(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 January 2017 (05.01.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/001357 A1

(51) International Patent Classification:
A61M 1/30 (2006.01) *A61M 1/36* (2006.01)

(21) International Application Number:
PCT/EP2016/064912

(22) International Filing Date:
28 June 2016 (28.06.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
15174230.1 29 June 2015 (29.06.2015) EP

(71) Applicant: **GAMBRO LUNDIA AB** [SE/SE]; P.O. Box 10101, 220 10 Lund (SE).

(72) Inventors: **COURT, Thierry**; Résidence Les Jardins d'Astrée, 26 A Rue Arago, 69100 Villeurbanne (FR). **ERICSON, Björn**; Kävlingevägen 68, S-226 52 Lund (SE). **NILSSON, Roger**; Höstgatan 1, 24334 Höör (SE). **HÅKANSSON, AnnMargret**; Lillö 1306, S-268 76 Kågeröd (SE).

(74) Agent: **SUTTO, Luca**; c/o PGA S.R.L., Via Mascheroni, 31, 20145 Milano (IT).

(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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, 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, SA, 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, ST, 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, KM, ML, MR, NE, SN, TD, TG).

Published:

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

(54) Title: EXTRACORPOREAL BLOOD TREATMENT APPARATUS FOR SINGLE-NEEDLE TREATMENTS

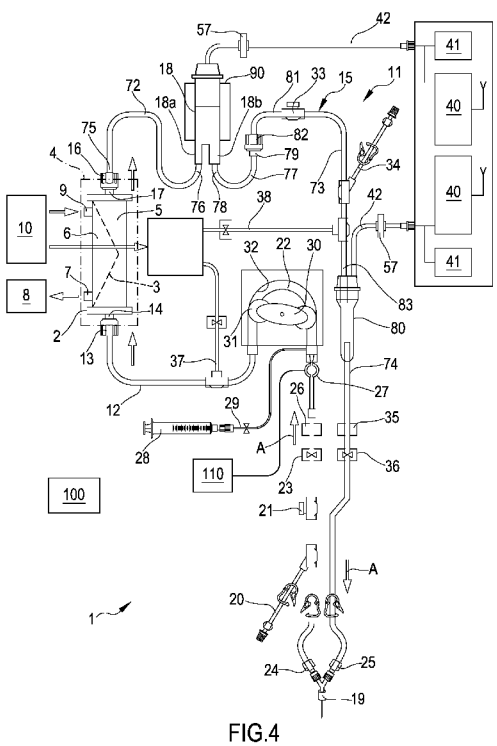


FIG.4

(57) Abstract: An extracorporeal blood circuit (11) cooperating with a single blood pump (30) and having at least one blood chamber (18; 80) in the blood return line but no blood chamber in the blood withdrawal line; and an extracorporeal blood treatment apparatus (1) configured for single needle treatments comprising the extracorporeal blood circuit (11) wherein the apparatus has a control unit (100) configured to control a pneumatic circuit (40) and the blood pump (30) such as to keep pressure in the blood circuit under control during both an arterial and a venous phase of the single needle cycles. A method for controlling the apparatus is also disclosed.

WO 2017/001357 A1

TITLE

Extracorporeal blood treatment apparatus for single-needle treatments

DESCRIPTION

TECHNICAL FIELD OF THE INVENTION

The present invention relates to an extracorporeal blood treatment apparatus which may be connected to a patient by means of a single access channel, such a single needle or a single cannula or a single lumen catheter. The apparatus may be for example an apparatus for treatment of renal insufficiency or a plasmapheresis apparatus. The invention also concerns new extracorporeal blood treatment circuits particularly suitable for use in single access configuration and methods of configuring the extracorporeal blood circuits.

BACKGROUND ART

An extracorporeal blood circuit may be connected to a patient cardiovascular system in either "double needle" mode or "single needle" mode. In double-needle mode, a first needle is used for the patient's arterial access, i.e. for withdrawing blood from the patient, and a second needle is used for the patient's venous access, i.e. for returning blood into the patient. Thus, blood flows in the extracorporeal circuit according to a single direction of flow from the first needle, through the arterial line, the blood compartment of a blood treatment unit, the venous line, finally reaching the second needle. Double-needle mode makes it possible to withdraw and simultaneously return blood but requires insertion of two needles into the patient, for example in the patient's fistula. Considering chronic patients receive several treatment sessions per week, repeated piercing of the fistula may cause damage to the vascular access and no longer

permit insertion. Furthermore, there are cases were a small fistula may prevent access of two needles, or may compel to insert two needles so close to each other causing, during treatment, an excessive recirculation thus compromising quality of the treatment.

In order to prevent or overcome the above problems single needle mode may be an available option.

In single-needle mode, the extracorporeal blood circuit is connected to the patient cardiovascular system by means of a single needle inserted into the patient access. Then, during a first phase, often referred to as the arterial phase, blood is taken from the patient via the single needle into the extracorporeal circuit, and in a second phase, often referred to as venous phase, blood is passed from the extracorporeal blood circuit back to the patient through the single needle.

Various solutions are known concerning single needle apparatus.

For instance, US4231366 discloses a single needle apparatus with a first blood pump 30 acting on the arterial line of the blood circuit and a second blood pump 30 acting on the venous line. The blood circuit also includes a venous chamber with level sensors configured to issue signals used to command the switch between the arterial and venous phases: arterial and venous clamps are used to selectively open and close the arterial and venous lines while the arterial and venous blood pumps 30 are alternatively operated.

US4464164 and US4490135 relate to a further single needle apparatus provided with an arterial blood pump 30, a venous blood pump 30 and a venous bag accumulator. The two blood pumps 30 are alternatively operated to execute the arterial and venous phases.

US4758336 also relates to a single needle apparatus with two blood pump 30s and with an arterial and a venous blood chambers. In particular, a first blood pump 30 operates upstream the arterial chamber during the arterial phase only and a second blood pump 30, located between the arterial chamber and the treatment unit,

continuously operates.

US5098373 discloses another double blood pump 30 single needle apparatus with the two blood pumps 30 operating on the arterial line respectively upstream and downstream an arterial bubble trap.

US8500671 and WO2010/037520 show a single needle apparatus with two blood pumps 30 in the arterial line, wherein a container is interposed between the two blood arterial pumps. Withdrawal and return phases are alternated by increasing and reducing speed of the upstream blood pump 30.

Various other embodiments of a single needle apparatus using an arterial and a venous pump are also disclosed in US8394047.

The above solutions use two blood pump 30s and may result in an architecture which would not be necessarily present in a double needle apparatus. Furthermore, the extracorporeal circuit of the above solutions may require a dedicated design significantly different from that of a typical double needle circuit. Moreover, the extracorporeal blood circuits of at least some of the above solutions may undesirably determine a relatively big volume of extracorporeal blood and a relatively big blood-air interface.

US5227049 shows various single needle apparatuses. In a first embodiment an arterial pump is located in the arterial line while a venous pump is located in the venous line downstream the venous chamber but upstream a further bubble trap. The arterial blood pump 30 is driven until filling of venous chamber, then the arterial pump is switched off and the venous pump is activated with pneumatic means controlling pressure in venous chamber. In a second embodiment, the arterial pump is located upstream an arterial chamber while the venous pump is located as in the first embodiment, namely downstream the venous chamber and upstream a further bubble trap. The arterial blood pump 30 is driven until filling of the arterial and venous chambers, then the venous pump is activated and the arterial pump switched off. Pressure is controlled in both the arterial and venous chambers by pneumatic

means while the arterial pump fills both chambers during arterial phase and venous pump empties both chambers during the venous phase. In a third embodiment, a single blood pump 30, namely an arterial pump, is used. The arterial pump operates downstream the arterial chamber to keep flow rate in the dialyzer substantially constant. A venous chamber is provided in the venous line, the venous chamber being connected to pneumatic means. The pneumatic means control respective pressures in the arterial and venous chambers. The arterial pump operates continuously while the arterial and venous phases are obtained by alternately opening and closing arterial and venous claims.

US20130079698, US2012/0251998 and WO2008/148505 disclose a single needle apparatus presenting a single blood pump 30 operative on the arterial line and a single blood chamber 18 located in the venous line. A sealed pneumatic circuit 40 controls pressure in venous chamber keeping pressure substantially constant during the venous phase, while the arterial pressure is necessarily variable in order to periodically recharge an air reservoir part of the sealed pneumatic circuit 40. This solution requires a pneumatic circuit 40 hermetically sealed from the external environment in order to control pressure during the venous phase. Furthermore, the need to cyclically refill the air reservoir requires a dedicated procedure in the arterial phase, which is thus made more complex. Additionally, during arterial phase, the arterial pump creates a progressively increasing pressure: the variable pressure in the blood circuit may have a negative impact on the patient fistula.

Although many solutions have been proposed in the past the Applicant has found that single needle apparatus may be further improved in order to reduce as possible complexity of the apparatus, and particularly of the extracorporeal blood circuit, while minimizing problems of haemocompatibility, coagulation and

fistula stress.

It is therefore an object of the present application to provide an extracorporeal blood treatment apparatus and/or an extracorporeal blood circuit overcoming one or more of the drawbacks or limitations typical of the above prior art solutions and at the same time particularly suitable for operation in a single-needle configuration.

In particular, it is a main object of the present application that of providing a single needle extracorporeal blood treatment apparatus and/or an extracorporeal blood treatment circuit having a lean design.

It is a further object of the present application providing a single needle extracorporeal blood treatment apparatus and circuit capable of minimizing extracorporeal blood volume and air blood interface.

A further object is to improve the hemodynamic conditions both in the arterial and venous lines in order to reduce as possible any negative impacts on the patient's fistula during treatment.

An auxiliary object is providing an apparatus which is suitable to maximize treatment efficiency in term of clearance and thus delivered treatment dialysis dose.

Finally, it is a further auxiliary object that of providing an apparatus which may easily configured to operate in double access, e.g. double needle, mode.

Additionally, it is an auxiliary object of the invention providing an apparatus suitable to be easily configured to operate in an HDF

(hemodiafiltration) mode without therapy interruption.

SUMMARY

At least one of the above objects is substantially reached by an apparatus according to one or more of the appended claims.

At least one of the above objects is substantially also reached by an apparatus and/or by a circuit and/or by a method according to one or more of below incorporated aspects.

Apparatus, circuits and methods for the extracorporeal treatment of blood according to aspects of the invention are here below described.

A 1st aspect concerns an extracorporeal blood treatment apparatus comprising:

- a treatment unit (2) having at least a semipermeable membrane (3) dividing the treatment unit (2) into a blood compartment (5), and a filtrate compartment (6);
- a blood withdrawal line (12) having a first end connected to an inlet port of the blood compartment of the treatment unit;
- a blood return line (15) having a first end connected to an outlet port of the blood compartment of the treatment unit, the blood return line (15) including at least one blood chamber (18) configured, in operation, to host a volume of blood and define a blood-air interface;
  wherein the blood withdrawal line (12), the blood compartment (5) and the blood return line (15) are part of an extracorporeal blood circuit (11);
- a single lumen access device (19) configured to be connected to a patient's cardiovascular system, wherein - in a single access configuration of the extracorporeal blood circuit - the blood withdrawal line (12) and the blood return line (15)

have respective second ends contemporaneously connected to the single lumen access device;

- a blood pump (30) positioned at, and configured to be operative on, the blood withdrawal line;
- an intercepting organ (36) positioned at, and configured to be operative on, a portion of the blood return line (15) and selectively positionable at least in an open condition and in a closed condition to respectively allow and prevent a passage of fluid through said second end of the blood return line;
- a pneumatic circuit (40) connected to the blood chamber (18) in the blood return line (15) and configured to supply gas to or withdraw gas from the blood chamber.

In a 2nd aspect according to the 1st aspect the apparatus further includes:

- a control unit (100), connected to the blood pump (30), to the pneumatic circuit (40) and to the intercepting organ (36), wherein – with the extracorporeal circuit (11) in said single access configuration – the control unit (100) is configured to repeatedly execute a cycle including an arterial phase and a venous phase,
  - wherein the arterial phase of the cycle includes the following steps the control unit (100) is configured to execute:
    - operating the blood pump (30) to withdraw blood via the single lumen access device (19) and convey it through the blood compartment (5) and to the blood chamber (18),
    - maintaining the intercepting organ (36) in the closed condition,
    - controlling the pneumatic circuit (40) to withdraw gas from the blood chamber (18) in synchrony with

operation of the blood pump (30) to facilitate inlet of blood in the blood chamber, wherein said controlling the pneumatic circuit (40) to withdraw gas includes maintaining pressure in the blood chamber (18) at a predetermined arterial phase pressure regimen at least for a major portion of the arterial phase;

- wherein the venous phase of the cycle includes the following steps the control unit (100) is configured to execute:
  - stopping operation of the blood pump (30),
  - maintaining the intercepting organ (36) in the open condition and cause blood in the venous line to return via the single lumen access device,
  - controlling the pneumatic circuit (40) to supply gas to the blood chamber (18) while the intercepting organ (36) is in the open condition, wherein said step of controlling the pneumatic circuit (40) to supply gas to the blood chamber (18) during the venous phase comprises maintaining pressure in the blood chamber (18) at a predetermined venous phase pressure regimen at least for a major portion of the venous phase.

Note that by major portion of the arterial phase it is intended about 80% or more of the duration of the arterial phase: in other words close to the entire duration of the arterial phase but for possible transitory periods which may take place. In a similar manner, by major portion of the venous phase it is intended about 80% or more of the duration of the venous phase, i.e., close to the entire duration of the venous phase but for possible transitory periods which may take place.

Also note that according to a less preferred alternative the

bubble trap (18) may be part of the blood withdrawal line instead of being part of the blood return line.

In a 3rd aspect according to the 2nd aspect said step of keeping pressure in the blood chamber (18) at a predetermined arterial phase pressure regimen, which the control unit (100) is configured to execute at each cycle during arterial phase, comprises one of:

keeping pressure in the blood chamber (18) at a substantially prefixed constant pressure value at least for a major portion of the arterial phase,

keeping pressure in the blood chamber (18) within a prefixed range around a constant pressure value at least for a major portion of the arterial phase.

In a 4th aspect according to any one of the preceding two aspects said step of keeping pressure in the blood chamber (18) at a predetermined venous phase pressure regimen, which the control unit (100) is configured to execute at each cycle during venous phase, comprises one of:

keeping pressure in the blood chamber (18) at a substantially prefixed constant pressure value at least for a major portion of the venous phase,

keeping pressure in the blood chamber (18) within a prefixed range around a constant pressure value at least for a major portion of the venous phase.

In a 5th aspect according to any one of the preceding three aspects further wherein the control unit (100) is configured to receive the constant pressure value (P_{0A}) to be kept during arterial phase and/or the constant venous pressure value (P_{0V}) to be kept during the venous phase either from a memory connected to the control unit (100) where said value(s) are pre-stored or from an input device connected to the control unit.

In a 6th aspect according to any one of the preceding four aspects said control unit (100) is configured such that said predetermined arterial phase pressure regimen is identical to the predetermined venous phase pressure regimen, in particular wherein said constant arterial pressure value is identical to said constant venous pressure value.

In a 7th aspect according to any one of the preceding aspects no blood pump (30) is operative on the blood return line.

In a 8th aspect according to any one of the preceding six aspects, during venous phase with the blood pump (30) positioned at the blood withdrawal line (12) being stopped, the control unit (100) is configured to cause blood in the venous line to return to the single lumen access device (19) exclusively by keeping the intercepting organ (36) in the open condition and controlling the pneumatic circuit (40) to supply gas to the blood chamber.

In a 9th aspect according to any one of the preceding aspects no blood chambers or blood reservoirs configured for air/blood separation is directly connected to, or part of, the blood withdrawal line.

In a 10th aspect according to any one of the preceding aspects from the 2nd to the 9th said controlling step which the control unit (100) is configured to execute during the arterial phase of the cycle comprises:

- estimating or receiving an arterial stroke volume value (VART), corresponding to a blood volume intended to be conveyed into the blood chamber (18) during the arterial phase, and
- commanding the pneumatic circuit (40) to withdraw from the

blood chamber, during the arterial phase, a volume of gas equal to said arterial stroke volume value (V_{ART}).

In a 11th aspect according to any one of the preceding aspects from the 2nd to the 10th the control unit (100) is configured for storing or receiving a first relationship: $V_{ART} = (Q_{B\_ART} - Q_{UF\_ART}) \cdot T_{ART}$

wherein:

V_{ART} is an estimated or set value of the arterial stroke volume,

T_{ART} is an estimated or set value of the duration of the arterial phase during which the blood pump (30) and the pneumatic circuit (40) are both active,

Q_{B_ART} is a measured or set value of the blood flow rate in the arterial line during the arterial phase,

Q_{UF_ART} is a measured or set value of the ultrafiltration flow rate through the semipermeable membrane (3) of the treatment unit (2) during the arterial phase,

said control unit (100) adopting said first relationship for calculating one of said value of the arterial stroke volume VART and said value of the duration of the arterial phase TART, using a set value of the other.

In a 12th aspect according to any one of the preceding aspects from the 2nd to the 11th said controlling step which the control unit (100) is configured to execute during the venous phase of the cycle comprises:

- estimating or receiving a venous stroke volume value (V_{VEN}), corresponding to a blood volume intended to be ejected from the blood chamber (18) and returned to the patient during the venous phase, and
- commanding the pneumatic circuit (40) to supply to the blood chamber (18), during the venous phase, a corresponding volume of gas equal to said venous stroke volume value (V_{VEN}).

In a 13th aspect according to the preceding aspect the control unit (100) is configured for commanding the pneumatic circuit (40) to supply to the blood chamber (18) a volume of gas equal to said venous stroke volume value (V_{VEN}) during a time interval (T_{VEN}) while keeping pressure constant and higher than blood pressure such that the same volume (V_{VEN}) of blood is returned to the patient.

In a 14th aspect according to any one of the preceding aspects from the 2nd to the 13th comprising at least one venous pressure sensor (41) connected to the blood return line (15) and configured to receive a pressure signal and supply it to the control unit (100).

In a 15th aspect according to the preceding aspect, the control unit (100) is configured to execute a pressure adjustment sequence during said arterial phase comprising:

receiving the pressure signal from the venous pressure sensor (41),

determining one or more measured values of the venous pressure from said pressure signal,

comparing said one or more measured values of the venous pressure with at least one set value representative of the predetermined arterial phase pressure regimen, and

adjusting the pneumatic circuit (40) to withdraw gas from the blood chamber (18) during the arterial phase to keep said one or more measured values of the venous pressure within a first prefixed tolerance from the at least one set value representative of said predetermined arterial pressure regimen.

As an alternative or in addition to the features of this aspect, maintaining pressure in the blood chamber (18) at a predetermined arterial phase pressure regimen comprises receiving

by the control unit (100) a level signal from a level sensor associated to the blood chamber and communicating with the control unit, and controlling, by the control unit, the pneumatic circuit to keep blood in the blood chamber at a constant level or at a level within a prefixed range around said constant level, at least during the major portion of the arterial phase.

In a 16th aspect according to any one of the preceding two aspects the control unit (100) is configured to execute a pressure adjustment sequence during said venous phase comprising:

receiving the pressure signal from the venous pressure sensor (41),

determining one or more measured values of the venous pressure from said pressure signal,

comparing said one or more measured values of the venous pressure with at least one set value representative of the predetermined venous phase pressure regimen, and

adjusting the pneumatic circuit (40) to supply gas to the blood chamber (18) during the venous phase to keep the one or more measured values of the venous pressure within a second prefixed tolerance from said at least one set value representative of said predetermined venous pressure regimen.

As an alternative or in addition to the features of this aspect, maintaining pressure in the blood chamber (18) at a predetermined venous phase pressure regimen comprises receiving by the control unit (100) a level signal from a level sensor associated to the blood chamber and communicating with the control unit, and controlling, by the control unit, the pneumatic circuit to keep blood in the blood chamber at a constant level or at a level within a prefixed range around said constant level, at least during the major portion of the venous phase.

In a 17th aspect according to any one of the preceding three aspects the pneumatic circuit (40) comprises an air pump having one side connected to the atmosphere and another side connected to the blood chamber (18) and wherein the control unit (100) receives said pressure signal from the pressure sensor (41) and acts on the air pump to keep pressure in the blood chamber (18) matching the arterial pressure regimen and the venous pressure regimen.

