(19) DANMARK

(10) **DK/EP 3603693 T3**

Patent- og Varemærkestyrelsen

(12) Oversættelse af europæisk patentskrift

(51) Int.Cl.: ***A 61 M 1/34 (2006.01)***

(45) Oversættelsen bekendtgjort den: **2022-05-16**

(80) Dato for Den Europæiske Patentmyndigheds bekendtgørelse om meddelelse af patentet: **2022-04-20**

(86) Europæisk ansøgning nr.: **19181860.8**

(86) Europæisk indleveringsdag: **2012-12-29**

(87) Den europæiske ansøgnings publiceringsdag: **2020-02-05**

(30) Prioritet: **2011-12-29 US 201161581496 P**

(62) Stamansøgningsnr: **18164476.6**

(84) Designerede stater: **AL AT BG CY CZ DK EE ES FI GR HR HU IS LT LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR**

(73) Patenthaver: **Delcath Systems, Inc., 1633 Broadway Suite 22C, New York, NY 10019, USA**

(72) Opfinder: **APPLING, William M, 566 Queensbury Avenue, Queensbury, NY New York 12804, USA**
ENGELHARD, Stephen N, 566 Queensbury Avenue, Queensbury, NY New York 12804, USA
BARTON, Matthew G, 566 Queensbury Avenue, Queensbury, NY New York 12804, USA

(74) Fuldmægtig i Danmark: **Plougmann Vingtoft A/S, Strandvejen 70, 2900 Hellerup, Danmark**

(54) Benævnelse: **FILTER OG RAMMEAPPARAT OG FREMGANGSMÅDE TIL ANVENDELSE**

(56) Fremdragne publikationer:
EP-A2- 1 101 502
US-A- 4 211 380

DESCRIPTION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is an international patent application filed in accordance with the patent cooperation treaty. This international application claims priority benefit of U.S. Provisional Patent Application Ser. No. 61/581,496 filed December 29, 2011, and entitled "Dual Filter Cartridge and Frame Apparatus and Method of Use."

BACKROUND

[0002] Filtering toxic compounds from blood has been an area of great importance for human health. Filters for adsorption of toxic compounds from blood are known in the art. An example is the use of extracorporeal filters to remove chemotherapeutic drugs from the blood stream during cancer treatments such as in hepatic chemosaturation therapy. This therapy also known as percutaneous hepatic perfusion (PHP) delivers ultra-high doses of intra-arterial chemotherapy directly into the isolated liver, saturating both the liver and the tumor cells. The blood from the liver is drained through an isolation-aspiration catheter, and then directed outside the body to specially designed, and often proprietary, filters which reduce the concentration of chemotherapeutic agent before this blood is returned to the body. The potential of chemosaturation therapy includes: the ability to administer higher doses of chemotherapeutic agent to a particular organ than could be delivered with traditional systemic-intravenous methods while significantly reducing systemic exposure to the high dose levels.

[0003] The filters used to absorb the drug from the blood are incorporated in an extracorporeal circuit. The blood drained from the liver through the isolation aspiration catheter is pumped by a venous bypass pump, such as is used in heart bypass surgery, through a filter or set of filters. The outlet of the filter(s) is connected by a tube set to a return catheter inserted in a central vein, through which the cleaned blood is returned to the patient's circulatory system. In use, the filter(s) are required to absorb drug at an efficiency which protect the patient's systemic circulation from toxic side effects of high drug concentrations. During use with certain drugs such as Melphalan Hydrochloride, poor filtration can cause side effects such as anemia, thrombocytopenia, neutropenia, together commonly known as Myelo Suppression. Other drugs at high concentrations have risk of cardio toxicities if poor filtration fails to reduce systemic concentrations to safe levels.

[0004] Filters, pumps, and connecting tubing are typically set up and assembled by a perfusionist, or other technician, prior to the case. Filters may be clamped or taped to equipment such as IV poles. Multiple filters are often used to aid efficiency. Many times hardware such as lab clamps can become misplaced between cases wasting time to find or forcing the technician to improvise a support method at the last minute.

[0005] The system, including filters, is connected to catheters for withdrawal and return of blood to the patient. For the entire system all surfaces exposed to body fluids should be kept sterile.

[0006] Prior to use, the filters, blood circuit tube set, and pump are prepared for the procedure. The filters are required to be primed with saline to remove all air from the filter media and to be flushed with saline to remove any fine particulate in the media prior to blood being introduced to the circuit. Proper priming is critical to filter performance. Removing air is necessary to eliminate the potential for air to be infused into the patient. Also, any air left in the filter reduces the surface area that blood will contact the filter media thus reducing filter efficiency.

[0007] Relevant prior art is for instance disclosed in documents EP1101502 A2 and US4211380 A.

SUMMARY

[0008] A kit of parts according to the present invention comprises the technical features of independent claim 1 or those of independent claim 7.

[0009] The inventors have recognized some problems with prior art filters and provide herein an apparatus that can solve many of the problems in the prior art.

[0010] Where multiple filters are used, the set up procedure can become cumbersome and unsteady. Technicians will need to use a variety of hardware to clamp the filters to a support.

[0011] If filters were to fall, sterility could be comprised, or catheters could be dislodged from the patient's body. Additionally, filters could crack or leak exposing technical staff and equipment to high concentrations of toxic compounds such as chemotherapeutic drugs.

[0012] If the filters are clamped in place to a support or taped together, it may be difficult to see the entire filter's circumference and this will hinder the priming process where air bubbles are to be removed. Additionally, if a technician attempts to turn the filters to visualize the circumference, the mounting method may need to be repeated.

