is a transverse section view of the heat transfer element of Figure 1;

15 Figure 4 is a perspective view of the heat transfer element of Figure 1 in use within a blood vessel;

Figure 5 is a schematic representation of the heat transfer element being used in an embodiment within the superior vena cava; and

Figure 6 is a flowchart showing an exemplary method of the invention.

20

DETAILED DESCRIPTION OF THE INVENTION

25 OVERVIEW

A one or two-step process and a one or two-piece device may be employed to intravascularly lower the temperature of a body in order to treat fever. A cooling element may be placed in a high-flow vein such as the vena cavae to absorb heat from the blood flowing into the heart. This transfer of heat causes a cooling of the blood
30 flowing through the heart and thus throughout the vasculature. Such a method and device may therapeutically be used to treat fever.

A heat transfer element that systemically cools blood should be capable of providing the necessary heat transfer rate to produce the desired cooling effect throughout the vasculature. This may be up to or greater than 300 watts, and is at least partially dependent on the mass of the patient and the rate of blood flow. Surface
5 features may be employed on the heat transfer element to enhance the heat transfer rate. The surface features and other components of the heat transfer element are described in more detail below.

One problem with treating fever with cooling is that the cause of the patient's fever attempts to defeat the cooling. Thus, a high power device is often required.

10

ANATOMICAL PLACEMENT

The internal jugular vein is the vein that directly drains the brain. The external jugular joins the internal jugular at the base of the neck. The internal jugular veins join the subclavian veins to form the brachiocephalic veins that in turn drain into the
15 superior vena cava. The superior vena cava drains into the right atrium of the heart and supplies blood to the heart from the upper part of the body.

A cooling element may be placed into the superior vena cava, inferior vena cava, or otherwise into a vein which feeds into the superior vena cava or otherwise into the heart to cool the body. A physician may percutaneously place the catheter into
20 the subclavian or internal or external jugular veins to access the superior vena cava. The blood, cooled by the heat transfer element, may be processed by the heart and provided to the body in oxygenated form to be used as a conductive medium to cool the body. The lungs have a fairly low heat capacity, and thus the lungs do not cause appreciable rewarming of the flowing blood.

25 The vasculature by its very nature provides preferential blood flow to the high blood flow organs such as the brain and the heart. Thus, these organs are preferentially cooled by such a procedure. The core body temperature may be measured by an esophageal probe. The brain temperature usually decreases more rapidly than the core body temperature. The inventors believe this effect to be due to the preferential supply
30 of blood provided to the brain and heart. This effect may be even more pronounced if thermoregulatory effects, such as vasoconstriction, occur that tend to focus blood supply to the core vascular system and away from the peripheral vascular system.

HEAT TRANSFER

When a heat transfer element is inserted approximately coaxially into an artery or vein, the primary mechanism of heat transfer between the surface of the heat transfer element and the blood is forced convection. Convection relies upon the movement of fluid to transfer heat. Forced convection results when an external force causes motion within the fluid. In the case of arterial or venous flow, the beating heart causes the motion of the blood around the heat transfer element.

The magnitude of the heat transfer rate is proportional to the surface area of the heat transfer element, the temperature differential, and the heat transfer coefficient of the heat transfer element.

The receiving artery or vein into which the heat transfer element is placed has a limited diameter and length. Thus, the surface area of the heat transfer element must be limited to avoid significant obstruction of the artery or vein and to allow the heat transfer element to easily pass through the vascular system. For placement within the superior vena cava via the external jugular, the cross sectional diameter of the heat transfer element may be limited to about 5-6 mm, and its length may be limited to approximately 10-15 cm. For placement within the inferior vena cava, the cross sectional diameter of the heat transfer element may be limited to about 6-7 mm, and its length may be limited to approximately 25-35 cm.

Decreasing the surface temperature of the heat transfer element can increase the temperature differential. However, the minimum allowable surface temperature is limited by the characteristics of blood. Blood freezes at approximately 0° C. When the blood approaches freezing, ice emboli may form in the blood, which may lodge downstream, causing serious ischemic injury. Furthermore, reducing the temperature of the blood also increases its viscosity, which results in a small decrease in the value of the convection heat transfer coefficient. In addition, increased viscosity of the blood may result in an increase in the pressure drop within the artery, thus compromising the flow of blood to the brain. Given the above constraints, it is advantageous to limit the minimum allowable surface temperature of the cooling element to approximately 5° C. This results in a maximum temperature differential between the blood stream and

the cooling element of approximately 32° C. For other physiological reasons, there are limits on the maximum allowable surface temperature of the warming element.

However, in certain situations, temperatures lower than 0°C may be used. For example, certain patients may have blood flows such that the flow per se prohibits or significantly inhibits freezing. To achieve such cooling, sub-zero temperatures may be used. In these cases, working fluids such as perfluorocarbons may be employed.

The mechanisms by which the value of the convection heat transfer coefficient may be increased are complex. However, it is well known that the convection heat transfer coefficient increases with the level of “mixing” or “turbulent” kinetic energy in the fluid flow. Thus it is advantageous to have blood flow with a high degree of mixing in contact with the heat transfer element.

The blood flow has a considerably more stable flux in the vena cava than in an artery. However, the blood flow in the vena cava still has a high degree of inherent mixing or turbulence. Reynolds numbers in the superior vena cava may range, for example, from 2,000 to 5,000. Thus, blood cooling in the vena cava may benefit from enhancing the level of mixing with the heat transfer element but this benefit may be substantially less than that caused by the inherent mixing.

BOUNDARY LAYERS

A thin boundary layer has been shown to form during the cardiac cycle. Boundary layers develop adjacent to the heat transfer element as well as next to the walls of the artery or vein. Each of these boundary layers has approximately the same thickness as the boundary layer that would have developed at the wall of the artery in the absence of the heat transfer element. The free stream flow region is developed in an annular ring around the heat transfer element. The heat transfer element used in such a vessel should reduce the formation of such viscous boundary layers.

HEAT TRANSFER ELEMENT CHARACTERISTICS AND DESCRIPTION

The intravascular heat transfer element should be flexible in order to be placed within the vena cavae or other veins or arteries. The flexibility of the heat transfer element is an important characteristic because the same is typically inserted into a vein such as the external jugular and accesses the vena cava by initially passing

though a series of one or more branches. Further, the heat transfer element is ideally constructed from a highly thermally conductive material such as metal in order to facilitate heat transfer. The use of a highly thermally conductive material increases the heat transfer rate for a given temperature differential between the working fluid within
5 the heat transfer element and the blood. This facilitates the use of a higher temperature coolant, or lower temperature warming fluid, within the heat transfer element, allowing safer working fluids, such as water or saline, to be used. Highly thermally conductive materials, such as metals, tend to be rigid. Therefore, the design of the heat transfer element should facilitate flexibility in an inherently inflexible material.

