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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
04 January 2018 (04.01.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/001994 A1

(51) International Patent Classification:
A61M 1/16 (2006.01) *A61M 1/36* (2006.01)

(21) International Application Number:
PCT/EP2017/065768

(22) International Filing Date:
27 June 2017 (27.06.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
1650949-9 30 June 2016 (30.06.2016) SE

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(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, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, 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.

(54) Title: CONNECTION TEST FOR BLOOD TREATMENT MACHINES I

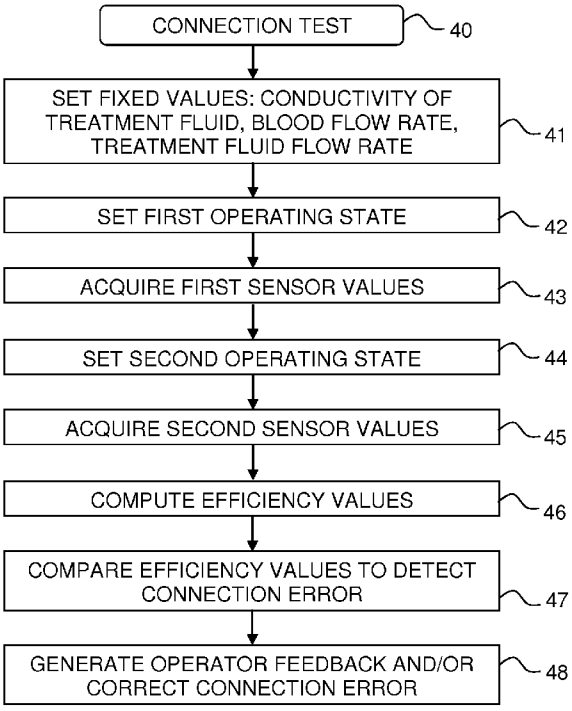

FIG. 4

(57) Abstract: A control device for a blood treatment machine performs a connection test (40) by causing (42, 44) the blood treatment machine to operate in first and second operating states, the second operating state differing from the first operating state by a change of flow direction in a dialyzer in the blood treatment machine and/or in access devices connected to a patient, without changing (41) the flow rate of blood, the flow rate of treatment fluid and a measured fluid property of the treatment fluid between the first and second operating states. Based on sensor values representing the fluid property (43, 45), the control device computes (46) efficiency values that represent the in-vivo clearance of the blood treatment machine in the first and second operating state, respectively, and evaluates (47) the efficiency values for detection of a connection error at the dialyzer and/or the access devices.

WO 2018/001994 A1

[Continued on next page]

(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).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *of inventorship (Rule 4.17(iv))*

Published:

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

CONNECTION TEST FOR BLOOD TREATMENT MACHINES I

Technical Field

The present invention relates to treatment of chronic renal failure, and in particular a technique of checking that a blood treatment machine is set up with correct flow directions before treatment.

Background Art

In treating chronic renal failure, various methods of purification and treatment of blood with machinery are used to replace the function of a healthy kidney. Such methods typically aim at withdrawing fluid and removing substances from the blood, and may also involve adding fluid and substances to the blood. Such purification and treatment may be performed by pumping a treatment fluid and blood through dedicated chambers of a blood filtration unit, commonly denoted a dialyzer. The treatment fluid chamber and the blood chamber of the dialyzer are separated by a semi-permeable membrane. While blood and treatment fluid flows on opposite sides of the membrane, fluid and substances are transported between the treatment fluid and the blood over the semi-permeable membrane. Diffusive mass transport through the membrane is predominant in hemodialysis (HD), whereas hemofiltration (HF) uses mainly convective mass transport through the membrane. Hemodiafiltration (HDF) is a combination of the two methods.

Machines for treatment of chronic renal failure, denoted "dialysis machines" in the following, comprise a first flow circuit which is connected to dedicated inlet and outlet connectors on the dialyzer and is configured to supply treatment fluid and pump the treatment fluid through the treatment fluid chamber, and a second flow circuit which is connected to the subject by an access device for blood withdrawal (e.g. an arterial needle or catheter adapter) and an access device for blood reintroduction (e.g. a venous needle or catheter adapter), which are connected to a dedicated blood vessel access (e.g. fistula, graft or catheter) on the subject. The second flow circuit is further connected to dedicated inlet and outlet connectors on the dialyzer and comprises a blood pump which is operable to draw blood from the subject via the access device for blood withdrawal, pump the blood through the blood chamber of the dialyzer and return the thus-treated blood to the subject via the access device for blood return. The second flow circuit is commonly referred to as an extracorporeal blood flow circuit.