In a 18th aspect according to any one of the preceding aspects from the 2nd to the 17th the pneumatic circuit (40) comprises a gas accumulator having:

- a variable volume chamber (60) in gas communication with the blood chamber (18),
- an actuator (60) associated to the variable volume chamber and controlled by the control unit (100) and active to cause a variation of the internal volume of the variable volume chamber (60) between a minimum volume and a maximum volume.

In a 19th aspect according to the preceding aspect, during the arterial phase, the control unit (100) is configured for commanding the pneumatic circuit (40) to withdraw from the blood chamber (18) a volume of gas equal to an/the estimated or set value of the arterial stroke volume VART, by acting on said actuator and increasing said internal volume to keep a combined volume – defined by the sum of the volume occupied by gas present in the blood chamber (18) with the internal volume of said variable volume chamber (60) – substantially constant during the entire or a major portion of said arterial phase.

In a 20th aspect according to any one of the preceding two aspects, during the venous phase, the control unit (100) is configured for commanding the pneumatic circuit (40) to supply to the blood

chamber (18) a volume of gas equal to an/the estimated or set value of the arterial stroke volume VVEN , by acting on said actuator and decreasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber (18) with the internal volume of said variable volume chamber (60) - substantially constant during the entire or a major portion of said venous phase.

In a 21st aspect according to any one of the preceding aspects the apparatus has at least one arterial pressure sensor - not shown - connected to a tract of the blood withdrawal line (12) positioned between the second end of the blood withdrawal line (12) and the blood pump (30) such as to operate upstream to the blood pump (30) at least during said arterial phase, said arterial pressure sensor being configured to receive a pressure signal from said tract of the blood withdrawal line (12) and supply it to the control unit (100), and wherein the control unit (100) is configured to detect if pressure is acceptable or not, e.g. if pressure is too low or too high with respect to an acceptable range which may be set by user or stored in the CPU memory.

In a 22nd aspect according to any one of the preceding aspects said blood chamber (18) is the only one on the blood return line, no other blood chambers being positioned at, part of, or directly connected to the blood return line.

In a 23rd aspect according to any one of the preceding aspects, the blood return line (15) further comprises:

- a first tube (70) extending from said first end to an inlet port of the blood chamber, and
- a second tube (71) extending from an outlet port of the blood chamber (18) to said second end of the blood return line;

wherein said venous pressure sensor (41) and said pneumatic

circuit (40) are fluidly connected to the blood chamber (18) via a pressure line having a first end connected to the blood chamber (18) and a second end connected to said pneumatic circuit (40).

In a 24th aspect according to the preceding aspect a transducer protector is positioned on said pressure line and comprises a casing housing a hydrophobic membrane (3) separating a casing internal volume into a first chamber communicating with the blood chamber (18) and a second chamber communicating with the pneumatic circuit.

In a 25th aspect according to any one of the preceding aspects from the 1st to the 21st said at least one blood chamber (18) is a reservoir of fixed internal volume having one single blood port (18a) configured to act both as blood inlet and as blood outlet port,

- said blood return line (15) comprises an additional blood chamber (80) positioned downstream said single blood port,
- said venous pressure sensor (41) is fluidly connected to either one of said blood chamber (18) or said additional blood chamber, and
- said pneumatic circuit (40) is fluidly connected to the blood chamber (18) via a pressure line (42) having a first end connected to the blood chamber (18) and a second end connected to said pneumatic circuit (40).

In a 26th aspect according to the preceding aspect a transducer protector is positioned on said pressure line and comprises a casing housing a hydrophobic membrane separating a casing internal volume into a first chamber communicating with the blood chamber (18) and a second chamber communicating with the pneumatic circuit.

In a 27th aspect according to any one of the preceding two aspects the blood return line (15) comprises:

- a first tube (84) extending from said first end to a blood inlet port of the additional blood chamber,
- a second tube (85) extending from a blood outlet port of the additional blood chamber (80) to said second end of the blood return line.

In a 28th aspect according to the preceding aspect the single blood port (18a) is connected to a branch-off point (86) of the first tube and wherein a tube segment (87) connects said single blood port to said branch-off point, this latter being located in an intermediate region of said first tube of the blood return line.

In a 29th aspect according to any one of the preceding two aspects the single blood port of the blood chamber (18) carries a connector configured to removably couple with a counter-connector carried by the tube segment to selectively couple and uncouple the blood chamber (18) to the return line.

In a 30th aspect according to any one of the preceding two aspects a clamp (89) acts in correspondence of said tube segment, further wherein said clamp is operable - either manually or under a command from said control unit (100) - between an open position allowing passage of fluid through said tube segment and a closed position preventing passage of fluid through said tube segment.

In a 31st aspect according to any one of the preceding aspects from the 1st to the 21st said at least one blood chamber (18) is a reservoir having two blood ports including an inlet port (18a), configured to receive all fluid coming from the first end of the blood return line, and an outlet port (18b), configured to discharge fluid exiting from the blood chamber;

- said blood return line (15) comprises an additional blood chamber (80), positioned downstream said outlet port (18b) of the blood chamber (18),
- said venous pressure sensor (41) is fluidly connected to either one of said blood chamber (18) or said additional blood chamber, and
- said pneumatic circuit (40) is fluidly connected to the blood chamber (18) via a pressure line having a first end connected to the blood chamber (18) and a second end connected to said pneumatic circuit (40).

In a 32nd aspect according to the preceding aspect a transducer protector is positioned on said pressure line and comprises a casing housing a hydrophobic membrane (3) separating a casing internal volume into a first chamber communicating with the blood chamber (18) and a second chamber communicating with the pneumatic circuit.

In a 33rd aspect according to any one of the preceding two aspects the blood chamber (18) is removably coupled to the rest of the blood return line.

In a 34th aspect according to any one of the preceding three aspects the blood return line (15) comprises

- a first tube (72) extending from said first end of the blood return line (15) and connected to the inlet port of the blood chamber (18) reservoir,
- a second tube (73) extending from the outlet port of the blood chamber (18) reservoir to a blood inlet port of the additional blood chamber,
- a third tube (74) extending from an outlet port of the additional blood chamber (80) to said second end of the blood return line.

In a 35th aspect according to the preceding aspect the first tube (72) has a first end, provided with a counter-connector adapted to removably couple with a connector of the outlet port of the blood compartment of the blood treatment unit, and a second end connected, in particular fixed, to the inlet port of the blood chamber (18) reservoir.

In a 36th aspect according to any one of the preceding two aspects the second tube (73) comprises:

- at least one first segment having a first end, connected, and in particular, fixed to outlet port of the blood chamber, and a second end provided with a connector, and
- a second segment having a first end with a respective counter-connector, configured for removable connection to the connector carried by the second end of the first segment, and a second end connected, in particular fixed, to the blood inlet port of the additional blood chamber, and
- wherein the counter-connector at the first end of the second segment is configured to also be removably connectable to the connector carried by the outlet port of the blood compartment of the treatment unit.

In a 37th aspect according to any one of the preceding aspects the apparatus includes:

- a support region defining a holder (90) for said blood chamber,
- a low level sensor (91) associated to the support region and connected to said control unit (100), the low level sensor being configured for issuing a signal to the control unit (100) at least when a liquid reaches a minimum liquid level in said blood chamber (18) and
- a high level sensor (92) associated to support region and

connected to said control unit (100), the high level sensor being configured for issuing a signal to the control unit (100) at least when a liquid reaches a maximum liquid level in said blood chamber.

In a 38th aspect according to the preceding aspect the apparatus includes: a foam sensor (93) associated to the support region in a position vertically above the high level sensor and connected to said control unit (100), the foam sensor being configured for issuing a signal to the control unit (100) at least when foam reaches a maximum foam level in said blood chamber, the maximum foam level being a level vertically higher than the maximum liquid level.

In a 39th aspect according to any one of the preceding aspects from the 2nd to the 38th the control unit (100) is configured to receive one or more of - optionally all - the following settings relating to the arterial phase:

- one or more set values representative of said predetermined arterial phase pressure regimen, in particular said prefixed constant arterial pressure value;
- a set value for a desired flow rate intended to be delivered by the blood pump (30) during said arterial phase,
- a value of a/the arterial stroke volume VART intended to be delivered into the blood chamber (18) during the arterial phase,

and to control the blood pump (30) and the pneumatic circuit (40) based on one or more of said settings relating to the arterial phase.

In a 40th aspect according to any one of the preceding aspects from the 2nd to the 39th the control unit (100) is configured to receive one or more of - optionally all - the following settings relating

to the venous phase:

- one or more set values representative of said predetermined venous phase pressure regimen, in particular said prefixed constant venous pressure value;
- a set value for a desired flow rate intended to be delivered through the venous line during said venous phase,
- a value of a/the venous stroke volume VVEN intended to be removed from the blood chamber (18) during the venous phase;

and to control the blood pump (30) and the pneumatic circuit (40) based on one or more of said settings relating to the venous phase.

In a 41st aspect according to any one of the preceding aspects from the 2nd to the 40th the control unit (100) is configured for commanding a switch from said arterial phase of the cycle into said venous phase of the cycle when one of the following events takes place:

- expiration of a predetermined arterial phase time interval as of start of the arterial phase,
- delivery into the blood chamber (18) of a predetermined quantity of liquid as of start of the arterial phase,
- reaching of a maximum liquid level of liquid in the blood chamber,
- reaching of a maximum level of foam in the blood chamber.

In a 42nd aspect according to any one of the preceding aspects from the 2nd to the 41st said control unit (100) is configured for commanding a switch from said venous phase of the cycle into said arterial phase of the cycle when one of the following events takes place:

- expiration of a predetermined venous phase time interval as of start of the venous phase,
- evacuation from the blood chamber (18) of a predetermined

quantity of liquid as of start of the arterial phase,

- reaching of a minimum liquid level of blood into the blood chamber.

In a 43rd aspect according to any one of the preceding aspects from the 2nd to the 42nd the control unit (100) is configured for:

- calculating a value for an actual flow rate delivered by the blood pump (30) during arterial phase as a function of:
  - o the quantity or the flow rate of air removed by the pneumatic circuit (40) from the blood chamber (18) during the arterial phase, and
  - o the pressure in the blood chamber (18) during the arterial phase.

In a 44th aspect according to the preceding aspect the control unit (100) is configured for calculating the value for an actual flow rate delivered by the blood pump (30) during arterial phase also as a function of optionally the temperature (for instance as detected by a temperature sensor detecting the temperature of the ambient or of extracorporeal blood or of the air removed by pneumatic circuit).

In a 45th aspect according to any one of the preceding aspects from the 2nd to the 44nd the control unit (100) is configured for:

- calculating a value for an actual flow rate delivered by the blood pump (30) during arterial phase as a function of the time for blood in the blood chamber (18) to pass from two prefixed liquid levels, optionally from a minimum liquid level to a maximum liquid level as detected by respective low level and high level sensors.

In a 46th aspect according to any one of the preceding three aspects the control unit (100) is configured for receiving a set

value for a desired flow rate intended to be delivered by the blood pump (30) during said arterial phase, comparing the calculated actual flow rate value with the desired flow rate value, and adjusting an angular speed of the blood pump (30) such that the calculated actual flow rate value matches, or stays in a range around, said desired flow rate value during said arterial phase.

In a 47th aspect according to any one of the preceding aspects from the 2nd to the 46th said pressure adjustment sequence during said arterial phase further comprises determining if said one or more measured values of the venous pressure deviate by more than a first safety tolerance, which is less stringent than said first prefixed tolerance, from the at least one set value, and generating an alarm signal, optionally stopping the blood pump; and/or
wherein said pressure adjustment sequence during said venous phase further comprises determining if said one or more measured values of the venous pressure deviate by more than a second safety tolerance, which is less stringent than said second prefixed tolerance, from the at least one set value, and generating an alarm signal, optionally closing the venous clamp.

In a 48th aspect according to any one of the preceding aspects the extracorporeal blood circuit is configurable according to a double access configuration where the blood withdrawal line (12) second end is connected to a withdrawal lumen and the blood return line (15) second end is connected to a return lumen.

In a 49th aspect according to the preceding aspect the withdrawal lumen and the return lumen are part of a same access device or each part of a respective and distinct access device.

In a 50th aspect according to any one of the preceding two aspects the control unit (100) – with the extracorporeal blood circuit in said double access configuration – is configured to:
operating the blood pump (30) to withdraw blood from a patient via the withdrawal lumen and convey it through the blood compartment and into the blood chamber,
maintaining the intercepting organ (36) in the open condition while operating the blood pump (30) to return blood to the patient via said return lumen.

In a 51st aspect according to the preceding aspect the control unit is configured to coordinate operation of the blood pump (30) and of the pneumatic circuit (40) such that – with the extracorporeal circuit in said double access configuration – blood occupies only a lower portion of said blood chamber (18) and – with the extracorporeal circuit in said single access configuration – at least during the arterial phase blood occupies also a higher portion of said blood chamber.

A 52nd aspect concerns an extracorporeal circuit, in particular an extracorporeal blood circuit, which may be used in the apparatus of any one of the preceding claims.

In a 53rd aspect according to the preceding aspect the extracorporeal circuit includes:
a blood treatment unit (2) having at least one blood compartment;
a blood withdrawal line (12) having a first end connected to an inlet port of the blood compartment of the blood treatment unit (2), wherein the blood withdrawal line (12) includes a blood pump segment (22) configured to receive a blood pump rotor of a peristaltic blood pump (30);
a blood return line (15) having a first end connected to an outlet port of the blood compartment of the blood treatment unit;

a single lumen access device (19) configured to be connected with a single access of a patient's cardiovascular system, wherein the blood withdrawal line (12) and the blood return line (15) have respective second ends configured to be both connected to the single lumen access device (19);
wherein the blood return line (15) - in a first configuration of the circuit includes - includes:
a blood chamber (18) comprising a reservoir having a fixed internal volume wherein the blood chamber (18) reservoir has one single blood port (18a) configured to act both as inlet port and as outlet port; and
an additional blood chamber (80) positioned in the blood return line (15) downstream said blood chamber (18) between the blood port(s) (18a; 18a, 18b) of the blood chamber (18) reservoir and said second end of the blood return line.

In a 54th aspect according to the 52nd aspect the extracorporeal circuit includes:
a blood treatment unit (2) having at least one blood compartment;
a blood withdrawal line (12) having a first end connected to an inlet port of the blood compartment of the blood treatment unit (2), wherein the blood withdrawal line (12) includes a blood pump segment (22) configured to receive a blood pump rotor of a peristaltic blood pump (30);
a blood return line (15) having a first end connected to an outlet port of the blood compartment of the blood treatment unit;
a single lumen access device (19) configured to be connected with a single access of a patient's cardiovascular system, wherein the blood withdrawal line (12) and the blood return line (15) have respective second ends configured to be both connected to the single lumen access device (19);
wherein the blood return line (15) - in a first configuration of the circuit includes - includes:

a blood chamber (18) comprising a reservoir having a fixed internal volume wherein the blood chamber (18) reservoir has two blood ports (18a, 18b) including an inlet port, configured to receive all fluid coming from the first end of the blood return line, and an outlet port configured to discharge fluid exiting from the blood chamber; and

an additional blood chamber (80) positioned in the blood return line (15) downstream said blood chamber (18) between the blood port(s) (18a; 18a, 18b) of the blood chamber (18) reservoir and said second end of the blood return line.

In a 55th aspect according to any one of the preceding two aspects said blood chamber (18) is removably coupled to said blood return line.

In a 56th aspect according to the preceding aspect, said blood chamber (18) is removably coupled to said blood return line in correspondence of a branch-off point.

In a 57th aspect according to any one of the preceding four aspects the internal volume of the blood chamber (18) reservoir is at least greater than 50% of the internal volume of the additional blood chamber.

In a 58th aspect according to any one of the preceding five aspects (with the exception of the 54th) said at least one blood chamber (18) reservoir has one single blood port (18a) configured to act both as blood inlet and as blood outlet port, while the additional blood chamber (80) comprises a blood inlet port and a blood outlet port, and wherein the blood return line (15) further comprises:

a first tube (84) extending from said first end to the blood inlet port of the additional blood chamber, wherein the single blood port is connected to a branch-off point (86) of the first tube,

a second tube (85) extending from the blood outlet port of the additional blood chamber (18) to said second end of the blood return line,

a tube segment (87) connecting said single blood port to said branch-off point, this latter being located on an intermediate region of said first tube of the blood return line.

In a 59th aspect according to the preceding aspect the single blood port of the blood chamber (18) carries a connector configured to removably couple with a counter-connector carried by the tube segment (87) to selectively couple and uncouple the blood chamber (18) to the return line.

In a 60th aspect according to the preceding aspect either said counter-connector carries a check valve which is configured to close fluid passage through said counter-connector upon disconnection of this latter from said connector.

In a 61st aspect according to the 59th aspect a clamp acts (89) in correspondence of said tube segment, further wherein said clamp is operable - either manually or under a command from a control unit (100) - between an open position allowing passage of fluid through said tube segment and a closed position squeezing the tube segment and preventing passage of fluid through said tube segment.

In a 62nd aspect according to the 52nd aspect or according to any one of aspects from the 54th to the 57th said at least one blood chamber (18) is a reservoir having two blood ports (18a, 18b) and wherein the blood return line (15) comprises

- a first tube (72) extending from said first end of the blood return line (15) and connected to the inlet port of the blood chamber (18) reservoir,
- a second tube (73)extending from the outlet port of the blood

chamber (18) reservoir to a blood inlet port of the additional blood chamber (80),

- a third tube (74) extending from an outlet port of the additional blood chamber (80) to said second end of the blood return line.

In a 63rd aspect according to the preceding aspect the first tube (72) has a first end - corresponding to the first end of the blood return line (15) - provided with a counter-connector adapted to removably couple with a connector of the outlet port (16) of the blood compartment of the blood treatment unit, and a second end connected, in particular fixed, to the inlet port (18a) of the blood chamber reservoir.

In a 64th aspect according to the preceding aspect the second tube comprises:

- at least one first segment (77) having a first end, connected, and in particular, fixed to outlet port of the blood chamber, and a second end provided with a connector, and
- a second segment (81) having a first end with a respective counter-connector, configured for removable connection to the connector carried by the second end of the first segment, and a second end connected, in particular fixed, to the blood inlet port of the additional blood chamber.

In a 65th aspect according to the preceding aspect the counter-connector at the first end of the second segment (81) is configured to also be removably connectable to the connector carried by the outlet port (16) of the blood compartment of the treatment unit, in particular wherein the counter-connector at the first end of the second segment (81) is identical to the counter-connector at the first end of the first tube.

In a 66th aspect according to any one of aspects from the 53rd to the 65th the circuit comprises a pressure line (42) connected to a top portion of the blood chamber (18) reservoir and leading to a terminal connector configured to be connected to a circuit for supplying pressurized gas.

In a 67th aspect according to any one of aspects from the 53rd to the 66th the circuit comprises at least one pressure line (42) having a first end connected to the blood chamber (18) and/or to the additional blood chamber (80). In an alternative a second end of the pressure line is configured to be connected to a pressure sensor.

In one example the circuit has one pressure line (42) with a first end connected to a top portion of the blood chamber (18) reservoir and a second end with a terminal connector configured to be connected to a circuit for supplying pressurized gas.
As mentioned said at least one pressure line (42) may a second end configured to be connected to a pressure sensor.

In a preferred variant of the example the circuit has a transducer protector (57) positioned on said at least one pressure line (42) and comprising a casing housing a hydrophobic membrane separating a casing internal volume into a first chamber communicating with the blood chamber (18), and a second chamber, configured for communicating with the circuit for supplying pressurized gas and/or with the pressure sensor.

In a 68th aspect according to any one of aspects from the 53rd to the 67th the circuit comprises no blood chambers or blood reservoirs configured for air/blood separation directly connected to, or part of, the blood withdrawal line (12).

In a 69th aspect according to any one of aspects from the 53rd to the 68th the circuit said circuit is configurable as follows:
- in a first configuration wherein the blood chamber (18) is connected to the blood return line (15) in correspondence of said port or ports and is placed in fluid communication with the blood return line (15) and
- in a second configuration wherein the blood chamber (18) is physically separated by the blood return line, this latter only including the additional blood chamber,
optionally wherein said circuit is further configurable according to a third configuration wherein
the blood chamber (18) is connected to the blood return line (15) in correspondence of said branch-off point, with fluid communication between the blood chamber (18) and the blood return line (15) being interrupted.