10 However, balloon designs may also be employed, such as those disclosed in co-pending U.S. Patent Application Serial No. 09/215,038, filed 12/16/98, entitled "Inflatable Catheter for Selective Organ Heating and Cooling and Method of Using the Same," now U.S. Patent No. 6,261,312 and incorporated herein by reference in its entirety.

15 It is estimated that the cooling element should absorb at least about 50 Watts of heat when placed in the vena cava to lower the temperature of the body to between about 30°C and 34°C. These temperatures are thought to be appropriate to lower most fevers. The power removed determines how quickly the target temperature can be reached. For example, in a fever therapy in which it is desired to lower brain
20 temperature, the same may be lowered about 4°C per hour in a 70 kg human upon removal of 300 Watts.

One embodiment of the invention uses a modular design. This design creates helical blood flow and produces a level of mixing in the blood flow by periodically forcing abrupt changes in the direction of the helical blood flow. The abrupt changes
25 in flow direction are achieved through the use of a series of two or more heat transfer segments, each included of one or more helical ridges. The use of periodic abrupt changes in the helical direction of the blood flow in order to induce strong free stream turbulence may be illustrated with reference to a common clothes washing machine. The rotor of a washing machine spins initially in one direction causing laminar flow.
30 When the rotor abruptly reverses direction, significant turbulent kinetic energy is created within the entire wash basin as the changing currents cause random turbulent

motion within the clothes-water slurry. These surface features also tend to increase the surface area of the heat transfer element, further enhancing heat transfer.

Figure 1 is an elevation view of one embodiment of a cooling element 14 according to the present invention. The heat transfer element 14 includes a series of
5 elongated, articulated segments or modules 20, 22, 24. Three such segments are shown in this embodiment, but two or more such segments could be used without departing from the spirit of the invention. As seen in Figure 1, a first elongated heat transfer segment 20 is located at the proximal end of the heat transfer element 14. A mixing-inducing exterior surface of the segment 20 includes four parallel helical
10 ridges 28 with four parallel helical grooves 26 therebetween. One, two, three, or more parallel helical ridges 28 could also be used without departing from the spirit of the present invention. In this embodiment, the helical ridges 28 and the helical grooves 26 of the heat transfer segment 20 have a left hand twist, referred to herein as a counter-clockwise spiral or helical rotation, as they proceed toward the distal end of the heat
15 transfer segment 20.

The first heat transfer segment 20 is coupled to a second elongated heat transfer segment 22 by a first bellows section 25, which provides flexibility and compressibility. The second heat transfer segment 22 includes one or more helical
20 ridges 32 with one or more helical grooves 30 therebetween. The ridges 32 and grooves 30 have a right hand, or clockwise, twist as they proceed toward the distal end of the heat transfer segment 22. The second heat transfer segment 22 is coupled to a third elongated heat transfer segment 24 by a second bellows section 27. The third heat transfer segment 24 includes one or more helical ridges 36 with one or more helical grooves 34 therebetween. The helical ridge 36 and the helical groove 34 have a
25 left hand, or counter-clockwise, twist as they proceed toward the distal end of the heat transfer segment 24. Thus, successive heat transfer segments 20, 22, 24 of the heat transfer element 14 alternate between having clockwise and counterclockwise helical twists. The actual left or right hand twist of any particular segment is immaterial, as long as adjacent segments have opposite helical twist.

30 In addition, the rounded contours of the ridges 28, 32, 36 allow the heat transfer element 14 to maintain a relatively atraumatic profile, thereby minimizing the

possibility of damage to the blood vessel wall. A heat transfer element according to the present invention may include two, three, or more heat transfer segments.

5 The bellows sections 25, 27 are formed from seamless and nonporous materials, such as metal, and therefore are impermeable to gas, which can be particularly important, depending on the type of working fluid that is cycled through the heat transfer element 14. The structure of the bellows sections 25, 27 allows them to bend, extend and compress, which increases the flexibility of the heat transfer element 14 so that it is more readily able to navigate through blood vessels. The bellows sections 25, 27 also provide for axial compression of the heat transfer element 10 14, which can limit the trauma when the distal end of the heat transfer element 14 abuts a blood vessel wall. The bellows sections 25, 27 are also able to tolerate cryogenic temperatures without a loss of performance. In alternative embodiments, the bellows may be replaced by flexible polymer tubes, which are bonded between adjacent heat transfer segments.

15 The exterior surfaces of the heat transfer element 14 can be made from metal, and may include very high thermal conductivity materials such as nickel, thereby facilitating heat transfer. Alternatively, other metals such as stainless steel, titanium, aluminum, silver, copper and the like, can be used, with or without an appropriate coating or treatment to enhance biocompatibility or inhibit clot formation. Suitable 20 biocompatible coatings include, *e.g.*, gold, platinum or polymer paralyene. The heat transfer element 14 may be manufactured by plating a thin layer of metal on a mandrel that has the appropriate pattern. In this way, the heat transfer element 14 may be manufactured inexpensively in large quantities, which is an important feature in a disposable medical device.

25 Because the heat transfer element 14 may dwell within the blood vessel for extended periods of time, such as 24-48 hours or even longer, it may be desirable to treat the surfaces of the heat transfer element 14 to avoid clot formation. In particular, one may wish to treat the bellows sections 25, 27 because stagnation of the blood flow may occur in the convolutions, thus allowing clots to form and cling to the surface to 30 form a thrombus. One means by which to prevent thrombus formation is to bind an antithrombogenic agent to the surface of the heat transfer element 14. For example, heparin is known to inhibit clot formation and is also known to be useful as a

biocoating. Alternatively, the surfaces of the heat transfer element 14 may be bombarded with ions such as nitrogen. Bombardment with nitrogen can harden and smooth the surface and thus prevent adherence of clotting factors. Another coating that provides beneficial properties may be a lubricious coating. Lubricious coatings, on both the heat transfer element and its associated catheter, allow for easier placement in the, *e.g.*, vena cava.