Maximum efficiency of the exchange process over the semi-permeable membrane in the dialyzer is achieved by having the blood and the treatment fluid flow in opposite

directions along the membrane ("counter-current configuration"). If the blood and the treatment fluid flow in the same direction ("co-current configuration"), a lower dialysis efficiency is achieved. Thus, in practice, the dialyzer is connected to the first and second flow circuits in the counter-current configuration.

It should be understood that the dialyzer is a disposable, which is regularly replaced by the operator of the dialysis machine. Further, the second flow circuit is at least partly formed by a second disposable which also needs to be regularly replaced by the operator of the dialysis machine. Typically, the second disposable comprises a set of blood lines, or a dedicated cassette. The second disposable may, but typically does not, include the blood pump. Instead, in current dialysis machines, the blood pump (e.g. a peristaltic pump) is integrated in a machine chassis that also hosts the first flow circuit, and the second disposable is attached onto the machine chassis in operative engagement with the blood pump, such that the blood pump is operable to displace blood through the second disposable.

As understood from the foregoing, it may be important to ensure after each replacement of one or more of the above-mentioned disposables that the dialyzer has been correctly connected to the first and second flow circuits, and specifically to avoid a co-current configuration of the dialyzer.

This problem is addressed by WO2012/016671, which proposes a technique for detecting the flow directions through a dialyzer. The technique is based on the following sequence of steps: producing a first bolus change in temperature or concentration in the treatment fluid provided to the dialyzer, measuring a corresponding first change in temperature or concentration downstream of the dialyzer, switching the direction of fluid flow through the dialyzer, producing a second bolus change in temperature or concentration in the treatment fluid provided to the dialyzer, and measuring a corresponding second change in temperature or concentration downstream of the dialyzer. The actual detection of the flow directions through the dialyzer is executed by computing integrals of the first and second bolus changes and the corresponding first and second changes, computing dialysance values before and after the switching based on the integrals, and analyzing the ratio of the dialysance values after and before the switching. If the ratio is smaller than 1, it is concluded that the dialyzer was operated in a counter-current configuration before the switching. Otherwise, it is concluded that the dialyzer was operated in a co-current configuration before the switching. WO2012/016671 proposes to achieve the switching of flow direction by reversing the flow direction of the treatment fluid through the dialyzer, but also mentions that it is in principle possible to instead reverse the flow direction of the blood.

The technique of measuring dialysance or clearance by generating a short-term bolus in concentration or temperature, as used in WO2012/016671, is in fact an established technique, e.g. known from EP0658352 and US6702774. This "bolus technique" has its inherent drawbacks when implemented in a dialysis machine. During each bolus generation, the dialysis machine needs to have a preparation system for treatment fluid that is capable of producing an intermittent, short-term change of composition or temperature of the treatment fluid. Even if the dialysis machine has such a preparation system, the intermittent change may cause subsequent instabilities in the composition and/or temperature of the treatment fluid. Thus, the bolus technique may only be applicable to certain dialysis machines and may require advanced mechanisms for controlling its operation. Furthermore, the bolus technique is relatively time-consuming, since even a short-term bolus results in a relatively long pulse downstream of the dialyzer, due to the exchange process in the dialyzer. It is also necessary to ensure that the bolus change in concentration or temperature of the treatment fluid lies within physiologically acceptable limits.

Summary

It is an objective of the invention to at least partly overcome one or more of limitations of the prior art.

Another objective is to provide a technique for detecting connection errors of a blood treatment machine.

Yet another objective is to provide such a technique with reduced requirements on the preparation system for treatment fluid in the blood treatment machine.

A still further objective is to provide such a technique which is simple to implement.

One or more of these objectives, as well as further objectives that may appear from the description below, are at least partly achieved by a control device, a blood treatment machine, a method and a computer-readable medium, embodiments thereof being defined by the dependent claims.