In a 70th aspect according to the preceding aspect said first configuration the blood withdrawal line (12) and the blood return line (15) second ends (24, 25) are both connected and in fluid communication with the lumen of the single lumen access device (19); and wherein in the second or third configuration the blood return line (15) second ends are each respectively connected to a corresponding lumen of a double lumen access device (19) or to a respective distinct access device.

A 71st aspect concerns a method of configuring a circuit according to any one of the preceding aspects from the 53rd to the 70th wherein said method comprises the following steps:
configuring the circuit in one of:
a first configuration wherein the blood chamber (18) is connected to the blood return line (15) and is placed in fluid communication with the blood return line (15) - optionally in correspondence of said branch-off point and exclusively via said single blood port,

a second configuration wherein the blood chamber (18) is physically separated from the blood return line;
a third configuration wherein the blood chamber (18) is connected to the blood return line (15) in correspondence of said branch-off point, with fluid communication between the blood chamber (18) and the blood return line (15) being interrupted,
configuring the circuit in another of said first or second or third configuration.

In a 72nd aspect according to the preceding aspect the first configuration has the blood chamber (18) connected to the blood return line (15) and placed in fluid communication with the blood return line (15) in correspondence of said branch-off point and exclusively via said single blood port.

In a 73rd aspect according to any one of the preceding two aspects the method comprises placing the circuit initially in the third configuration either by causing closure of said check valve upon disconnection of said counter-connector from said connector, or by closing the clamp acting in correspondence of said tube segment,
and then placing the circuit in the second configuration by physically separating the blood chamber (18) from the blood return line.

In a 74th aspect according to any one of the 71st or 72nd aspects the method comprises initially placing the circuit in the first configuration, then flowing priming liquid through the circuit such as to remove air from the blood circuit and fill the blood circuit with priming liquid also filling said blood chamber (18),
and then placing the circuit in one of said second or third configurations.

A 75th aspect concerns a method of extracorporeal treatment of

blood using a circuit according to any one of the preceding aspects from the 53rd to the 70th comprising the following sequential steps:

configuring said circuit in one of:

a first configuration wherein the blood chamber (18) is connected to the blood return line (15) in correspondence of said branch-off point and is placed in fluid communication with the blood return line (15) exclusively via said single blood port,

a second configuration wherein the blood chamber (18) is connected to the blood return line (15) in correspondence of said branch-off point, with fluid communication between the blood chamber (18) and the blood return line (15) being interrupted,

a third configuration wherein the single blood port and consequently the blood chamber (18) are physically separated from the blood return line;

circulating a patient blood in the extracorporeal blood circuit;

configuring the circuit in another of said first or second or third configuration;

circulating a patient blood in the extracorporeal blood circuit.

In a 76th aspect according to the preceding aspect the methods comprises the steps

configuring said circuit in said first configuration,

circulating a patient blood in the extracorporeal blood circuit (11) in the first configuration with the second ends of the blood withdrawal line (12) and the blood return line (15) both connected to the lumen of the single lumen access device (19) such that an extracorporeal blood treatment session lasting a first time interval is carried out with the circuit in said first configuration;

configuring said circuit in said second or third configuration,

circulating a patient blood in the extracorporeal blood circuit (11) in the second or third configuration with each one of the

second ends of the blood withdrawal line (12) and the blood return line (15) both connected to a respective lumen of a double lumen access device (19) such that an extracorporeal blood treatment session lasting a second time interval is carried out with the circuit in said second or third configuration.

In a 77th aspect according to any one of the preceding aspects the extracorporeal blood circuit is entirely made in plastic material and is intended for single use (disposable).

A 78th aspect concerns a method of controlling the extracorporeal treatment apparatus of anyone of preceding aspects from the 1st to the 51st by means of the control unit (100) – the method comprising the steps executed by the control unit (100) as indicated in anyone of preceding aspects from the 1st to the 51st.

In a 79th aspect the method of the preceding aspect uses an extracorporeal circuit as per any one of aspects fro the 53rd to the 70th.

DEFINITIONS

In the claims and in the following description the below listed terms or terminology have the following meaning:

- 'single lumen access' is used to cover a single needle or any other type of access device (such as a single lumen cannula or a single lumen catheter) having a single channel designed to receive both the second end of the blood withdrawal and the second end of the blood return line and configured to be connected to a respective single access point in the patient cardiovascular system;
- single access configuration: refers to a configuration of an extracorporeal blood circuit exclusively having a single lumen access device to which both the blood withdrawal line and the

blood return line are connected; an extracorporeal blood circuit in 'single access configuration' is suitable for connection to the patient's cardiovascular system at a single access point;

- double access configuration: refers to a configuration of an extracorporeal blood circuit exclusively having either a double lumen access device or two distinct access devices (e.g., two needles) to which the blood withdrawal line and the blood return line are respectively connected;

- blood chamber: a reservoir having a fluid passage cross section sensibly larger than that of the tubing to which the chamber is connected to promote blood speed reduction and gas expansion, accumulation of a certain quantity of blood and formation of a blood air interface for the separation of air bubbles contained in blood; in order to fall under the definition of 'blood chamber' a reservoir shall present a minimum internal volume of at least 20 ml. This 20 ml internal volume corresponds to the whole air and liquid volume in the blood chamber: generally the optimal liquid volume in the chamber during a dialysis session double access configuration corresponds around to 65% of whole chamber volume.

DESCRIPTION OF THE DRAWINGS

Aspects of the invention are shown in the attached drawings, which are provided by way of non-limiting example, wherein:

Figure 1 schematically shows a first example of a blood treatment apparatus in a single lumen or single needle configuration, according to one aspect of the invention;

Figure 2 shows a portion of the apparatus of figure 1 comprising a blood chamber 18 positioned on the blood return line and a pneumatic circuit 40 connected to the blood chamber; in particular figure 2 shows a condition during use in single access configuration of the apparatus;

Figure 3 shows the same portion of the apparatus of figure 1 as shown in figure 2, but during use in a double lumen or double

needle configuration.

Figure 4 schematically shows a second example of a blood treatment apparatus in a single lumen or single needle configuration, according to another aspect of the invention;

Figure 5 shows a portion of the apparatus of figure 4 comprising a blood chamber 18 positioned on the blood return line and a pneumatic circuit 40 connected to the blood chamber; in particular figure 5 shows a condition during use in single access configuration of the apparatus;

Figure 6 shows the same portion of the apparatus of figure 4 as shown in figure 3, but during use in a double lumen or double needle configuration.

Figure 7 schematically shows a third example of a blood treatment apparatus in a single lumen or single needle configuration, according to a further aspect of the invention;

Figure 8 shows a portion of the apparatus of figure 7 comprising a blood chamber 18 positioned on the blood return line and a pneumatic circuit 40 connected to the blood chamber; in particular figure 8 shows a condition during use in single access configuration of the apparatus;

Figure 9 shows the same portion of the apparatus of figure 7 as shown in figure 8, but during use in a double lumen or double needle configuration.

Figure 10 shows a first exemplifying structure of a pneumatic circuit 40 which may be connected to the blood chamber 18 of figures 2, 5 and 8.

Figure 11 shows a second exemplifying structure of a pneumatic circuit 40 which may be connected to the blood chamber 18 of figures 2, 5 and 8.

Figure 12 shows a third exemplifying structure of a pneumatic circuit 40 which may be connected to the blood chamber 18 of figures 2, 5 and 8;

Figure 13 shows a fourth exemplifying structure of a pneumatic

circuit 40 which may be connected to the blood chamber 18 of figures 2, 5 and 8; and

Figure 14 shows a flowchart representative of the arterial and venous phase control steps taken the control unit of the apparatus according to aspects of the invention.

DETAILED DESCRIPTION

Description common to embodiments of figures 1-9

Figures 1, 4 and 7 show a respective example of an apparatus for extracorporeal treatment of blood 1. Note that same components are identified by same reference numerals in the attached figures.

The extracorporeal blood treatment apparatus 1 comprises a treatment unit 2, which in use is supported by a treatment unit holder 4 carried by the apparatus 1. In the examples, the treatment unit 2 has at least a semipermeable membrane 3 dividing the treatment unit into a blood compartment 5 and a filtrate compartment 6. Depending upon the type of blood treatment apparatus the treatment unit may be a hemofilter, an ultrafilter, a hemodiafilter, a plasmafilter, a dialyzer, or other type of treatment unit. The filtrate compartment 6 has at least an outlet port 7 connected to a waste handling circuit 8. In certain embodiments (e.g. in the case where the blood treatment unit is a hemodiafilter or a hemodialyzer), the inlet port 9 to the filtrate compartment 6 is connected to a source of fresh treatment fluid 10, such as a container of fresh dialysis fluid or a section of the apparatus devoted to the on line preparation of fresh dialysis and/or fresh replacement fluid.

The waste handling circuit is connected to the filtrate compartment 6 of the treatment unit 2 and comprises at least one pump for controlling ultrafiltration of fluid crossing the semipermeable membrane 3 (for instance the waste handling circuit may include an ultrafiltration pump located on a line branching off the main waste line connected to the filtrate compartment).

Other ways for controlling ultrafiltration may be possible as it is known in the art. The control unit may be configured to control the at least one pump of the waste handling circuit during said arterial phase while keeping pressure in the blood chamber 18 at said predetermined arterial phase pressure regimen, such that control of ultrafiltration is made easier. In an analogous manner the control unit may configured to control the at least one pump of the waste handling circuit during said venous phase while keeping pressure in the blood chamber 18 at said predetermined venous phase pressure regimen so that control of ultrafiltration is made easier also during the venous phase.

The apparatus comprises an extracorporeal blood circuit 11 which, in its turn, includes the blood compartment 5 of the treatment unit 2, a blood withdrawal line 12 having a first end 13 connected to an inlet port 14 of the blood compartment 5 of the treatment unit, and a blood return line 15 having a first end 16 connected to an outlet port 17 of the blood compartment of the treatment unit.

The blood return line 15 presents at least one blood chamber 18 configured, in operation, to host a volume of blood and define a blood-air interface; as shown in figure 1 the blood chamber 18 is a reservoir having a prefixed internal volume (i.e., designed to host a prefixed quantity of liquid): the blood chamber 18 is received by a respective holder 90 for instance carried by a front panel of the apparatus 1. The blood chamber 18 receives in use blood coming from the outlet port 17 of the blood compartment.

In figures 1, 4 and 7 the extracorporeal blood circuit 12 is connected to a single lumen access device 19 (for instance a single needle or a single lumen cannula) configured to be connected to a patient's cardiovascular system at a single access point and able to alternatively receive blood to be treated coming from the patient or return treated blood to the patient. In

figures 1, 4 and 7 the extracorporeal blood circuit 11 is represented in a single access configuration wherein the blood withdrawal line and the blood return line 12 and 15 have respective second ends 24 and 25 contemporaneously connected to the single lumen access device 19. In figures 1, 4 and 7 it is also shown that the extracorporeal blood circuit 11 may include an optional arterial service line 20 and an arterial sampling port 21 both connected to the arterial line upstream (with reference to the direction of circulation of blood during treatment indicated by arrow A) a blood pump segment 22 of the arterial line 12. Note that an arterial clamp 23, for instance carried by the apparatus front panel, may operate on a section of the arterial line 12 positioned between the arterial line second end 24 and the blood pump segment 22. Furthermore, other sensors such as an arterial bubble detector 26, for instance carried by the apparatus front panel, a pressure transducer 27, and a blood volume sensor (also for example carried by the apparatus front panel) may be coupled to the tract of arterial line extending upstream the blood pump segment: in the examples of figures 1, 4 and 7 the optional arterial bubble detector, pressure transducer and blood volume sensor are all operative between the arterial clamp and the blood pump segment. It is also noted that an anticoagulant source 28, for instance in the form of an anticoagulant container, may be connected via an anticoagulant line 29 to the arterial line: in the examples shown the anticoagulant line leads to a point of the arterial line immediately upstream the blood pump segment 22. Of course other locations for the anticoagulant injection points may be envisaged. Also note that the anticoagulant container may be part of a syringe pump or, alternatively, it may be connected to a peristaltic pump active on the anticoagulant line.

A blood pump 30, also for example carried by the apparatus front panel, is positioned and configured to be operative on the blood withdrawal line 12 and, in particular, is configured to act on the

blood pump segment 22: as shown in the enclosed figures the blood pump 30 may be a peristaltic pump comprising a plurality of active elements 31 (such as rollers) periodically squeezing and releasing successive portions of the blood pump segment which is received in a respective runway 32 defined by the apparatus next to the blood pump 30.

As above mentioned, the blood return line 15 has its first end 16 connected to the outlet port 17 of the treatment unit blood compartment 5 and leads to the blood chamber. An optional venous sampling port 33 and venous service line 34 may be present on the blood return line as well, as shown in figures 1, 4 and 7. In a tract of the venous line which in use is positioned downstream the blood chamber 18 operates a venous bubble detector 35 (for instance carried by the apparatus front panel) and an intercepting organ 36, operative on a portion of the blood return line also located downstream the blood chamber. The intercepting organ 36 may be in the form of a venous clamp operated by the apparatus 1 and selectively positionable at least in an open condition and in a closed condition to respectively allow and prevent a passage of fluid through said second end of the blood return line.

According to a variant, which is shown in figures 1, 4 and 7, the apparatus may also include one or more infusion lines 37, 38 connected to a source of infusion liquid. Note that the source of infusion liquid may be a container housing sterile replacement fluid ready for infusion or - as mentioned in connection with the source of dialysis fluid - the section 10 of the apparatus devoted to the on line preparation of fresh dialysis and/or fresh replacement fluid. In the examples of figures 1, 4 and 7, the apparatus 1 has at least one pre-dilution infusion line 37 connecting the source of replacement fluid to a point of the blood withdrawal line, for instance positioned between the blood pump segment and the first end of the blood withdrawal line. The apparatus represented in the mentioned figures also includes a

post-dilution infusion line 38 connecting the source of replacement fluid to a point of the blood return line, which may be positioned upstream, downstream or at the blood chamber.

Finally, as shown in figures 1, 4 and 7, it is noted that the apparatus 1 presents no blood chambers or blood reservoirs configured for air/blood separation directly connected to, or part of, the blood withdrawal line 12, which - with the possible exclusion of sensors and/or injection sites - only includes tubing for conveying blood to the inlet port of the blood compartment of the treatment unit, thereby simplifying and standardizing the design of the arterial line.

The apparatus also has at least one control unit 100, which is in general connected to all the apparatus actuators and sensors described above and in particular to the arterial and venous clamps 23, 36, to the anticoagulant pump 28, to the bubble detector(s) 26, 35 etcetera in order to receive signals from the sensors and to control the various actuators.

In accordance with one aspect of the invention, the apparatus 1 also includes a pneumatic circuit 40 connected to the blood chamber 18 present in the blood return line 15 and configured to supply gas to or withdraw gas from the blood chamber 18 in order to keep the pressure regimen under control as it will be herein after further described. The control unit 100 is connected to the blood pump 30, to the pneumatic circuit 40 and to the intercepting organ 36 (venous clamp) such that - when the extracorporeal circuit 11 is in the single access configuration as shown in figures 1, 4 and 7 - the control unit 100 is configured to repeatedly execute a single access treatment cycle, including a respective arterial phase and a respective venous phase, during which the pressure in the blood chamber 18 is kept under control.

In particular, the control unit 100 is configured to control at least the blood pump 30, the intercepting organ 36 and the pneumatic circuit 40, so that during the arterial phase of the

cycle the control unit 100 causes the execution of the following steps (see flowchart of figure 14):

- receive (step 101 in figure 14) the value or values representative of the desired arterial phase pressure regiment P_{ART} and venous phase pressure regimen P_{VEN};
- verify if the arterial or venous phase shall be started (step 102);
- at the beginning of the arterial phase the blood pump 30, which was previously stopped, is activated (step 103) and operated during the arterial phase to withdraw blood from a patient via the single lumen access device 19 and convey it through the blood compartment 5 and to the blood chamber, such that blood level in the blood chamber 18 raises;
- the intercepting organ 36 is closed (step 104) and is maintained in the closed condition during the arterial phase, so that no blood is returned to the patient and a certain amount of blood accumulates in the blood chamber 18;
- furthermore, the pneumatic circuit 40 (step 105) is controlled to withdraw gas from the blood chamber 18 in synchrony with operation of the blood pump 30 to thereby facilitate inlet of blood in the blood chamber.

On the other hand, the control unit 100 is configured to control at least the blood pump 30, the intercepting organ 36 and the pneumatic circuit 40, so that during the venous phase of the cycle the control unit 100 causes the execution of the following steps:

- at the beginning of the venous phase the operation of the blood pump 30 is stopped (step 106) so that blood is no longer withdrawn from the patient;
- at the beginning of the venous phase the intercepting organ 36 which was closed during the arterial phase is opened (step 107) and maintained in the open condition to cause blood in the venous line to return to the patient via the single lumen access device 19;

- furthermore, the pneumatic circuit 40 is controlled to supply gas to the blood chamber 18 (step 108) while the intercepting organ 36 is in the open condition, thereby facilitating expulsion of blood from the blood chamber 18 under controlled pressure conditions.

In particular, according to aspects of the invention, the control unit 100 is configured to control the pneumatic circuit 40, so that during the arterial phase of the cycle, the pneumatic circuit 40 withdraws gas (step 105) from the blood chamber 18 in a controlled manner to maintain pressure in the blood chamber 18 at a predetermined arterial phase pressure regimen P_{ART} at least for a major portion of the arterial phase.

Moreover, the control unit 100 is configured to control the pneumatic circuit 40, so that during the venous phase of the cycle, the pneumatic circuit 40 supplies gas (step 108) to the blood chamber 18 and maintains pressure in the blood chamber 18 at a predetermined venous phase pressure regimen P_{VEN} at least for a major portion of the venous phase. In other words, during both the arterial phase and the venous phase the pressure in the blood chamber 18 is kept under control and in particular matching a prescribed pressure regimen which may be either a pre-set pressure value or a pre-set range around a pressure value.

Note that by major portion of the arterial phase it is intended about 80% or more of the duration of the arterial phase: in other words close to the entire duration of the arterial phase but for possible transitory periods which may take place. In a similar manner, by major portion of the venous phase it is intended about 80% or more of the duration of the venous phase, i.e., close to the entire duration of the venous phase but for possible transitory periods which may take place.

In accordance with a possible execution, the predetermined arterial phase pressure regimen P_{ART} is either a substantially prefixed constant pressure value P_{0A} (slight oscillations in the

range of 10 mm of Hg are considered acceptable) which the pressure in the blood chamber 18 shall follow at least for a major portion of the arterial phase, or a first prefixed range around a constant pressure value within which the pressure in the blood chamber 18 shall fall at least for a major portion of the arterial phase.

In an analogous manner the predetermined venous phase pressure regimen P_{VEN} is either a substantially prefixed constant pressure value P_{0V} (slight oscillations in the range of 5 mm of Hg are considered acceptable) which the pressure in the blood chamber 18 shall follow at least for a major portion of the venous phase, or a second prefixed range around a constant pressure value within which the pressure in the blood chamber 18 shall fall at least for a major portion of the venous phase.

Note that the control unit 100 may be configured to receive the constant pressure value P_{0A} to be kept during arterial phase and/or the constant venous pressure value P_{0V} to be kept during the venous phase and/or the value of said first and second prefixed ranges either from a memory connected to the control unit 100 where said value(s) and range(s) are pre-stored or from an input device (not shown) connected to the control unit 100.

In accordance with a further possibility, the control unit 100 may be configured such that said predetermined arterial phase pressure regimen is identical to the predetermined venous phase pressure regimen: in particular a same constant value for the pressure in the blood chamber 18 may be selected or pre-set and kept by the control unit 100 as arterial pressure value and as venous pressure value such that during both the arterial and the venous phases the pressure in the blood chamber 18 is kept always constant with the result of a reduced stress on the fistula, a reduced duration of the overall cycle as the venous pressure is maintained at the ideal value for returning blood to the patient, and less discomfort to the patient.