Figure 2 is a longitudinal sectional view of the heat transfer element 14 of an embodiment of the invention, taken along line 2-2 in Figure 1. Some interior contours are omitted for purposes of clarity. An inner tube 42 creates an inner lumen 40 and an outer lumen 46 within the heat transfer element 14. Once the heat transfer element 14 is in place in the blood vessel, a working fluid such as saline or other aqueous solution may be circulated through the heat transfer element 14. Fluid flows up a supply catheter into the inner lumen 40. At the distal end of the heat transfer element 14, the working fluid exits the inner lumen 40 and enters the outer lumen 46. As the working fluid flows through the outer lumen 46, heat is transferred from the working fluid to the exterior surface 37 of the heat transfer element 14. Because the heat transfer element 14 is constructed from a high conductivity material, the temperature of its exterior surface 37 may reach very close to the temperature of the working fluid. The tube 42 may be formed as an insulating divider to thermally separate the inner lumen 40 from the outer lumen 46. For example, insulation may be achieved by creating longitudinal air channels in the wall of the insulating tube 42. Alternatively, the insulating tube 42 may be constructed of a non-thermally conductive material like polytetrafluoroethylene or another polymer.

It is important to note that the same mechanisms that govern the heat transfer rate between the exterior surface 37 of the heat transfer element 14 and the blood also govern the heat transfer rate between the working fluid and the interior surface 38 of the heat transfer element 14. The heat transfer characteristics of the interior surface 38 are particularly important when using water, saline or other fluid that remains a liquid as the working fluid. Other coolants such as Freon undergo nucleate boiling and create mixing through a different mechanism. Saline is a safe working fluid, because it is non-toxic, and leakage of saline does not result in a gas embolism, which could occur with the use of boiling refrigerants. Since mixing in the working fluid is enhanced by

the shape of the interior surface 38 of the heat transfer element 14, the working fluid can be delivered to the cooling element 14 at a warmer temperature and still achieve the necessary cooling rate. Similarly, since mixing in the working fluid is enhanced by the shape of the interior surface of the heat transfer element, the working fluid can be delivered to the warming element 14 at a cooler temperature and still achieve the necessary warming rate.

This has a number of beneficial implications in the need for insulation along the catheter shaft length. Due to the decreased need for insulation, the catheter shaft diameter can be made smaller. The enhanced heat transfer characteristics of the interior surface of the heat transfer element 14 also allow the working fluid to be delivered to the heat transfer element 14 at lower flow rates and lower pressures. High pressures may make the heat transfer element stiff and cause it to push against the wall of the blood vessel, thereby shielding part of the exterior surface 37 of the heat transfer element 14 from the blood. Because of the increased heat transfer characteristics achieved by the alternating helical ridges 28, 32, 36, the pressure of the working fluid may be as low as 5 atmospheres, 3 atmospheres, 2 atmospheres or even less than 1 atmosphere.

Figure 3 is a transverse sectional view of the heat transfer element 14 of the invention, taken at a location denoted by the line 3-3 in Figure 1. Figure 3 illustrates a five-lobed embodiment, whereas Figure 1 illustrates a four-lobed embodiment. As mentioned earlier, any number of lobes might be used. In Figure 3, the construction of the heat transfer element 14 is clearly shown. The inner lumen 40 is defined by the insulating tube 42. The outer lumen 46 is defined by the exterior surface of the insulating tube 42 and the interior surface 38 of the heat transfer element 14. In addition, the helical ridges 32 and helical grooves 30 may be seen in Figure 3. Although Figure 3 shows four ridges and four grooves, the number of ridges and grooves may vary. Thus, heat transfer elements with 1, 2, 3, 4, 5, 6, 7, 8 or more ridges are specifically contemplated.

Figure 4 is a perspective view of a heat transfer element 14 in use within a blood vessel, showing only one helical lobe per segment for purposes of clarity. Beginning from the proximal end of the heat transfer element (not shown in Figure 4), as the blood moves forward, the first helical heat transfer segment 20 induces a

counter-clockwise rotational inertia to the blood. As the blood reaches the second segment 22, the rotational direction of the inertia is reversed, causing mixing within the blood. Further, as the blood reaches the third segment 24, the rotational direction of the inertia is again reversed. The sudden changes in flow direction actively reorient and randomize the velocity vectors, thus ensuring mixing throughout the bloodstream. During such mixing, the velocity vectors of the blood become more random and, in some cases, become perpendicular to the axis of the vessel. Thus, a large portion of the volume of warm blood in the vessel is actively brought in contact with the heat transfer element 14, where it can be cooled by direct contact rather than being cooled largely by conduction through adjacent laminar layers of blood.

Referring back to Figure 1, the heat transfer element 14 has been designed to address all of the design criteria discussed above. First, the heat transfer element 14 is flexible and is made of a highly conductive material. The flexibility is provided by a segmental distribution of bellows sections 25, 27 that provide an articulating mechanism. Bellows have a known convoluted design that provide flexibility. Second, the exterior surface area 37 has been increased through the use of helical ridges 28, 32, 36 and helical grooves 26, 30, 34. The ridges also allow the heat transfer element 14 to maintain a relatively atraumatic profile, thereby minimizing the possibility of damage to the vessel wall. Third, the heat transfer element 14 has been designed to promote mixing both internally and externally. The modular or segmental design allows the direction of the grooves to be reversed between segments. The alternating helical rotations create an alternating flow that results in mixing the blood in a manner analogous to the mixing action created by the rotor of a washing machine that switches directions back and forth. This action is intended to promote mixing to enhance the heat transfer rate. The alternating helical design also causes beneficial mixing, or turbulent kinetic energy, of the working fluid flowing internally.

METHOD OF USE

The practice of the present invention is illustrated in the following non-limiting example.

Exemplary Procedure

1. The patient is initially assessed as having a fever, resuscitated, and stabilized.

2. The procedure may be carried out in an angiography suite, NICU, ICU, or surgical suite equipped with fluoroscopy.
3. An ultrasound or angiogram of the superior vena cava and external jugular can be used to determine the vessel diameter and the blood flow; a catheter with an appropriately sized heat transfer element can be selected.
4. After assessment of the veins, the patient is sterilely prepped and infiltrated with lidocaine at a region where the appropriate vein may be accessed.
5. The external jugular is cannulated and a guide wire may be inserted to the superior vena cava. Placement of the guide wire is confirmed with fluoroscopy.
- 10 6. An angiographic catheter can be fed over the wire and contrast media injected into the vein to further to assess the anatomy if desired.
7. Alternatively, the external jugular is cannulated and a 10-12.5 french (f) introducer sheath is placed.
8. A guide catheter is placed into the superior vena cava. If a guide catheter is placed, it can be used to deliver contrast media directly to further assess anatomy.
- 15 9. The cooling catheter is placed into the superior vena cava via the guiding catheter or over the guidewire.
10. Placement is confirmed if desired with fluoroscopy.
- 20 11. Alternatively, the cooling catheter shaft has sufficient pushability and torqueability to be placed in the superior vena cava without the aid of a guide wire or guide catheter.
12. The cooling catheter is connected to a pump circuit also filled with saline and free from air bubbles. The pump circuit has a heat exchange section that is immersed into a water bath and tubing that is connected to a peristaltic pump.
- 25 The water bath is chilled to approximately 0° C.
13. Cooling is initiated by starting the pump mechanism. The saline within the cooling catheter is circulated at 5 cc/sec. The saline travels through the heat exchanger in the chilled water bath and is cooled to approximately 1° C.
- 30 14. The saline subsequently enters the cooling catheter where it is delivered to the heat transfer element. The saline is warmed to approximately 5-7° C as it travels

along the inner lumen of the catheter shaft to the end of the heat transfer element.

