

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
6 September 2013 (06.09.2013)



(10) International Publication Number
WO 2013/128013 A9

- (51) International Patent Classification:
A61M 25/00 (2006.01)
- (21) International Application Number:
PCT/EP2013/054203
- (22) International Filing Date:
1 March 2013 (01.03.2013)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
12157765.4 1 March 2012 (01.03.2012) EP
- (71) Applicant: **MEDICAL DEVICE WORKS NV** [BE/BE];
Joseph Wybranlaan 40, B-1070 Brussel (BE).
- (72) Inventors: **FIERENS, Joop**; Vroenenbosstraat 16, B-1653
Dworp (BE). **NACKARD, Jason**; 1801 S Highland Mesa,
Flagstaff, Arizona 86001 (US). **MARCOUX, Eric Thi-**
erry Jean; Alboom 17 bte2, B-1780 Wemmel (BE).
BARTHOLOME, Emmanuel J.; Vlazendaallaan 20, B-
1701 Itterbeek (BE).
- (74) Agent: **BRANTS, Johan Philippe Emile**; Brantsandpat-
ents BVBA, Guldensporenpark 75, B-9820 Merelbeke
(BE).
- (81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU,
RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA,
ZM, ZW.

- (84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

— *with information concerning authorization of rectification
of an obvious mistake under Rule 91.3 (b) (Rule 48.2(i))*

[Continued on next page]

(54) Title: PERFUSION-OCCLUSION DEVICE

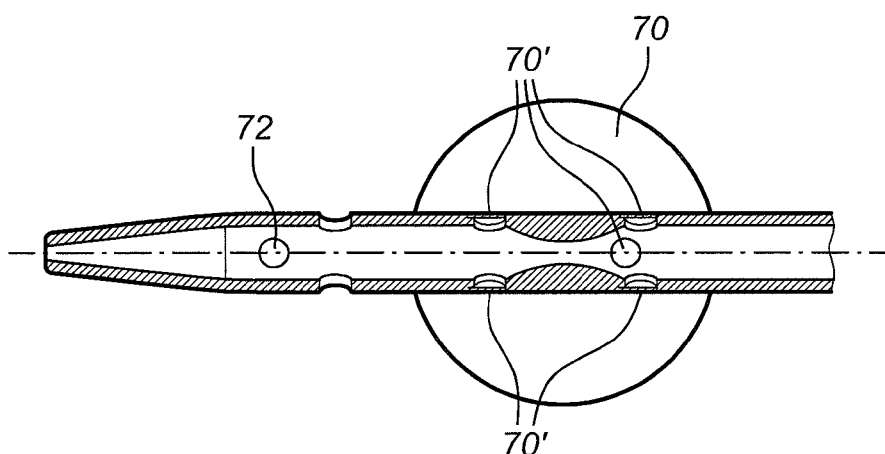


Fig. 11B

(57) Abstract: The present application provides a device for the simultaneous or the separate perfusion and occlusion of a vessel comprising a body having a distal end, a proximal end, a single lumen (66, 80) extending between the proximal end and the distal end, and at least one opening (63, 72) which is in fluid communication with the lumen for delivering a therapeutic treatment to a vessel; and at least one expandable balloon (65, 70, 81) coupled with the body of the device, said balloon is provided with an interior which is in fluid communication with the lumen of the device through at least one opening (68, 69, 70), said opening is provided with at least one valve (71) which is movable from a closed position, in which fluid communication of the lumen with the interior of the balloon is prevented, to an open position in which the lumen is in fluid communication with the interior of the balloon.



WO 2013/128013 A9



(48) Date of publication of this corrected version:

24 October 2013

(15) Information about Correction:

see Notice of 24 October 2013

Perfusion-occlusion device

Field of the invention

5 The present invention generally relates to the field of medical treatment systems. More particularly, the present invention relates to a device for delivering a therapeutic agent to a vessel and thereby to an organ blood flow.

Background

10

Perfusion devices are largely used to deliver a therapeutic treatment to a vessel and thereby to an organ blood flow. Said devices are preferred as they provide minimal invasive tools to allow repetitive perfusion procedures in a relatively short time. Several devices have been developed for the perfusion of a vessel and thereby to an organ blood flow.

15

US 2010/0222637 discloses a catheter comprising a body, at least one expandable balloon and at least one sensor coupled with the body. The body of the catheter comprises a proximal open end, a distal end, a lumen extending between the proximal open end and the distal end, and a plurality of orifices disposed thereon. Each of the orifices is in fluid communication with the lumen of the catheter body. The body of the catheter is configured for placement within a venous vessel. Each of the at least one expandable balloons of the catheter is coupled with the body and comprises an interior that is in fluid communication with the lumen. Further, each expandable balloon is adapted to move between an expanded configuration and a deflated configuration. The body of the catheter may further comprise one or more pores disposed thereon to facilitate fluid communication between the lumen and the interior of each of the expandable balloons. Each of the at least one expandable balloons may be adapted to move from the deflated configuration to the expanded configuration when a fluid flows through the lumen of the body, through the one or more pores, and into the interior of the expandable balloon.

30

US 2004/0249401 discloses a medical device comprising an ultrasonic probe having a proximal end, a distal end and a longitudinal axis there between; a catheter surrounding the ultrasonic probe, the catheter having a proximal end, a distal end and longitudinal axis there between; an inflation lumen located along the longitudinal axis of the catheter; and a balloon supported by the catheter, an inner surface of the balloon is in communication with the inflation lumen. The catheter comprises a catheter tip at the distal end of the catheter and a plurality of fenestrations along a longitudinal axis of the catheter. The balloon engages the catheter at an at least one engagement position along the longitudinal axis of the catheter. A connective tubing engages the catheter at the port and the connective tubing can be opened or closed with one or more valves. The connective tubing is used to deliver a medium to inflate the balloon.

40

The devices of the prior art only allow for the simultaneous perfusion and occlusion of a vessel. When the perfusion is stopped, the occluding element of the device, in general an inflatable balloon, is deflated thereby terminating the occlusion. The perfused therapeutic agent will be partially conveyed to the patient's non-targeted organs through the systemic blood flow. This is disadvantageous for the patient as (i) it leads to a dilution of the perfused therapeutic agent dose which inhibits the effect on the targeted organ (ii) it limits the maximum dose that can be perfused to a targeted organ to the maximum dose leaked out of said organ which can be accepted by other non-targeted organs of the patient's body (iii) the agent will have not enough time to bond to the diseased tissue of the organ, indeed said agent needs optimum conditions to bond or settle in the organ to be treated. In addition, some therapeutic agents are more effective at specific conditions, such as administration at a temperature which is different from the systemic temperature. It is hence beneficial to occlude the vessel for a certain period of time after the therapeutic agent has been delivered. Surgical perfusions wherein blood flow is controlled by clamping off the blood vessel provide a solution for the above mentioned problems. However, said surgical perfusions are invasive traumatic methods, expensive and cannot be repeated on short term. Therefore, there is a need to provide a device for the simultaneous or the separate perfusion and occlusion of a vessel.

An object of the present invention is to provide a solution to overcome at least part of the above mentioned disadvantages. The invention thereto aims to provide a device for the perfusion or the occlusion of a vessel.

Summary of the invention

The present invention provides a device for the simultaneous or the separate perfusion and occlusion of a vessel. The device comprises a body having a distal end a proximal end, a single lumen extending between the proximal end and the distal end, and at least one opening which is in fluid communication with the lumen for delivering a therapeutic treatment to a vessel; and at least one expandable balloon coupled with the body of the device, said balloon is provided with an interior which is in fluid communication with the lumen of the device through at least one opening of the lumen, said opening is provided with at least one valve which is movable from a closed position, in which fluid communication of the lumen with the interior of the balloon is prevented, to an open position in which the lumen is in fluid communication with the interior of the balloon. In a further preferred embodiment, the interior of the balloon is in fluid communication with the lumen of the device through a plurality of openings of the lumen. In a preferred embodiment each of said openings, allowing fluid communication between the balloon interior and the lumen, is provided with a valve.

In a preferred embodiment, the valves are movable from a closed position to an open position in which said valves are completely contained outside the lumen of the device and inside the interior of the balloon.

In a preferred embodiment, the valves are movable from a closed position to an open position in which said valves are at least partially contained inside the lumen of the device. The open position,

in which the valves are at least partially contained inside the lumen of the device, is obtained by creating a negative pressure inside the lumen for deflating the balloon.

5 In a preferred embodiment, the valves are selected from the group comprising pressure-sensitive valve, mechanically steered valves and magnetically steered valves. Preferably said valves are pressure-sensitive valves.

10 In a preferred embodiment, the diameter of the lumen at the distal end is reduced by at least 10% compared to the diameter of the lumen at the proximal end. In a preferred embodiment, the diameter of the lumen at the distal end is of from 1 mm to 3 mm.

15 In a preferred embodiment, the perfusion rate of the device is at least 50 ml/min. In a preferred embodiment, the distal end of the device is a closed end. The proximal end of the device is an open end.

In a preferred embodiment, the opening, which is in fluid communication with the lumen for delivering a therapeutic treatment to a vessel, is positioned proximal to the proximal end of the balloon and/or distal to the distal end of the balloon.

20 In a preferred embodiment, the body is made of a material selected from the group comprising silicone, polyvinyl chloride and rubber. In a preferred embodiment, the valves are made of the same material as the body of the device.

25 In a preferred embodiment, the valves are made of a material different than the material of the body of the device.

In a preferred embodiment, the balloon is made of the same material as the body and/or the valves of the device.

30 In a preferred embodiment, the balloon is made of a material different than the material of the body and/or the valves of the device.

35 The device of the present invention presents several advantages. The device is of a small size and is flexible which allows its introduction into tortuous vessels to be positioned close to or in an organ. Hence, the device allows the simultaneous or the separate perfusion AND occlusion of very small and tortuous vessels. Said small device allows high rate perfusions and provides for minimal invasive perfusion. In addition, the device is a single lumen device which reduces its cost as less material will be used for the production. Furthermore, the device of the present invention provides a tool for the simultaneous perfusion and occlusion of a vessel and for the separate occlusion of the
40 vessel when the perfusion is terminated, thereby enhancing the efficiency of the delivered therapeutic agent.

Description of the figures

Fig. 1 illustrates an embodiment of the second medical device in the expanded state comprising a tubular member (dumb-bell shaped) attached to a catheter. **FIG. 1A** shows a transverse cross-section across the catheter where the pusher means is a pusher rod. **FIG. 1B** shows a transverse cross-section across the catheter where the pusher means is formed from the wall of the inner tube.

Fig. 1C illustrates another embodiment of the second medical device in the expanded state comprising a tubular member (dumb-bell shaped) attached to a catheter. The liner is attached to the inner wall of the tubular member.

Fig. 1D illustrates a side view of another embodiment of the second medical device wherein the distal end of the inner tube have a cup or a spoon shape **Fig. 1E** illustrates a top view of the same embodiment **Fig. 1F** illustrates a cross-section view along A-A shown in **Fig. 1D**.

Fig 1G illustrates another embodiment of the second medical device in the expanded state wherein the device has a bell shape.

Fig. 2A illustrates an embodiment of the second medical device of **Fig. 1** where the tubular member is in its collapsed, compressed state and is provided with a closed tip.

Fig. 2B illustrates another embodiment of the second medical device of **Fig. 1** where the tubular member is in its collapsed, compressed state and is provided with a conical closed tip.

Fig. 3 illustrates the second medical device which has been placed in situ, wherein: **A** illustrates a liner on the exterior of the carrier, and **B** illustrates a liner on the interior of the carrier.

Fig. 3 C and **D** illustrate the use of the second medical device for the delivery of a therapeutic agent to the right and left lung respectively. **Fig. 3 E** and **F** illustrate the use of the second medical device having a bell shape for the delivery of a therapeutic agent to the right and left lung respectively.

Fig. 4 illustrates an embodiment of the kit wherein the first medical device, the second medical device and the separation device are used for delivering a therapeutic agent and removing the therapeutic agent excess from the liver.

Fig. 5 illustrates the second medical device when introduced in the vena cava.

Fig. 6 illustrates an embodiment showing the position of the separation device within the second medical device.

Fig. 7 illustrates another embodiment showing the position of the separation device within the second medical device.

Fig. 8 detailed schematic illustration of the first medical device.

Fig. 9 detailed schematic illustration of an embodiment of the third medical device.

Fig. 10 detailed schematic illustration of another embodiment of the third medical device.

Fig. 11A and **Fig. 11B** illustrates an embodiment of the first medical device.

Fig. 11C, Fig. 11D and **Fig. 11E** illustrate an embodiment of the first medical device wherein each opening allowing fluid communication of the lumen with the interior of the balloon is provided with a valve.

Fig. 11F illustrates an embodiment of the first medical device wherein the lumen diameter at the distal end of the device is not reduced compared to the proximal diameter of the lumen and wherein each opening allowing fluid communication of the lumen with the interior of the balloon is provided with a valve, said valves are pressure-controlled or pressure sensitive.