A first aspect of the invention is a control device for a blood treatment machine. The blood treatment machine comprises an extracorporeal blood flow circuit with first and second access devices for connection to upstream and downstream portions, respectively, of a vascular access of a patient and having a blood pump operable to generate a flow of blood in the extracorporeal blood flow circuit from one of the first and second access devices through a blood compartment of a dialyzer and to another of the first and second access devices, and a treatment fluid flow circuit configured to generate a flow of treatment fluid through a treatment fluid compartment of the

dialyzer, the treatment fluid compartment being separated from the blood compartment by a semi-permeable membrane. The control device is configured to, during a connection test: cause the blood treatment machine to operate in a first operating state with fixed values of the flow rate of blood, the flow rate of treatment fluid and a fluid property of the treatment fluid; cause the blood treatment machine to operate in a second operating state with said fixed values, the second operating state differing from the first operating state by a change of flow direction in at least one of the dialyzer and the first and second access devices; acquire an output signal of at least one sensor which is arranged in the blood treatment machine to measure the fluid property of the treatment fluid; compute, based on the output signal, a first efficiency value that represents the in-vivo clearance of the blood treatment machine in the first operating state; compute, based on the output signal, a second efficiency value that represents the in-vivo clearance of the blood treatment machine in the second operating state; and evaluate the first and second efficiency values for detection of a connection error at the dialyzer and/or the access devices when the blood treatment machine is operated in the first operating state.

The first aspect goes against the common understanding in the field of blood treatment that the established bolus technique should be used in combination with flow reversal for detection of connection errors in blood treatment machines. The first aspect is based on the surprising and groundbreaking finding that, under certain conditions, it is possible to estimate and compare in-vivo clearance or dialysance based on a measured fluid property without generating bolus changes in the fluid property to be measured. Specifically, bolus changes are not necessary if the following operating parameters of the blood treatment machine remain the same during the measurements of the fluid property, i.e. before and after the flow reversal: the flow rate of blood in the extracorporeal blood flow circuit, the flow rate of treatment fluid in the treatment fluid flow circuit, and the measured fluid property of the treatment fluid that is supplied to the dialyzer.

Depending on the implementation of the flow reversal, the first aspect allows the control unit to detect connection errors either at the dialyzer or at the access devices in a blood treatment machine, or at both the dialyzer and the access devices in a blood treatment machine.

By operating, according to the first aspect, the blood treatment machine with fixed values of the flow rate of blood, the flow rate of treatment fluid and the measured fluid property, in both of the first and second operating states, connection errors can be detected significantly faster than by use of conventional techniques that require a bolus change of the fluid property to be generated in each of the first and second operating

states. Also, by the fixed values, the first aspect overcomes the difficulty of computing accurate clearance values based on measurements made during two individual and time-separated bolus changes. Further, it is realized that the requirements on the system for preparing the treatment fluid in the blood treatment machine are significantly reduced. For example, the above-mentioned risk of subsequent instabilities in the composition and/or temperature of the treatment fluid is completely eliminated.

Furthermore, the first aspect opens up a possibility to detect connection errors even if the blood treatment machine is unable by its design to generate bolus changes in any relevant fluid property of the treatment fluid.

Still further, the first aspect is simple to implement since the extracorporeal blood flow circuit and the treatment fluid flow circuit merely need to be operated to perform, during the connection test, the same tasks that they regularly perform during each blood treatment session, namely to provide consistent and well-controlled flow rates of blood and treatment fluid and to provide a treatment fluid with well-controlled and consistent properties such as composition and temperature.

It should be the noted that the control device may be configured to cause the blood treatment machine to operate in the first and second operating state by prompting an operator to manually set the machine in the respective state (if not already in this state), e.g. by manipulating a flow switching device in the treatment fluid flow circuit and/or the extracorporeal blood flow circuit. Alternatively, the control device may be configured to set the blood treatment machine in the respective operating state by generating a dedicated control signal for the blood treatment machine.

The first and second efficiency values are typically computed to be proportional to the in-vivo clearance. In one embodiment, the control unit is configured to compute each of the first and second efficiency values to represent a difference in the fluid property between an inlet and an outlet of the treatment fluid chamber.

In one embodiment, the connection error causes a detectable reduction in the in-vivo clearance compared to a correct operating state of the blood treatment machine, in which the blood pump is operated to generate the flow of blood from the upstream portion of the vascular access, via the first access device, through the blood compartment and via the second access device to the downstream portion of the vascular access, and in which the treatment fluid flow circuit is operated to generate the flow of treatment fluid through the treatment fluid compartment along the semipermeable membrane in opposite direction to the flow of blood through the blood compartment along the semipermeable membrane.