[0013] Additionally, during use filters may not see the same resistance to flow if they are angled or set at different heights relative to each other. When filtering drugs from blood it is desirable that each filter provides the same flow resistance so that blood equally flows through each filter. A reduction in flow in one filter may allow thrombus formation in the low flow filter which can continue to develop until flow is completely stopped in that filter. The other filter then provides for the majority, and possibly 100% of the flow and filtration. If the flow rate remains the same, and the total filter volume is decreased or possibly reduced by 50%, the residence time will decrease thus reducing filter efficiency. Additionally, having all flow forced through only

one filter may lead to complete saturation of the filter media and limit the filters ability to absorb or filter drug from the blood. Reduced filter efficiency may lead to an increase in adverse reactions caused by the toxic effects of the chemotherapeutic drug not adsorbed by the filter.

[0014] The inventors recognized that that these problems could be solved by providing, in some embodiments of the invention, a filter system, apparatus, and method which allows the technician to quickly and securely attach the filter housing to a support without the need for additional hardware. Filter cartridges can be easier to prime and verify all air is removed if the housing allows the cartridges to be rotated so that all areas of the filter can be visualized. The system will guarantee that filters have the same flow conditions if the housing mounts all filter cartridges at the same height and orientation. Combining filter cartridges in a rugged frame housing will increase durability of the product. In some embodiments of the invention, provided herein is a filter system and apparatus wherein the housing of the apparatus enables the filter cartridges to be rotated so that all areas of the filter can be visualized, the housing mounts all of the filter cartridges at the same height and orientation, and the filter cartridges are combined in a rugged frame housing that provides durability. The combination of these features results in an easy to use and robust filter system that protects the equipment and staff from inadvertent breakage. The apparatus allows for the holding of filter cartridges in about the same orientation. The filter cartridges being held in about the same orientation allows for the flow to be about the same in the different cartridges.

[0015] In some embodiments, the invention is a filter system where multiple filter cartridges are mounted in a single frame housing. The housing includes a built in clamping mechanism that deploys to allow the filter to be mounted to an IV pole or other suitable and available structure in an operating room. A technician can simply open the sterile supplied filter system, deploy the mounting mechanism, and clamp the assembly to an available IV pole or other supporting member available in the operating room. The housing is mechanically strong and provides a very solid attachment to the support with no risk of falling and no need to improvise a clamping means. The cartridge is allowed to rotate within the housing during priming so that all areas of the filter can be visualized to verify air has been removed. The housing also insures that both filters are mounted in the same orientation and height which guarantees that each filter sees the same flow conditions.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016]

FIG. 1 shows a perspective view from the front of dual filter cartridges mounted in a single frame;

FIG. 2 shows a top view of dual filter cartridges mounted in a single frame with the mounting means deployed for connection;

FIG. 3 shows a bottom view of dual filter cartridges mounted in a single frame with the

mounting means deployed for connection;

FIG. 4 shows a front view of dual filter cartridges mounted in a single frame;

FIG. 5 shows a perspective view from the back of dual filter cartridges mounted in a single frame with mounting means stowed for packaging;

FIG. 6 shows a back view of dual filter cartridges mounted in a single frame with mounting means stowed for packaging;

FIG. 7 shows a side view of dual filter cartridges mounted in a single frame with the mounting means deployed for connection;

FIG. 8 shows an exploded view of dual filter cartridges and housing;

FIG. 9 shows a perspective view from back of dual filter cartridges mounted in a single frame with mounting means deployed and connected to a pole such as an IV pole; and

FIG. 10 shows dual filter cartridges mounted in a single frame in an extracorporeal blood filtration set up incorporated into a percutaneous hepatic perfusion procedure.

DETAILED DESCRIPTION

[0017] A filter cartridge is made by assembling lower inlet flange **12** to the cartridge tube **11,** to the upper outlet flange **18.** Inlet connector **15** is connected to lower inlet flange **12.** An inlet screen (not shown) is incorporated at the inside end of a cartridge tube **11** at the joint between the lower inlet flange **12** and cartridge tube **11.** Filter media is added to the assembly by filling the inside volume of cartridge tube **11.** Outlet connector **19** is connected to upper outlet flange **18.** An outlet screen (not shown) is incorporated at the inside ends of cartridge tube **11** at the joint between the upper outlet flange **18** and cartridge tube **11.** The screens provide a means to keep filter media (not shown), typically small spheres or beads, within the filter cartridge while allowing blood to flow into, through, and out of the filter. The screens may be formed of a suitable polymer with a 200 - 400 micron mesh. The flanges **12** and **18** and tube **11** is formed from any suitable transparent plastic such as polysulfone, polycarbonate, or polypropylene. The connections between components can be joints formed by adhesive such as two part epoxy or ultraviolet light curing epoxy, or the joints can be heat welded by means such as radio frequency welding, induction welding, or ultrasonic welding.

[0018] The housing is assembled from structural components. Lower plate **1** is attached to six tie rods **7** with six tamper proof flat head cap screws **10.** Center support plates **2** and **3** are assembled with the pole clamp **5** to create a deployable mounting mechanism. Pivot pin **4** is pressed fit into center support plate **2,** and is passed through pole clamp **5** and is press fit into opposite center support plate **3.** Three stop pins **6** are pressed into receiving holes in center

support plate **2** and **3.** Two stop pins **6** form the stop for the pole clamp **5** deployed position, one stop pin **6** form the stop for the stowed position. Clamp knob **8** has a threaded shaft that is screwed through pole clamp **5.** The sub assembly of center support plates **2** and **3,** pins **4** and **6,** and pole clamp **5** and knob **8** creates the deployable mounting mechanism. The sub assembly is then attached to lower plate **1** with four tamper proof flat head cap screws **10.** Herein, item **1** is used for both upper plate and lower plate as the plates are the same part. Face plate **25** is inserted into grooves in the center support plates **2** and **3** and slid towards the lower plate **1** until it contacts the lower plate **1.** O ring **9** is formed from an elastomeric material such as Silicone or Viton. One O ring **9** is added to the top of each cartridge assembly at the upper outlet flange **18.** A cartridge assembly with O ring **9** is inserted into each side of the frame housing between tie rods **7** and center support plates **2** and **3.** Upper plate **1** is placed on top of the assembly and secured to the tie rods **7** and center support plates **2** and **3** with ten tamper proof flat head cap screws **10.** The O rings **9** are captured between upper plate **1** and upper outlet flanges 18 such that the cartridges can smoothly rotate within the housing frame without being loose or creating excessive compression of the cartridge within the housing frame.