Fig. 11G illustrates an embodiment of the first medical device wherein the lumen diameter at the distal end of the device is not reduced compared to the proximal diameter of the lumen and wherein each opening allowing fluid communication of the lumen with the interior of the balloon is provided with a valve, said valves controlled using an internal plug.

Fig. 11H illustrates an embodiment of the first medical device wherein the lumen diameter at the distal end of the device is not reduced compared to the proximal diameter of the lumen and wherein each opening allowing fluid communication of the lumen with the interior of the balloon is provided with a valve, said valves are magnetically controlled.

Fig. 12A and **Fig. 12B** longitudinal cross-section view of the first medical device

Fig. 13 illustrates an embodiment of the third medical device.

Fig. 14 is a schematic view of a system that can be used to perfuse a medical treatment through an organ. The system can be controlled by an algorithm.

Fig. 15 is a flowchart of an algorithm that can be used to control the perfusion system of **Fig.14**.

Fig. 16A shows a vessel having a lesion **Fig. 16B** shows the second retrievable medical device introduced in the vessel having a lesion.

Detailed description of the invention

Unless otherwise defined, all terms used in disclosing the invention, including technical and scientific terms, have the meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. By means of further guidance, term definitions are included to better appreciate the teaching of the present invention.

As used herein, the following terms have the following meanings:

"A", "an", and "the" as used herein refers to both singular and plural referents unless the context clearly dictates otherwise. By way of example, "a compartment" refers to one or more than one compartment.

"About" as used herein referring to a measurable value such as a parameter, an amount, a temporal duration, and the like, is meant to encompass variations of +/-20% or less, preferably +/-10% or less, more preferably +/-5% or less, even more preferably +/-1% or less, and still more preferably +/-0.1% or less of and from the specified value, in so far such variations are appropriate to perform in the disclosed invention. However, it is to be understood that the value to which the modifier "about" refers is itself also specifically disclosed.

"Comprise," "comprising," and "comprises" and "comprised of" as used herein are synonymous with "include", "including", "includes" or "contain", "containing", "contains" and are inclusive or open-ended terms that specifies the presence of what follows e.g. component and do not exclude or preclude the presence of additional, non-recited components, features, element, members, steps, known in the art or disclosed therein.

The recitation of numerical ranges by endpoints includes all numbers and fractions subsumed within that range, as well as the recited endpoints.

The expression "% by weight" (weight percent), here and throughout the description unless otherwise defined, refers to the relative weight of the respective component based on the overall weight of the formulation.

The term "therapeutic agent" is used herein to refer to a treatment fluid or particles delivered to a patient's organ.

The terms "particles", "microspheres" and "beads" are used herein as synonyms and refer to an object that is substantially spherical in shape and has a diameter less than 1 millimeter.

The term "glass" refers to a hard, brittle, non-crystalline, inorganic substance, which is usually transparent; glasses are often made by fusing silicates with soda, as described by Webster's New World Dictionary. Ed. Guralnik, D B 1984.

The terms "inflow" and "outflow" herein refer respectively to the blood flowing inside an organ and the blood flowing outside an organ.

5 The present invention provides a device for the simultaneous or the separate perfusion and occlusion of a vessel. Said device is herein also called first retrievable medical device. The device comprises a body having a distal end a proximal end, a single lumen extending between the proximal end and the distal end, and at least one opening which is in fluid communication with the lumen for delivering a therapeutic treatment to a vessel; and at least one expandable balloon coupled with the body of the device, said balloon is provided with an interior which is in fluid
10 communication with the lumen of the device through at least one opening of the lumen, said opening is provided with at least one valve which is movable from a closed position, in which fluid communication of the lumen with the interior of the balloon is prevented, to an open position in which the lumen is in fluid communication with the interior of the balloon. In a further preferred embodiment, the interior of the balloon is in fluid communication with the lumen of the device
15 through a plurality of openings of the lumen.

The device of the present invention is suitable to be used in a kit for the delivery a therapeutic agent to an organ blood flow and the removal of the excess of said therapeutic agent from said organ blood flow. The kit comprises:

- 20 (a) optionally the therapeutic agent,
(b) a first retrievable medical device, for delivering said therapeutic agent into the organ artery blood, comprising a catheter and an injection device such as a syringe, said catheter have a proximal end, a distal end and a lumen; the distal end is in fluid communication with the proximal end via the lumen; said injection device is suitable to be connected to the proximal end of the
25 catheter,
(c) a second retrievable medical device for isolating the organ vein blood, having a distal end and a proximal end; said second medical device comprises a catheter at the distal end suitable for deploying a self-expanding hollow tubular member at the proximal end of the device; the proximal end of the tubular member is attached to the distal end of the catheter ; said tubular member is
30 configured to expand radially to form a central part flanked by two annular ridges, a distal annular ridge and a proximal annular ridge; the tubular member comprises a liquid-impermeable area disposed with one or more fluid ports for the collection of organ vein and two liquid-permeable regions, one distal to the distal annular ridge and one proximal to the proximal annular ridge so forming a passageway between the distal end and the proximal end of the tubular member for the
35 flow the organ blood devoid of therapeutic agent, whereby the liquid-impermeable area is disposed in an area defined by the region flanked by the annular ridges, the distal annular ridge and at least part of the proximal annular ridge for isolating organ vein blood containing therapeutic agent excess from the organ blood flow devoid of therapeutic agent, and
(d) a separation device comprising at least one filter able to separate the therapeutic agent excess
40 from the organ vein blood, having an inlet for the organ vein blood having a particle excess and an outlet for filtered organ vein blood.

The kit, devices and method of the present invention will be further detailed for a treatment of the liver and/or the lungs. However, any other organ can be treated using the kit, devices and method of the present invention. For liver treatment, the kit is intended to control blood flow in and/or out of the hepatic veins, while maintaining continuous blood flow through the inferior vena cava. The kit is used to collect the hepatic vein outflow in order to filter chemotherapy, particles or a fluid treatment or any other therapeutic agent.

Therapeutic agent

The therapeutic agent of can be a treatment fluid or particles or beads containing said treatment. Particles are known for the person skilled in the art and for instance described in US 2004/197264, the content of which is incorporated herein by reference. The particles comprise a material selected from the group consisting of glass, polymer and resin; a first radioisotope that emits a therapeutic [beta]-particle; and a second radioisotope that emits a diagnostic [gamma]-ray; wherein the atomic number of the first radioisotope is not the same as the atomic number of the second radioisotope. In a preferred embodiment of the present invention, the particles are beads comprising a radioactive element, preferably polymer or glass beads. It is to be understood that the therapeutic agent can be used with any device suitable to deliver said agent to an organ blood flow.

The particles are used to treat organ tumors. The particles are delivered into the organ blood flow through an artery of the organ to be treated. The radioactive particles are selectively implanted in the microvascular supply of the tumor wherein they become trapped. The particles emit beta radiation for a certain period of time which will kill the tumor.

The particles might be used to treat liver cancer for instance. Patients with primary or metastatic tumors can be treated by radio-embolization via a catheter which tip is placed in the hepatic artery. A direct injection of beads into the tumor is also possible using a needle. The spheres eventually lodge in the microvasculature of the liver and tumor, remaining until the complete decay of the radioisotope.

The diameter of said particles is in the range from about 1-500 micrometers, preferably 2-400 micrometers, more preferably 4-300 micrometers, most preferably 5-200 micrometers. The diameter of said particles can be any value comprised within the mentioned ranges.

In a further preferred embodiment, the size of the particles is comprised between 10 and 300 micrometers, preferably between 15 and 200 micrometers, more preferably between 20 and 60 micrometers, most preferably the particles size is around 30 micrometers.

Preferably the diameter of said particles is comprises between 50 and 70 micrometers, more preferably between 40 and 60 micrometers, most preferably around 30 micrometers.

First retrievable medical device

The first medical device (**26, FIG. 4**) of the present invention is a device used for the introduction of the therapeutic agent into the patient's body, more in particular into an organ blood flow of the patient. The therapeutic agent may be administered to the patient through the use of syringes or catheters either alone or in combination with vasoconstricting agents or by any other means of administration that effectively causes the microspheres to become embedded in the cancerous or tumor-bearing tissue (U.S. Pat. No. 5,302,369; incorporated herein by reference).

The device can be used for the simultaneous or the separate perfusion and occlusion of a vessel, thereby occluding and/or delivering a therapeutic agent to an organ blood flow while occluding the natural inflow. Said device comprises a body having a distal end; a proximal end; a single lumen through which a fluid is delivered to said vessel, said lumen is extending between the proximal end and the distal end; and at least one opening which is in fluid communication with the lumen for delivering a therapeutic treatment to the vessel and thereby to the organ blood flow. In a preferred embodiment, the body of the device is provided with a plurality of openings which are in fluid communication with the lumen for delivering a therapeutic treatment to the vessel and thereby to the organ blood flow.

The device also comprises at least one expandable balloon coupled with the body of the device, said balloon is provided with an interior which is in fluid communication with the lumen of the device through at least one opening, said opening is provided with at least one valve which is movable from a closed position in which fluid in the lumen is prevented from flowing to the interior of the balloon to an open position, in which fluid in the lumen flows to the interior of the balloon, thereby moving the balloon from a deflated configuration to an inflated configuration. The valve is herein movable from a closed position to an open position wherein the valve is completely contained outside the lumen of the device and inside the interior of the balloon.

The presence of valves is advantageous as the device allows maintaining the balloon in expanded state even if the perfusion flow and/or pressure is low or is inexistent. This is in contradiction with the devices of the prior art wherein the balloon is deflated as soon as the perfusion is stopped or when the perfusion fluid and/or pressure is very low.

The valve is also movable from a closed position in which fluid in the interior of the balloon is prevented from flowing to the lumen, to an open position in which fluid flows from the interior of the balloon to lumen of the device, thereby moving the balloon from an inflated configuration to a deflated configuration. The valve is herein movable from a closed position to an open position wherein the valve is at least partially contained inside the lumen of the device.

In a preferred embodiment, the lumen of the device is provided with a plurality of openings which are in fluid communication with the interior of the balloon. Each of said openings is provided with at least one valve.

The device will be further described as a device having openings provided with pressure-sensitive valves. However, it is to be understood that any other valves known to the person skilled in the art are suitable to be used and are enclosed by the description. Said valves can for instance be mechanically steered valves or magnetically steered valves.

In a preferred embodiment, the distal end of the device is a closed end. The proximal end is an open end suitable to be connected to at least one injection means for injecting the therapeutic agent into the lumen of the device. Said injection means can be a syringe or any other means known to the person skilled in the art. In a further preferred embodiment, the device is provided at its proximal end with a grip area to facilitate the handling of the device by the practitioner. Said grip area can be of any design and any material known to the person skilled in the art.

The first retrievable medical device (**26, FIG. 4**) is preferably a catheter. For liver tumor treatment, said catheter will be introduced in the hepatic artery (HA). The insertion of said catheter occurs via the right femoralis artery into the hepatic communis artery.

The openings, which are in fluid communication with the lumen for delivering a therapeutic treatment to a vessel or an organ blood flow, can be positioned proximal to the proximal end of the balloon. This means that the openings are positioned on the body of the device between the proximal end of the device and the balloon. Said openings can be positioned distal to the distal end of the balloon, meaning that the openings are positioned on the body of the device between the balloon and the distal end of the device. Said openings can also be positioned distal to the distal end of the balloon and proximal to the proximal end of the balloon.

In a preferred embodiment, the first medical device (**26, FIG. 4**) allows shunt debits in the range of 10 – 500 cc/min allowing slow supply of agents with unwanted tissue reactions, like spasms, and higher flows for bolus treatments.

In a preferred embodiment, the perfusion rate of the device is at least 20 ml/min, preferably at least 40 ml/min, more preferably at least 50 ml/min, even more preferably at least 70 ml/min, most preferably at least 80 ml/min or at least any value comprised between the mentioned values. The perfusion rate is at most 90 ml/min, preferably at most 110 ml/min, more preferably at most 120 ml/min, even more preferably at most 130 ml/min, even more more preferably at most 150 ml/min, even most preferably at most 180 ml/min, even most preferably at most 200 ml/min or at most any value comprised between the mentioned values.

In a preferred embodiment, the first medical device has a small size and is a flexible device such as it can be positioned following torturous pathways. The diameter of said device is comprised between 1 and 5 mm, preferably between 1.5 and 4 mm, more preferably between 1.6 and 3 mm, most preferably between 5F (= about 1.67 mm) and 7F (= about 2.3 mm).

In a preferred embodiment, the lumen diameter at the distal end of the device is reduced by at least 10%, compared to the diameter of the lumen at the proximal end of the device. The lumen diameter at the distal end of the device is preferably reduced by at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or any value comprised between these values, compared to the lumen diameter at the proximal end of the device. The lumen diameter reduction is advantageous as it creates, in a short time, a pressure inside the lumen leading to a fast expansion of the balloon due to the entry of the fluid in the interior of the balloon through the opening of the device body which is in fluid communication with said balloon.

In a preferred embodiment, the diameter of the lumen at the distal end is of from 1 mm to 3 mm, preferably from 1.2 mm to 2.5 mm, more preferably from 1.5 to 2 mm.