15. The saline then flows back through the heat transfer element in contact with the inner metallic surface. The saline is further warmed in the heat transfer element to 12-15° C, and in the process, heat is absorbed from the blood, cooling the blood to 30°C to 35°C.
16. The chilled blood then goes on to chill the body. It is estimated that less than an hour will be required to substantially reduce a fever down to normothermia.
17. The warmed saline travels back the outer lumen of the catheter shaft and is returned to the chilled water bath where the same is cooled to 1° C.
18. The pressure drops along the length of the circuit are estimated to be between 1 and 10 atmospheres.
19. The cooling can be adjusted by increasing or decreasing the flow rate of the saline. Monitoring of the temperature drop of the saline along the heat transfer element will allow the flow to be adjusted to maintain the desired cooling effect.
20. The catheter is left in place to provide cooling for, *e.g.*, 6-48 hours.

Of course, the use of the superior vena cava is only exemplary. It is envisioned that the following veins may be appropriate to percutaneously insert the heat transfer element: femoral, internal jugular, subclavian, and other veins of similar size and position. It is also envisioned that the following veins may be appropriate in which to dispose the heat transfer element during use: inferior vena cava, superior vena cava, femoral, internal jugular, and other veins of similar size and position. Arteries may also be employed if a fever therapy selective to a particular organ or region of the body is desired.

Figure 5 shows a cross-section of the heart in which the heat transfer element 14 is disposed in the superior vena cava 62. The heat transfer element 14 has rotating helical grooves 22 as well as counter-rotating helical grooves 24. Between the rotating and the counter-rotating grooves are bellows 27. It is believed that a design of this nature would enhance the Nusselt number for the flow in the superior vena cava by about 5 to 80.

In some cases, a heating blanket may be used. The heating blanket serves several purposes. By warming the patient, vasoconstriction is avoided. The patient is

also made more comfortable. For example, it is commonly agreed that for every one degree of core body temperature reduction, the patient will continue to feel comfortable if the same experiences a rise in surface area (skin) temperature of five degrees. Spasms due to total body hypothermia may be avoided. Temperature control
5 of the patient may be more conveniently performed as the physician has another variable (the amount of heating) which may be adjusted.

As an alternative, the warming element may be any of the heating methods proposed in U.S. Patent Application Serial No. 09/292,532, filed on 4/15/99, and entitled "Isolated Selective Organ Cooling Method and Apparatus," and incorporated
10 by reference above.

Anti-shivering drugs may be used to provide the features of the heating blanket. In this connection, meperidine is an analgesic of the phenyl piperidine class that is known to bind to the opiate receptor. Meperidine may be used to treat shivering due to post-operative anesthesia as well as hypothermia induced in a fever suppression
15 treatment.

In a method according to an embodiment of the invention for treating patients with fever, the heat transfer element as described may be placed in any of several veins, including the femoral, the IVC, the SVC, the subclavian, the braichiocephalic, the jugular, and other such veins. The heat transfer element may also be placed in
20 appropriate arteries for more selective fever reduction.

The amount of cooling performed may be judged to a first approximation by the rate of cool-down. The amount of cooling is proportional to the difference between the temperature of the blood and the temperature of the heat transfer element or cooling element. Thus, if the temperature of the blood is 40°C and the temperature
25 of the cooling element is 5°C, the power extracted will be greater than if the temperature of the blood is 38°C and the temperature of the cooling element is maintained at 5°C. Thus, the cool-down or cooling rate is generally greatest at the beginning of a cooling procedure. Once the patient temperature begins to approach the target temperature, usually normothermia or 37oC, the cooling rate may be
30 reduced because the temperature differential is no longer as great.

In any case, once the patient reaches the normothermic temperature, it is no longer easy to guess whether, in the absence of the cooling therapy, the patient would

otherwise be feverish or whether the fever has abated. One embodiment of the invention allows a determination of this.

First, it is noted that the power extracted can be calculated from the temperature differential between the working fluid supply temperature and the working fluid return temperature. In particular:

$$P_{\text{catheter}} = M c_f \Delta T_f$$

Where P_{catheter} is the power extracted, M is the mass flow rate of the working fluid, c_f is the heat capacity of the working fluid, and ΔT is the temperature differential between the working fluid as it enters the catheter and as it exits the catheter.

Accordingly, P_{catheter} can be readily calculated by measuring the mass flow of the circulating fluid and the temperature difference between the working fluid as it enters and exits the catheter. The power removed by the catheter as determined above may be equated to a close approximation to the power that is lost by the patient's body. In general, a closed-form solution for the power P required to cool (or heat) a body at temperature T to temperature T_0 is not known. One possible approximation may be to assume an exponential relationship:

$$P = \alpha (\exp \beta(T - T_0) - 1)$$

Taking the derivative of each side with respect to temperature:

$$\frac{\partial P}{\partial T} = \alpha \beta e^{\beta(T - T_0)}$$

and taking the inverse of each side:

$$\frac{\partial T}{\partial P} = \frac{1}{\alpha \beta e^{\beta(T - T_0)}}$$

or

$$\Delta T \approx \frac{\partial T}{\partial P} \Delta P$$

where ΔT is the temperature differential from nominal temperature and ΔP is the measured power.

A close approximation may be obtained by assuming the relationship is linear. Equivalently, a power series expansion may be taken, and the linear term retained. In any case, integrating, assuming a linear relationship, and rearranging:

$P = \alpha (T - T_0)$, where the constant of proportionality has units of watts/degree Celsius.

One can determine the constant of proportionality α using two points during the therapy when both T and P are finite and known. One may be when therapy begins, i.e., when the patient has temperature T and the catheter is drawing power P . Another

5 point may be obtained when $T = T_0$ and $P = P_0$.