[0019] In some embodiments of the invention, the filter system can be packaged, labeled, and sterilized by the manufacturer. It can be shipped to the customer alone or as a component of a comprehensive kit containing all components needed to perform a procedure. Once in use the technician setting up the system will open the packaging while maintaining sterility of inlet connector **15** and outlet connector **19.** As shown in figure 9, the pole clamp **5** can be deployed from its storage position between center support plates **2** and **3.** The pole clamp **5** can rotate around pivot pin **4** and contact stop pins **6,** which limits the clamp rotation to a perpendicular orientation. The pole clamp **5** can be placed around an available IV pole or similar available structure in the operating room. The frame is secured to a pole by tightening clamp knob **8** on to the pole.

[0020] The technician and physician team can then assemble the system connect tubing between the filter system and other components which make up a complete circuit such as pump, saline supply bags, and flow rate monitor. The tube set which connects to the filter uses rotatable connectors to connect to inlet connectors **15** and outlet connector **19.** All components are primed and flushed with saline. The technician will slowly fill the filters with saline from the bottom up allowing air to escape from the top. Due to the high surface area of some filter media, air will often be trapped in the filter cartridge and will need to be coaxed to leave by slowly flushing saline through the filter while tapping the filter cartridge walls to break the air bubbles free. To insure that all air has been removed the technician can rotate the cartridge within the frame to view the entire circumference of the cartridge. Once the filters are primed, the final connections can be made to the isolation aspiration catheter which acts as a supply catheter and the venous return catheter, already placed in location in the patient as shown in fig 10. The procedure can then be performed with a secure and safe system.

REFERENCES CITED IN THE DESCRIPTION

Cited references

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US61581496 [0001]
- EP1101502A2 [0007]
- US4211380A [0007]

Patentkrav

1. Kit af dele som kan samles til levering af et kemoterapeutisk middel til en lever hos en patient, omfattende:

et isolations-aspirations-kateter, og

et filtersystem eller filterapparat omfattende to eller flere filterpatroner monteret i et enkelt rammehus,

hvor huset omfatter en øvre plade (1) og en nedre plade (1) til at holde de to eller flere filterpatroner i omtrent den samme orientering, idet den øvre plade (1) og den nedre plade (1) omfatter åbninger til drejeligt at gribe ind i de to eller flere filterpatroner, og et eller flere støtteelementer, som forbinder den øvre plade (1) og den nedre plade (1),

idet det enkelte rammehus omfatter en klemmemekanisme, som anvendes for at lade filtersystemet eller filterapparatet blive monteret på en IV-stang eller en anden passende og tilgængelig struktur på en operationsstue,

eventuelt er klemmemekanismen en IV-stangklemme forbundet til det enkelte rammehus.

2. Kit af dele ifølge krav 1, yderligere omfattende et venøst tilbageløbshylster eller et venøst tilbageløbskateter; og/eller yderligere omfattende et leverarterie-infusionskateter.

3. Kit af dele ifølge et hvilket som helst af de foregående krav, hvor de to eller flere filterpatroner strækker sig gennem åbningerne, den øvre plade (1) og den nedre plade (1).

4. Kit af dele ifølge et hvilket som helst af de foregående krav, hvor de to eller flere patroner omfatter et filtermedium af aktivt kul; og eventuelt hvor filtermediet af aktivt kul er hydrogel belagt aktivt kul.

5. Kit af dele ifølge krav 1, hvor klemmemekanismen er en IV-stangklemme forbundet til et eller flere af det ene eller flere støtteelementer; og/eller hvor det ene eller flere støtteelementer omfatter en kombination af stænger (7) og støtteplader (2, 3).

6. Kit af dele ifølge et hvilket som helst af de foregående krav, yderligere omfattende melphalanhydrochlorid.

7. Kit af dele som kan samles til levering af et kemoterapeutisk middel til en lever hos en patient, omfattende:

et isolations-aspirations-kateter, og

et filterapparat, omfattende to eller flere filterpatroner med en første ende med et indløb og sigte og en anden ende med et udløb og en sigte, og vægge til at indeholde et filtermedium; et hus omfattende en øvre plade (1) og en nedre plade (1) til at holde de to eller flere filterpatroner i omtrent den samme orientering, idet den øvre plade (1) og den nedre plade (1) omfatter åbninger til drejeligt at gribe ind i de to eller flere filterpatroner, og et eller flere støtteelementer, som forbinder den øvre plade (1) og den nedre plade (1); og en IV-stangklemme forbundet til huset.

8. Kit af dele ifølge krav 7, yderligere omfattende et venøst tilbageløbshylster eller et venøst tilbageløbskateter.

9. Kit af dele ifølge krav 7 eller 8, hvor de to eller flere filterpatroner strækker sig gennem åbningerne, den øvre plade (1) og den nedre plade (1).