The length of the device is about 600 mm, preferably about 700 mm, more preferably about 800 mm, most preferably about 900 mm, even most preferably about 1000 mm. The length of the device allows the positioning of the device close to, or in, an organ. The device provides for the control of the blood flow through the targeted organ and provides a non-limited infusion/perfusion debit.

In a preferred embodiment, the length of the device having a reduced lumen diameter is of from 50 to 300 mm, preferably from 70 to 250 mm, more preferably from 100 to 200 mm, most preferably about 150 mm. The balloon can be coupled to the body of the device where the lumen has a reduced diameter or to the body of the device where the diameter of the lumen is not reduced.

The device is shown in **Fig. 11A** and comprises a grip area **67**, a proximal end **Y**, a distal end **X**, a single lumen **66** and at least one balloon **65**. The expansion of the balloon is induced and controlled by the infusion/perfusion liquid. The device can occlude, at least partly and/or temporarily, the vessel to control the blood flow and to inject a therapeutic agent into that organ in flow rates of at least 20 ml/min. During delivery of the therapeutic agent into the vessel, the infusion/perfusion liquid containing said therapeutic agent flow in the lumen **66** and inflates the balloon **65** by flowing through the openings **68** and **69** (**FIG. 11A**) to the interior of the balloon **65**.

Fig. 11B shows another embodiment of the catheter wherein the openings **70'** allow the flow of the infusion/perfusion liquid to the interior of the balloon leading to the expansion of said balloon **70**. Said openings are provided with a plurality of valves **71** as shown in **Fig. 11C, 11D** and **11E**. Said valves **71** are located on the surface of the openings. When the perfusion liquid is injected, a pressure is created in the lumen of the device. Said pressure is created in a short time as the distal end of lumen has a reduced diameter compared to its proximal end. The pressurized liquid forces the valves, initially in a closed position shown in **Fig. 11B**, to be in an open position in which they are completely contained outside the lumen and inside the interior of the balloon as shown in **Fig. 11C**. The pressurized liquid opens the pressure-sensitive valves **71** and accumulates in the interior of the balloon **70** thereby inflating it as illustrated by the arrows in **Fig. 11C**. When the injection of

the perfusion liquid is terminated the valves **71** close and the balloon remains in an inflated state (**Fig. 11D**). This allows maintaining the occlusion of the vessel after completion of the perfusion and before retrieving the device from the vessel. Optimal conditions, such as time and temperature, can hence be provided to ensure an optimal use of the therapeutic agent. When the device is to be retrieved at the end of the treatment, a negative pressure is created inside the lumen of the device which leads to the opening of the valves **71** inside the lumen and to the deflation of the balloon **70** (**Fig. 11E**). The valves are made of any suitable flexible material such as but not limited to silicone. A pull can be provided in the device to control the opening and closing of the valves.

Fig. 12A shows the device when the balloon **81** is not in an expanded state, i.e. in a deflated state. The lumen **80** diameter is reduced at one end **82** which is the distal end **X** of the catheter. The narrowed end can be provided with a conical tip. Reducing the diameter at one end of the catheter, i.e. the distal end, leads to a pressure increase during the perfusion and/or delivery of the therapeutic agent. The latter accelerates the expansion of the balloon. The diameter reduction ensures that the balloon segment will expand at minimal defined flows. The diameter at the end **82** of the catheter is reduced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or any value comprised between these values, compared to the diameter of the lumen to assure the expansion of the balloon during perfusion. **Fig. 12B** shows the catheter when the balloon **81** is in an expanded state due to the flow of the infusion/perfusion liquid in the lumen **80**. Said infusion/perfusion liquid creates a pressure inside the lumen due to the reduced diameter at the distal end. Said fluid and fluid pressure leads to the inflation of the balloon **81**.

In other embodiments, at least one guidewire and/or other means can be used to increase and/or lower the perfusion fluid pressure inside the lumen of the device, thereby opening the valves leading to the inflation of the balloon or to the deflation of the balloon.

Fig. 11F illustrates an embodiment of the first medical device wherein the lumen diameter at the distal end **X** of the device is not reduced compared to the proximal diameter **Y** of the lumen. Each opening allowing fluid communication of the lumen with the interior of the balloon **70** is provided with a valve **71**; said valves are pressure-controlled or pressure sensitive. Having a non-reduced lumen will increase the flow of the perfusate compared to use of a device having a reduced lumen diameter at the distal end of the device. This allows a reduction of the perfusion time.

In a preferred embodiment, the tip **151** of the device is provided with a guidewire **150** having a means **152** for locking the tip **151** to the catheter. Said means can for instance be a knot or any other means known to the person skilled in the art. When perfusion starts, the pressure inside the lumen **166** will increase due to the presence of the closed tip **151**. The valves **171** will open and the fluid will accumulate in the balloon leading to the inflation of said balloon **170**. The guidewire can then be moved in a direction which is from the proximal end **Y** to the distal end **X** of the device **X**. By moving the guidewire, the tip **151** will be unlocked and moved in the same direction as the guidewire and away from the catheter body. This leads to the decline of the pressure inside the lumen **166** which results in the closure of the valves **171**. The perfusion rate of the organ is

ensured by the opening created when the tip is pushed away from the catheter body but also because said opening has the same diameter as the lumen. At the end of the perfusion procedure, the guide wire **150** is pulled back until the tip **151** is locked to the catheter body. The pressure can be reduced inside the lumen and/or a negative pressure can be created inside said lumen **166**, thereby deflating the balloon **170**. The device with the guidewire and the tip can then be retrieved from the subject's body.

Fig. 11G illustrate an embodiment of the first medical device wherein the lumen diameter at the distal end **X** of the device is not reduced compared to the proximal diameter **Y** of the lumen. Each opening allowing fluid communication of the lumen with the interior of the balloon **70** is provided with a valve **71**, said valves controlled using an internal plug.

In a preferred embodiment, the device is positioned in the desired vessel using a retrievable guidewire. Said guidewire is afterwards retrieved and a rod **154** with a plug **153** is introduced in the lumen **166** of the device. The plug **153** will occlude the distal end of the lumen. The size of said plug **153** is smaller than the lumen **166** of the catheter. Preferably the diameter of said plug is at least 1% smaller than the diameter of said lumen **166**. When perfusion starts, the pressure inside the lumen **166** will increase due to the presence of the plug **153**. The valves **172** will open and the fluid will accumulate in the balloon leading to the inflation of said balloon **170**. The rod **154** and the plug **153** can then be retrieved from the device. This leads to the decline of the pressure inside the lumen **166** which results in the closure of the valves **172**. The perfusion rate of the organ is ensured by the opening created when the rod **154** and the plug **153** are retrieved from the catheter body but also because said opening has the same diameter as the lumen. At the end of the perfusion procedure, the rod **154** and the plug **153** are inserted in the catheter via the lumen **166**. The pressure can be reduced inside the lumen and/or a negative pressure can be created inside said lumen **166**, thereby deflating the balloon **170**. The rod **154**, the plug **153** and the device can then be retrieved from the subject's body. In a preferred embodiment, the rod **154** is permanently fixed to the plug **153**. In another preferred embodiment, the rod **154** is dismountably fixed to the plug **153**. This allows the adaptation of the plug size to different devices having different lumen diameter.

Fig. 11H illustrate an embodiment of the first medical device wherein the lumen diameter at the distal end **X** of the device is not reduced compared to the proximal diameter **Y** of the lumen. Each opening allowing fluid communication of the lumen with the interior of the balloon **70** is provided with a valve **71**, said valves are magnetically controlled.

In a preferred embodiment, the device is positioned in the desired vessel using a retrievable guidewire. Said guidewire is afterwards retrieved and a rod **156** having at least one magnetic means **157** and a stopper **155** is introduced in the lumen **166** of the device. The size of said stopper **155** is smaller than the lumen **166** of the catheter. Preferably the diameter of said stopper is at least 1% smaller than the diameter of said lumen **166**. During the introduction of the rod **156**, the magnetic means will open the valves **173** and the stopper **155** will occlude the distal end of the lumen **166**. When perfusion starts, the pressure inside the lumen **166** will increase due to

the presence of the stopper **155**. The fluid will accumulate in the balloon leading to the inflation of said balloon **170**. The rod **156** and the stopper **155** can then be retrieved from the device. This leads to the decline of the pressure inside the lumen **166** which results in the closure of the valves **173**. The perfusion rate of the organ is ensured by the opening created when the rod **156** and the stopper **155** are retrieved from the catheter body but also because said opening has the same diameter as the lumen.

At the end of the perfusion procedure, the rod **156** and the stopper **155** are inserted in the catheter via the lumen **166**. The pressure can be reduced inside the lumen and/or a negative pressure can be created inside said lumen **166**, thereby deflating the balloon **170**. The rod **156**, the stopper **155** and the device can then be retrieved from the subject's body. In a preferred embodiment, the rod **156** is permanently fixed to the stopper **155**. In another preferred embodiment, the rod **156** is dismountably fixed to the stopper **155**. This allows the adaptation of the stopper size to different devices having different lumen diameter.

In a preferred embodiment, the device according to the present invention allows the withdrawal of fluid from the vessel or the organ into which said device is introduced. This is due to the fact that the balloon of the device can be maintained inflated even in the absence of perfusion flow inside the lumen of the device. The balloon can be maintained inflated thanks to the presence of the valves which makes the occlusion of the vessel independent from the perfusate flow rate in the lumen of the device.

It is to be understood that devices comprising any type of valve described herein is suitable to be used for the simultaneous or the separate perfusion and occlusion of a vessel and in addition said devices are suitable to be used for the withdrawal or drainage of fluid from said vessel.

The device body is made of a biocompatible materials generally applied for short term (< 120 minutes) endovascular procedures. The balloon **81** can be the most flexible part of the catheter, for instance by having smaller wall thickness, or made from other materials bonded to the catheter. The device according to the present invention is a percutaneous device having a minimum quantity of material to ensure the vessel occlusion, to increase the flexibility and maximize the infusion/perfusion flow.

Fig. 8 shows the catheter having a guide wire **52** and a lumen **51**. The balloon is substantially spherical and is positioned at the distal end **X** of the device. The length **c** of the expanded balloon is about 10 mm. The catheter comprises a tube **44**, also called a body, having a lumen **51**. The diameter **j** of said tube **44** is about 2.5 mm. The diameter **e** of distal end **X** portion of the first retrievable medical device is about 2 mm said portion extends over a length **g** of about 150 mm. The length **h** of the catheter is about 900 mm. The tube **44** is provided at the proximal end **Y** with a female luer adapter **49**. At the distal end **X**, the tube **44** is provided with a balloon that inflates when the user pushes the inflation bladder **47**. The latter is provided with an inflation check valve **46** and a male luer adapter **48**. The inflation bladder **47** is connected to the catheter via a female luer adapter **49** and a connector tube **50**. It is to be understood that the presence of the inflation

bladder is optional. The balloon of the device can be inflated by the therapeutic agent through openings which are in fluid connection with the interior of the balloon as described above. Said openings can be provided with valves also as described above.

- 5 In a preferred embodiment, the guide wire can be used to increase the perfusion pressures to support inflation or deflation of the balloon, or can be used to trigger the valves to open or to close.

- 10 In a preferred embodiment, the body of the device is made of a material selected from the group comprising silicone, polyvinyl chloride and rubber.

In a preferred embodiment, the valves are made of the same material as the body of the device. Preferably, the valves are made of silicone. Said valves can be made of a material different from the material of the body of the device.

- 15 In a preferred embodiment, the balloon is made of the same material as the body of the device and/or the valves. Said balloon can be made of a material different from the material of the body of the device and/or the valves.

- 20 When liver is treated for example, the main blood vessels connected to the liver are occluded: the vena porta (PV, hepatic portal vein) using the third retrievable medical device, hepatic artery (HA) using the first retrievable medical device and hepatic vein (HV) using the second retrievable medical device to achieve site specific blood isolation and collection. The isolation of the liver vascular system makes it possible to reach high local chemotherapy concentration. The introduction of the third retrievable medical device and the first medical device can be achieved by means of an introducer sheath.

- 25 Although the present invention has been described with reference to preferred embodiments thereof, many modifications and alternations may be made by a person having ordinary skill in the art without departing from the scope of this invention which is defined by the appended claims.