In one embodiment, the connection error results in at least one of a co-current dialyzer configuration, in which the flow of blood through the blood compartment and

the flow of treatment fluid through the treatment fluid compartment are in a common direction along the semi-permeable membrane, and a reversed access device configuration, in which the first and second access devices are connected to the downstream and upstream portions, respectively, of the vascular access.

In one implementation, the second operating state differs from the first operating state by the flow direction in the dialyzer, and the connection error results in the co-current dialyzer configuration. Alternatively or additionally, the second operating state differs from the first operating state by the flow direction in the first and second access devices, and the connection error results in the reversed access device configuration. In these implementations, the control unit may be configured to detect the connection error when the first efficiency value is smaller than the second efficiency value.

In one embodiment, the control unit is operatively associated with an interface device configured to output instructions for an operator of the blood treatment machine, and the control device is configured to, when detecting the connection error, operate the interface device to inform the operator that the connection test has failed, and optionally to instruct the operator on how to correct the connection error.

In one embodiment, the control device is further configured to obtain at least the fixed values of the flow rate of blood and the flow rate of treatment fluid from an electronic memory.

In one embodiment, the fixed values define the flow rate of blood to a value in the approximate range of 200-300 ml/min.

In one embodiment, the fixed values define the flow rate of treatment fluid to a value in the approximate range of 200-400 ml/min.

In one embodiment, the control device is further configured to, in advance of the connection test, compute at least one of the first and second efficiency values and, if said at least one of the first and second efficiency values is lower than a predefined minimum value, control a source of treatment fluid in the treatment fluid flow circuit to adjust the fluid property of the treatment fluid so that said at least one of the first and second efficiency values exceeds the predefined minimum value.

In one embodiment, the control unit is configured to cause the blood treatment machine to be switched between the first and second operating states by causing at least one flow switching device in the blood treatment machine to change the flow direction in at least one of the dialyzer and the first and second access devices. In one example, the control unit is configured to generate a control signal for the at least one flow switching device to switch the blood treatment machine between the first and second operating states.

In one embodiment, the at least one flow switching device comprises the blood pump, wherein the blood pump is set to operate in a forward pumping direction in the first operating state of the blood treatment machine and in a reverse pumping direction in the second operating state of the blood treatment machine.

In one embodiment, the control unit is further configured to correct the connection error by selectively operating the at least one flow switching device to change the flow direction in at least one of the dialyzer and the first and second access devices in the first operating state.

In one embodiment, the fluid property is a physical and/or chemical property of the treatment fluid.

In one embodiment, the fluid property is one of a temperature and a concentration of a substance that is present in the blood and is capable of exchanging across the semi-permeable membrane.

In one embodiment, said at least one sensor is one of a concentration sensor, a temperature sensor, a conductivity sensor, an optical absorbance sensor, a polarimetry sensor and a density sensor.

A second aspect of the invention is a blood treatment machine, comprising an extracorporeal blood flow circuit with first and second access devices for connection to upstream and downstream portions, respectively, of a vascular access of a patient and having a blood pump operable to generate a flow of blood from one of the first and second access devices through a blood compartment of a dialyzer and to another of the first and second access devices, a treatment fluid flow circuit configured to generate a flow of treatment fluid through a treatment fluid compartment of the dialyzer, the treatment fluid compartment being separated from the blood compartment by a semi-permeable membrane, and the control device of the first aspect.

A third aspect of the invention is a method of performing a connection test of a blood treatment machine comprising an extracorporeal blood flow circuit with first and second access devices for connection to upstream and downstream portions, respectively, of a vascular access of a patient and having a blood pump operable to generate a flow of blood in the extracorporeal blood flow circuit from one of the first and second access devices through a blood compartment of a dialyzer and to another of the first and second access devices, and a treatment fluid flow circuit configured to generate a flow of treatment fluid through a treatment fluid compartment of the dialyzer, said treatment fluid compartment being separated from the blood compartment by a semi-permeable membrane. The method comprises the steps of: causing the blood treatment machine to operate in a first operating state with fixed values of the flow rate of blood, the flow rate of treatment fluid and a fluid property of the treatment fluid;

causing the blood treatment machine to operate in a second operating state with said fixed values, the second operating state differing from the first operating state by a change of flow direction in at least one of the dialyzer and the first and second access devices; acquiring an output signal of at least one sensor which is arranged in the blood treatment machine to measure the fluid property of the treatment fluid; computing, based on the output signal, a first efficiency value that represents the in-vivo clearance of the blood treatment machine in the first operating state; computing, based on the output signal, a second efficiency value that represents the in-vivo clearance of the blood treatment machine in the second operating state; and evaluating the first and second efficiency values for detection of a connection error at the dialyzer and/or the access devices when the blood treatment machine is operated in the first operating state.