In accordance with further aspects of the invention the control

unit 100 is configured to receive one or two or all three of the following settings relating to the arterial phase:

- one or more set values representative of said predetermined arterial phase pressure regimen, in particular said prefixed constant arterial pressure value;
- a set value for a desired flow rate intended to be delivered by the blood pump 30 during said arterial phase (or a desired T_{ART} time),
- a value of a/the arterial stroke volume V_{ART} intended to be delivered into the blood chamber 18 during the arterial phase.

Based on the above settings, the control unit 100 may be configured to control the blood pump 30 and the pneumatic circuit 40 during arterial phase.

Furthermore, the control unit 100 may be configured to receive one, two or three of the following settings relating to the venous phase:

- one or more set values representative of said predetermined venous phase pressure regimen, in particular said prefixed constant venous pressure value;
- a set value for a desired flow rate intended to be delivered through the venous line during said venous phase (or a desired T_{VEN} time),
- a value of a/the venous stroke volume V_{VEN} intended to be removed from the blood chamber 18 during the venous phase (which is normally equal to the arterial stroke volume);

The control unit 100 may be configured - during the venous phase - to control the blood pump 30 and the pneumatic circuit 40 based on one or more of said settings relating to the venous phase.

Furthermore, the control unit 100 may be configured for commanding a switch from said arterial phase of the cycle into said venous phase of the cycle when one of the following events takes place:

- expiration of a predetermined arterial phase time interval as

of start of the arterial phase,

- delivery into the blood chamber 18 of a predetermined quantity of liquid as of start of the arterial phase (e.g. delivery of V_{ART}),
- reaching of a maximum liquid level of liquid in the blood chamber (which may be detected by the sensor or sensors described in further detail herein below),
- reaching of a maximum level of foam in the blood chamber (which may be detected by the sensor or sensors described in further detail herein below).

On the other hand, control unit 100 may be configured for commanding a switch from said venous phase of the cycle into said arterial phase of the cycle when one of the following events takes place:

- expiration of a predetermined venous phase time interval as of start of the venous phase,
- evacuation from the blood chamber 18 of a predetermined quantity of liquid as of start of the arterial phase,
- reaching of a minimum liquid level of blood into the blood chamber (which may be detected by the sensor or sensors described in further detail herein below).

In accordance with another aspect of the invention, it is noted that no blood pump (other than the above described blood pump 30 active of the arterial line) is operative on the extracorporeal blood circuit. In particular, no blood pump 30 is operative on the blood return line 15: thus during the venous phase with the single blood pump 30 of the apparatus being positioned at and active on the blood withdrawal line and being stopped, the control unit 100 causes blood to return to the single lumen access device exclusively by keeping the intercepting organ 36 in the open condition and controlling the pneumatic circuit 40 to supply gas to the blood chamber. This allows to reliably control the pressure regimen in the blood chamber 18 (avoiding pressure oscillations

caused by any active peristaltic pump) basically during a major portion of the venous phase while at the same time allowing an efficient return of blood to the patient.

In order to maintain pressure within a controlled regimen the control unit 100 may be configured to adopt one or both the following criteria.

In accordance with a 1st control criterion the control unit is configured for introducing (during venous phase) or removing (during arterial phase) gas/air in the expansion volume of the blood chamber 18 while keeping pressure constant; in this case the control process is governed by the control unit 100 using one or more pressure sensors for receiving, continuously or at short time intervals, signals useful for adjusting pressure and acting in control loop on the pneumatic circuit 40; this control requires frequent or continuous pressure monitoring and a frequent pressure adjustment by frequent removal or addition of gas in the venous chamber. Level sensors may be associated to the blood chamber 18 to switch from between arterial and venous phases.

In accordance with a 2nd control criterion, the control unit may be configured for introducing (during venous phase) or removing (during arterial phase) in the blood chamber 18 a known amount of air (i.e. a volume of air at known pressure) and therefore keep pressure constant by balancing, with an air volume exchange, the liquid volume change in the blood chamber; in this case the control process is governed by the control unit 100 which controls supply/removal of gas volume in synchrony with blood volume removal/supply to and from the blood chamber 18 in order to continuously compensate the change in volume of the blood inside the same chamber. Knowing the pressure to be kept and the change in volume caused by incoming or leaving blood, and also knowing the pressure/volume characteristic of the pump or pumps used to supply and/or withdraw gas it is possible to achieve a stable pressure in the blood chamber.

In order to implement the first of the above two criteria, the apparatus 1 also includes at least one venous pressure sensor 41 connected to the blood return line and configured to receive a pressure signal and supply it to the control unit 100: the pressure sensor 41 may be connected to a pressure line 42 directly linked to the blood chamber 18 or it may be connected to a pressure line 42 linked to an additional blood chamber 80 possibly present on the blood return line or it can be connected to and receive a pressure signal directly from the blood return line. During the arterial phase the control unit 100 is configured for: receiving the pressure signal from the venous pressure sensor, determining one or more measured values of the venous pressure from said pressure signal, comparing said one or more measured values of the venous pressure with at least one set value representative of the predetermined arterial phase pressure regimen, and adjusting the pneumatic circuit 40 to withdraw gas from the blood chamber 18 during the arterial phase to keep said one or more measured values of the venous pressure within a first prefixed tolerance from the at least one set value representative of said predetermined arterial pressure regimen.

In an analogous manner, the control unit 100 is configured to execute a pressure adjustment sequence during said venous phase comprising: receiving the pressure signal from the venous pressure sensor, determining one or more measured values of the venous pressure from said pressure signal, comparing said one or more measured values of the venous pressure with at least one set value representative of the predetermined venous phase pressure regimen, and adjusting the pneumatic circuit 40 to supply gas to the blood chamber 18 during the venous phase to keep the one or more measured values of the venous pressure within a second prefixed tolerance from said at least one set value representative of said predetermined venous pressure regimen.

On the other hand, in order to implement the second of the above

control criteria the control unit 100 is configured - during the arterial phase of the cycle - to estimate or receive an arterial stroke volume value (V_{ART}), corresponding to a blood volume intended to be conveyed into the blood chamber 18 during the arterial phase. During the arterial phase, in synchrony with activation of the blood pump 30, the control unit 100 commands the pneumatic circuit 40 to withdraw from the blood chamber 18 a volume of gas equal to said arterial stroke volume value (V_{ART}), such that pressure inside the blood chamber 18 remains constant or substantially constant.

In detail, the control unit 100 may store or receive a first relationship (step 201):

$$V_{ART} = (Q_{B\_ART} - Q_{UF\_ART}) \cdot T_{ART} \quad (1)$$

wherein: V_{ART} is an estimated or set value of the arterial stroke volume, T_{ART} is an estimated or set value of the duration of the arterial phase during which the blood pump 30 and pneumatic circuit 40 are both active, Q_{B_ART} is a calculated or set value of the blood flow rate in the arterial line during the arterial phase, Q_{UF_ART} is a set value of the ultrafiltration flow rate through the semipermeable membrane of the treatment unit during the arterial phase.

Considering that Q_{B_ART} and Q_{UF_ART} are known (either set or measured), then adopting said first relationship, the control unit 100 may calculate the arterial stroke volume value V_{ART} (step 202), based on a set duration of the arterial phase T_{ART} and impose that during the same T_{ART} an identical volume of gas is withdrawn from the blood chamber (step 203).

If on the other hand V_{ART} is set (by user or pre-stored), then the control unit 100 may determine the T_{ART} (and impose it by proper alternation of the venous and arterial phases) for achieving the set V_{ART} value and consequently also impose that a same volume of gas is withdrawn from the blood chamber 18 during the same T_{ART} of arterial phase.

In order to maintain pressure within a controlled regimen during the venous phase of the cycle, the control unit 100 may be configured to estimate or receive a venous stroke volume value V_{VEN}, corresponding to a blood volume intended to be expelled by the blood chamber 18 and returned to the patient during the venous phase. During the venous phase, in synchrony with de-activation of the blood pump 30 and opening of the intercepting organ 36, the control unit 100 commands the pneumatic circuit 40 to supply to the blood chamber 18 a volume of gas equal to said venous stroke volume value V_{VEN} during a time interval T_{VEN} while keeping pressure constant; note pressure is kept sufficiently high such that the same volume V_{VEN} of blood is returned to the patient.

In order to actuate the above described procedure, the control unit 100 controls the pneumatic circuit which may have different configurations.

In a first example, which is shown in figure 10, the pneumatic circuit 40 comprises an air pump 43, having one side connected to the atmosphere 44 (i.e. connected with the environment external to apparatus 1 which is therefore at atmospheric pressure) and another side connected to the blood chamber. The air pump 43 in the example shown is of the unidirectional type and is inserted between two three-way valves 45 and 46 such that depending upon the position of the three-way valves the pump outlet may either be connected and pump gas to the blood chamber 18 or it may be connected to the atmosphere 44, while the pump inlet is respectively connected either to the atmosphere 44 (and thus suck fluid from the atmosphere) or to the blood chamber 18 (and thus suck gas from the blood chamber). In greater, detail the pneumatic circuit 40 may be connected to the pressure line 42 leading to the blood chamber 18: the pressure line has a first end in direct communication with the blood chamber 18 and a second end connected, at a bifurcation point 47, with a first circulating line 48 part of the pneumatic circuit 40. The first circulating

line 48 has opposite ends respectively connected with a first port 49 of the first three-way valve 45 and with the first port 50 of the second three-way valve 46. A second circulating line 51, which is connected to the atmosphere 44 (e.g. at an intermediate region of the second circulating line) and which is also part of the pneumatic circuit 40, has opposite ends respectively connected to the second port 52 of the first three-way valve 45 and to the second port 53 of the second three-way valve 46. Finally, the unidirectional pump 43 has an outlet port connected to a third port 54 of the first three-way valve 45 and an inlet port connected to the third port 55 of the second three-way valve 45. The control unit 100 is configured to control the first and second three-way valves and the unidirectional pump as follows.

When the pneumatic circuit 40 has to supply gas to the blood chamber, then the control unit 100 switches the first three-way valve in a first configuration, i.e. with the third port 54 communicating with the first port 49, and at the same time, switches the second three-way valve in a second configuration, i.e. with the third port 55 communicating with the second port 53 (fig.10 - dashed lines). When - on the other hand - the pneumatic circuit 40 has to withdraw gas from the blood chamber, then the control unit 100 switches the first three-way valve in a second configuration, i.e. with the third port 54 communicating with the second port 52, and at the same time, switches the second three-way valve in a second configuration, i.e. with the third port 55 communicating with the first port 50 (fig. 10).

The pressure sensor 41 for detecting pressure in the blood chamber 18 may be connected to the pressure line 42, for instance via a branch line 56 branching off said pressure line 42. Furthermore, again as shown in fig.10), a transducer protector 57 is positioned on said pressure line and comprises a casing housing a hydrophobic membrane separating a casing internal volume into a first chamber communicating with the blood chamber, and a second chamber,

communicating with the pneumatic circuit 40. The transducer protector 57 is preferably positioned between a gas port of the blood chamber, located at the blood chamber 18 top, and the point 58 where the branch line 56 branches off the pressure line 42 such as to protect both the pressure sensor 41 and the pneumatic circuit 40 from contamination with liquid (e.g. blood or priming liquid) coming from the blood return line. In practice during the arterial phase, the control unit 100 receives pressure signals from the pressure sensor 41 and commutes the first three-way valve 45 to the second configuration while the second three-way valve 46 is placed in the first configuration such that operation of the unidirectional pump 43 causes gas to be withdrawn from the blood chamber 18 and pressure to be kept in line with the arterial pressure regimen. On the other hand, during the venous phase, the control unit 100 again receives pressure signals from the pressure sensor 41 and commutes the first three-way valve 45 to the first configuration while the second three-way valve 46 is placed in the second configuration such that operation of the unidirectional pump causes gas to be fed to the blood chamber 18 and pressure to be kept in line with the venous pressure regimen.

In the example shown in figure 11 all components of the example of figure 10 are present and are identified with the same reference numerals. In addition, the pneumatic circuit 40 of figure 11 includes a gas accumulator 59, which in the instant case may take the form of a syringe pump, having: a variable volume chamber 60 in gas communication with either the blood chamber 18 or the atmosphere, and an actuator 61 associated to the variable volume chamber 60 and active to cause a variation of the internal volume of the variable volume chamber between a minimum volume and a maximum volume. A third three-way valve 62 may present in the pneumatic circuit 40 and has a first port 63 connected to the pressure line 42 and leading to the gas port of the blood chamber,

a second port 64 connected to the atmosphere 44, and a third port 65 connected to an inlet and outlet port 66 (i.e. the same port acts both as inlet and as outlet) of the gas accumulator 59. In the case where the third three-way valve is not present, then the inlet and outlet port 66 of the gas accumulator is directly connected to the pressure line 42 to feed gas to or withdraw gas from the blood chamber 18.

During the arterial phase, the control unit 100 is configured to switch the first and second three way valves as described for the arterial phase of the circuit of figure 10, while the third three-way valve (if present) is kept in a configuration connecting the third port to the first port. The control unit 100 commands therefore the pneumatic circuit 40 to withdraw from the blood chamber 18 a volume of gas equal to an/the estimated or set value of the arterial stroke volume V_{ART}, by acting on said actuator and increasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber 18 with the internal volume of said variable volume chamber - substantially constant during the entire or a major portion of said arterial phase; at the same time the unidirectional pump 43 makes sure that pressure as detected by the venous pressure sensor remains constant or substantially constant.

During the venous phase, the control unit 100 is configured to switch the first and second three way valves 45, 46 as described for the venous phase of the circuit of figure 10, while the third three-way valve 62 (if present) is kept in a configuration connecting the third port to the first port). The control unit 100 then commands the pneumatic circuit 40 to supply to the blood chamber 18 a volume of gas equal to an/the estimated or set value of the arterial stroke volume V_{VEN} , by acting on said actuator and decreasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber 18 with the internal volume of said variable volume

chamber - substantially constant during the entire or a major portion of said venous phase; at the same time the unidirectional pump makes sure that pressure as detected by the venous pressure sensor remains constant or substantially constant.

In the example shown in figure 12 the pneumatic circuit comprises an air pump 43, having one side connected to the atmosphere 44 (i.e. connected with the environment external to apparatus 1) and another side connected to the blood chamber. The air pump 43 in the example shown is of the bidirectional type and is inserted in the pneumatic circuit 40 such as to pump gas to the blood chamber 18 during the venous phase and to suck gas from the blood chamber 18 during the arterial phase. In greater, detail the bidirectional pump 43 is connected to a pressure line 42 leading to the blood chamber 18: the pressure line 42 has a first end in direct communication with the blood chamber 18 and a second end connected with the bidirectional pump 43.

The pressure sensor 41 for detecting pressure in the blood chamber 18 may be connected to the pressure line 42, for instance via a branch line 56 branching off said pressure line at point 58. Furthermore, again as shown in fig.10), a transducer protector 57 is positioned on said pressure line and comprises a casing housing a hydrophobic membrane separating a casing internal volume into a first chamber communicating with the blood chamber, and a second chamber, communicating with the pneumatic circuit 40. The transducer protector 57 is preferably positioned between a gas port of the blood chamber, located at the blood chamber 18 top, and the point 58 where the branch line branches off the pressure line such as to protect both the pressure sensor and the pneumatic circuit 40 from contamination with liquid (e.g. blood or priming liquid) coming from the blood return line.

In practice during the arterial phase, the control unit 100 receives pressure signals from the pressure sensor and operates the bidirectional pump to keep pressure inside the blood chamber

18 in line with said prescribed arterial pressure regimen. On the other hand, during the venous phase, the control unit 100 again receives pressure signals from the pressure sensor 41 and controls the bidirectional pump such that pressure to be kept in line with the venous pressure regimen.

In addition, the pneumatic circuit 40 of figure 12 includes a gas accumulator 59, which in the instant case may take the form of a syringe pump, having: a variable volume chamber 60 in gas communication with either the blood chamber 18 or the atmosphere 44, and an actuator 61 associated to the variable volume chamber and active to cause a variation of the internal volume of the variable volume chamber between a minimum volume and a maximum volume. During the arterial phase, the control unit 100 commands therefore the pneumatic circuit 40 to withdraw from the blood chamber 18 a volume of gas equal to an/the estimated or set value of the arterial stroke volume V_{ART}, by acting on said actuator and increasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber 18 with the internal volume of said variable volume chamber 60 - substantially constant during the entire or a major portion of said arterial phase; at the same time the bidirectional pump 43 makes sure that pressure as detected by the venous pressure 41 sensor remains constant or substantially constant.

During the venous phase, the control unit 100 is configured to command the pneumatic circuit 40 to supply to the blood chamber 18 a volume of gas equal to an/the estimated or set value of the arterial stroke volume V_{VEN} , by acting on said actuator and decreasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber 18 with the internal volume of said variable volume chamber 60 - substantially constant during the entire or a major portion of said venous phase; at the same time the bidirectional pump makes sure that pressure as detected by the venous pressure

sensor remains constant or substantially constant.

In the example shown in figure 13 all components of the example of figure 10 are present and are identified with the same reference numeral. In addition, the pneumatic circuit 40 of figure 11 includes a gas container 97, which is kept above atmospheric pressure and which is selectively connectable to an inlet port of the air pump 43: in practice a further three-way valve 67 is interposed between the gas container 97 and the second circulating line 51 and has a first port 68 connected to the second circulating line, a second port 69 connected to the external atmosphere 44 and a third port 70 connected to the single port of the gas container 96. In this way the unidirectional pump (depending upon the position of the further three-way valve) may receive/send gas either from/to the external atmosphere or from/to the gas container so that no or limited external air is used. Additionally a heat exchanger 95 for dissipating heat and/or a cooler 96 for cooling incoming fluid may be positioned in the pneumatic circuit 40 as shown in figure 13 in order keep temperature of the gas as stable as possible. A temperature sensor may be connected to pressure line 42 and to the control unit 100 which may act on heat exchanger 95 and/or cooler 96 based on the temperature detections of said temperature sensor to keep the temperature of fluid in line 42 substantially constant, i.e. in the range of a constant value a part for a minimum tolerance.

It is noted that the apparatus 1 may also include one arterial pressure sensor (not shown) connected to said pressure transducer 27 or in other manners connected to the blood withdrawal line, such as to detect a pressure in a tract of the blood withdrawal line 12 positioned between the second end 24 of the blood withdrawal line 12 and the blood pump 30. This arterial pressure sensor may receives a pressure signal relating to a pressure in said tract of the blood withdrawal line and supply it to the control unit 100; the control unit 100 would in this case be

configured to monitor pressure and issue a warning signal (which is e.g. sent to the user interface) in case pressure goes too much down.

Variants in the design of the extracorporeal blood circuit.

After the above description of the apparatus 1, here below certain variants in the structure of the extracorporeal blood circuit are described. The above described features of the apparatus 1 may be associated and combined with each one of the below described variants of the extracorporeal blood circuit structure.

A first variant of the extracorporeal blood circuit 11 is shown in figures 1-3. According to this variant, the only blood chamber is the blood chamber 18 present in/or connected to the blood return line and to the blood circuit in general: in other words the extracorporeal blood circuit has one single blood chamber 18 and no other blood chambers are positioned at, part of, or directly connected to the blood return line. The internal total volume (liquid + air may occupy the internal volume) of the blood chamber 18 is at least 90 ml. The internal total volume of the blood chamber (i.e. these at least 90 ml) is the sum of:

- the blood volume in the chamber when in a double access configuration (at least about 25 ml) with a maximum operating blood flow-rate of 600mL/min (bottom chamber volume), plus
- the stroke volume when operating in single access configuration (at least about 50 ml for a single access mean blood flowrate of 300ml/min), plus
- the volume of air at the top of chamber (at least about 15ml at the end of arterial phase in single access configuration).

Therefore, during use of the extracorporeal blood circuit in double lumen configuration, only the bottom part of the blood chamber 18 internal volume is occupied by liquid, while during use in single access configuration also the top half internal volume

of the blood chamber 18 may at least in part be occupied by liquid.

The extracorporeal blood circuit 11 has a blood return line 15 comprising a first tube 70 extending from the first end 16 of the blood return line - which in figure 1 is coupled with the blood treatment unit - to an inlet port of the blood chamber 18- which is for instance positioned in correspondence of the top half of the blood chamber. The return line, also includes a second tube 71 extending from an outlet port, for instance positioned at the bottom half of the blood chamber 18, to the second end 25 of the blood return line which is connected or connectable to the single lumen access device 19. As it can be seen from figure 1 the venous pressure sensor 41 and the pneumatic circuit 40 are fluidly connected to the blood chamber 18 via said pressure line 42.