10. Kit af dele ifølge et hvilket som helst af kravene 7-9, hvor IV-stangklemmen er forbundet til et eller flere af det ene eller flere støtteelementer; og/eller hvor det ene eller flere støtteelementer omfatter en kombination af stænger (7) og støtteplader (2,3).

11. Kit af dele ifølge et hvilket som helst af kravene 7-10, hvor indløbet og udløbet omfatter et indløbsforbindelsesstykke (15) og et udløbsforbindelsesstykke (19), og hvor udløbsforbindelsesstykket (19) er forbundet til patronrøret (11) via en konisk udløbsflange (18).

12. Kit af dele ifølge et hvilket som helst af kravene 7-11, hvor væggene, som indeholder filtermediet, omfatter et patronrør (11); og eventuelt hvor patronrørene (11) er transparente, og hvor patronrørene (11), som er

transparente, eventuelt er omfattet et af transparent materiale valgt fra gruppen bestående af en polysulfon, et polycarbonat, en polypropylen og en acryl.

13. Kit til dele ifølge et hvilket som helst af kravene 7-12, hvor filtermediet omfatter aktivt kul; og eventuelt hvor filtermediet er hydrogel belagt aktivt kul.

14. Kit af dele ifølge et hvilket som helst af kravene 7-13, yderligere omfattende melphalanhydrochlorid.

15. Kit af dele ifølge et hvilket som helst af de foregående krav, hvor isolations-aspirations-katetret er et dobbeltballonkateter.