Then, for any P , T is given by:

$$T_{\text{absence of therapy}} = T_0 + \frac{P_{\text{at } T_0}}{\alpha}$$

An example of this may be seen in Fig. 6, which shows a flowchart of an embodiment of a method of the invention. Referring to the figure, a patient presents
10 at a hospital or clinic with a fever (step 202). Generally, such a patient will have a fever as a result of a malady or other illness for which hospitalization is required. For example, the majority of patients in ICUs present with a fever.

A catheter with a heat transfer element thereon may be inserted (step 204). The initial power withdrawn P_{start} and body temperature T_{start} may be measured (step
15 206), and the therapy begun (step 208). The therapy continues (step 210), and P and T are periodically, continuously, or otherwise measured (step 212). The measured T is compared to the normothermic $T = T_0$, which is usually about 37°C (step 214). If T is greater than T_0 , the therapy continues (step 210). If T is less than T_0 , then the power P_0 is measured at $T = T_0$ (step 216). By the equations above, a constant of
20 proportionality α may be uniquely determined (step 218) by knowledge of T_{start} , P_{start} , P_0 , and T_0 . From α , T_{start} , P_{start} , P_0 , and T_0 , $T_{\text{absence of cooling}}$ may be determined (step 220). $T_{\text{absence of cooling}}$ is then compared to T_0 (step 222). If $T_{\text{absence of cooling}} > T_0$, then the patient is still generating enough power via their metabolism to cause a fever if the therapy were discontinued. Thus, therapy is continued (step 224). If $T_{\text{absence of cooling}}$
25 $\leq T_0$, then the patient is no longer generating enough power via their metabolism to cause a fever if the therapy were discontinued. Thus, therapy is discontinued (step 226). Variations of the above method will be apparent to those of ordinary skill in the art.

While the invention herein disclosed is capable of obtaining the objects
30 hereinbefore stated, it is to be understood that this disclosure is merely illustrative of

the presently preferred embodiments of the invention and that no limitations are intended other than as described in the appended claims.

What is claimed is:

CLAIMS

- 1 1. A method for treating fever in a patient's body intravascularly,
2 comprising:
3 providing a catheter having a cooling element attached to a distal end
4 thereof;
5 inserting the catheter through the vascular system of a patient with a
6 fever to place the cooling element in a vein that drains into the
7 heart of a patient;
8 circulating fluid through the cooling element;
9 transferring heat from the blood in the vein to the cooling element; and
10 thereby lowering the temperature of the patient.
- 1 2. The method of claim 1, further comprising inducing mixing in the
2 blood of the vascular system of the patient.
- 1 3. The method of claim 1, further comprising administering a
2 thermoregulatory drug to the patient.
- 1 4. The method of claim 3, wherein the thermoregulatory drug is selected
2 from the group consisting of clonidine, meperidine, propofol,
3 magnesium, dexmedetomidine, and combinations thereof.

- 1 5. The method of claim 1, wherein the cooling element is disposed in a
2 vein selected from the group consisting of the superior vena cava, the
3 inferior vena cava, the femoral, the iliac, the subclavian, the
4 braichiocephalic, or combinations of these.

1 6. A method for determining duration of a intravascular fever treatment,
2 comprising:
3 providing a catheter having a cooling element attached to a distal end
4 thereof;
5 inserting the catheter through the vascular system of a patient with a
6 fever to place the cooling element in a vein that drains into the
7 heart of a patient;
8 circulating fluid through the cooling element, and measuring a starting
9 power withdrawn and starting body temperature at the
10 beginning of the circulating;
11 transferring heat from the blood in the vein to the cooling element, and
12 thereby lowering the temperature of the patient;
13 measuring a power withdrawn and body temperature during the
14 circulating;
15 measuring a power withdrawn at substantially the time when the body
16 temperature equals a normothermic temperature;
17 calculating a $T_{\text{absence of cooling}}$ from the power withdrawn at substantially
18 the time when the body temperature equals a normothermic
19 temperature, the normothermic temperature, the starting power
20 withdrawn and the starting body temperature; and
21 comparing the $T_{\text{absence of cooling}}$ with the normothermic temperature, and
22 continuing the circulating if $T_{\text{absence of cooling}}$ is greater than the
23 normothermic temperature, and discontinuing the circulating if
24 $T_{\text{absence of cooling}}$ is less than the normothermic temperature.

1 7. A computer program, residing on a computer-readable medium, containing
2 instructions for causing a chiller console, circulating set, and
3 intravascularly inserted catheter having a heat transfer element at a distal
4 end thereof to:
5 circulate fluid through a heat transfer element, and measuring a starting
6 power withdrawn and starting body temperature corresponding
7 to a body temperature of a patient at the beginning of the
8 circulating;
9 transfer heat from the blood in the vasculature to the heat transfer
10 element, and thereby lowering the body temperature of a
11 patient;
12 measure a power withdrawn and body temperature during the
13 circulating;
14 measure a power withdrawn at substantially the time when the body
15 temperature equals a normothermic temperature;
16 calculate a $T_{\text{absence of cooling}}$ from: the power withdrawn at substantially
17 the time when the body temperature equals a normothermic
18 temperature, the normothermic temperature, the starting power
19 withdrawn, and the starting body temperature; and
20 compare the $T_{\text{absence of cooling}}$ with the normothermic temperature, and
21 continuing the circulating if $T_{\text{absence of cooling}}$ is greater than the
22 normothermic temperature, and discontinuing the circulating if
23 $T_{\text{absence of cooling}}$ is less than the normothermic temperature.