A second variant of the extracorporeal blood circuit is shown in figures 4-6. According to this variant, and with specific reference to figure 4, the blood chamber 18 is a reservoir having two blood ports: an inlet port 18a, configured to receive all fluid coming from the first end 16 of the blood return line 15, and an outlet port 18b configured to discharge fluid exiting from the blood chamber 18. In practice the blood chamber 18 has an inlet and an outlet port positioned at the bottom half of the chamber wherein one serves as inlet for liquid coming from the extracorporeal blood circuit and the other serves as outlet for liquid accumulated in the blood chamber 18. The blood return line 15 comprises an additional blood chamber 80, positioned downstream (considering the direction of flow during treatment) the outlet port 18b of the blood chamber 18: in practice blood coming from the blood treatment unit enters the blood chamber 18, exits the blood chamber 18 and then reaches the additional blood chamber 80, before then reaching the second end 25 of the blood return line 15 where the access device is or may be positioned. In greater

detail, the blood return line 15 comprises a first tube 72 extending from said first end 16 of the blood return line to the inlet port 18a of the blood chamber reservoir, a second tube 73 extending from the outlet port 18b of the blood chamber reservoir to a blood inlet port of the additional blood chamber 80, and a third tube 74 extending from an outlet port of the additional blood chamber 80 to said second end 25 of the blood return line 15.

The venous pressure sensor 41 is fluidly connected to either one of or to both said blood chamber 18 or said additional blood chamber 80. The pneumatic circuit 40 is fluidly connected to either one or to both the blood chamber 18 and the additional blood chamber 80 via a respective pressure line 42 having a first end connected to the blood chamber 18 (or to the additional blood chamber 80) and a second end connected to said pneumatic circuit 40. Note how a transducer protector 57 of the type described above may be present on each one of pressure lines 42. When the pneumatic circuit 40 is connected to the additional blood chamber 80 it may be controlled by the control unit 100 to adjust pressure and/or inlet and outlet of gas to/from the additional blood chamber 80 as described above in connection with the blood chamber.

According to one aspect of the invention the blood chamber 18 is removably coupled to the rest of the blood return line, such that in single access configuration both the blood chamber 18 and the additional blood chamber 80 may be used, while in double access configuration the blood chamber 18 may be removed and the circuit used with a blood return line exclusively provided with the additional blood chamber 80. In the example shown in figure 4, the first tube 72 has a first end 75, provided with a counter-connector configured to removably couple with a connector of the outlet port 17 of the blood compartment of the blood treatment unit, and a second end 76 connected, in particular fixed, to the

inlet port 18a of the blood chamber reservoir. The second tube 73 comprises at least one first segment 77 having a first end 78, connected, and in particular, fixed to outlet port 18b of the blood chamber 18, and a second end 79 provided with a connector; the second tube also has a second segment 81 with a first end 82 carrying a respective counter-connector, configured for removable connection to the connector carried by the second end 79 of the first segment 77, and a second end 83 connected, in particular fixed, to the blood inlet port of the additional blood chamber 80. The counter-connector at the first end 82 of the second segment is configured to also be removably connectable to the connector carried by the outlet port 16 of the blood compartment of the treatment unit. In this way, the assembly formed by blood chamber 18, first tube 72 and first segment 77 of the second tube 73 may is removably engaged to the blood circuit and may be removed when the extracorporeal blood circuit is used in double access configuration, with the possibility of connecting the second segment directly to the outlet port of the extracorporeal blood treatment unit.

Finally a third variant is shown in figures 7-9. In this case, the blood chamber 18 is a reservoir of fixed internal volume having one single blood port 18a configured to act both as blood inlet and as blood outlet port. The blood return line 15 comprises an additional blood chamber 80 positioned downstream said single blood port 18a (again with reference to a direction of blood circulation during treatment - see arrow A). More in detail, the blood return line comprises a first tube 84 extending from said first end 16 of the blood return line 15 to a blood inlet port of the additional blood chamber 80, a second tube 85 extending from a blood outlet port of the additional blood chamber 80 to said second end 25 of the blood return line: the single blood port 18a is connected to a branch-off point 86 of the first tube 84, for

instance located in an intermediate zone of the first tube. A tube segment 87 may connect the single blood port 18a of the blood chamber reservoir to the branch-off point 86. In the example shown, the single blood port 18a of the blood chamber carries (directly or via interposition of a further tube element 88) a connector configured to removably couple with a counter-connector carried by the tube segment 87 to selectively couple and uncouple the blood chamber 18 to the return line 15, such that the blood return line may be configured to include or not the blood chamber. It should be noted that a clamp 89 (either of the disposable type like a plastic and manually actuatable tube clamp or of the type controlled by the control unit 100) acts in correspondence of said tube segment: the clamp is operable - either manually or under a command from said control unit 100 - between an open position allowing passage of fluid through said tube segment and a closed position preventing passage of fluid through said tube segment. Also note that according to a variant, said counter-connector associated to tube segment 87 may carry a check valve which is configured to close fluid passage through said counter-connector upon disconnection of this latter from the said connector. The venous pressure sensor 41 is fluidly connected to either one of or to both said blood chamber 18 or said additional blood chamber 80. The pneumatic circuit 40 is fluidly connected to either one or to both the blood chamber 18 and the additional blood chamber 80 via a respective pressure line 42 having a first end connected to the blood chamber 18 (or to the additional blood chamber 80) and a second end connected to said pneumatic circuit 40. Note how a transducer protector 57 of the type described above may be present on each one of pressure lines 42. When the pneumatic circuit 40 is connected to the additional blood chamber 80 it may be controlled by the control unit 100 to adjust pressure and/or inlet and outlet of gas to/from the additional blood chamber 80 as described above in connection with the blood chamber. According to one aspect of

the invention the blood chamber 18 is removably coupled to the rest of the blood return line, such that in single access configuration both the blood chamber 18 and the additional blood chamber 80 may be used, while in double access configuration the blood chamber 18 may be removed and the circuit used with a blood return line exclusively provided with the additional blood chamber. Before connecting or disconnecting the blood chamber 18 said clamp is moved to the closed position.

In conclusion each of the three variants described above offers the possibility to configure the circuit in a configuration optimal for single access and in a configuration optimal for double access. In use the extracorporeal blood circuit is configurable according to the single access configuration (as described above and shown in figures 1, 4 and 7) or according to a double lumen configuration, where the blood withdrawal line second end is connected to a withdrawal lumen and the blood return line second end is connected to a return lumen: note the withdrawal lumen and the return lumen being either part of a same access device or each part of a respective and distinct access device. When the extracorporeal circuit is in the double lumen configuration, the control unit 100 is configured to:

- operating the blood pump 30 to withdraw blood from a patient via the withdrawal lumen and convey it through the blood compartment and into the blood chamber,
- maintaining the intercepting organ 36 in the open condition while operating the blood pump 30 to return blood to the patient via said return lumen.

The control unit 100 may also be configured to coordinate operation of the blood pump 30 and of the pneumatic circuit 40 such that – with the extracorporeal circuit in said double lumen configuration – blood occupies only a lower portion of said blood chamber 18 (this is particularly applicable with the first variant

of the extracorporeal blood circuit, but is not excluded also with the second and third variant in case the blood chamber 18 is not disconnected from the blood return line) and - with the extracorporeal circuit in said single access configuration - during the arterial phase blood occupies also a higher portion of said blood chamber.

Other aspects of the apparatus

The apparatus 1 in the variants of the extracorporeal blood circuit disclosed above may include the following further features.

In particular the apparatus 1 includes a support region, which is for instance part of the front panel of the apparatus cabinet, defining the holder 90 for said blood chamber. A low level sensor 91 and an high level sensor 92 may be associated to the support region and connected to said control unit 100: the low level sensor 91 is configured for issuing a signal to the control unit 100 at least when a liquid reaches a minimum liquid level in said blood chamber 18 and the high level sensor 92 is configured for issuing a signal to the control unit 100 at least when a liquid reaches a maximum liquid level in said blood chamber. Optionally a foam sensor 93 may also be associated to the support region in a position vertically above the high level sensor 92 and connected to said control unit 100: the foam sensor is configured for issuing a signal to the control unit 100 at least when foam reaches a maximum foam level in said blood chamber 18 (the maximum foam level being a level vertically higher than the maximum liquid level). In practice, the low level sensor 91 defines a mandatory minimum liquid level in the expansion volume present in the blood chamber 18, in order to prevent air to enter into the return tube downstream the blood chamber 18 or air backflow to the treatment unit. The high level sensor 92 defines a mandatory maximum liquid

level in the expansion volume of the blood chamber 18 to prevent wetting of transducer protector or propagation of liquid into the pressure line.

According to a further aspect of the invention, the control unit 100 may be configured for calculating a value for an actual flow rate delivered by the blood pump 30 during arterial phase as a function of: the quantity or the flow rate of air removed by the pneumatic circuit 40 from the blood chamber 18 during the arterial phase, and the pressure, and optionally the temperature, in the blood chamber 18 during the arterial phase. Alternatively a further way of calculating – by the suitably configured control unit 100 – the actual flow rate delivered by the blood pump 30 during arterial phase may be as a function of the time for blood in the blood chamber 18 to pass from two prefixed liquid levels, optionally from a minimum liquid level to a maximum liquid level as detected by respective low level and high level sensors. In both cases the actual flow rate determined by the control unit 100 may be used to correct the blood pump 30 angular speed using the following process: receiving a set value for a desired flow rate intended to be delivered by the blood pump 30 during said arterial phase, comparing the calculated actual flow rate value with the desired flow rate value, and adjusting an angular speed of the blood pump 30 such that the calculated actual flow rate value matches, or stays in a range around, said desired flow rate value during said arterial phase.

Finally, it should be noted that certain safety limits may be set in order to avoid risks during pressure adjustment. In detail, the pressure adjustment sequence during said arterial phase may include determining if said one or more measured values of the venous pressure deviate by more than a first safety tolerance, which is less stringent (i.e. with a broader acceptability range) than said first prefixed tolerance, from the at least one set

value, and generating an alarm signal, optionally stopping the blood pump 30. Analogously the pressure adjustment sequence during said venous phase may further comprise determining if said one or more measured values of the venous pressure deviate by more than a second safety tolerance, which is less stringent than said second prefixed tolerance, from the at least one set value, and generating an alarm signal, optionally closing the venous clamp.
In other words if pressure values are detected which are too far from respective venous or arterial pressure regimen values then alarms are generated and safety measures taken by the control unit 100.

Control unit 100

The apparatus 1 according to the invention makes use of at least one control unit 100. The control unit 100 may comprise a respective digital processor (CPU) with memory (or memories), an analog type circuit, or a combination of one or more digital processing units with one or more analog type circuits. In the present description and in the claims it is indicated that the control unit 100 may be "configured" or "programmed" to execute certain steps: this may be achieved in practice by any means which allow configuring or programming the control unit 100. For instance, in case of a control unit 100 comprising one or more CPUs and one or more memories, one or more programs may be stored in an appropriate memory banks connected to the CPU or CPUs; the program or programs contain instructions which, when executed by the CPU or CPUs, cause the control unit 100 to execute the steps described or claimed in connection with the control unit 100. Alternatively, if the control unit 100 is or comprises analog type circuitry, then the circuitry of the control unit 100 may be designed to include circuitry configured, in use, to process electric signals such as to execute the control unit 100 steps herein disclosed or claimed.

The above described aspects of the present invention related to the pressure control in the arterial and venous phases achieve appreciable advantages. Just to mention some of them: the ability to control the pressure regimen such that pressure in the blood chamber during arterial phase and venous phase is kept substantially constant for the major portion of said phases leads to a reduction of fistula stress. Moreover, control of the ultrafiltration is made simpler as pressure in the blood chamber and thus in the blood side 5 of the blood treatment unit may be kept substantially constant basically during the majority of the treatment: this is particularly evident when the pressure regimen kept during the arterial phase is the same as the pressure regimen kept during venous phase.

While the invention has been described in connection with what is presently considered to be the most practical and preferred embodiments, it is to be understood that the invention is not to be limited to the disclosed embodiments, but on the contrary, is intended to cover various modifications and equivalent arrangements included within the spirit and the scope of the appended claims.

For example according to an alternative the blood chamber 18 (onto which the pneumatic circuit acts) may be part of the blood withdrawal line, preferably being located in the tract between the blood pump tract and the blood treatment unit, instead of being located as part of the blood return line.

CLAIMS

1. An extracorporeal blood treatment apparatus comprising:

- a treatment unit (2) having at least a semipermeable membrane (3) dividing the treatment unit (2) into a blood compartment (5), and a filtrate compartment (6);
- a blood withdrawal line (12) having a first end connected to an inlet port of the blood compartment of the treatment unit;
- a blood return line (15) having a first end connected to an outlet port of the blood compartment of the treatment unit, the blood return line (15) including at least one blood chamber (18) configured, in operation, to host a volume of blood and define a blood-air interface;

wherein the blood withdrawal line (12), the blood compartment (5) and the blood return line (15) are part of an extracorporeal blood circuit (11);

- a single lumen access device (19) configured to be connected to a patient's cardiovascular system, wherein – in a single access configuration of the extracorporeal blood circuit – the blood withdrawal line (12) and the blood return line (15) have respective second ends contemporaneously connected to the single lumen access device;
- a blood pump (30) positioned at, and configured to be operative on, the blood withdrawal line;
- an intercepting organ (36) positioned at, and configured to be operative on, a portion of the blood return line (15) and selectively positionable at least in an open condition and in a closed condition to respectively allow and prevent a passage of fluid through said second end of the blood return line;
- a pneumatic circuit (40) connected to the blood chamber (18) in the blood return line (15) and configured to supply gas to or withdraw gas from the blood chamber; and
- a control unit (100), connected to the blood pump (30), to the

pneumatic circuit (40) and to the intercepting organ (36), wherein – with the extracorporeal circuit (11) in said single access configuration – the control unit (100) is configured to repeatedly execute a cycle including an arterial phase and a venous phase,

- o wherein the arterial phase of the cycle includes the following steps the control unit (100) is configured to execute:
  - operating the blood pump (30) to withdraw blood via the single lumen access device (19) and convey it through the blood compartment (5) and to the blood chamber (18),
  - maintaining the intercepting organ (36) in the closed condition,
  - controlling the pneumatic circuit (40) to withdraw gas from the blood chamber (18) in synchrony with operation of the blood pump (30) to facilitate inlet of blood in the blood chamber, wherein said controlling the pneumatic circuit (40) to withdraw gas includes maintaining pressure in the blood chamber (18) at a predetermined arterial phase pressure regimen at least for a major portion of the arterial phase,
- o wherein the venous phase of the cycle includes the following steps the control unit (100) is configured to execute:
  - stopping operation of the blood pump (30),
  - maintaining the intercepting organ (36) in the open condition and cause blood in the venous line to return via the single lumen access device,
  - controlling the pneumatic circuit (40) to supply gas to the blood chamber (18) while the intercepting organ (36) is in the open condition, wherein said

step of controlling the pneumatic circuit (40) to supply gas to the blood chamber (18) during the venous phase comprises maintaining pressure in the blood chamber (18) at a predetermined venous phase pressure regimen at least for a major portion of the venous phase.

2. The apparatus of claim 1, wherein said step of keeping pressure in the blood chamber (18) at a predetermined arterial phase pressure regimen, which the control unit (100) is configured to execute at each cycle during arterial phase, comprises one of:

keeping pressure in the blood chamber (18) at a substantially prefixed constant pressure value at least for a major portion of the arterial phase,

keeping pressure in the blood chamber (18) within a prefixed range around a constant pressure value at least for a major portion of the arterial phase.

3. The apparatus of claim 2, wherein the control unit (100) is configured to receive the constant pressure value (P_{0A}) to be kept during arterial phase either from a memory connected to the control unit (100) where said value(s) are pre-stored or from an input device connected to the control unit.

4. The apparatus of claim 2 or 3, wherein the predetermined arterial phase pressure regimen (P_{ART}) is either a prefixed constant pressure value (P_{0A}) or the prefixed constant pressure value (P_{0A}) ± 10 mm of Hg.

5. The apparatus of any one of the preceding claims, wherein said step of keeping pressure in the blood chamber (18) at a predetermined venous phase pressure regimen, which the control unit (100) is configured to execute at each cycle during venous

phase, comprises one of:

keeping pressure in the blood chamber (18) at a substantially prefixed constant pressure value at least for a major portion of the venous phase,

keeping pressure in the blood chamber (18) within a prefixed range around a constant pressure value at least for a major portion of the venous phase.

6. The apparatus of claim 5, wherein the control unit (100) is configured to receive the constant pressure value (P_{0V}) to be kept during venous phase either from a memory connected to the control unit (100) where said value(s) are pre-stored or from an input device connected to the control unit.

7. The apparatus of claim 5 or 6, wherein the predetermined venous phase pressure regimen (P_{VEN}) is either a prefixed constant pressure value (P_{0V}) or the prefixed constant pressure value (P_{0V}) ± 10 mm of Hg.

8. The apparatus of any one of the preceding claims, wherein said control unit (100) is configured such that said predetermined arterial phase pressure regimen is identical to the predetermined venous phase pressure regimen

9. The apparatus of any one of the preceding claims wherein said constant arterial pressure value (P_{0A}) is identical to said constant venous pressure value(P_{0V}).

10. The apparatus of any one of the preceding claims, wherein the major portion of the arterial phase is 80% or more of the duration of the entire arterial phase.

11. The apparatus of any one of the preceding claims, wherein the major portion of the venous phase is 80% or more of the duration of the entire venous phase.

12. Apparatus according to any one of the preceding claims wherein no blood pump (30) is operative on the blood return line, wherein no blood chambers or blood reservoirs configured for air/blood separation is directly connected to, or part of, the blood withdrawal line, and wherein during venous phase with the blood pump (30) positioned at the blood withdrawal line (12) being stopped, the control unit (100) is configured to cause blood in the venous line to return to the single lumen access device (19) exclusively by keeping the intercepting organ (36) in the open condition and controlling the pneumatic circuit (40) to supply gas to the blood chamber.

13. Apparatus according to any one of the preceding claims wherein said controlling step which the control unit (100) is configured to execute during the arterial phase of the cycle comprises:

- estimating or receiving an arterial stroke volume value (V_{ART}), corresponding to a blood volume intended to be conveyed into the blood chamber (18) during the arterial phase, and
- commanding the pneumatic circuit (40) to withdraw from the blood chamber, during the arterial phase, a volume of gas equal to said arterial stroke volume value (V_{ART}).

14. Apparatus according to any one of the preceding claims wherein the control unit (100) is configured for storing or receiving a first relationship: $V_{ART} = (Q_{B\_ART} - Q_{UF\_ART}) \cdot T_{ART}$

wherein:

V_{ART} is an estimated or set value of the arterial stroke volume,

T_{ART} is an estimated or set value of the duration of the

arterial phase during which the blood pump (30) and the pneumatic circuit (40) are both active,

Q_{B_ART} is a measured or set value of the blood flow rate in the arterial line during the arterial phase,

Q_{UF_ART} is a measured or set value of the ultrafiltration flow rate through the semipermeable membrane (3) of the treatment unit (2) during the arterial phase,

said control unit (100) adopting said first relationship for calculating one of said value of the arterial stroke volume (V_{ART}) and said value of the duration of the arterial phase (T_{ART}), using a set value of the other.

15. Apparatus according to any one of the preceding claims wherein said controlling step which the control unit (100) is configured to execute during the venous phase of the cycle comprises:

- estimating or receiving a venous stroke volume value (V_{VEN}), corresponding to a blood volume intended to be ejected from the blood chamber (18) and returned to the patient during the venous phase, and
- commanding the pneumatic circuit (40) to supply to the blood chamber (18), during the venous phase, a corresponding volume of gas equal to said venous stroke volume value (V_{VEN}).

16. Apparatus according to the preceding claim wherein the control unit (100) is configured for commanding the pneumatic circuit (40) to supply to the blood chamber (18) a volume of gas equal to said venous stroke volume value (V_{VEN}) during a time interval (T_{VEN}) while keeping pressure constant and higher than blood pressure such that the same volume (V_{VEN}) of blood is returned to the patient.