In one embodiment, each of the first and second efficiency values are computed to represent a difference in the fluid property between an inlet and an outlet of the treatment fluid chamber.

In one embodiment, the connection error causes a detectable reduction in the in-vivo clearance compared to a correct operating state of the blood treatment machine, in which the blood pump is operated to generate the flow of blood from the upstream portion of the vascular access, via the first access device, through the blood compartment and via the second access device to the downstream portion of the vascular access, and in which the treatment fluid flow circuit is operated to generate the flow of treatment fluid through the treatment fluid compartment along the semipermeable membrane in opposite direction to the flow of blood through the blood compartment along the semipermeable membrane.

In one embodiment, the connection error results in at least one of a co-current dialyzer configuration, in which the flow of blood through the blood compartment and the flow of treatment fluid through the treatment fluid compartment are in a common direction along the semi-permeable membrane, and a reversed access device configuration, in which the first and second access devices are connected to the downstream and upstream portions, respectively, of the vascular access.

In one implementation, the second operating state differs from the first operating state by the flow direction in the dialyzer, and wherein the connection error results in the co-current dialyzer configuration. Alternatively or additionally, the second operating state differs from the first operating state by the flow direction in the first and second access devices, and the connection error results in the reversed access device configuration. In these implementations, the connection error is detected when the first efficiency value is smaller than the second efficiency value.

In one embodiment, the method further comprises: detecting the connection error, and subsequently operating an interface device to inform an operator of the blood treatment machine that the connection test has failed, and optionally to instruct the operator on how to correct the connection error.

In one embodiment, the method further comprises: obtaining at least the fixed values of the flow rate of blood and the flow rate of treatment fluid from an electronic memory.

In one embodiment, the fixed values define the flow rate of blood to a value in the approximate range of 200-300 ml/min.

In one embodiment, the fixed values define the flow rate of treatment fluid to a value in the approximate range of 200-400 ml/min.

In one embodiment, the method further comprises a preparatory adjustment procedure, said preparatory adjustment procedure comprising: computing at least one of the first and second efficiency values and, if said at least one of the first and second efficiency values is lower than a predefined minimum value, adjusting the fluid property of the treatment fluid so that said at least one of the first and second efficiency values exceeds the predefined minimum value.

In one embodiment, the method further comprises: causing at least one flow switching device in the blood treatment machine to change the flow direction in at least one of the dialyzer and the first and second access devices so as to switch the blood treatment machine between the first and second operating states. In one example, the method further comprises: generating a control signal for the at least one flow switching device to switch the blood treatment machine between the first and second operating states.

In one embodiment, the at least one flow switching device comprises the blood pump, wherein the blood pump is set to operate in a forward pumping direction in the first operating state of the blood treatment machine and in a reverse pumping direction in the second operating state of the blood treatment machine.

In one embodiment, the method further comprises: correcting the connection error by selectively operating the at least one flow switching device to change the flow direction in at least one of the dialyzer and the first and second access devices in the first operating state.

In one embodiment, the fluid property is a physical and/or chemical property of the treatment fluid.

In one embodiment, the fluid property is one of a temperature and a concentration of a substance that is present in the blood and is capable of exchanging across the semi-permeable membrane.

In one embodiment, said at least one sensor is one of a concentration sensor, a temperature sensor, a conductivity sensor, an optical absorbance sensor, a polarimetry sensor and a density sensor.

A fourth aspect of the invention is a computer-readable medium comprising computer instructions which, when executed by a processor, cause the processor to perform the method of the third aspect.

Any one of the above-identified embodiments of the first aspect may be adapted and implemented as an embodiment of the second to fourth aspects.

Still other objectives, features, aspects and advantages of the present invention will appear from the following detailed description, from the attached claims as well as from the drawings.

Brief Description of the Drawings

Embodiments of the invention will now be described in more detail with reference to the accompanying schematic drawings.

FIG. 1 is a schematic overview of a dialysis system connected to a patient.

FIGS 2A-2B are schematic side views of withdrawal and return devices in a normal and reversed configuration, respectively, at a vascular access.