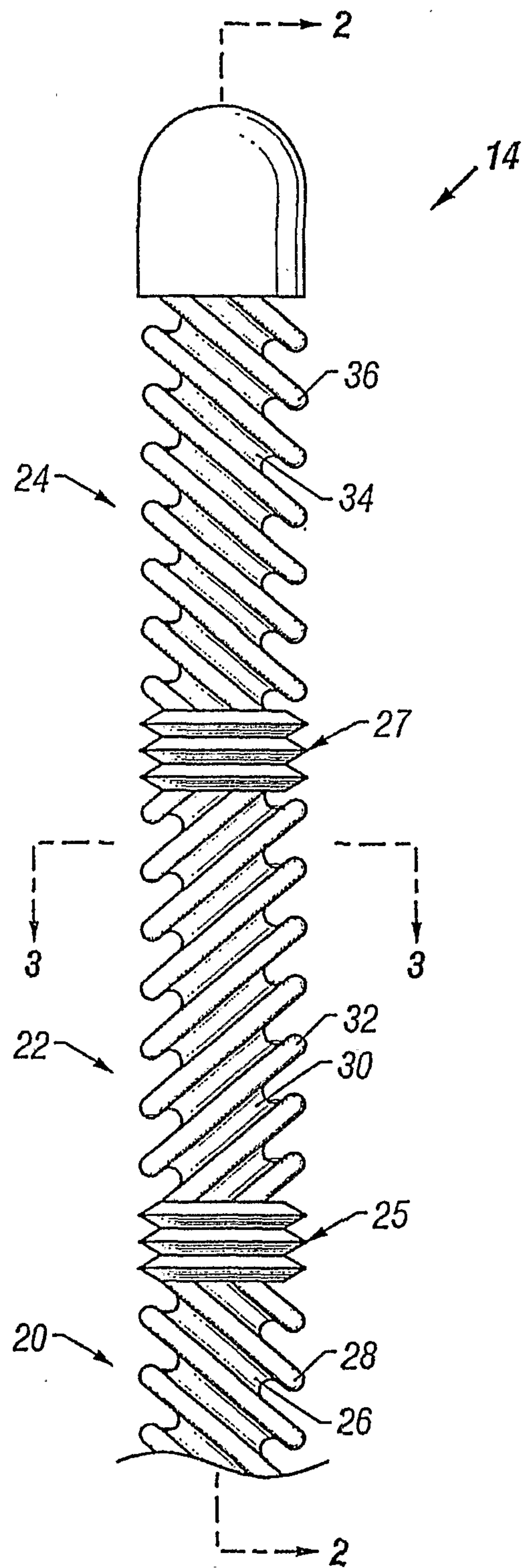


FIG. 1

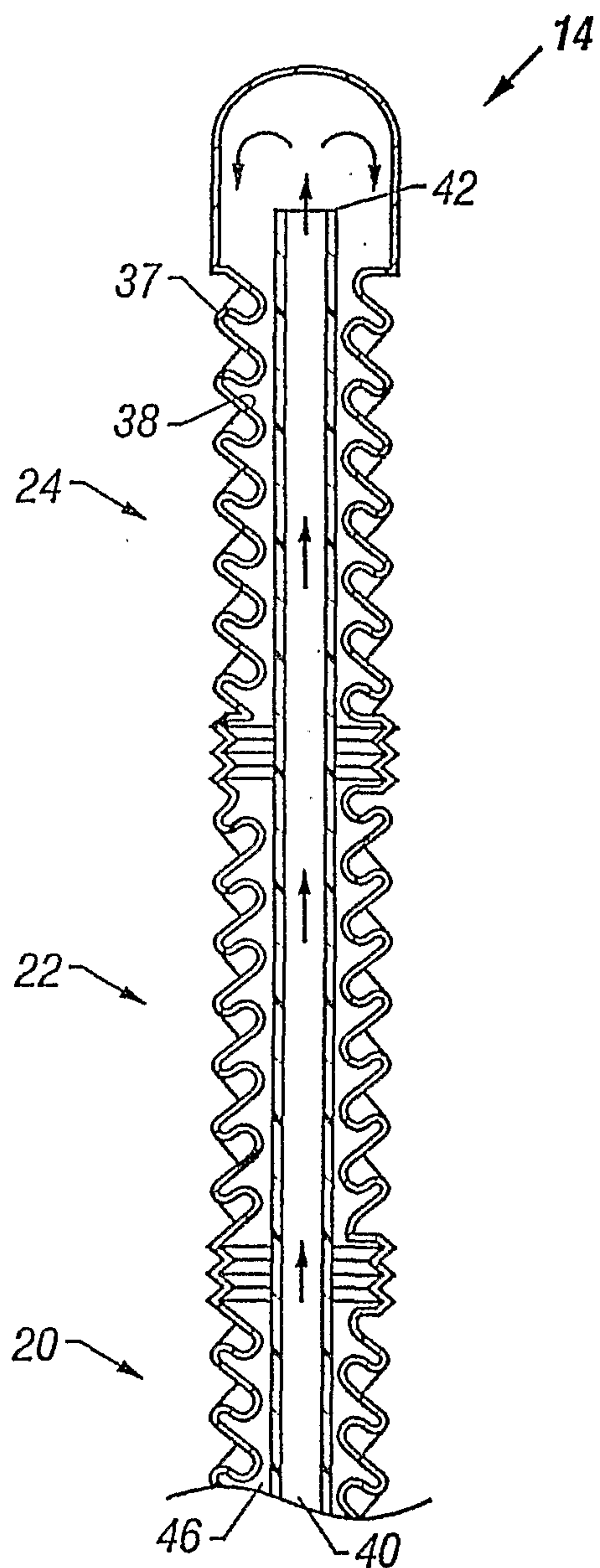


FIG. 2