17. Apparatus according to any one of the preceding claims comprising at least one venous pressure sensor (41) connected to

the blood return line (15) and configured to receive a pressure signal and supply it to the control unit (100),

wherein the control unit (100) is configured to execute a pressure adjustment sequence during said arterial phase comprising:

receiving the pressure signal from the venous pressure sensor (41),

determining one or more measured values of the venous pressure from said pressure signal,

comparing said one or more measured values of the venous pressure with at least one set value representative of the predetermined arterial phase pressure regimen, and

adjusting the pneumatic circuit (40) to withdraw gas from the blood chamber (18) during the arterial phase to keep said one or more measured values of the venous pressure within a first prefixed tolerance from the at least one set value representative of said predetermined arterial pressure regimen;

18. Apparatus according to any one of the preceding claims wherein the control unit (100) is configured to execute a pressure adjustment sequence during said venous phase comprising:

receiving the pressure signal from the venous pressure sensor (41),

determining one or more measured values of the venous pressure from said pressure signal,

comparing said one or more measured values of the venous pressure with at least one set value representative of the predetermined venous phase pressure regimen, and

adjusting the pneumatic circuit (40) to supply gas to the blood chamber (18) during the venous phase to keep the one or more measured values of the venous pressure within a second prefixed tolerance from said at least one set value representative of said predetermined venous pressure regimen.

19. Apparatus according to claim 17 or 18, wherein the pneumatic circuit (40) comprises an air pump having one side connected to the atmosphere and another side connected to the blood chamber (18) and wherein the control unit (100) receives said pressure signal from the pressure sensor and acts on the air pump to keep pressure in the blood chamber (18) matching the arterial pressure regimen.

20. Apparatus according to claim 17 or 18 or 19, wherein the pneumatic circuit (40) comprises an air pump having one side connected to the atmosphere and another side connected to the blood chamber (18) and wherein the control unit (100) receives said pressure signal from the pressure sensor and acts on the air pump to keep pressure in the blood chamber (18) matching the venous pressure regimen.

21. Apparatus according any one of the preceding claims in combination with claim 13 or claim 14, wherein the pneumatic circuit (40) comprises a gas accumulator having:

- a variable volume chamber (60) in gas communication with the blood chamber (18),
- an actuator (60) associated to the variable volume chamber and controlled by the control unit (100) and active to cause a variation of the internal volume of the variable volume chamber (60) between a minimum volume and a maximum volume,

wherein, during the arterial phase, the control unit (100) is configured for commanding the pneumatic circuit (40) to withdraw from the blood chamber (18) a volume of gas equal to an/the estimated or set value of the arterial stroke volume (V_{ART}), by acting on said actuator and increasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber (18) with the internal volume

of said variable volume chamber (60) - substantially constant during the entire or a major portion of said arterial phase.

22. Apparatus according any one of the preceding claims in combination with claim 15 or claim 16, wherein the pneumatic circuit (40) comprises a gas accumulator (59) having:

- a variable volume chamber (60) in gas communication with the blood chamber,
- an actuator (61) associated to the variable volume chamber and controlled by the control unit (100) and active to cause a variation of the internal volume of the variable volume chamber between a minimum volume and a maximum volume,

wherein, during the venous phase, the control unit (100) is configured for commanding the pneumatic circuit (40) to supply to the blood chamber (18) a volume of gas equal to an/the estimated or set value of the arterial stroke volume (V_{VEN}), by acting on said actuator and decreasing said internal volume to keep a combined volume - defined by the sum of the volume occupied by gas present in the blood chamber (18) with the internal volume of said variable volume chamber (60) - substantially constant during the entire or a major portion of said venous phase.

23. Apparatus according to any one of the preceding claims wherein said blood chamber (18) is the only one on the blood return line, no other blood chambers being positioned at, part of, or directly connected to the blood return line, the blood return line (15) further comprising:

- a first tube (70) extending from said first end to an inlet port of the blood chamber, and
- a second tube (71) extending from an outlet port of the blood chamber (18) to said second end of the blood return line;

wherein said venous pressure sensor (41) and said pneumatic circuit (40) are fluidly connected to the blood chamber (18) via a

pressure line having a first end connected to the blood chamber (18) and a second end connected to said pneumatic circuit (40).

24. Apparatus of claim 23, wherein a transducer protector is positioned on said pressure line and comprises a casing housing a hydrophobic membrane (3) separating a casing internal volume into a first chamber communicating with the blood chamber (18) and a second chamber communicating with the pneumatic circuit.

25. Apparatus according to any one of the preceding claims from 1 to 22 wherein:

- said at least one blood chamber (18) is a reservoir of fixed internal volume having one single blood port (18a) configured to act both as blood inlet and as blood outlet port,
- said blood return line (15) comprises an additional blood chamber (80) positioned downstream said single blood port,
- said venous pressure sensor (41) is fluidly connected to either one of said blood chamber (18) or said additional blood chamber, and
- said pneumatic circuit (40) is fluidly connected to the blood chamber (18) via a pressure line (42) having a first end connected to the blood chamber (18) and a second end connected to said pneumatic circuit (40).

26. Apparatus according to claim 25, wherein a transducer protector is positioned on said pressure line and comprises a casing housing a hydrophobic membrane separating a casing internal volume into a first chamber communicating with the blood chamber (18) and a second chamber communicating with the pneumatic circuit.

27. Apparatus of claim 25 or 26, wherein the blood return line (15) comprises

- a first tube (84) extending from said first end to a blood inlet port of the additional blood chamber,
- a second tube (85) extending from a blood outlet port of the additional blood chamber (80) to said second end of the blood return line, wherein the single blood port (18a) is connected to a branch-off point (86) of the first tube and wherein a tube segment (87) connects said single blood port to said branch-off point, this latter being located in an intermediate region of said first tube of the blood return line;

yet further wherein the single blood port of the blood chamber (18) carries a connector configured to removably couple with a counter-connector carried by the tube segment to selectively couple and uncouple the blood chamber (18) to the return line, and wherein a clamp (89) acts in correspondence of said tube segment, further wherein said clamp is operable - either manually or under a command from said control unit (100) - between an open position allowing passage of fluid through said tube segment and a closed position preventing passage of fluid through said tube segment.

28. Apparatus according to any one of the preceding claims from 1 to 22 wherein:

- said at least one blood chamber (18) is a reservoir having two blood ports including an inlet port (18a), configured to receive all fluid coming from the first end of the blood return line, and an outlet port (18b), configured to discharge fluid exiting from the blood chamber;
- said blood return line (15) comprises an additional blood chamber (80), positioned downstream said outlet port (18b) of the blood chamber (18),
- said venous pressure sensor (41) is fluidly connected to either one of said blood chamber (18) or said additional blood chamber, and

- said pneumatic circuit (40) is fluidly connected to the blood chamber (18) via a pressure line having a first end connected to the blood chamber (18) and a second end connected to said pneumatic circuit (40).

29. Apparatus of claim 28, wherein a transducer protector is positioned on said pressure line and comprises a casing housing a hydrophobic membrane (3) separating a casing internal volume into a first chamber communicating with the blood chamber (18) and a second chamber communicating with the pneumatic circuit.

30. Apparatus of claim 28 or 29, wherein the blood chamber (18) is removably coupled to the rest of the blood return line;
and wherein the blood return line (15) comprises

- a first tube (72) extending from said first end of the blood return line (15) and connected to the inlet port of the blood chamber (18) reservoir,
- a second tube (73) extending from the outlet port of the blood chamber (18) reservoir to a blood inlet port of the additional blood chamber,
- a third tube (74) extending from an outlet port of the additional blood chamber (80) to said second end of the blood return line.

31. Apparatus of claim 28 or 29 or 30, wherein the first tube (72) has a first end, provided with a counter-connector adapted to removably couple with a connector of the outlet port of the blood compartment of the blood treatment unit, and a second end connected, in particular fixed, to the inlet port of the blood chamber (18) reservoir,
and wherein the second tube (73) comprises:

- at least one first segment having a first end, connected, and in particular, fixed to outlet port of the blood chamber, and

a second end provided with a connector, and

- a second segment having a first end with a respective counter-connector, configured for removable connection to the connector carried by the second end of the first segment, and a second end connected, in particular fixed, to the blood inlet port of the additional blood chamber, and
- wherein the counter-connector at the first end of the second segment is configured to also be removably connectable to the connector carried by the outlet port of the blood compartment of the treatment unit.

32. Apparatus according to any one of the preceding claims comprising:

- a support region defining a holder (90) for said blood chamber,
- a low level sensor (91) associated to the support region and connected to said control unit (100), the low level sensor being configured for issuing a signal to the control unit (100) at least when a liquid reaches a minimum liquid level in said blood chamber (18) and
- a high level sensor (92) associated to support region and connected to said control unit (100), the high level sensor being configured for issuing a signal to the control unit (100) at least when a liquid reaches a maximum liquid level in said blood chamber.

33. Apparatus of claim 32, comprising a foam sensor (93) associated to the support region in a position vertically above the high level sensor and connected to said control unit (100), the foam sensor being configured for issuing a signal to the control unit (100) at least when foam reaches a maximum foam level in said blood chamber, the maximum foam level being a level vertically higher than the maximum liquid level.

34. Apparatus according to any one of the preceding claims wherein at least one level sensor is associated to the blood chamber (18) and connected to the control unit (100) and wherein maintaining pressure in the blood chamber (18) at a predetermined venous phase pressure regimen comprises receiving by the control unit (100) a level signal from the level sensor and controlling, by the control unit, the pneumatic circuit to keep blood in the blood chamber at a constant level or at a level within a prefixed range around said constant level.

35. Apparatus according to any one of the preceding claims wherein at least one level sensor is associated to the blood chamber (18) and connected to the control unit (100) and wherein maintaining pressure in the blood chamber (18) at a predetermined arterial phase pressure regimen comprises receiving by the control unit (100) a level signal from the level sensor and controlling, by the control unit, the pneumatic circuit to keep blood in the blood chamber at a constant level or at a level within a prefixed range around said constant level.

36. Apparatus according to any one of the preceding claims wherein the control unit (100) is configured to receive one or more of - optionally all - the following settings relating to the arterial phase:

- one or more set values representative of said predetermined arterial phase pressure regimen, in particular said prefixed constant arterial pressure value;
- a set value for a desired flow rate intended to be delivered by the blood pump (30) during said arterial phase,
- a value of a/the arterial stroke volume (V_{ART}) intended to be delivered into the blood chamber (18) during the arterial phase,

and to control the blood pump (30) and the pneumatic circuit (40) based on one or more of said settings relating to the arterial phase;

wherein the control unit (100) is configured to receive one or more of - optionally all - the following settings relating to the venous phase:

- one or more set values representative of said predetermined venous phase pressure regimen, in particular said prefixed constant venous pressure value;
- a set value for a desired flow rate intended to be delivered through the venous line during said venous phase,
- a value of a/the venous stroke volume (V_{VEN}) intended to be removed from the blood chamber (18) during the venous phase;

and to control the blood pump (30) and the pneumatic circuit (40) based on one or more of said settings relating to the venous phase.

37. Apparatus according to any one of the preceding claims wherein said control unit (100) is configured for commanding a switch from said arterial phase of the cycle into said venous phase of the cycle when one of the following events takes place:

- expiration of a predetermined arterial phase time interval as of start of the arterial phase,
- delivery into the blood chamber (18) of a predetermined quantity of liquid as of start of the arterial phase,
- reaching of a maximum liquid level of liquid in the blood chamber,
- reaching of a maximum level of foam in the blood chamber;

and wherein said control unit (100) is configured for commanding a switch from said venous phase of the cycle into said arterial phase of the cycle when one of the following events takes place:

- expiration of a predetermined venous phase time interval as of start of the venous phase,

- evacuation from the blood chamber (18) of a predetermined quantity of liquid as of start of the arterial phase,
- reaching of a minimum liquid level of blood into the blood chamber.

38. Apparatus according to any one of the preceding claims wherein the control unit (100) is configured for:

- calculating a value for an actual flow rate delivered by the blood pump (30) during arterial phase as a function of:
  - o the quantity or the flow rate of air removed by the pneumatic circuit (40) from the blood chamber (18) during the arterial phase, and
  - o the pressure, and optionally the temperature, in the blood chamber (18) during the arterial phase;

  or as a function of the time for blood in the blood chamber (18) to pass from two prefixed liquid levels, optionally from a minimum liquid level to a maximum liquid level as detected by respective low level and high level sensors;
- receiving a set value for a desired flow rate intended to be delivered by the blood pump (30) during said arterial phase,
- comparing the calculated actual flow rate value with the desired flow rate value, and
- adjusting an angular speed of the blood pump (30) such that the calculated actual flow rate value matches, or stays in a range around, said desired flow rate value during said arterial phase.

39. Apparatus according to any one of the preceding claims wherein the extracorporeal blood circuit is configurable according to a double access configuration where the blood withdrawal line (12) second end is connected to a withdrawal lumen and the blood return line (15) second end is connected to a return lumen, the withdrawal lumen and the return lumen being either part of a same

access device or each part of a respective and distinct access device,

wherein the control unit (100) – with the extracorporeal blood circuit in said double access configuration – is configured to:

- operating the blood pump (30) to withdraw blood from a patient via the withdrawal lumen and convey it through the blood compartment and into the blood chamber,
- maintaining the intercepting organ (36) in the open condition while operating the blood pump (30) to return blood to the patient via said return lumen,

and wherein the control unit (100) is configured to coordinate operation of the blood pump (30) and of the pneumatic circuit (40) such that – with the extracorporeal circuit in said double access configuration – blood occupies only a lower portion of said blood chamber (18) and – with the extracorporeal circuit in said single access configuration – at least during the arterial phase blood occupies also a higher portion of said blood chamber.

40. Apparatus according to any one of the preceding claims comprising a waste handling circuit (8) configured to be connected to the filtrate compartment (6) of the treatment unit (2) and comprising at least one pump for controlling ultrafiltration of fluid crossing the semipermeable membrane (3).

41. Apparatus of claim 40, wherein the control unit is configured to control the at least one pump of the waste handling circuit during said arterial phase and while keeping pressure in the blood chamber (18) at said predetermined arterial phase pressure regimen.

42. Apparatus of claim 40 or 41, wherein the control unit is configured to control the at least one pump of the waste handling

circuit during said venous phase and while keeping pressure in the blood chamber (18) at said predetermined venous phase pressure regimen.

5

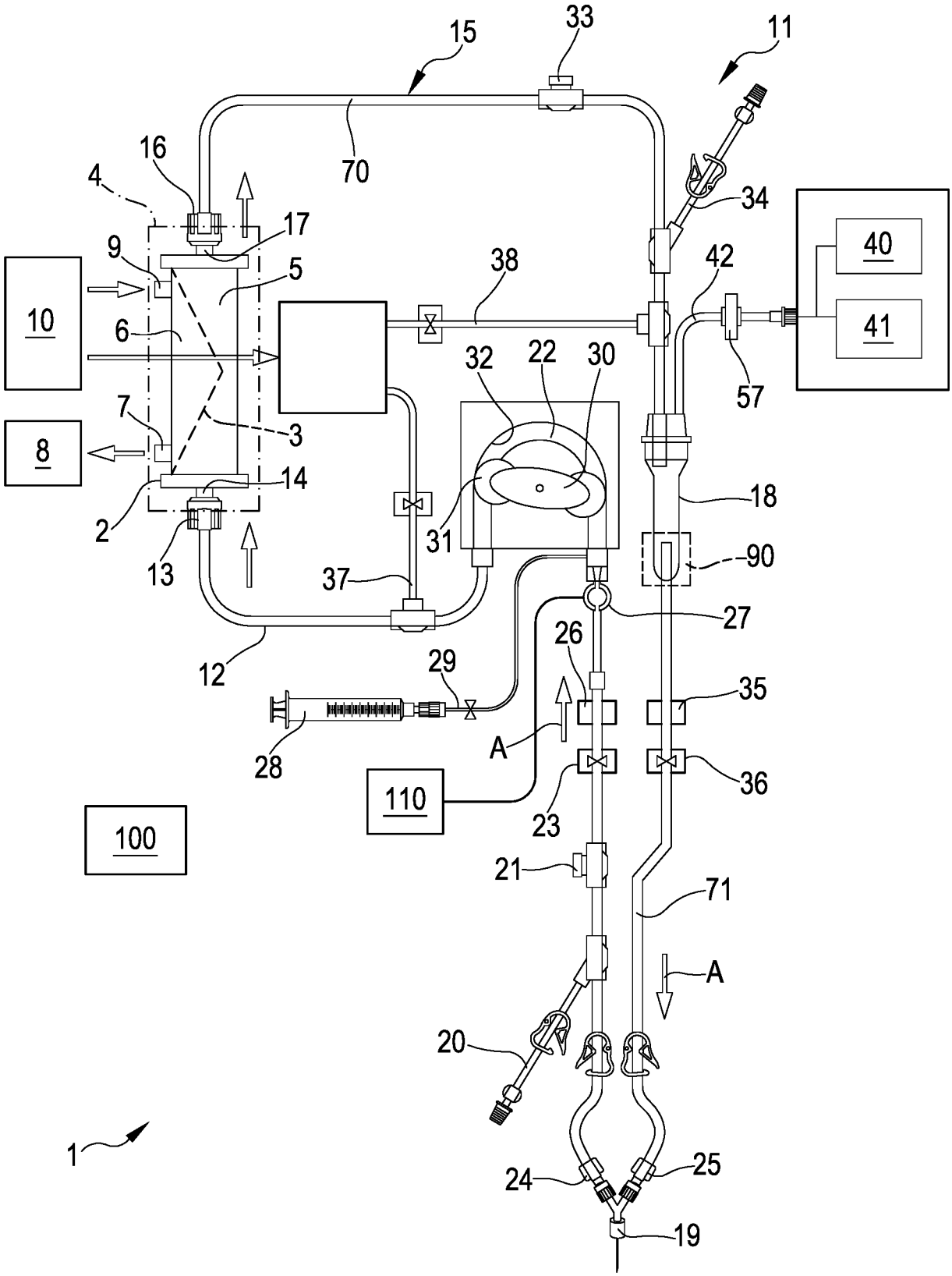

15
33
11
16
70
4
34
17
9
5
38
42
40
10
6
41
32
22
30
57
7
3
8
14
18
2
31
90
13
37
27
12
26
29
35
A
28
110
36
23
100
21
71
A
20
1
24
25
19