FIG. 3A is a block diagram of a dialysis system enabling flow direction switching in the dialyzer, and FIG. 3B is a block diagram of a variant.

FIG. 4 is a flow chart of a method implemented by the control unit in FIG. 3A.

FIG. 5 is plot of calculated conductivity differences obtained over the dialyzer for counter-current and co-current flows in the dialyzer in FIG. 3A, as function of blood flow rate in the EC circuit.

FIG. 6A is a hydraulic model of a patient connected to a dialysis system by access devices in a normal configuration, with counter-current flow in the dialyzer and without recirculation in the vascular access, FIG. 6B corresponds to FIG. 6A for a situation with recirculation in the vascular access, and FIG. 6C corresponds to FIG. 6A for a situation with the access devices in a reversed configuration.

FIGS 7A-7B are plots of calculated conductivity differences obtained over the dialyzer for different flow direction statuses attainable in dialysis systems, as function of blood flow rate in the EC circuit.

FIGS 8A-8D are block diagrams dialysis systems enabling flow direction switching in the access devices and/or in the dialyzer.

FIGS 9A-9C show examples of ranges that may be applied by the method in FIG. 4 for determining a fluid direction status of the dialysis system of FIG. 8D.

Detailed Description of Example Embodiments

Embodiments of the present invention will now be described more fully hereinafter with reference to the accompanying drawings, in which some, but not all, embodiments of the invention are shown. Indeed, the invention may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure may satisfy applicable legal requirements. Like numbers refer to like elements throughout.

Also, it will be understood that, where possible, any of the advantages, features, functions, devices, and/or operational aspects of any of the embodiments of the present invention described and/or contemplated herein may be included in any of the other embodiments of the present invention described and/or contemplated herein, and/or vice versa. In addition, where possible, any terms expressed in the singular form herein are meant to also include the plural form and/or vice versa, unless explicitly stated otherwise. As used herein, "at least one" shall mean "one or more" and these phrases are intended to be interchangeable. Accordingly, the terms "a" and/or "an" shall mean "at least one" or "one or more," even though the phrase "one or more" or "at least one" is also used herein. As used herein, except where the context requires otherwise owing to express language or necessary implication, the word “comprise” or variations such as “comprises” or “comprising” is used in an inclusive sense, that is, to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

Before describing embodiments of the invention detail, a few further definitions will be given.

As used herein, "clearance" is given its ordinary meaning and is a measure of the purification efficiency of a dialyzer, typically given as ml/min. Clearance may sometimes be defined to exclusively refer to removal, from the blood, of one or more substances that are absent in the fresh treatment fluid fed to the dialyzer, such as urea. The term "dialysance" may sometimes be used to designate an approximation of clearance so as to represent removal, from the blood, of one or more substances that are present also in the fresh treatment fluid, such as sodium or another electrolyte that passes the semi-permeable membrane of the dialyzer. With these definitions, the clearance and the dialysance will be equal for a given dialyzer in the absence of ultrafiltration. Within the present disclosure, no distinction is made between clearance and dialysance, and these terms are thus considered to be synonymous. Clearance may be measured directly on the dialyzer under well-controlled, non-patient specific, laboratory conditions. This type of clearance is commonly known as "*in-vitro* clearance" or "dialyzer clearance" and makes it possible to assess the relative efficacy of

different dialyzers. Clearance may also be measured for a dialyzer under actual dialysis treatment conditions involving a patient. This type of clearance is commonly known as "*in-vivo* clearance" or "effective clearance" and is influenced by, e.g., the dialyzer, the effective blood flow rate, ultrafiltration, recirculation, and the flow rate of treatment fluid. Unless explicitly stated otherwise, the term clearance refers to the in-vivo clearance in the following description.

FIG. 1 illustrates a human subject or patient which is connected to an extracorporeal blood flow circuit 1a by way of access devices 2', 2" inserted into a dedicated vascular access 3 (also known as "blood vessel access") on the subject. The extracorporeal blood flow circuit 1a (denoted "EC circuit" in the following) is configured to draw blood from the vascular access 3 via access device 2' and pump the blood through a blood filter unit 4 and back to the vascular access 3 via access device 2". Thus, access device 2' is designated for blood withdrawal and access device 2" is designated for blood return. The vascular access 3 may be a fistula or a graft provided in the forearm of the patient, and the access devices 2', 2" may be needles or catheters, as is well-known in the art. The blood filter unit 4 may be any type of filtering device, such as a coil dialyzer, a parallel plate dialyzer, a hollow fiber dialyzer, etc. For simplicity, the blood filter unit 4 is denoted "dialyzer" in the following. The dialyzer 4 defines a blood chamber 4A and a treatment fluid chamber 4B separated by a semipermeable membrane 4'.