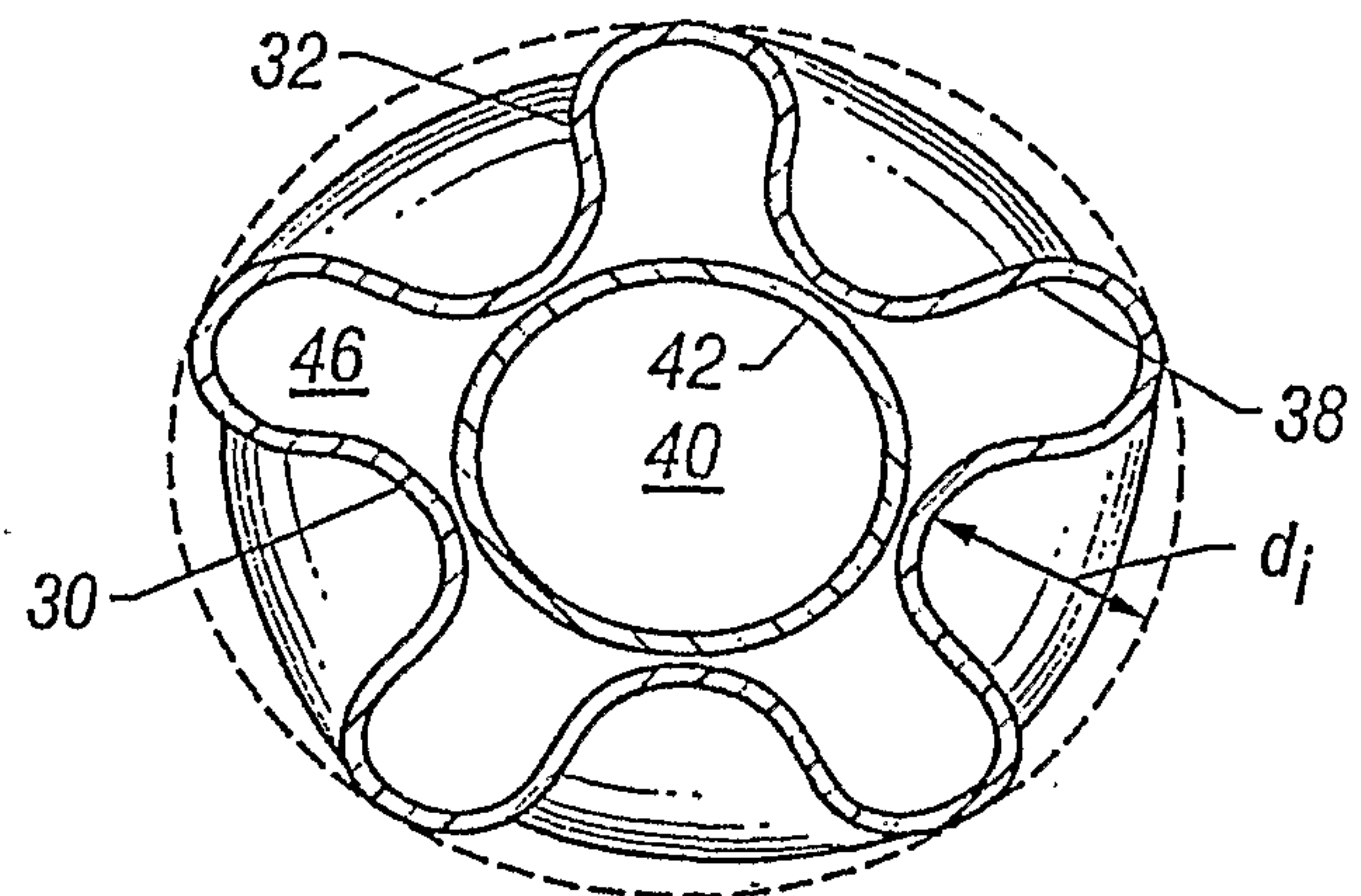


FIG. 3

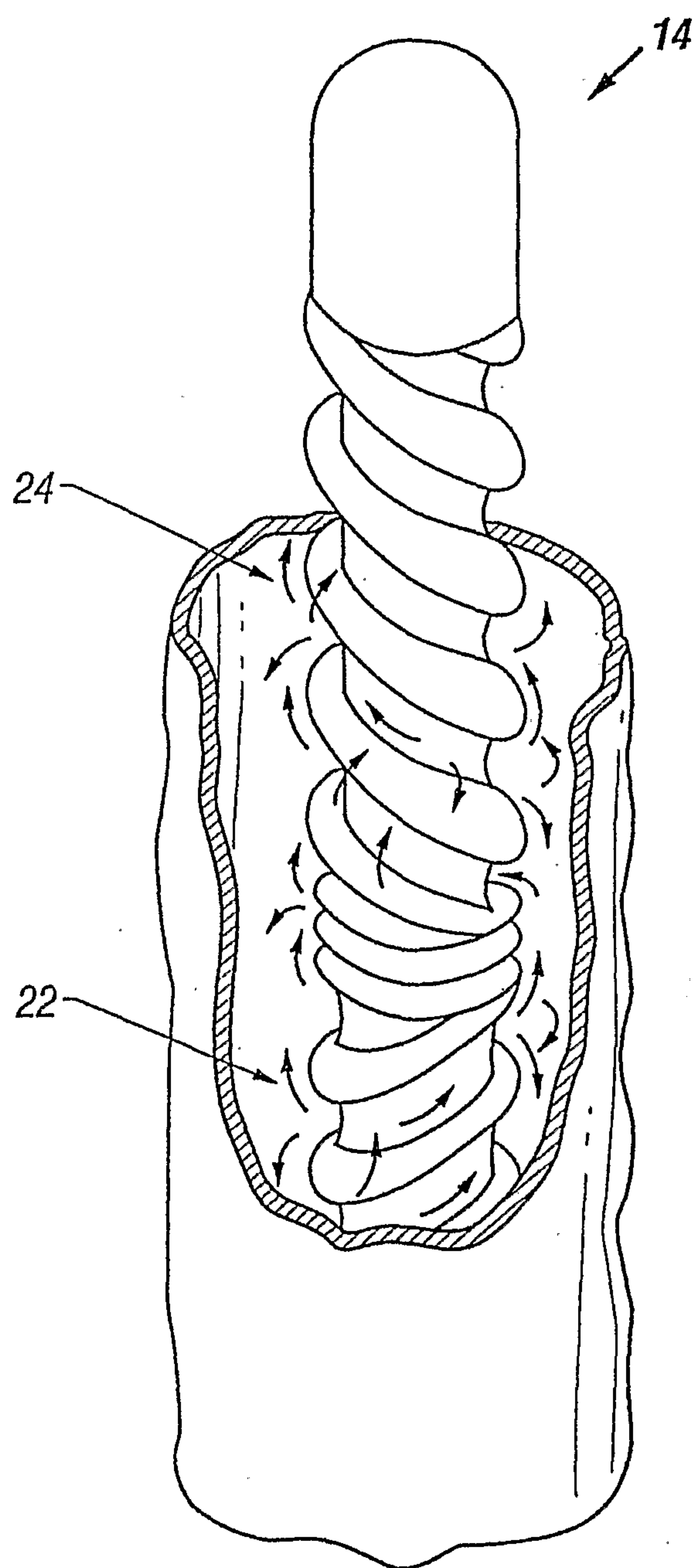


FIG. 4