Claims

1. A device for the simultaneous or the separate perfusion and occlusion of a vessel comprising:
 - a body having a distal end (X), a proximal end (Y), a single lumen (66, 80) extending between the proximal end (Y) and the distal end (X), and at least one opening (63, 72) which is in fluid communication with the lumen for delivering a therapeutic treatment to a vessel; and
 - at least one expandable balloon (65, 70, 81) coupled with the body of the device, said balloon is provided with an interior which is in fluid communication with the lumen (66, 80) of the device through at least one opening (68, 69, 70'), said opening (68, 69, 70') is provided with at least one valve which is movable from a closed position, in which fluid communication of the lumen with the interior of the balloon is prevented, to an open position in which the lumen is in fluid communication with the interior of the balloon.
2. The device according to claim 1, wherein the valve is movable from a closed position to an open position in which said valve is completely contained outside the lumen (66, 80) of the device and inside the interior of the balloon (65, 70, 81).
3. The device according to any of the preceding claims, wherein the valve is movable from a closed position to an open position in which said valve is at least partially contained inside the lumen (66, 80) of the device.
4. The device according to any of the preceding claims, wherein the valve is selected from the group comprising pressure-sensitive valve, mechanically steered valve and magnetically steered valve.
5. The device according to any of the preceding claims, wherein the open position, in which the valve is at least partially contained inside the lumen (66, 80) of the device, is obtained by creating a negative pressure inside the lumen for deflating the balloon.
6. The device according to any of the preceding claims, wherein the diameter of the lumen (66, 80) at the distal end (X) is reduced by at least 10% compared to the diameter of the lumen (66, 80) at the proximal end (Y).
7. The device according to any of the preceding claims, wherein the diameter of the lumen (66, 80) at the distal end (X) is of from 1 mm to 3 mm.
8. The device according to any of the preceding claims, wherein the perfusion rate is at least 50 ml/min.
9. The device according to any of the preceding claims, wherein the opening (63, 72), which is in fluid communication with the lumen (66, 80) for delivering a therapeutic treatment to a vessel,

is positioned proximal to the proximal end (Y) of the balloon (65, 70, 81) and/or distal to the distal end (X) of the balloon (65, 70, 81).

- 5
10. The device according to any of the preceding claims, wherein the distal end (X) is a closed end.
11. The device according to any of the preceding claims, wherein the body is made of a material selected from the group comprising silicone, polyvinyl chloride and rubber.
- 10 12. The device according to any of the preceding claims, wherein the valves are made of the same material as the body of the device.
13. The device according to any of the preceding claims, wherein the valves are made of a material different than the material of the body of the device.
- 15 14. The device according to any of the preceding claims, wherein the balloon is made of the same material as the body and/or the valves of the device.
15. The device according to any of the preceding claims, wherein the balloon is made of a material different than the material of the body and/or the valves of the device.

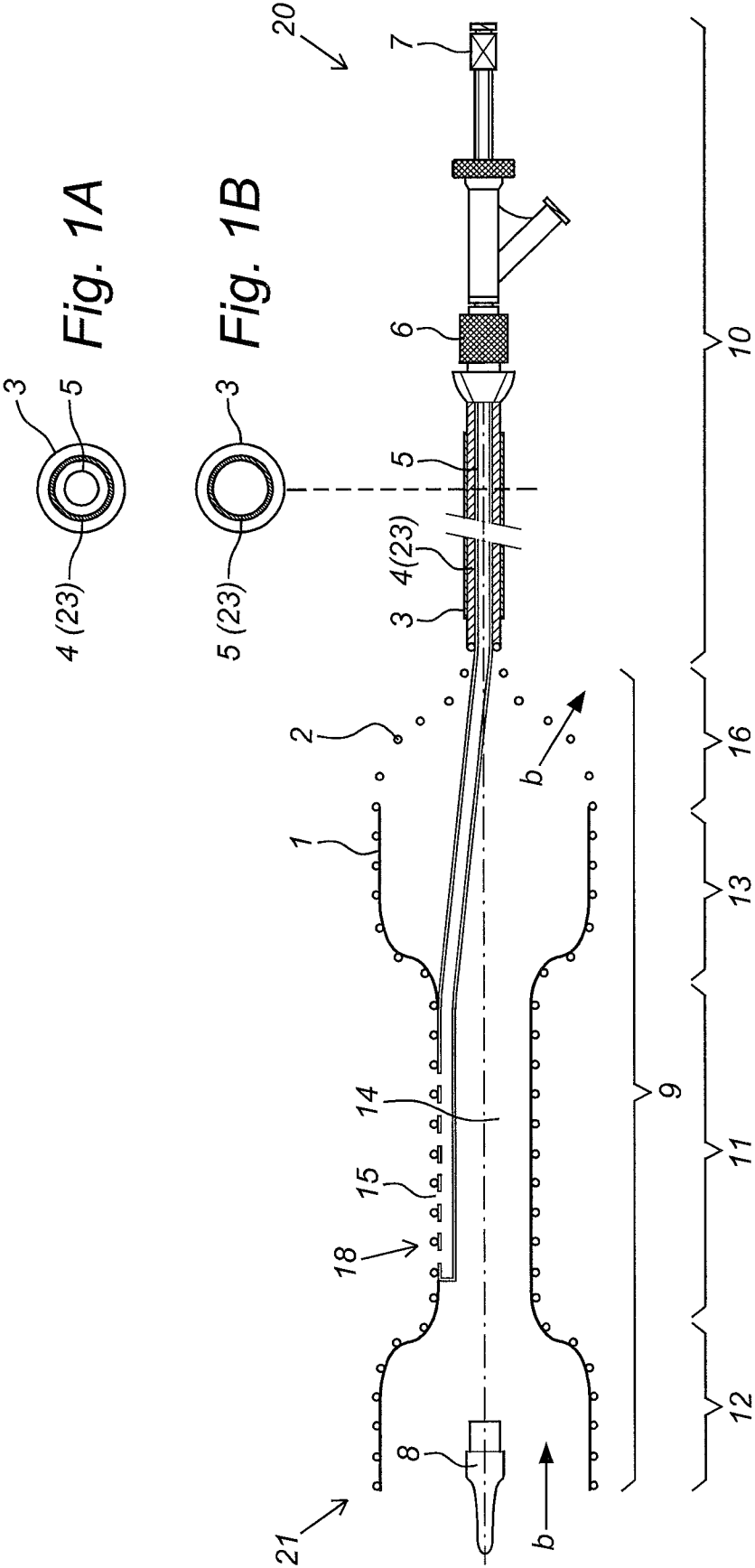


Fig. 1

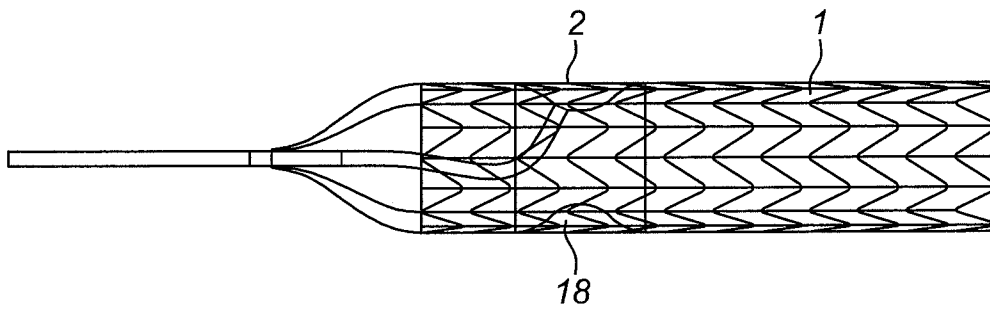


Fig. 1C

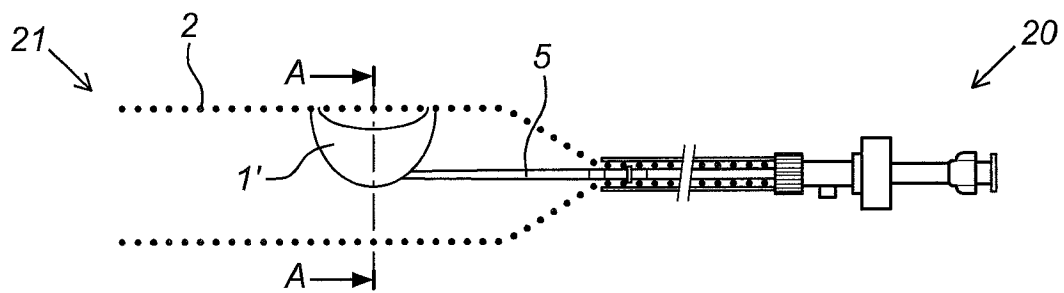


Fig. 1D

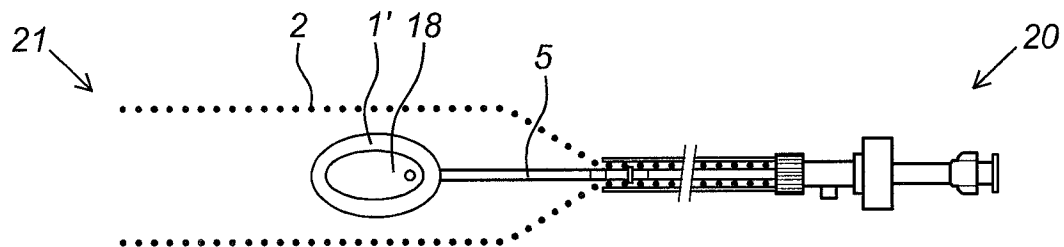


Fig. 1E

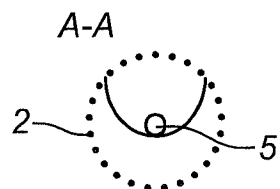
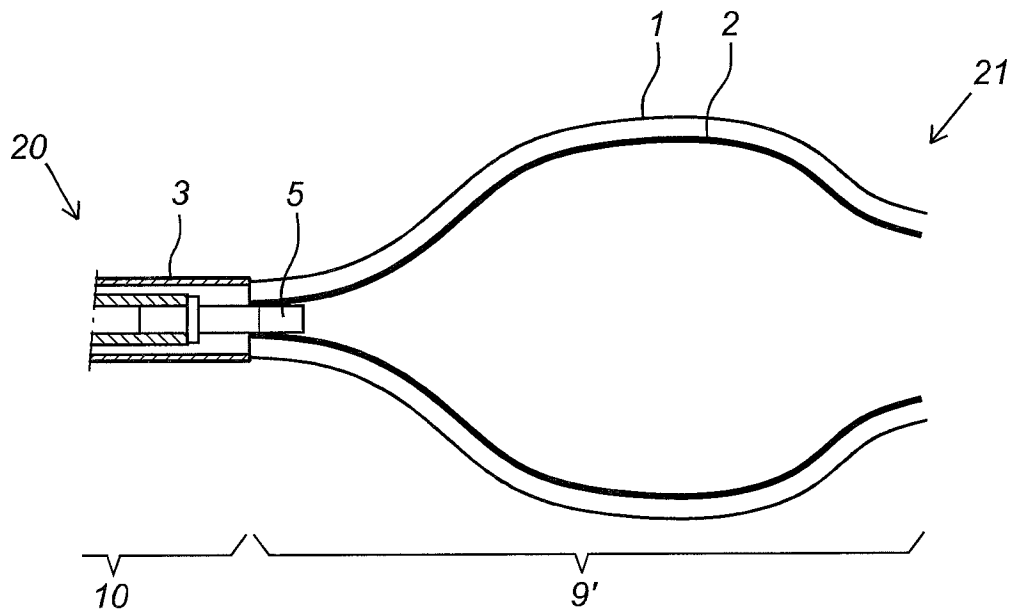