FIG.1

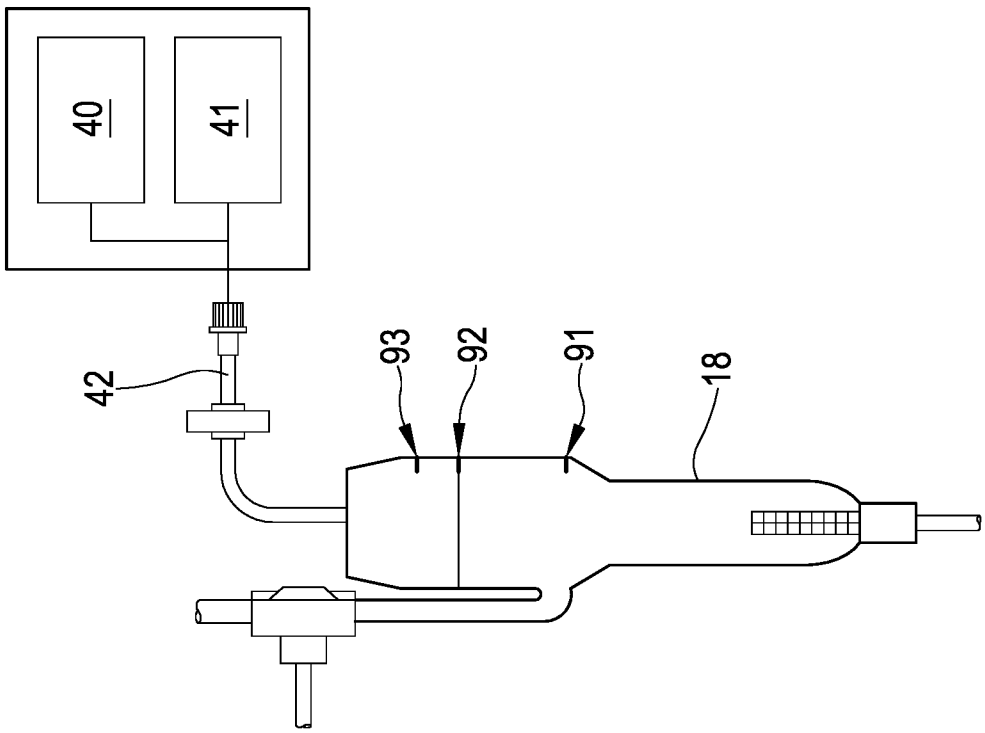


FIG.3

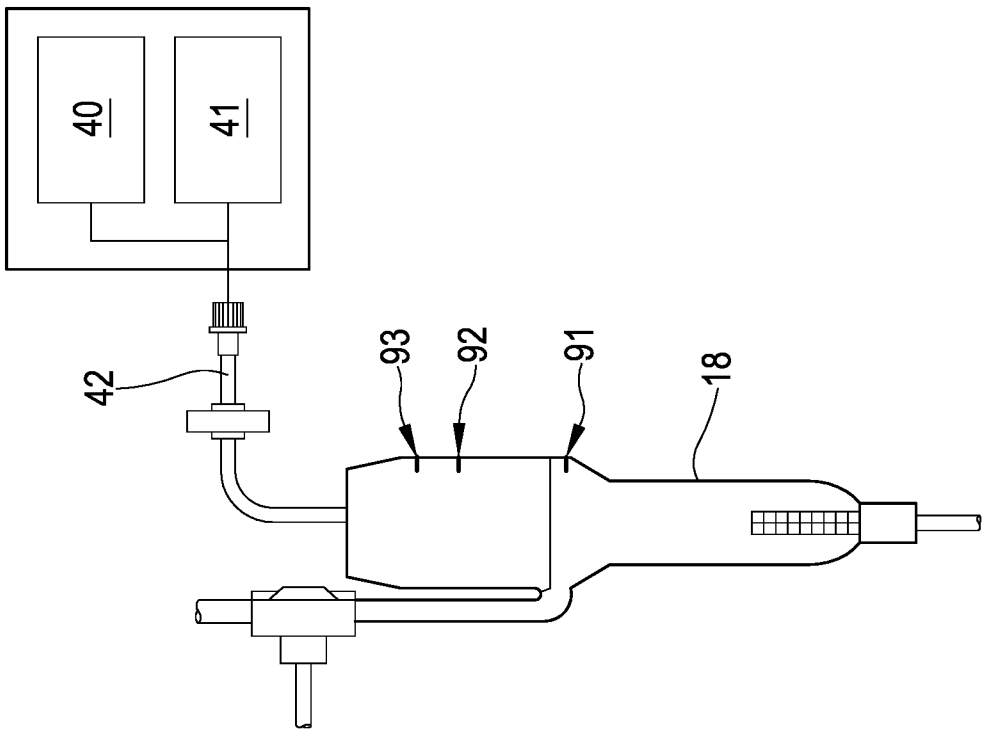


FIG.2

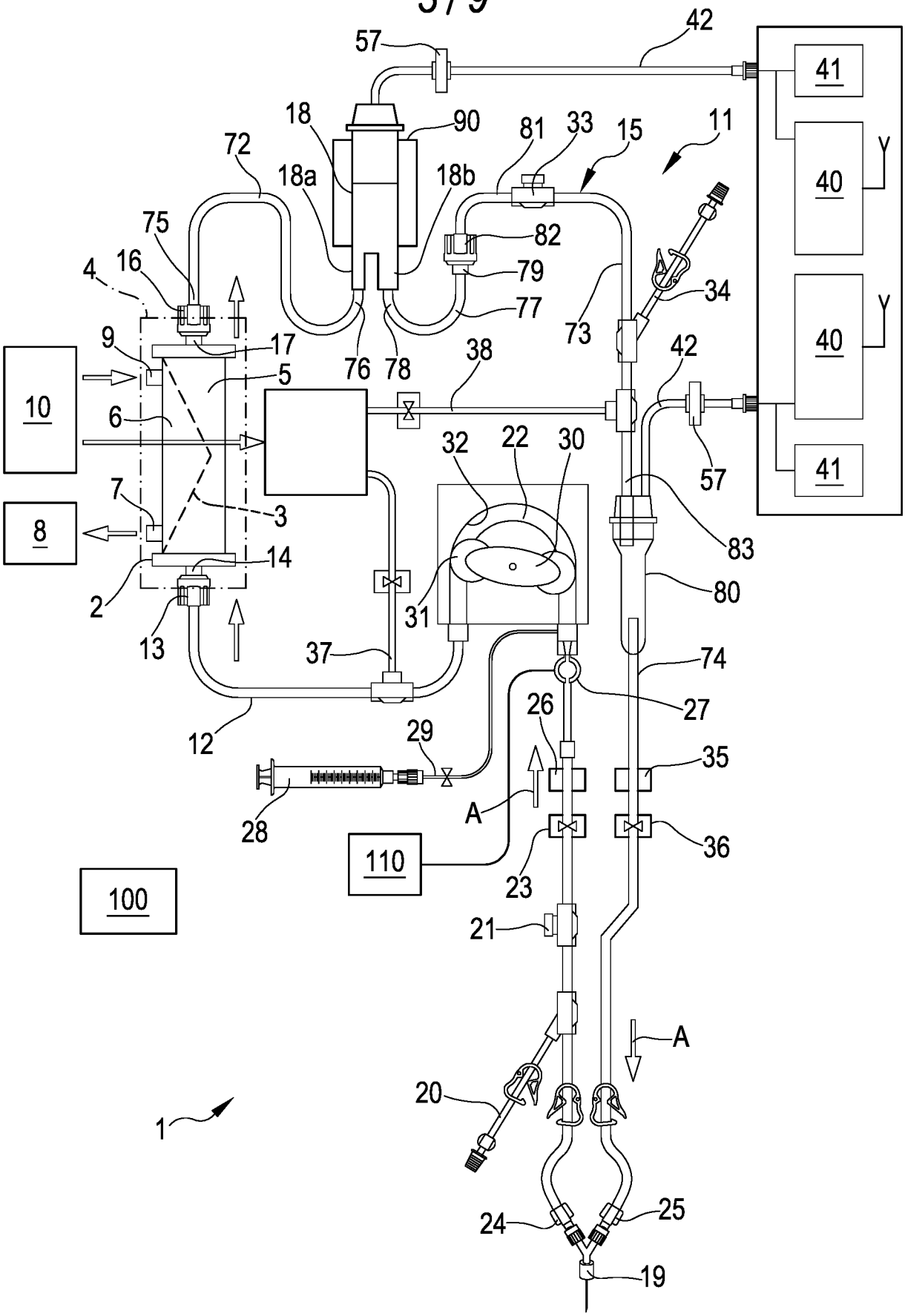

42
57
41
18
90
81
33
15
11
72
18a
18b
40
Y
75
82
16
4
79
34
77
73
9
17
42
38
76
78
10
5
6
32
22
30
57
41
7
3
8
83
14
80
2
31
13
37
74
27
26
12
29
35
A
28
110
36
23
100
21
A
20
1
24
25
19

FIG.4

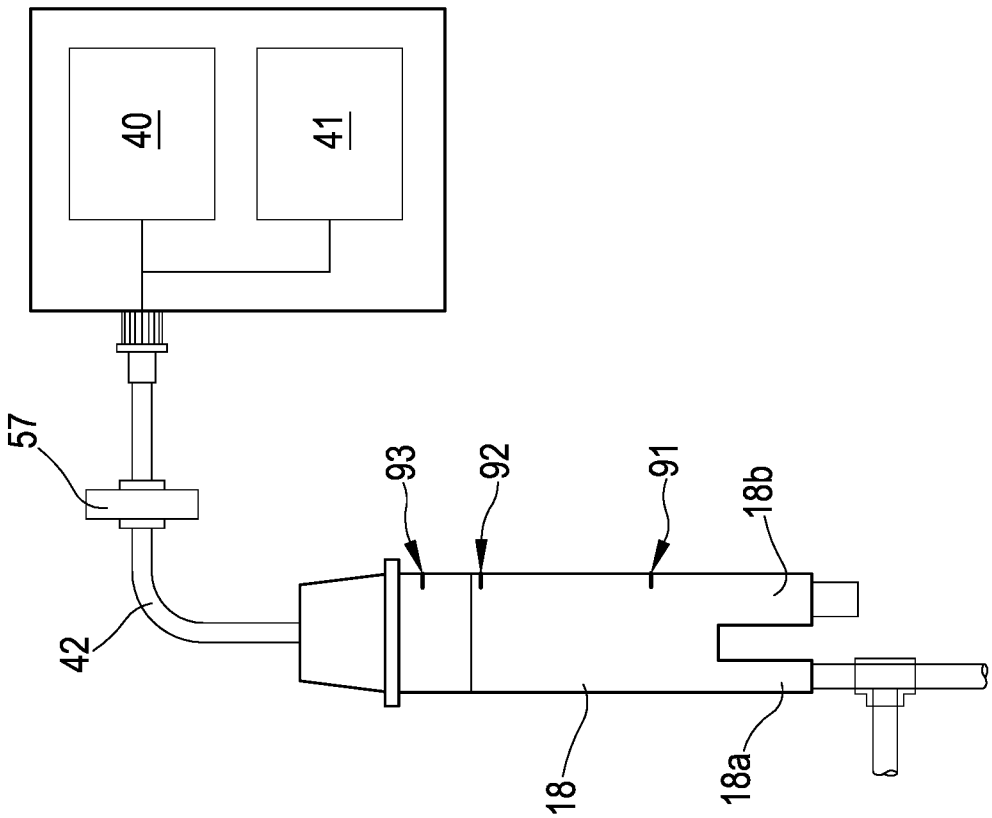


FIG.6

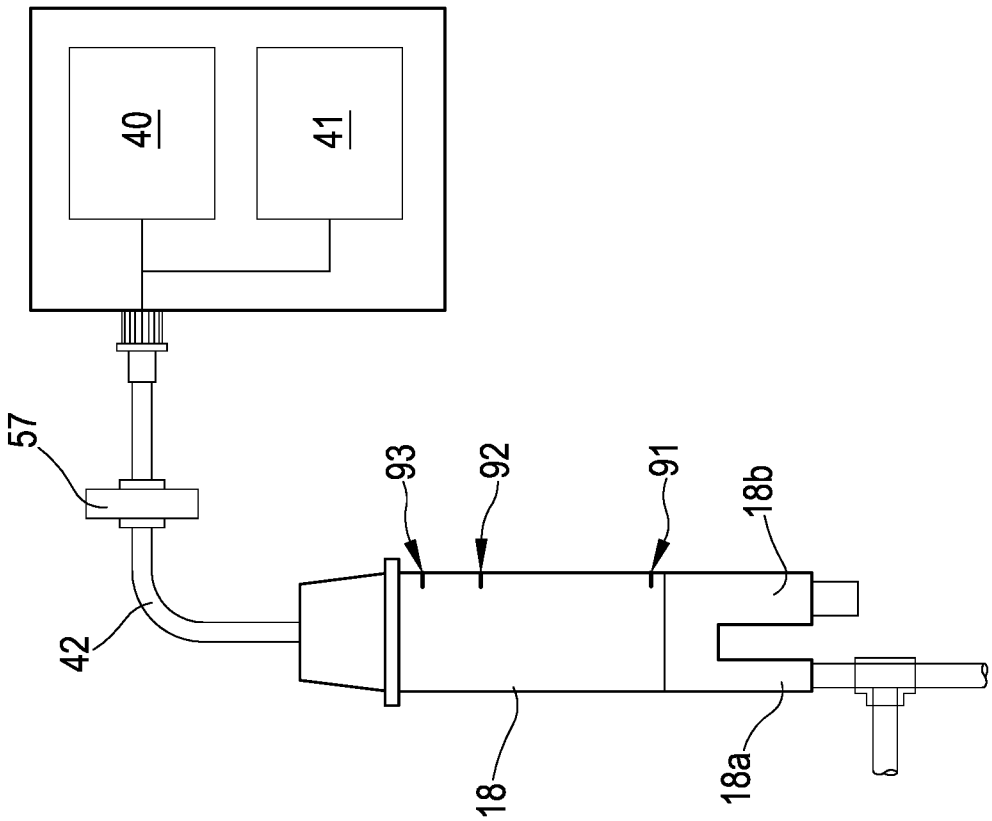


FIG.5

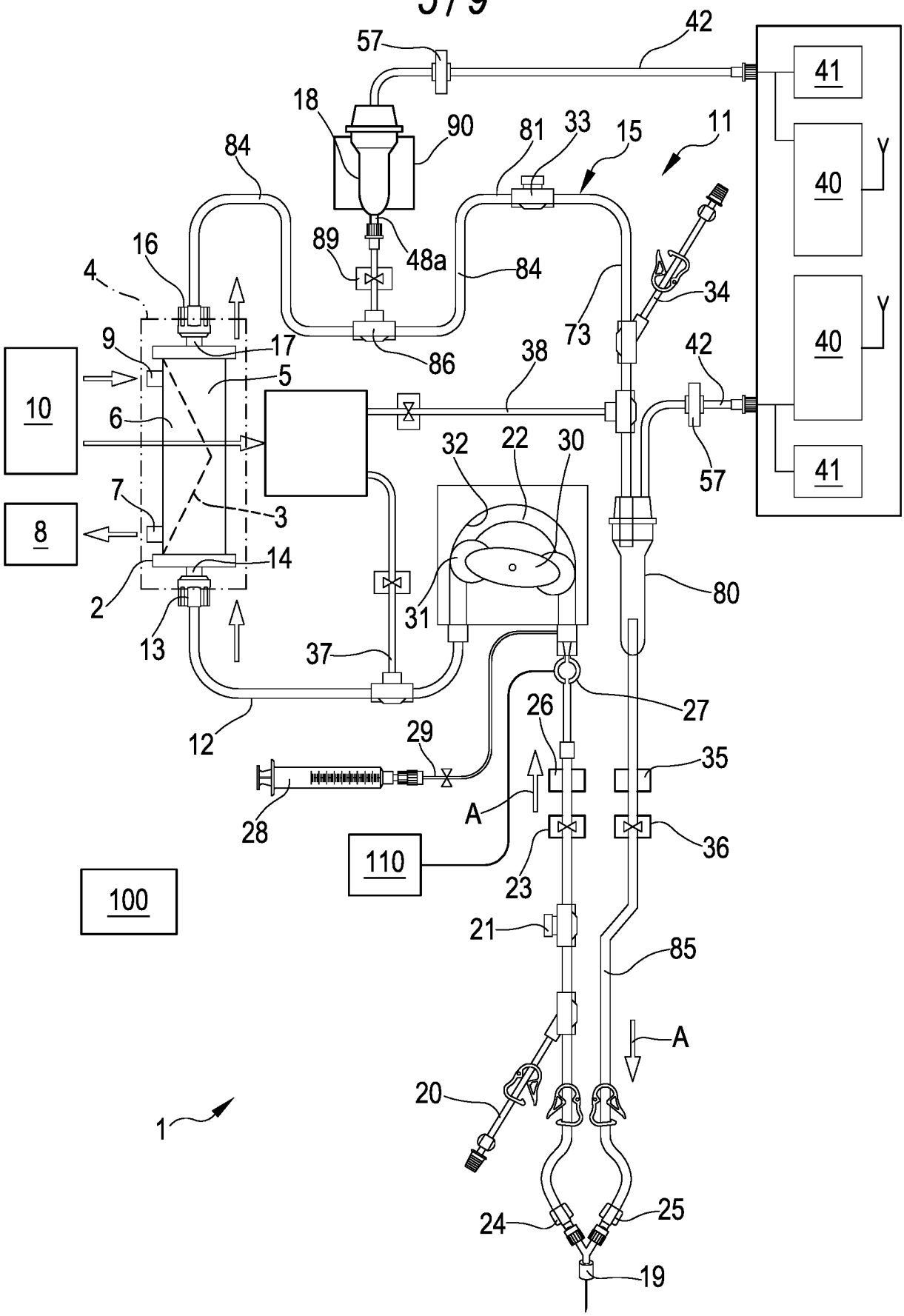

42
57
41
18
90
81
33
15
11
84
40
Y
16
89
48a
84
4
34
9
17
86
73
38
42
40
Y
10
5
6
32
22
30
57
41
7
3
8
14
80
2
31
13
37
27
26
12
29
35
A
28
110
36
23
100
21
85
A
20
1
24
25
19