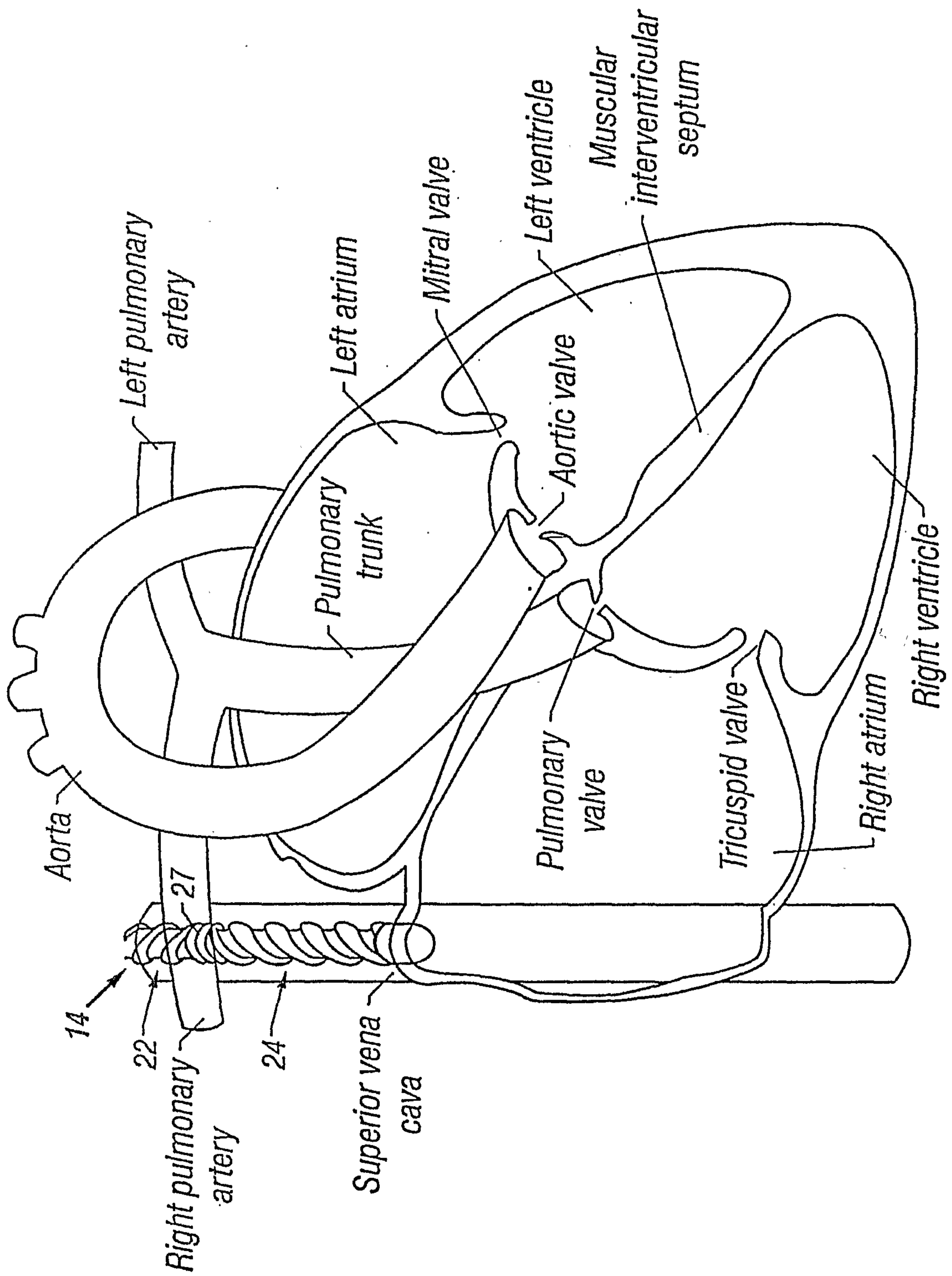


FIG. 5

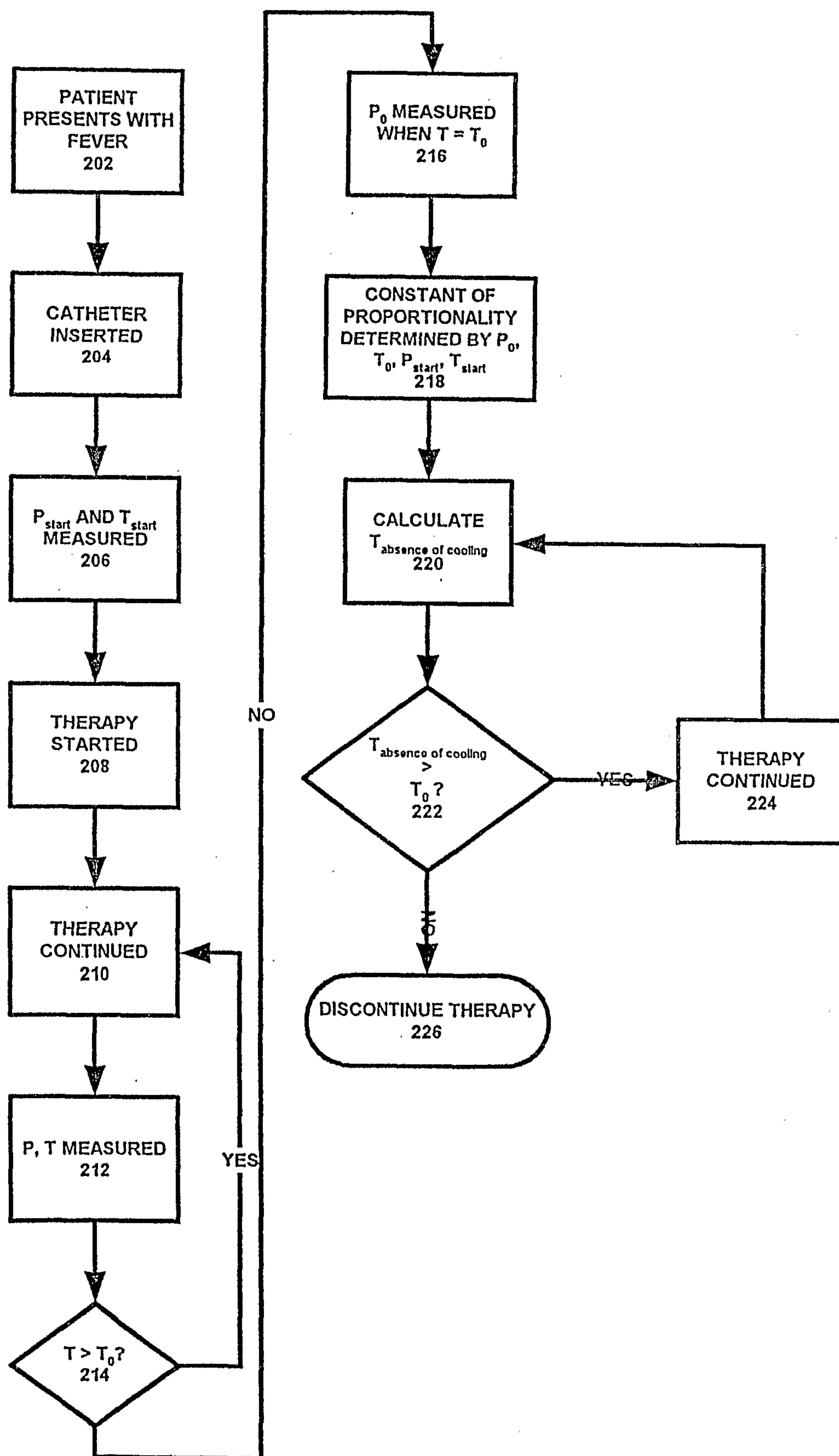


FIG. 6