Fig. 1F

*Fig. 1G*

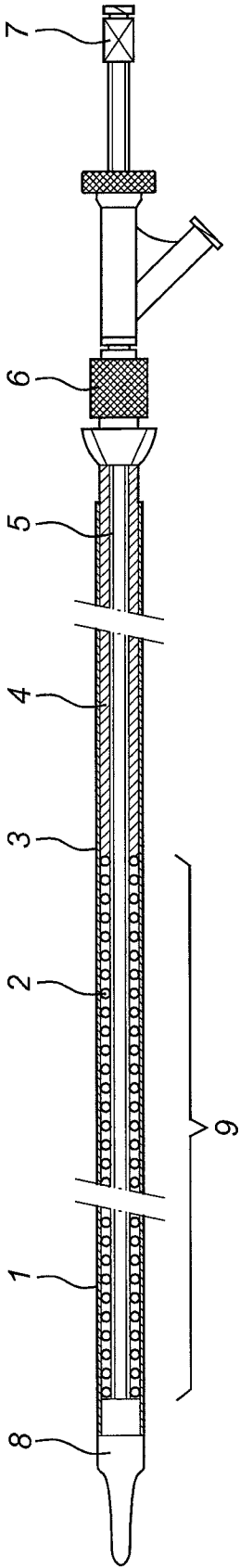


Fig. 2A

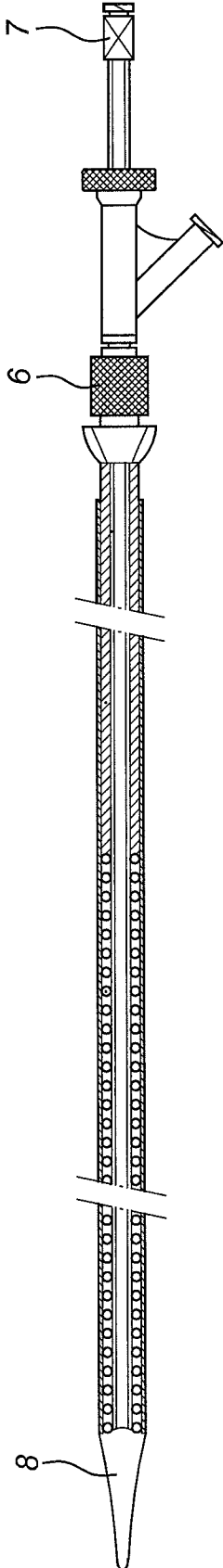
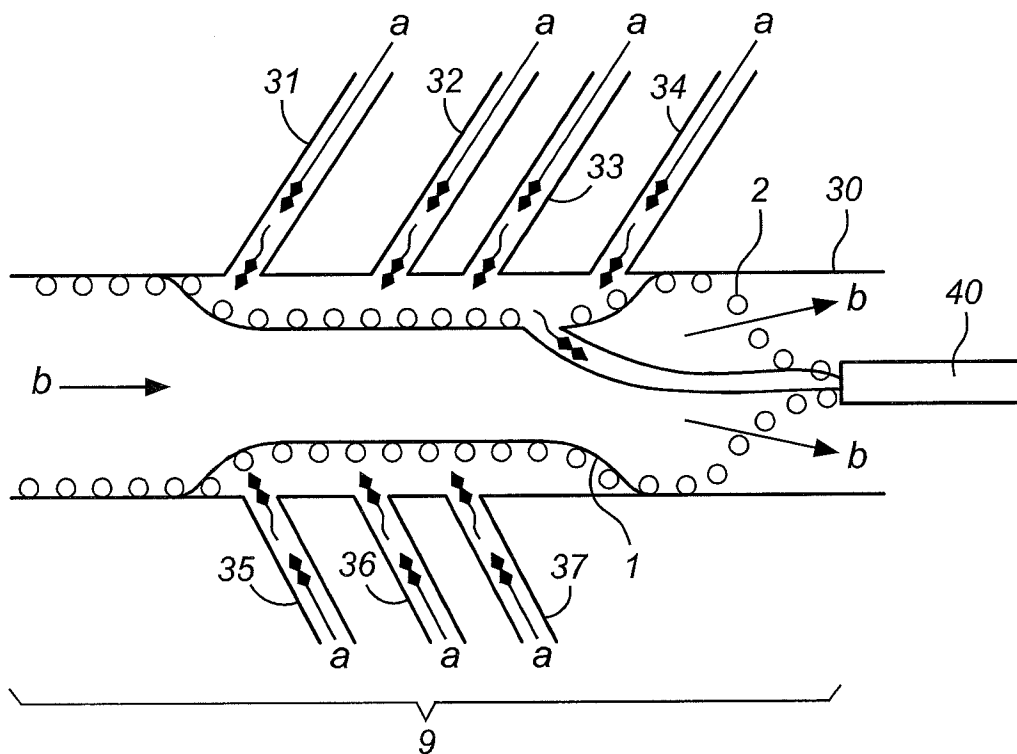
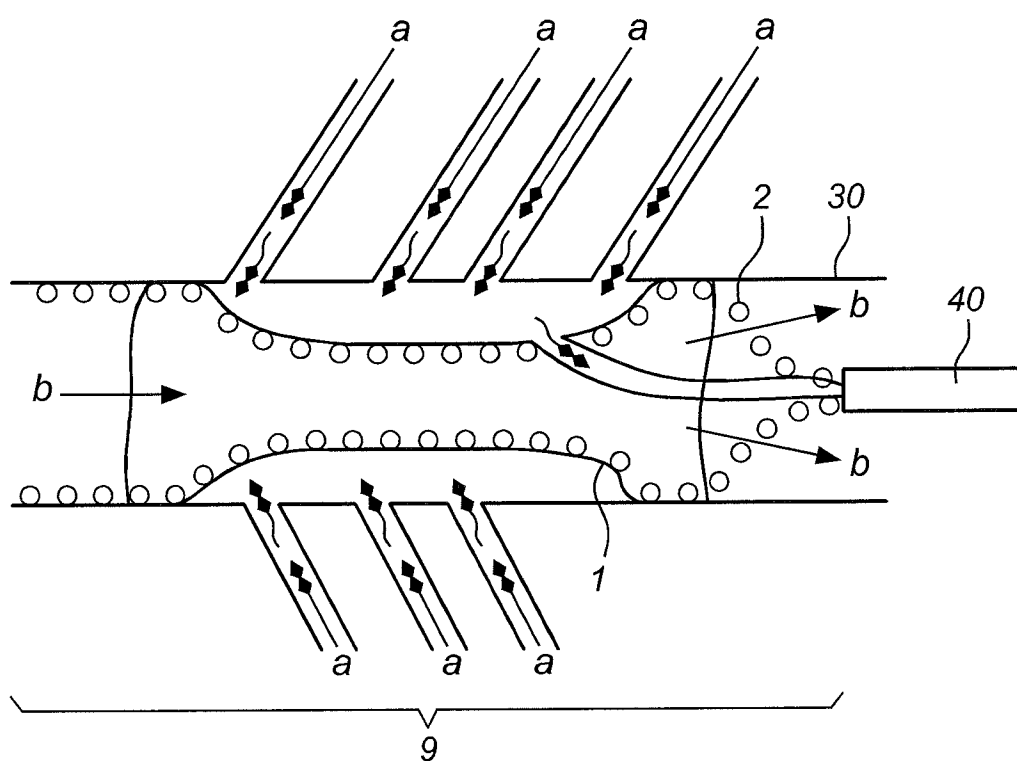
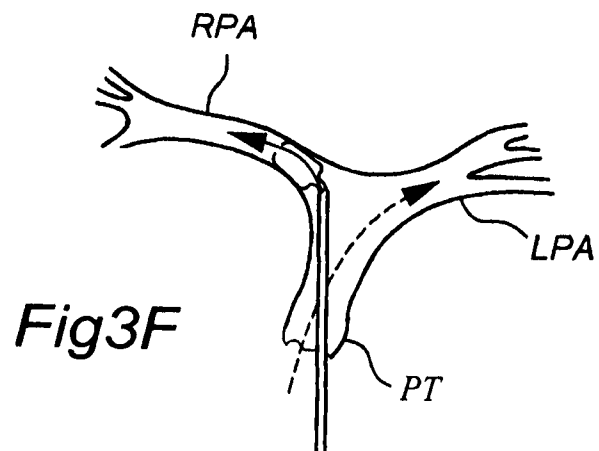
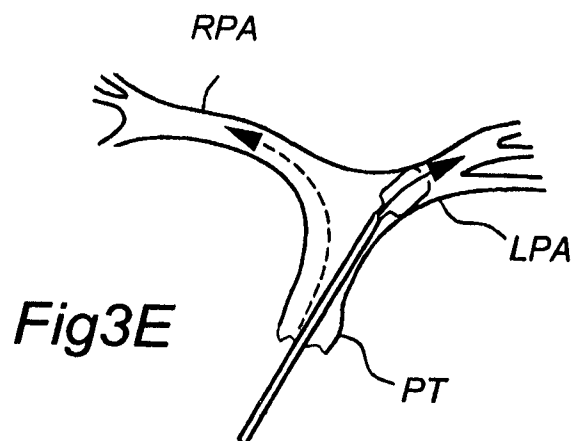
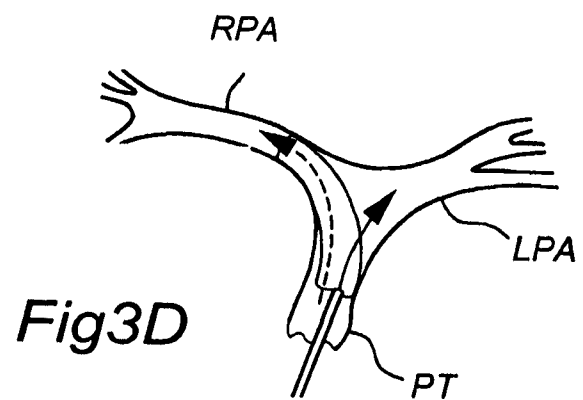
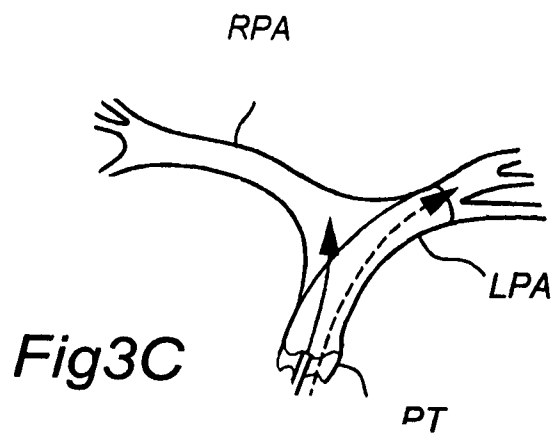
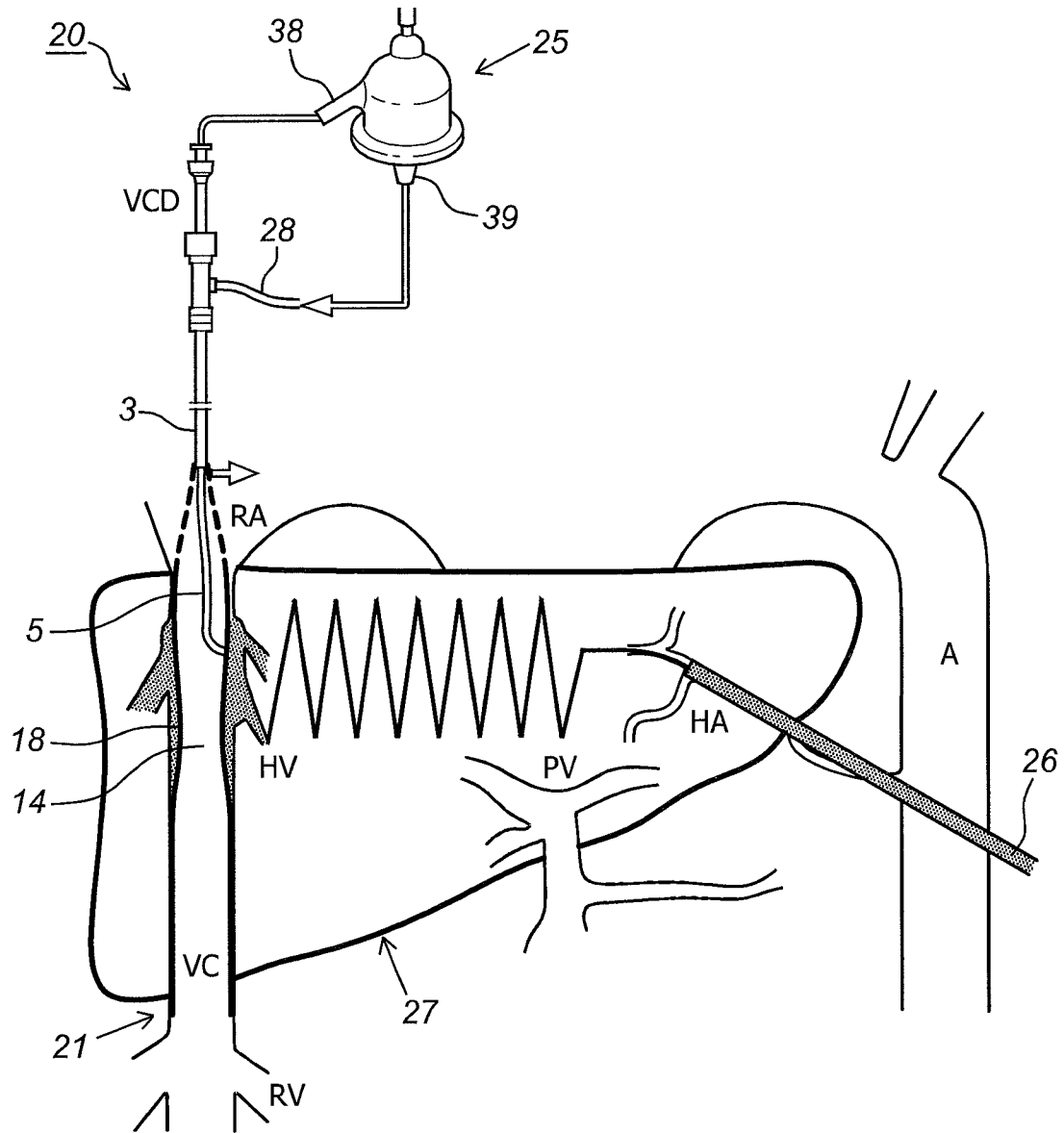
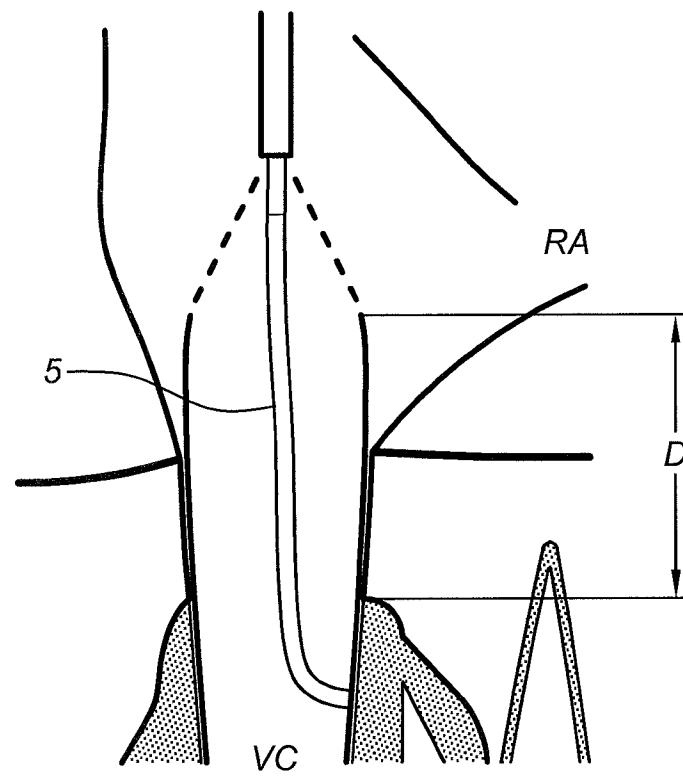