The EC circuit 1a is part of an apparatus or machine 1 for blood treatment, such as a dialysis machine, at least when the machine 1 has been prepared for a treatment session. In the illustrated example, the EC circuit 1a comprises bloodlines connected to the access device 2´, 2", a blood pump 5 and the blood chamber 4A of the dialyzer 4. The skilled person realizes that FIG. 1 is a simplified illustration and that the EC circuit 1a may comprise further components, such as a venous drip chamber, one or more pressure sensor, clamps, valves, etc.

The machine 1 further comprises a supply system 1b for treatment fluid (denoted "TF circuit" in the following). The TF circuit 1b is arranged to pump a treatment fluid through the treatment fluid side 4B of the dialyzer 4, while the blood pump 5 is operated to pump blood through the blood side 4A of the dialyzer 4, whereby solutes are transported over the membrane 4' due to a concentration gradient and/or ultrafiltrate is transported over the membrane 4' due to a pressure gradient. In the illustrated example, the TF circuit 1b comprises a source 6 of fresh treatment fluid (e.g. dialysis fluid), various fluid lines, the treatment fluid chamber 4B of the dialyzer 4, a treatment fluid pump 7, and is connected to a receptacle/drain 8 for receiving spent treatment fluid. The skilled person understands that the TF circuit 1b may include a plurality of other

functional components such as further pumps, balancing chambers, valves, mixing chambers, heaters, etc. In the particular example of FIG. 1, the TF circuit also includes sensors 10A, 10B, which are configured to generate measurement signals that allow a control unit (not shown) to assess the dialysis efficiency, represented by the above-mentioned in-vivo clearance.

In practice, the machine 1 is typically formed as a combination of a permanent machine part and one or more disposables attached to the permanent machine part. The permanent machine part is enclosed in a machine chassis, often denoted "monitor", which exposes holders for mounting the disposable(s) in operative engagement with components such as connectors, pumps, sensors, clamps, etc. The disposables are exposed to the circulating blood in the EC circuit 1a and are typically discarded after each treatment session.

One such disposable is a bloodline set which includes the bloodlines of the EC circuit 1a, and connectors 11A, 11B on the bloodlines for coupling to dedicated inlet and outlet ports on the dialyzer 4, as indicated in FIG. 1. The access devices 2', 2" may also be integrated with the bloodlines in the bloodline set. Alternatively, the access devices 2', 2" may be provided as a separate disposable for connection to dedicated connectors 12A, 12B on the bloodlines, as indicated in the FIG. 1. The bloodline set may include further components, such as a venous drip chamber, valves, clamps, etc. For reasons of economy, components of the EC circuit 1a that are not exposed to the circulating blood are normally integrated in the machine chassis. For example, the blood pump 5 may be implemented as a peristaltic pump that engages with the exterior of a bloodline to push the blood though the bloodline, as is well known in the art. However, it is conceivable that the blood pump 5, if exposed to blood, is included in the disposable.

The dialyzer 4 may be provided as a separate disposable for installation on the machine chassis. When mounted on the machine chassis, the connectors 11A, 11B of the bloodline set are coupled to the dedicated inlet and outlet ports of the blood chamber 4A, and dedicated connectors 13A, 13B on the fluid lines of the TF circuit 1b are connected to dedicated inlet and outlet ports of the treatment fluid chamber 4B.

In an alternative, the dialyzer 4 is included in the bloodline set. In a further alternative, the bloodline set is replaced or supplemented by a cassette that defines internal fluid paths for blood. Such as cassette may also be integrated with the dialyzer 4.

Embodiments of the present invention addresses the risk that the operator of the machine 1 inadvertently makes an error when installing the dialyzer 4 in the machine 1, e.g. by confusing the connectors 11A, 11B or the connectors 13A, 13B. It is to be

understood that the EC circuit 1a and the TF circuit 1b have a respective default pumping direction for blood and treatment fluid, respectively, so as to achieve a counter-current flow of blood and treatment fluid in the dialyzer 4. Thus, if the connectors 11A, 11B or 13A, 13B are confused, the machine 1 will inadvertently be operated in a co-current configuration. As explained in the Background section, this is undesirable since the co-current configuration results in lower dialysis efficiency than the counter-current configuration.