FIG.7

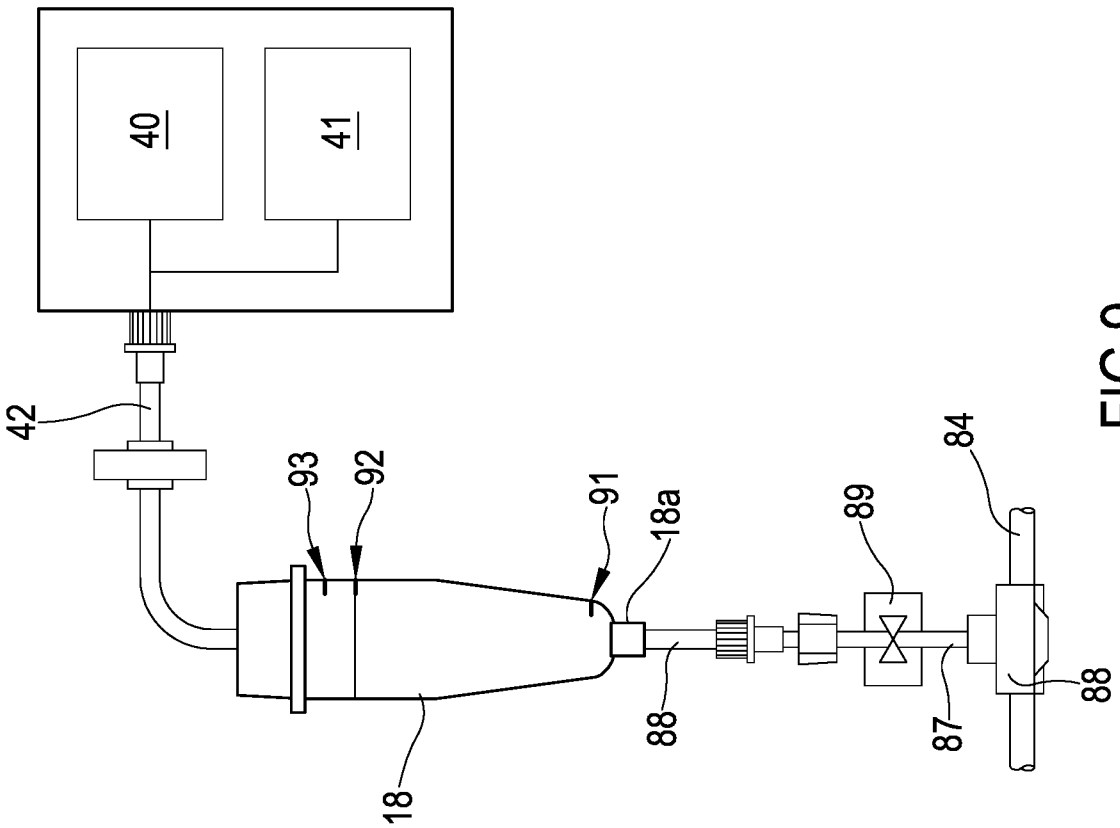

40
41
42
93
92
91
18a
89
84
88
87
88
18

FIG.9

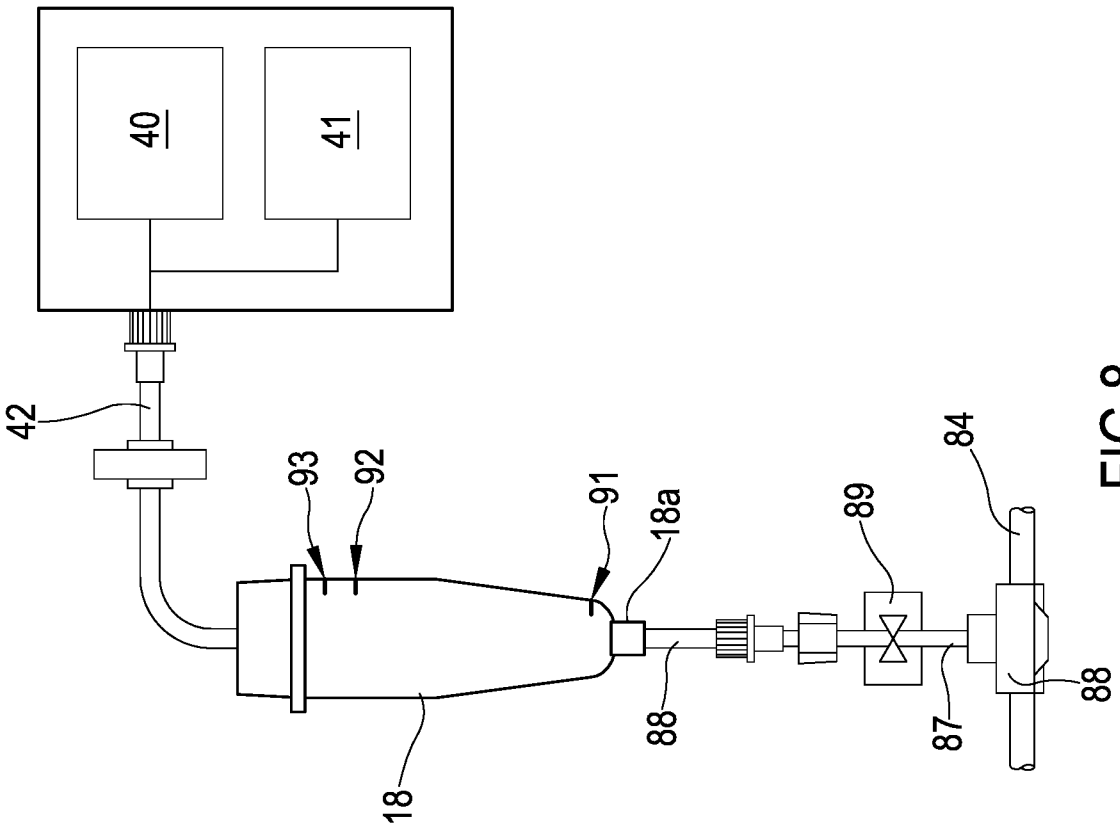

40
41
42
93
92
91
18a
89
84
88
87
88
18

FIG.8

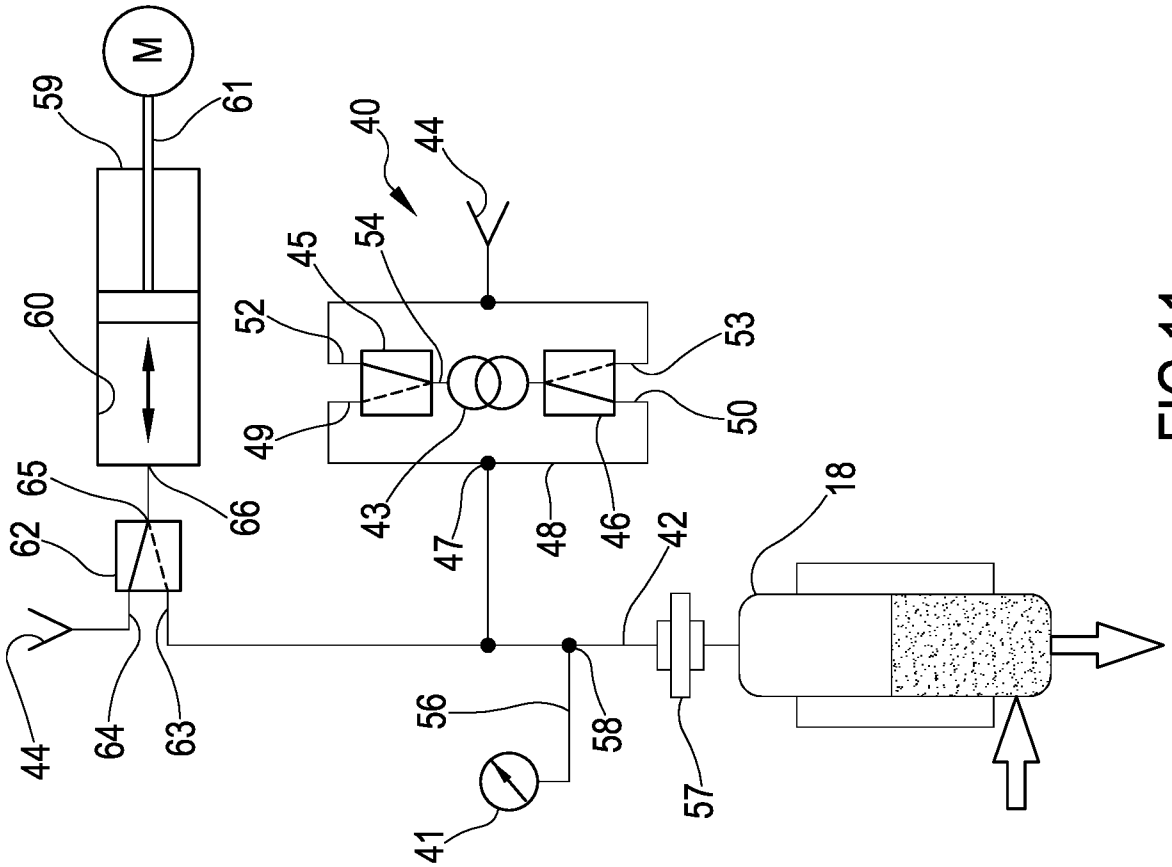

M
59
61
60
65
66
62
64
63
44
40
44
45
54
52
53
49
50
43
47
48
46
42
18
56
58
41
57

FIG.11

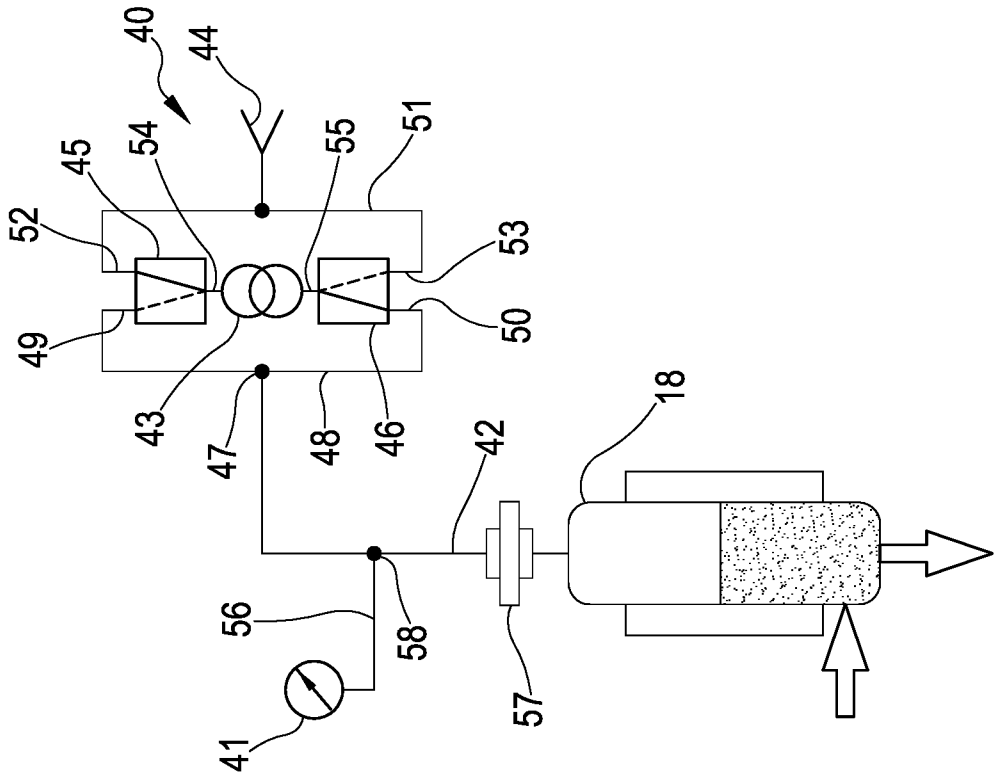
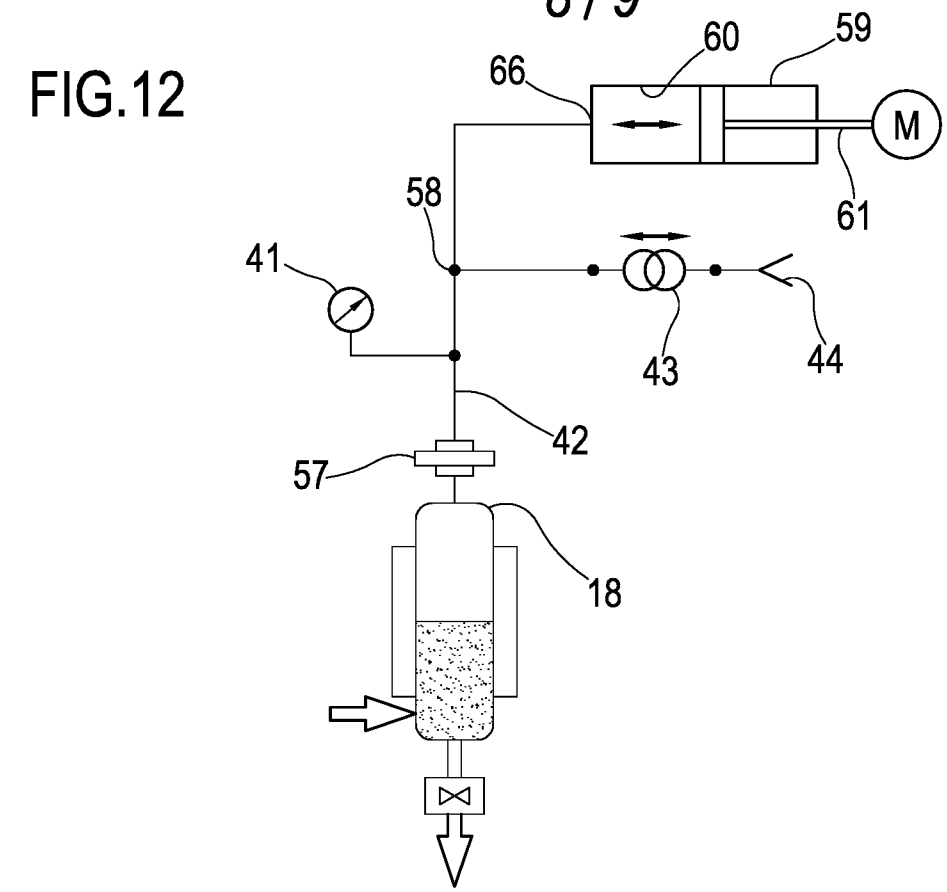

40
44
45
54
55
51
52
53
49
50
43
47
48
46
42
18
56
58
41
57

FIG.10

FIG.12


60
59
66
M
61
58
41
43
44
42
57
18

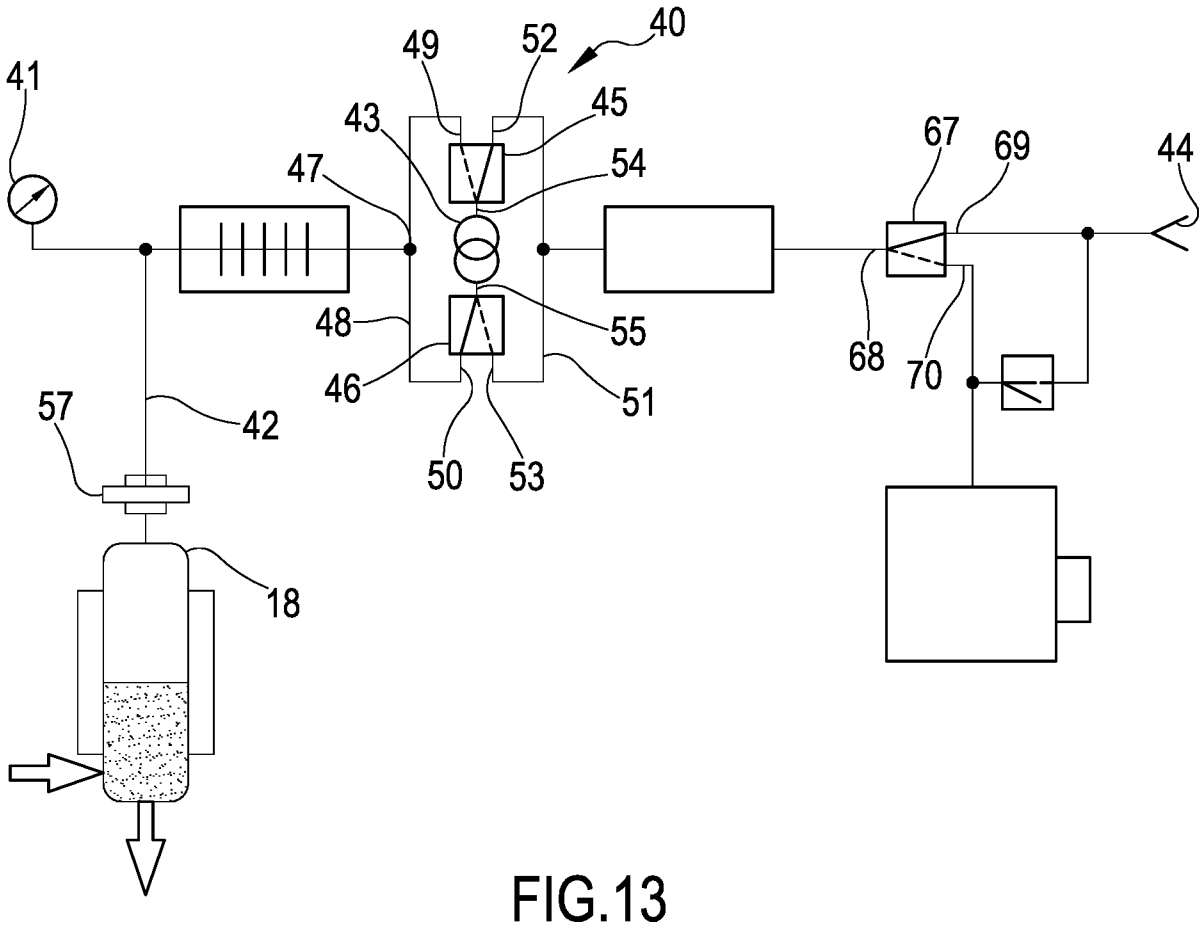

40
49
52
41
43
45
47
54
67
69
44
48
55
68
70
46
51
57
42
50
53
18

FIG.13

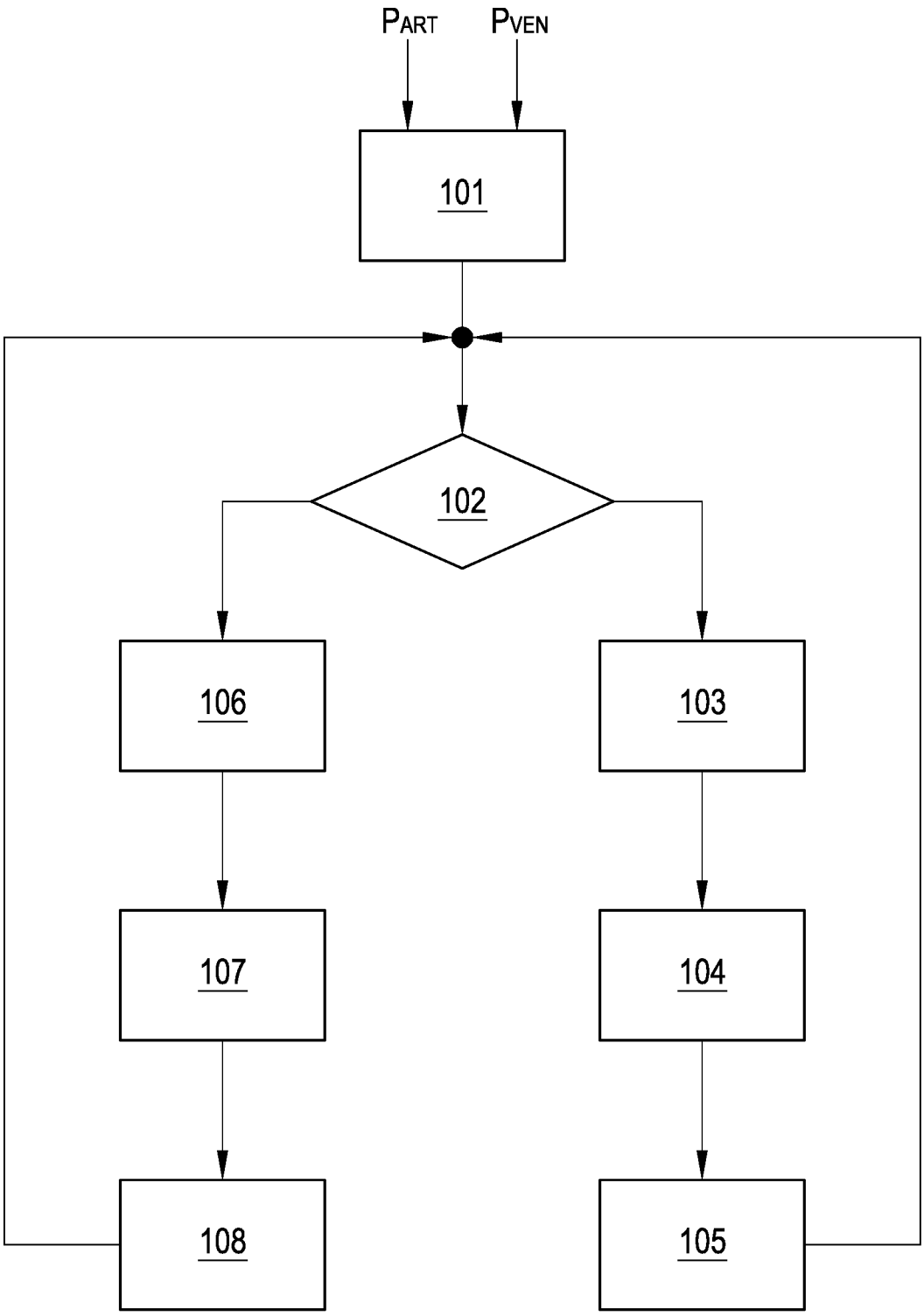


FIG.14

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/064912

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M1/30 A61M1/36
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, COMPENDEX, INSPEC, IBM-TDB, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2013/079698 A1 (BOCKLET CHRISTOPH [DE] ET AL) 28 March 2013 (2013-03-28) cited in the application	1-3,5,6, 10-12, 17,18, 36,37,40
A	paragraph [0033] - paragraph [0079] paragraph [0095] figures 1,3	4,7-9, 13-16, 19-35, 38,39, 41,42

X	US 5 227 049 A (CHEVALLET JACQUES [FR] ET AL) 13 July 1993 (1993-07-13) cited in the application column 2, line 64 - column 4, line 10 figure 1	1,2,5, 17-20, 32,34-37

	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
30 August 2016	06/09/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Aguilar, María

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/064912

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 318 511 A (RIQUIER JEAN-CLAUDE [FR] ET AL) 7 June 1994 (1994-06-07) column 3, line 21 - column 5, line 52 figures -----	1,2,5, 17-20, 32,34-37

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/064912

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2013079698 A1	28-03-2013	DE 102010022776 A1	08-12-2011
		EP 2575924 A1	10-04-2013
		ES 2546235 T3	21-09-2015
		US 2013079698 A1	28-03-2013
		WO 2011151075 A1	08-12-2011
US 5227049 A	13-07-1993	AT 125714 T	15-08-1995
		CA 2049465 A1	21-02-1992
		DE 69111716 D1	07-09-1995
		DE 69111716 T2	04-04-1996
		DK 0472480 T3	11-12-1995
		EP 0472480 A1	26-02-1992
		ES 2076497 T3	01-11-1995
		JP 3177268 B2	18-06-2001
		JP H05168704 A	02-07-1993
		US 5227049 A	13-07-1993
US 5318511 A	07-06-1994	CA 2060693 A1	07-08-1992
		DE 69203250 D1	10-08-1995
		DE 69203250 T2	18-01-1996
		EP 0498741 A1	12-08-1992
		ES 2075663 T3	01-10-1995
		FR 2672219 A1	07-08-1992
		JP 3210716 B2	17-09-2001
		JP H04317659 A	09-11-1992
		US 5318511 A	07-06-1994