DRAWINGS

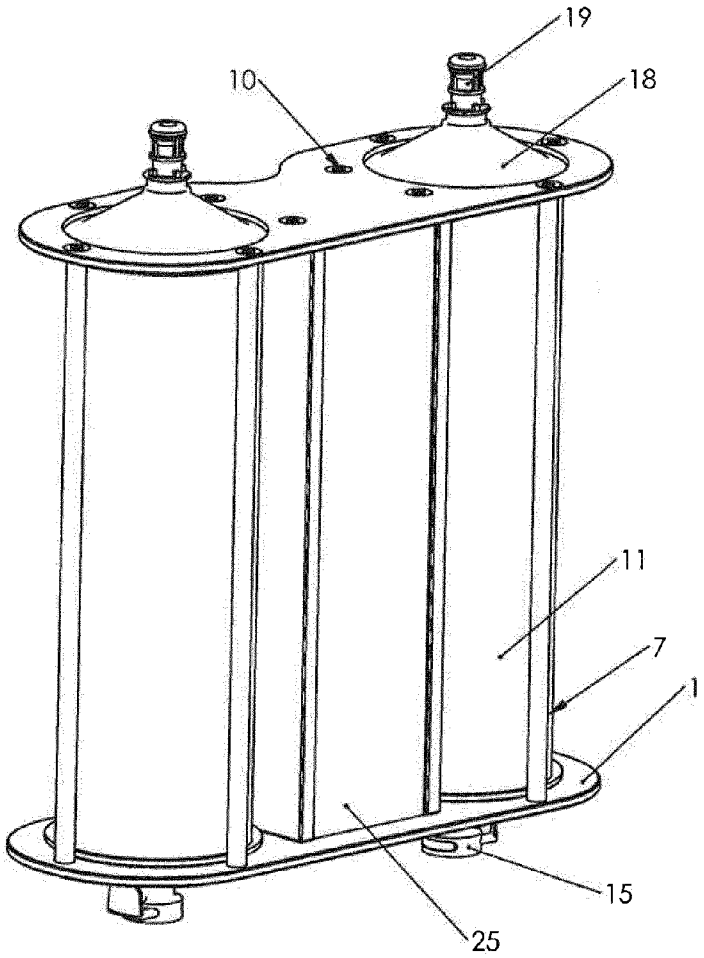

FIG.1

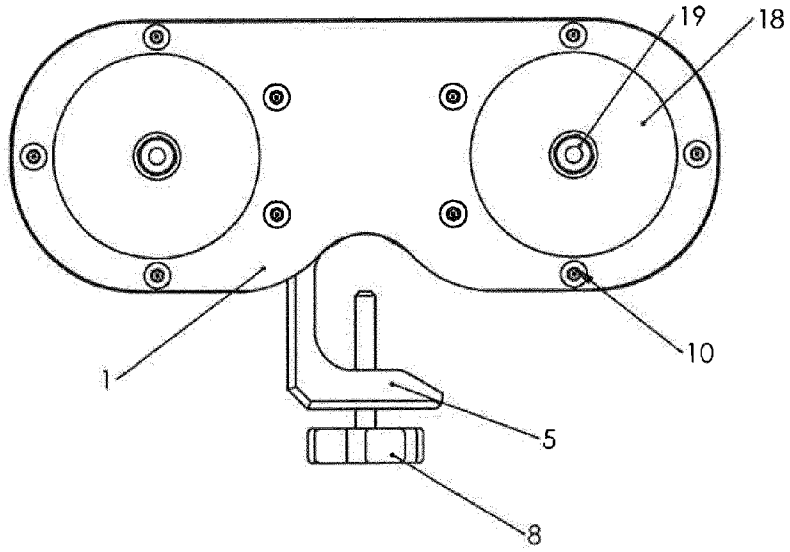

FIG.2

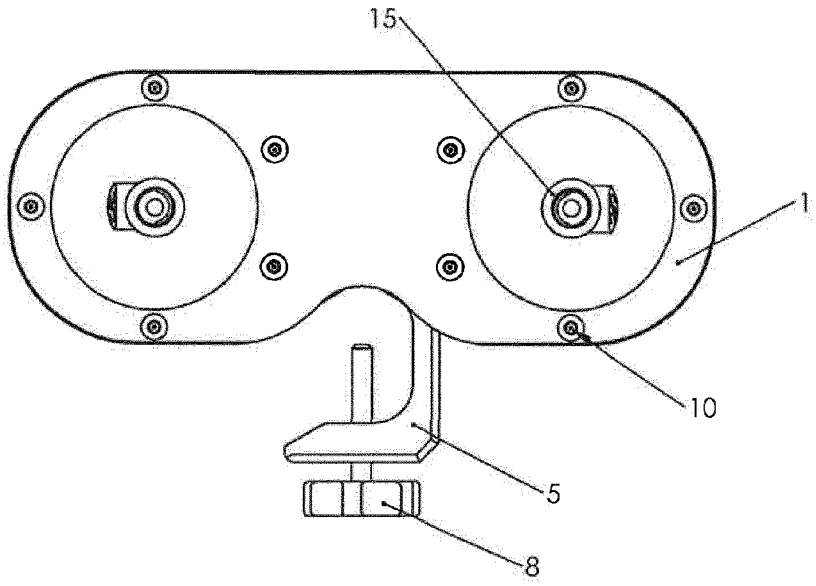

FIG.3

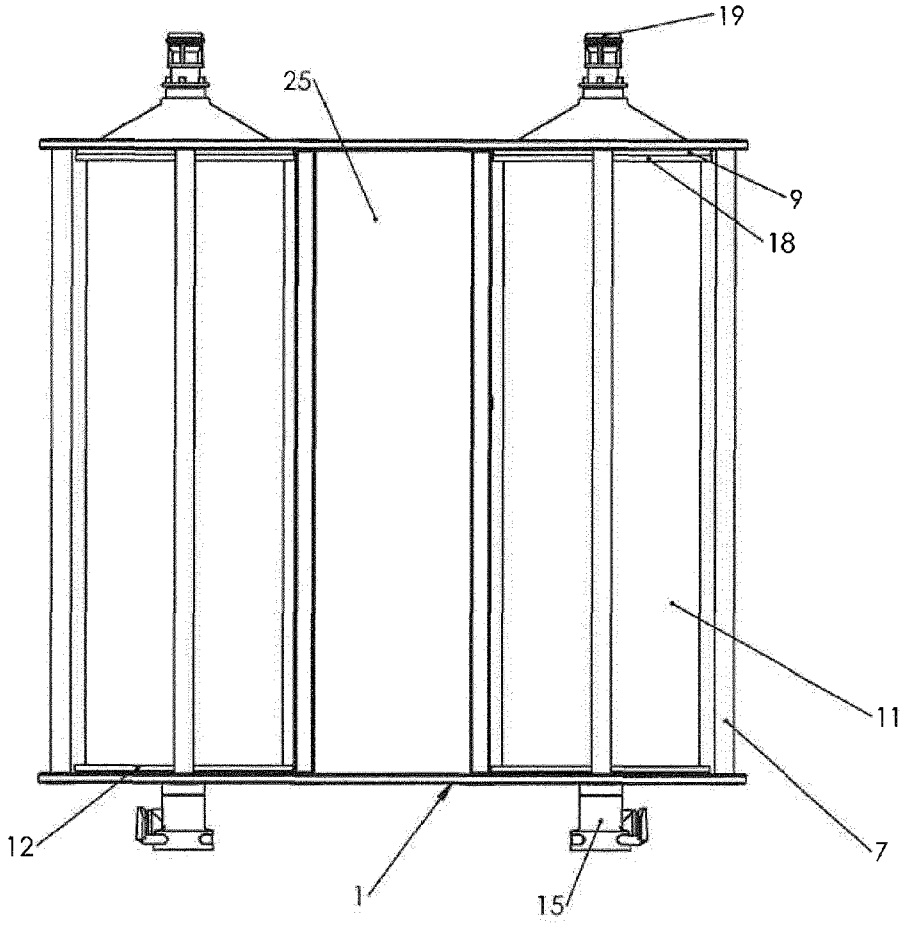