Fig. 2B

*Fig. 3A**Fig. 3B*



*Fig. 4*

*Fig. 5*

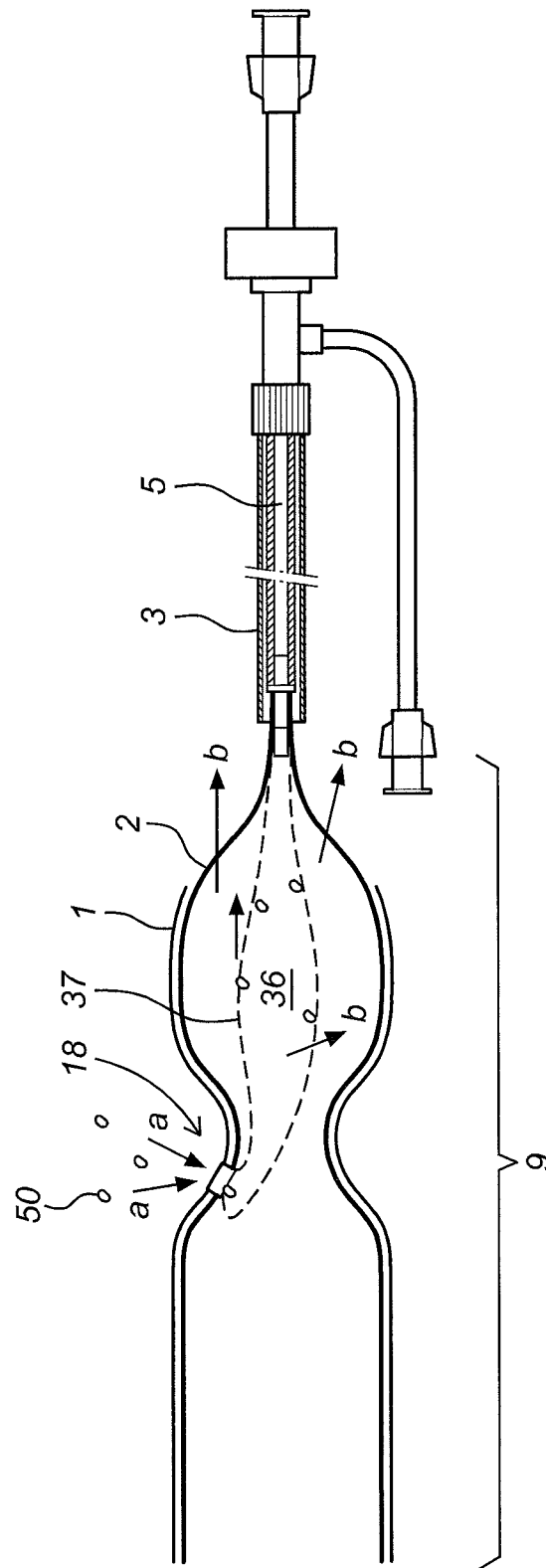


Fig. 6

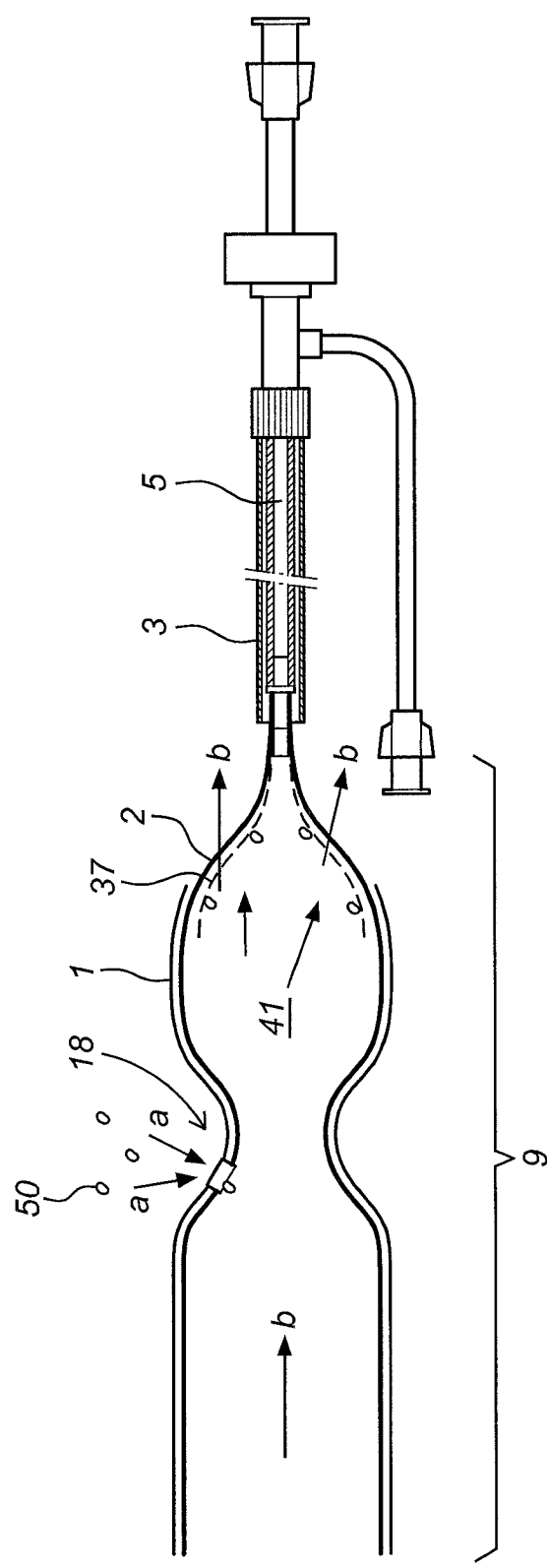


Fig. 7

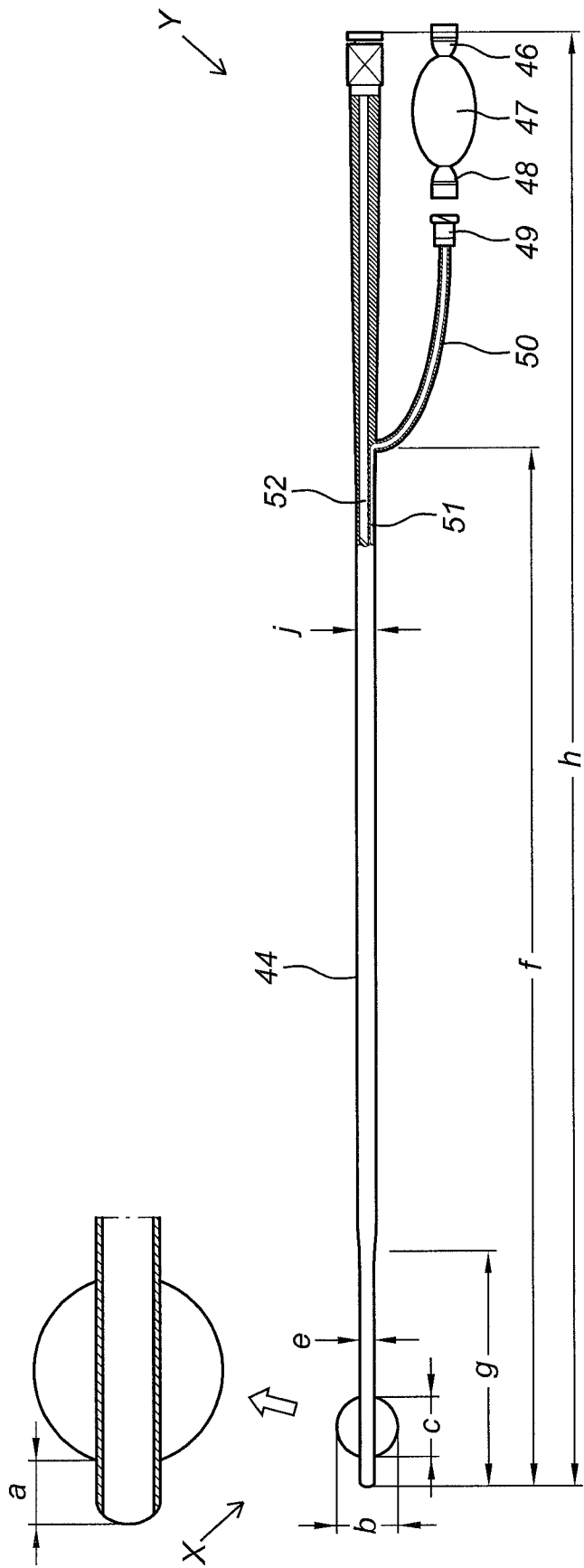


Fig. 8

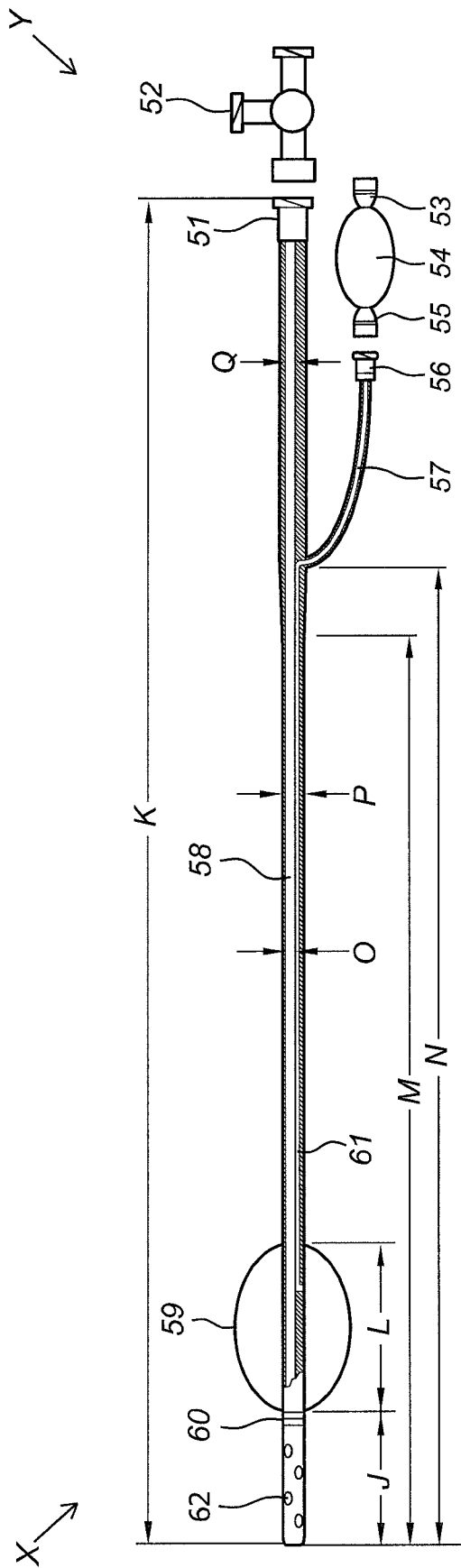


Fig. 9

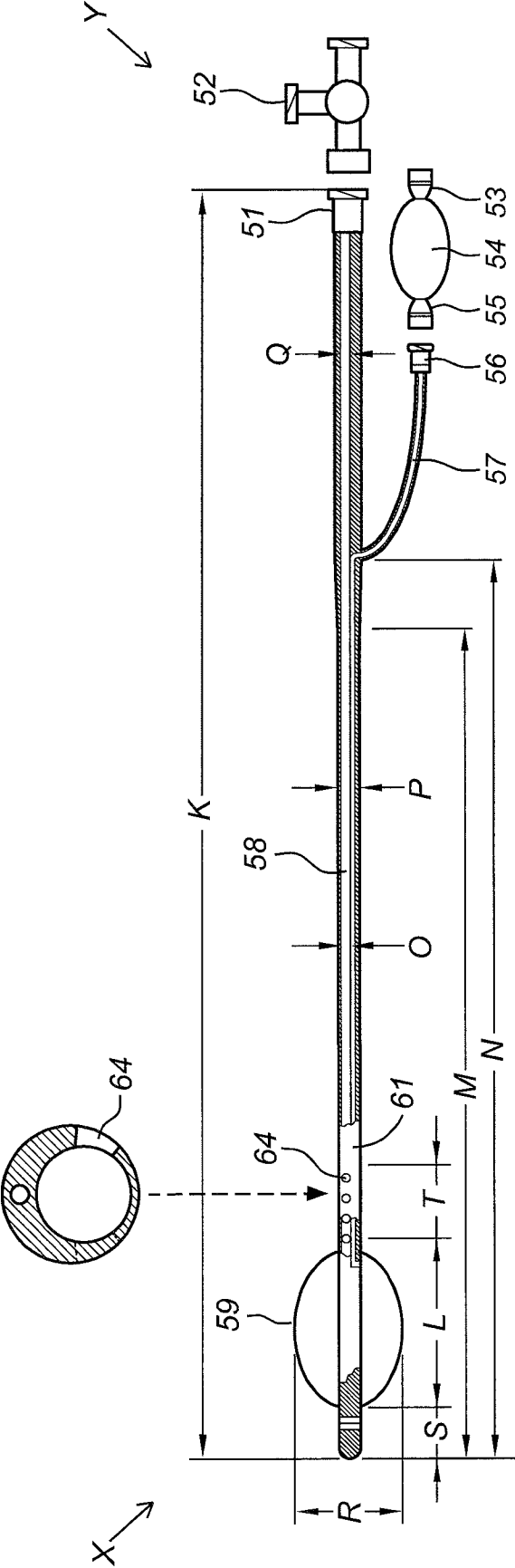


Fig. 10

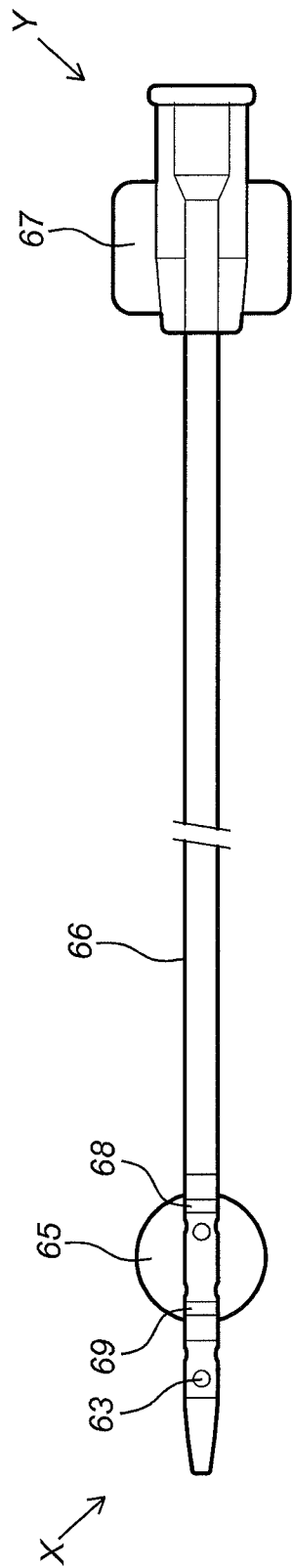


Fig. 11A

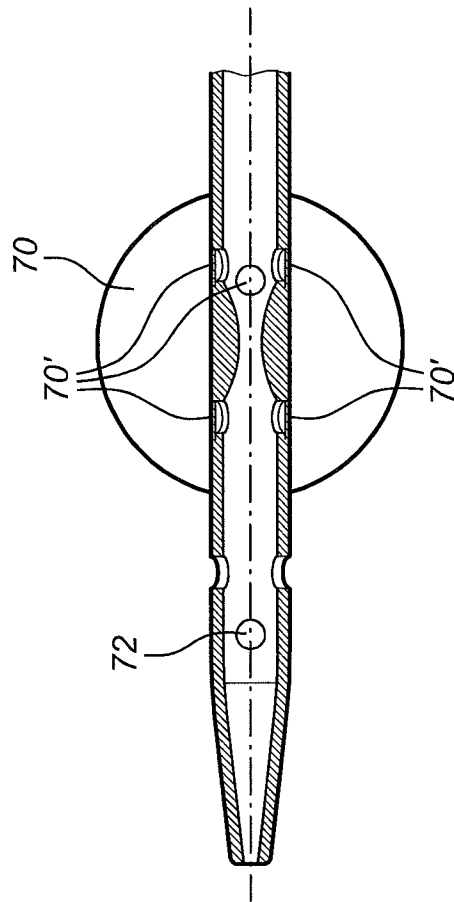


Fig. 11B

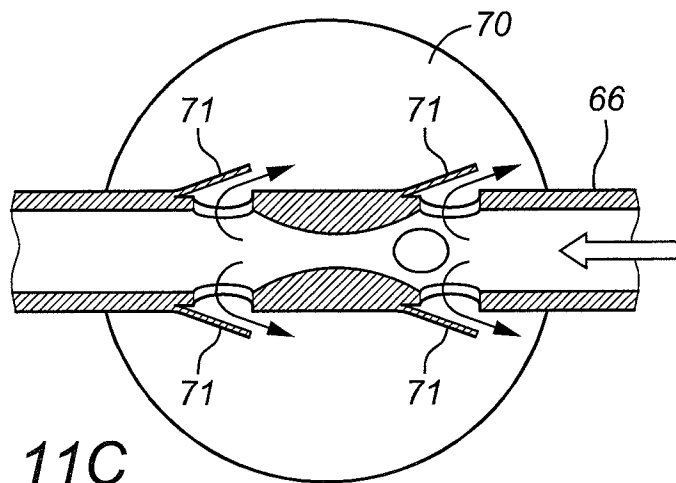


Fig. 11C

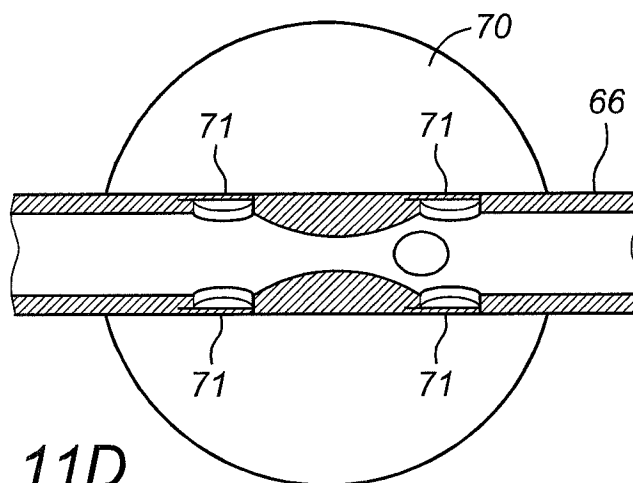


Fig. 11D

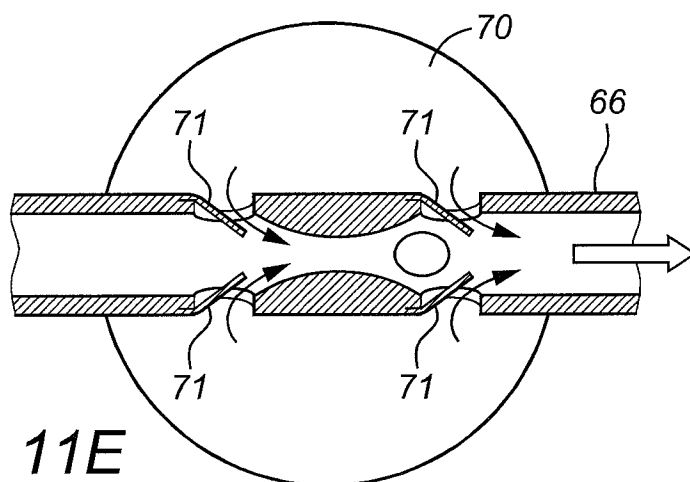


Fig. 11E

16/21

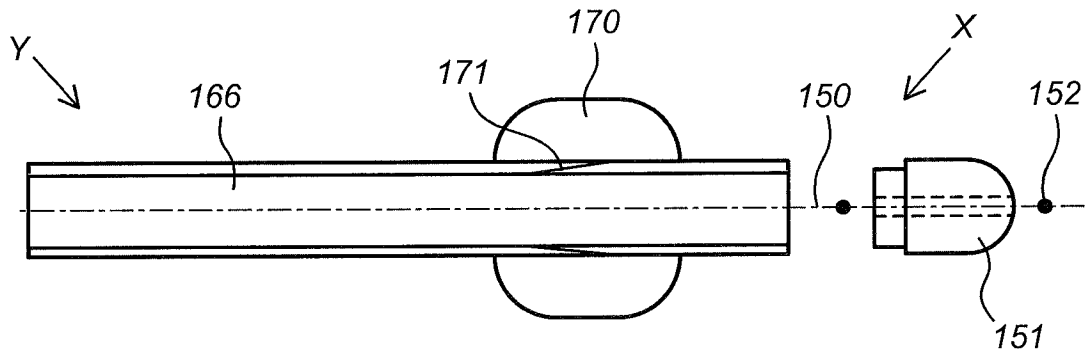


Fig. 11F

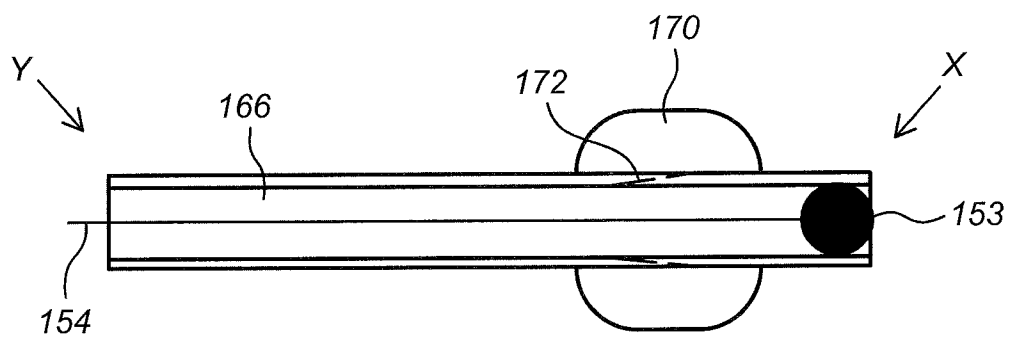


Fig. 11G

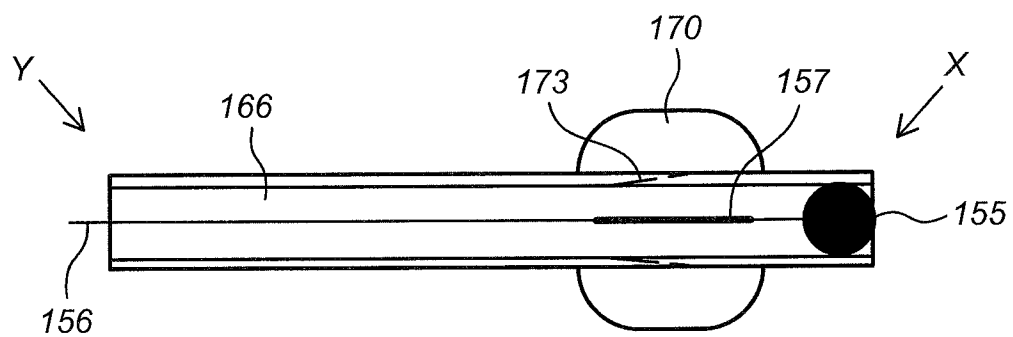