FIG.4

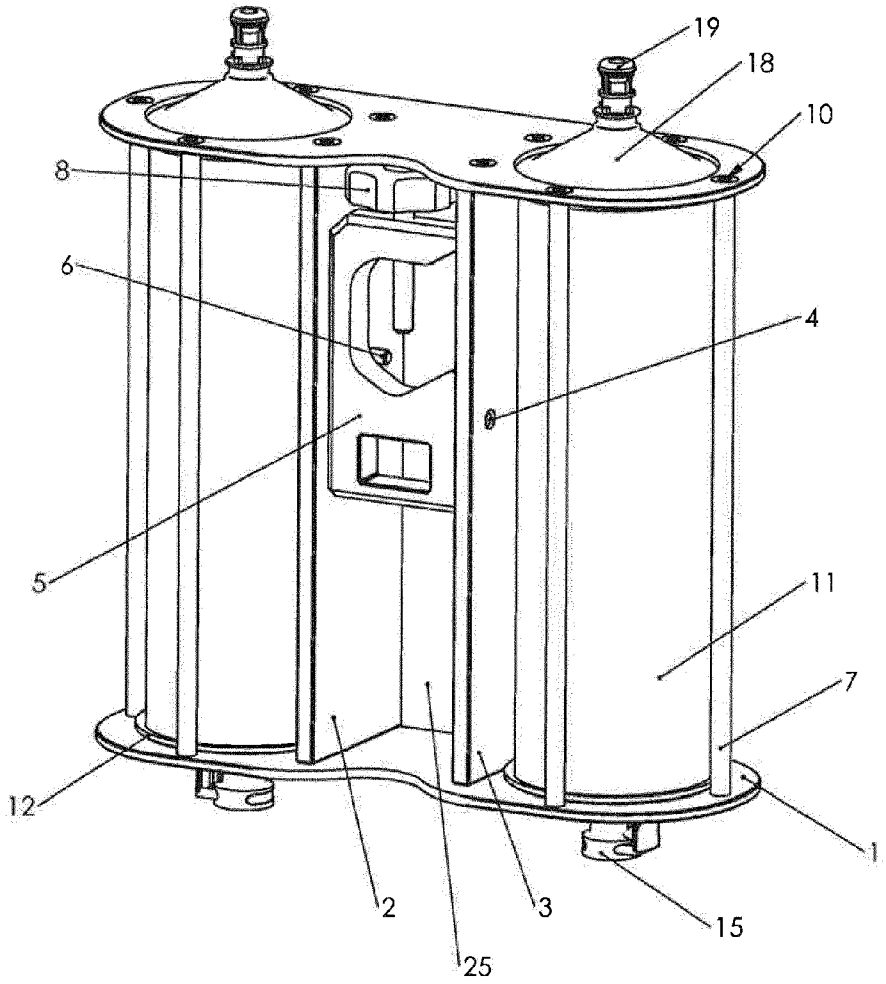

FIG.5

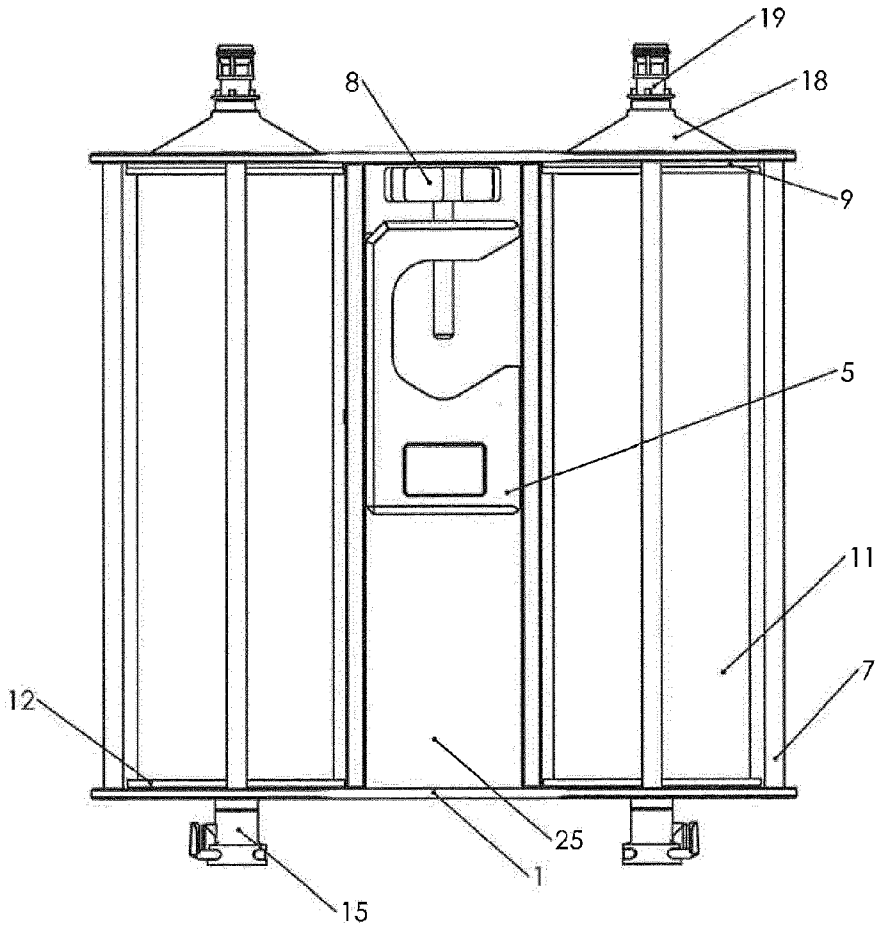

FIG. 6

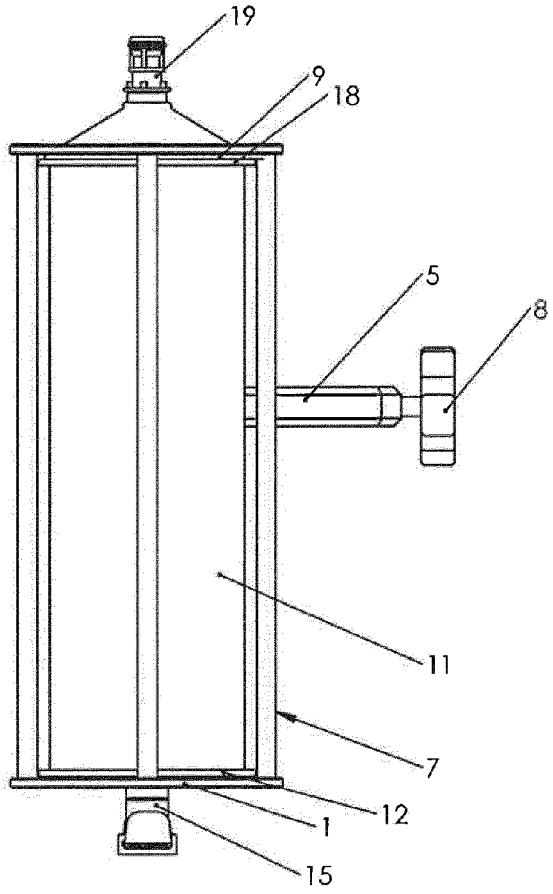

FIG.7

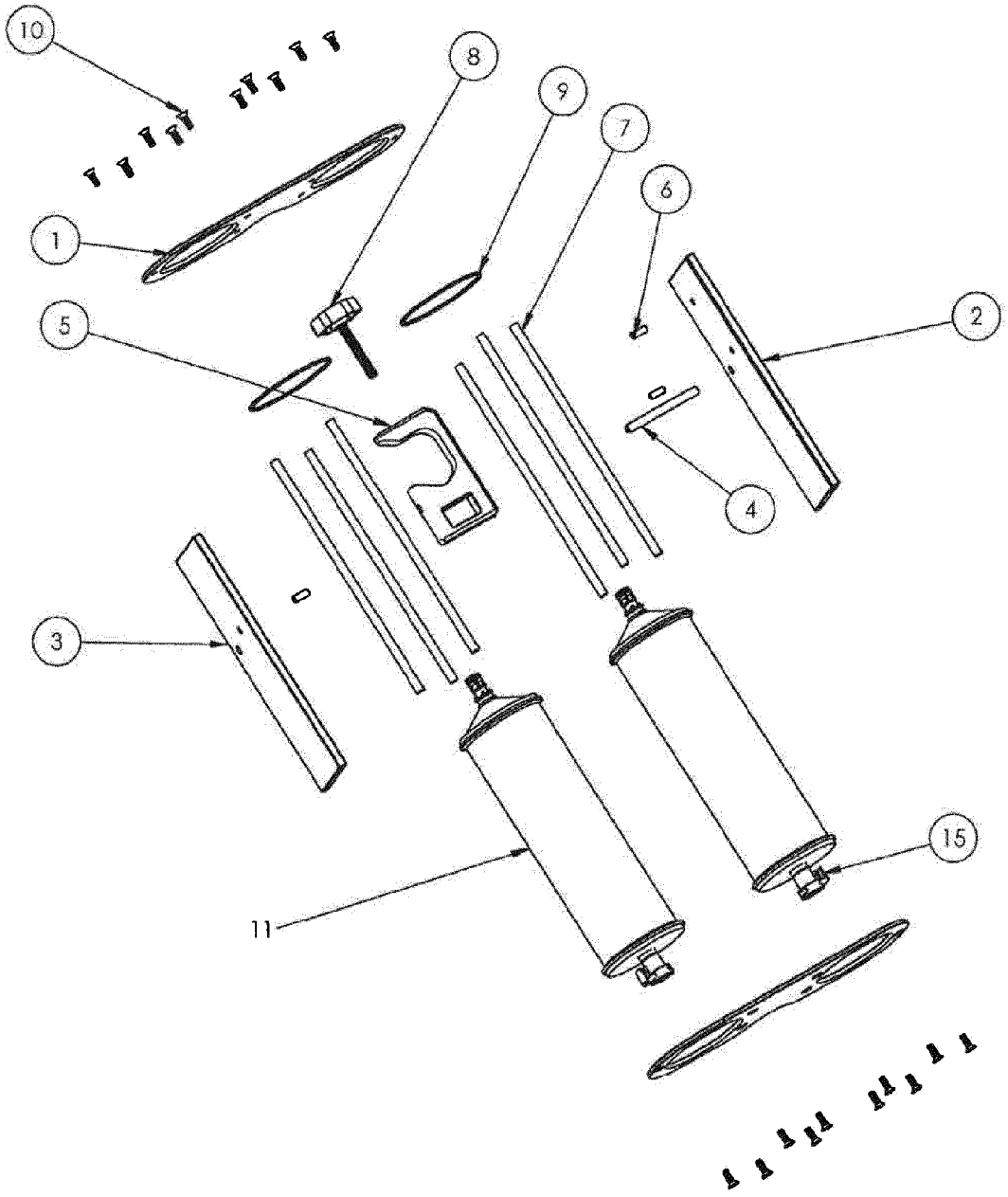

FIG. 8

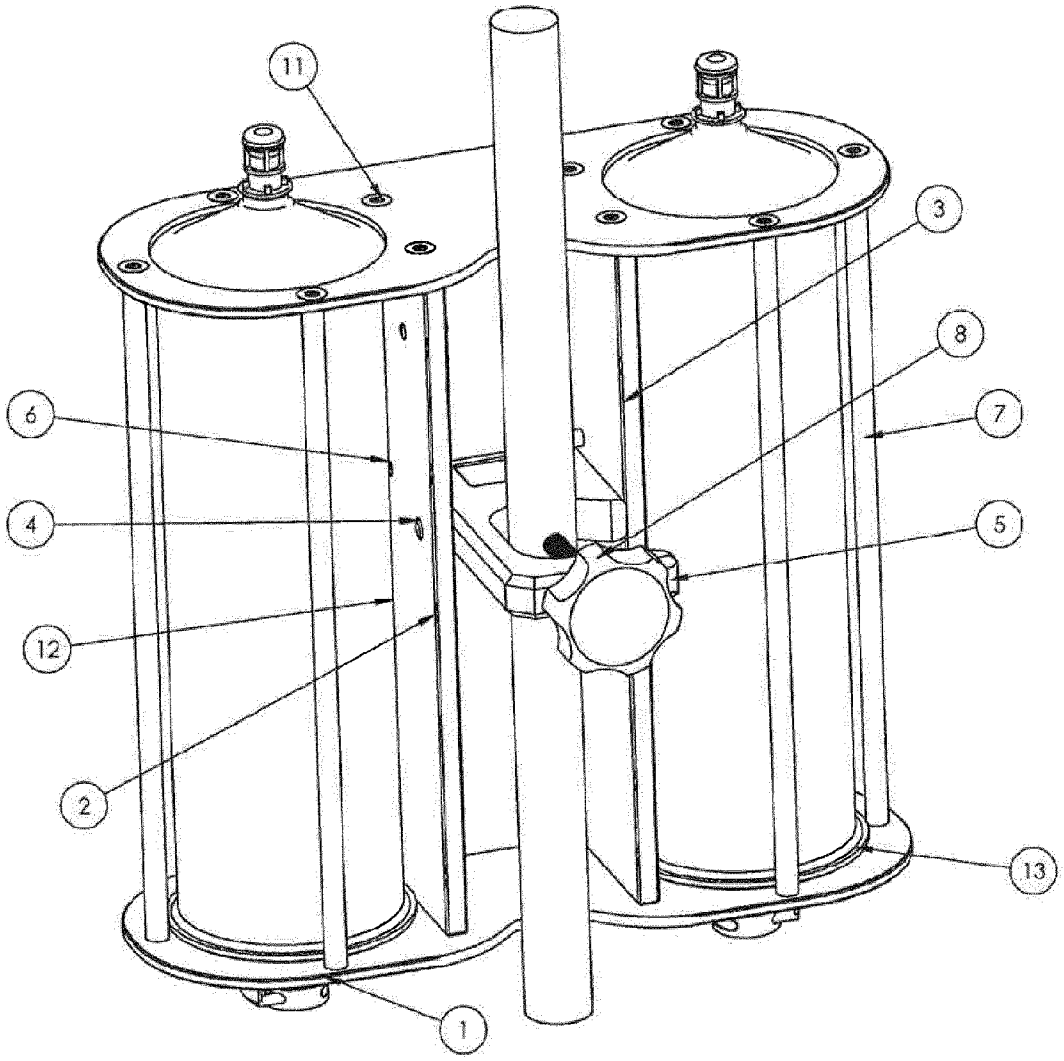

FIG.9

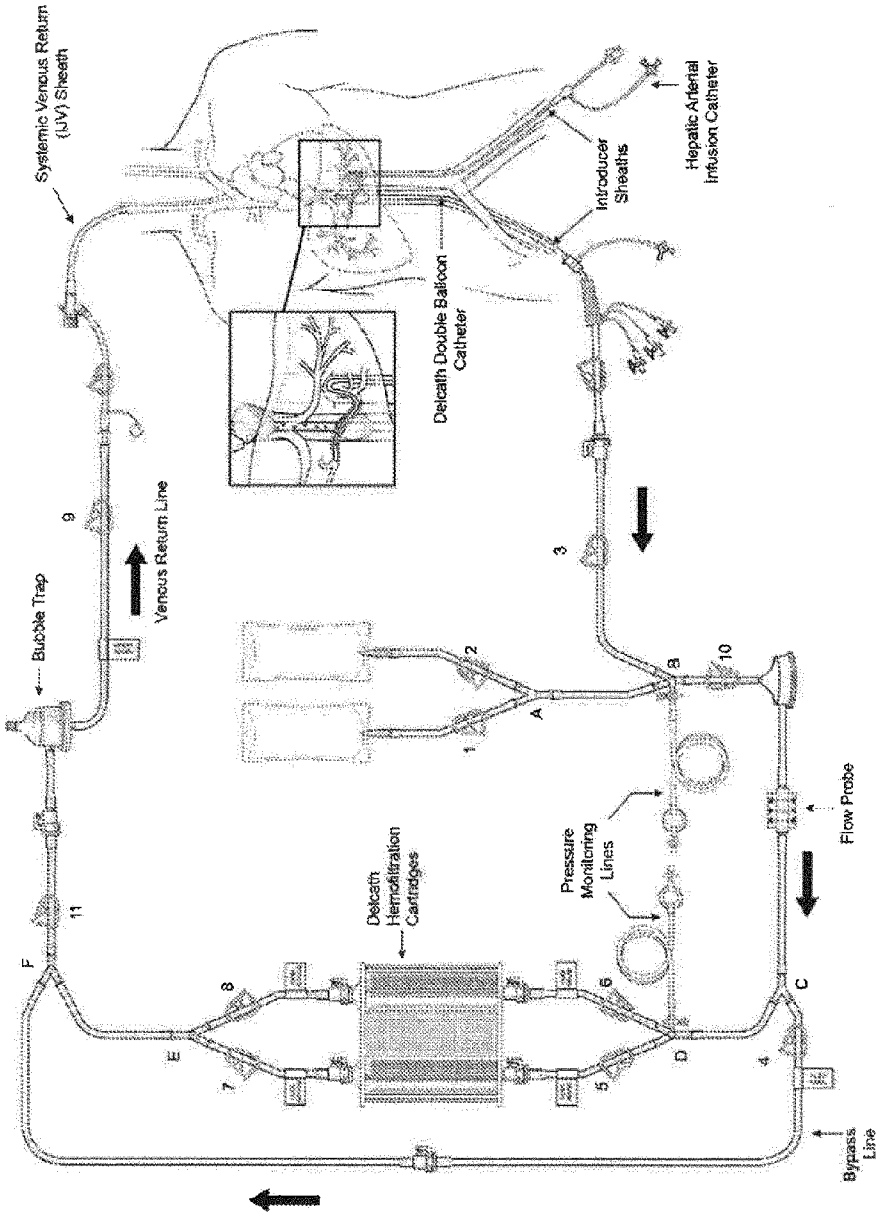
Systemic Venous Return (IJV) Sheath
Hepatic Arterial Infusion Catheter
Introducer Sheaths
Delcath Double Balloon Catheter
Bubble Trap
Venous Return Line
Delcath Hemofiltration Cartridges
Pressure Monitoring Lines
Flow Probe
Bypass Line
A
B
C
D
E
F
1
2
3
4
5
6
7
8
9
10
11

FIG. 10