Fig. 11H

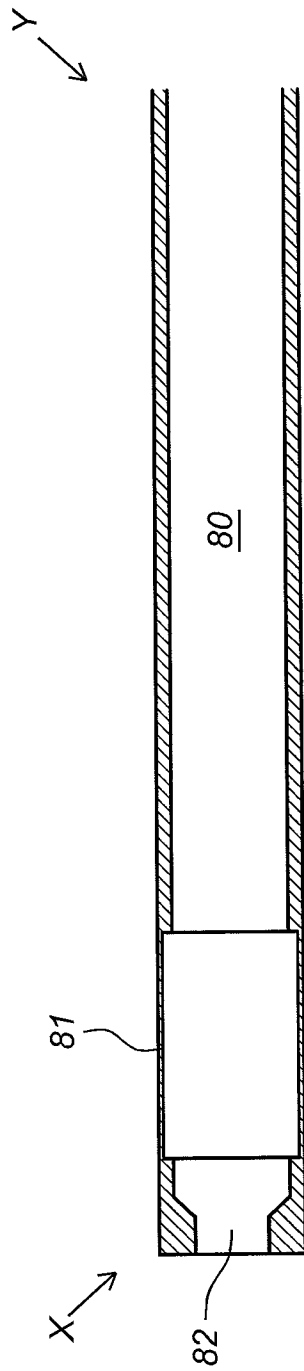


Fig. 12A

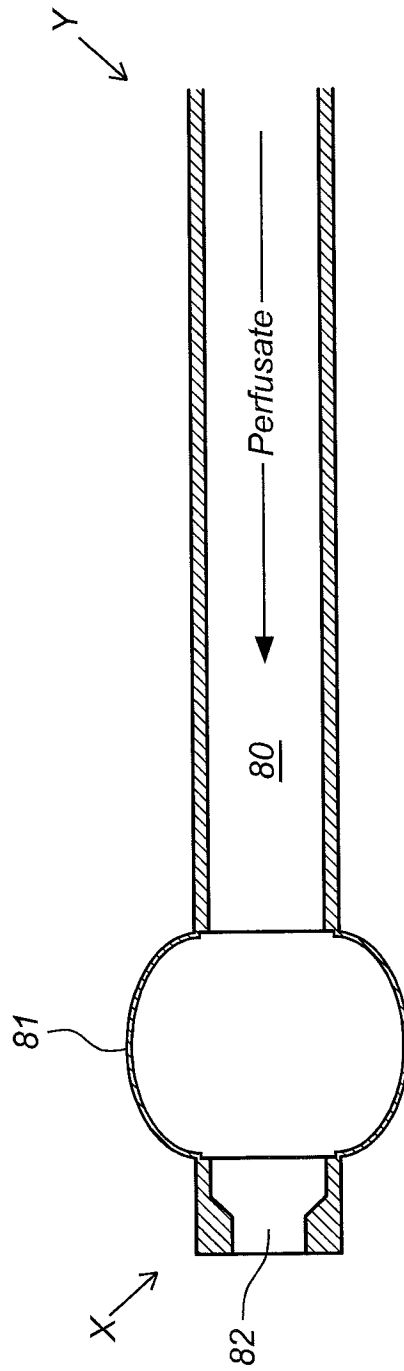


Fig. 12B

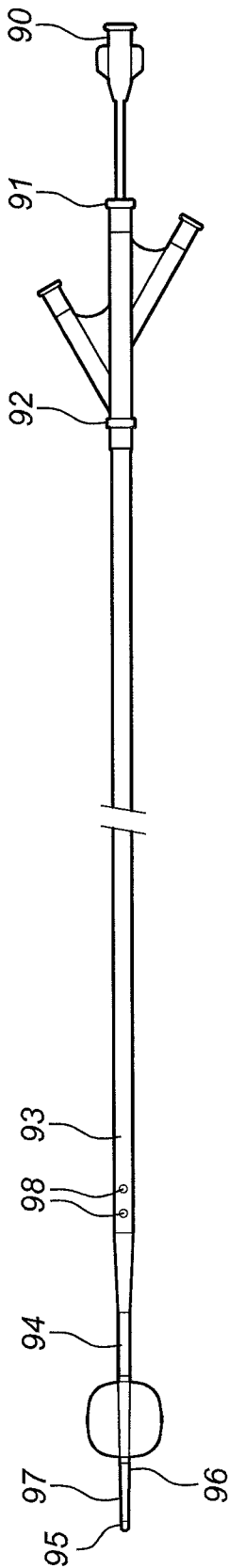


Fig. 13

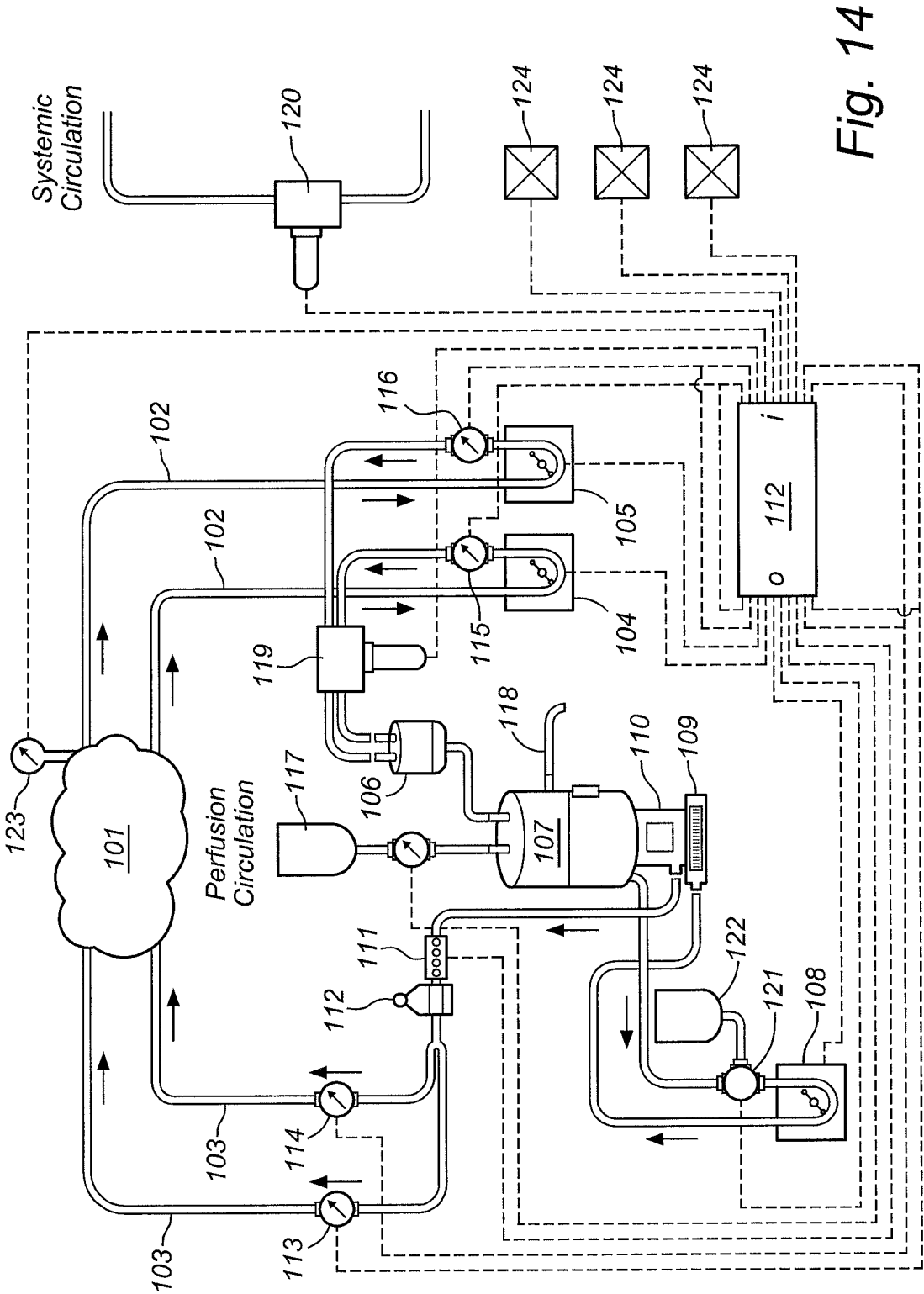
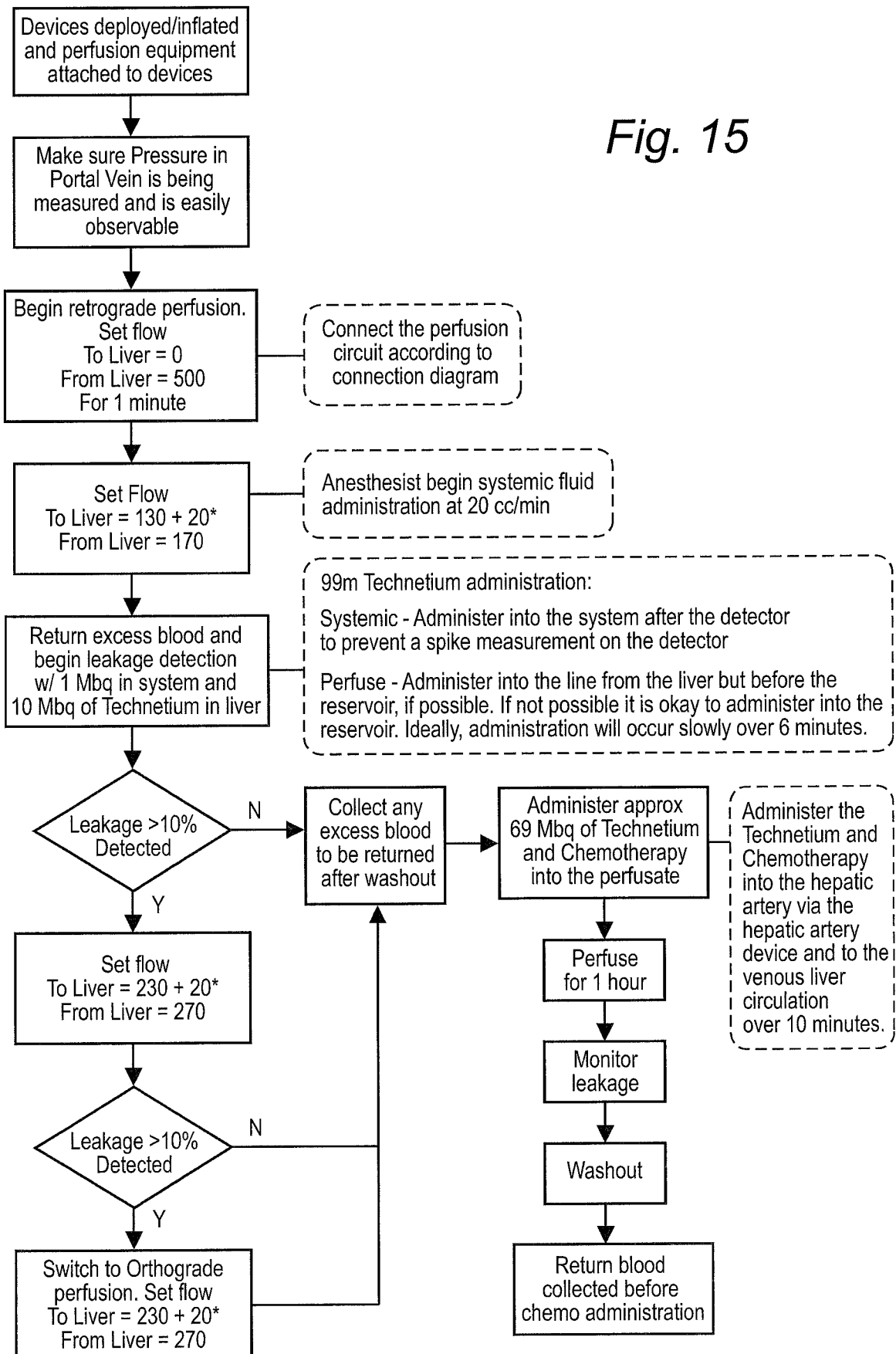
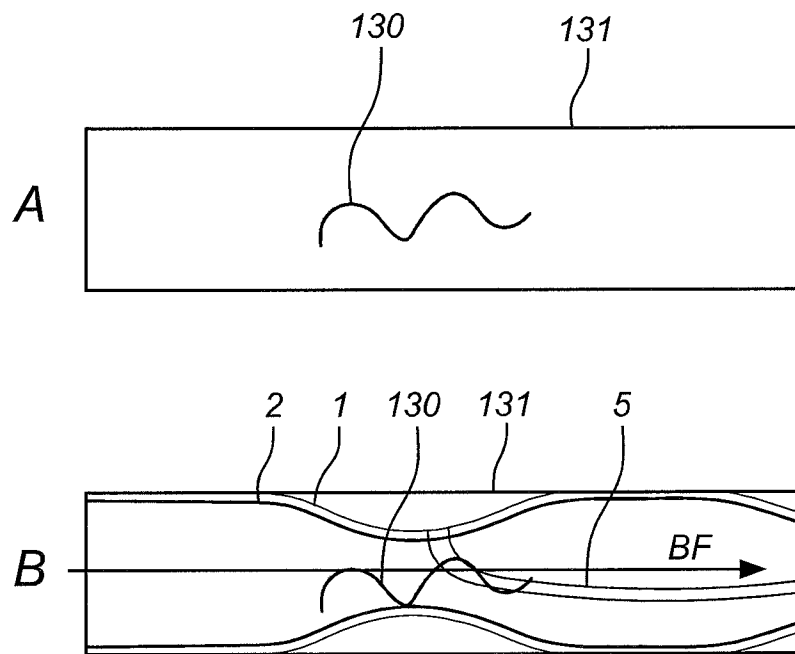


Fig. 14

20/21

Fig. 15



*Fig. 16*

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/054203

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M25/00
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 807 328 A (BRISCOE RODERICK E [US]) 15 September 1998 (1998-09-15) column 10, line 13 - line 41 figures 19,20 -----	1
A	US 6 102 891 A (MARIA VAN ERP WILHELMUS PETRUS [NL]) 15 August 2000 (2000-08-15) column 6, line 47 - line 60 figures 1,2,7 -----	1
A	US 2003/163115 A1 (GERSHOWITZ ARTHUR D [US]) 28 August 2003 (2003-08-28) paragraph [0026] paragraph [0029] paragraph [0031] figure 1 -----	1



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

7 June 2013

Date of mailing of the international search report

18/06/2013

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Amaro, Henrique

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2013/054203

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5807328	A	15-09-1998	NONE	

US 6102891	A	15-08-2000	NL 1008051 C2	19-07-1999
			US 6102891 A	15-08-2000

US 2003163115	A1	28-08-2003	US 2003163115 A1	28-08-2003
			US 2005085792 A1	21-04-2005