Embodiments of the present invention also address the risk that the operator of the machine 1 inadvertently confuses the access devices 2', 2" when connecting them to the vascular access 3 or when connecting them to the connectors 12A, 12B (if present). FIGS 2A-2B schematically illustrate a vascular access 3 and access devices 2', 2" in a normal configuration and a reversed configuration, respectively. The blood flow in the vascular access 3 and access devices 2', 2" are indicated by arrows. As seen, blood flows in a given direction through the vascular access 3. In the normal configuration of FIG. 2A, the access device 2' for blood withdrawal is positioned at an upstream portion for extracting blood and the access device 2" for blood return is positioned at a downstream portion for returning blood to the vascular access 3. In the reversed configuration of FIG. 2B, the access device 2' is positioned at the downstream position and the access device 2" is positioned at the upstream position, with the consequence of treated blood being returned upstream and being extracted downstream. In the reversed configuration, some of the already treated blood is again withdrawn into the EC circuit 1a, as phenomenon commonly known as recirculation and indicated by a dashed arrow in FIG. 2B. By the recirculation, less blood flowing from the body into the vascular access 3 will be treated, leading to reduced treatment efficiency. It is realized that the reversed configuration in FIG. 2B may also arise if the connectors 12A, 12B are confused, leading to a situation in which the access device 2' for blood withdrawal effectively is converted into an access device 2" for blood return, and vice versa. As is well-known to the skilled person, recirculation may occur even with access devices 2', 2" in the normal configuration, if the blood flow rate in the EC circuit 1a exceeds the incoming blood flow rate to the vascular access 3 (denoted "access flow rate" in the following).

Although the access device 2', 2" are illustrated in FIGS 2A-2B as needles that puncture the skin to gain access to the patient's blood supply, a reversed placement may occur with other types of access devices as well. For example, the access devices 2', 2" may be implemented as a double lumen catheter (not shown) which comprises two parallel channels which terminate at a distance from each other. One lumen is configured to remove blood for treatment, and the other lumen to return the treated

blood. Like in FIG. 2B, a reversed configuration occurs if the double lumen catheter is inserted in a reversed direction into the vascular access or if the double lumen is incorrectly connected to the bloodlines.

Embodiments of the invention enable automatic verification before a treatment session that the dialyzer 4 is properly installed in the machine 1 and/or that the access devices 2', 2" are properly connected to the patient. Embodiments of the invention also enable signaling of connection errors resulting in a co-current configuration of the dialyzer 4 and/or a reversed configuration of the access devices 2', 2".

FIG. 3A illustrates an embodiment of the invention that comprises a control unit 15 (also denoted control device or controller) which is configured to control the operation of the machine 1 in FIG. 1, at least during a test phase aiming to detect connection errors and, if needed, take corrective action. A further difference compared to the machine 1 in FIG. 1 is that a flow switching device (FSD) 9 is installed in the TF circuit 1b, intermediate the sensors 10A, 10B and the inlet and outlet ports of the treatment fluid chamber 4B. The FSD 9 is operable in two configurations with different flow paths of treatment fluid to and from the dialyzer 4: a first configuration with straight paths through the FSD 9 so as to provide a flow of treatment fluid from bottom to top in the chamber 4B in FIG. 3A, and a second configuration with crossed paths so as to provide a flow of treatment fluid from top to bottom in the chamber 4B in FIG. 3A. This type of FSD 9 is well-known in the art. For example, the FSD 9 may be implemented as a combination of fluid lines and one or more valves, e.g. four on/off valves as shown in above-mentioned WO2012/016671, or a dedicated valve as shown in US7896831.

The control unit 15 comprises a signal interface for input and output of signals. Specifically, in the example of FIG. 3A, the control unit 15 is configured to generate and output control signals C1, C2, C3, C4 for the treatment fluid pump 7, the blood pump 5, the FSD 9 and the source 6 of treatment fluid, and to receive and process measurement signals S1, S2 from sensors 10A, 10B arranged in the TF circuit 1b, on both sides of the treatment fluid chamber 4B. The control unit 15 is also connected, by wire or wirelessly, to a user interface (UI) device 16 for interacting with the operator of the machine 1. The control unit 15 is configured to generate and output a control signal C5 for operating the UI device 16, e.g. to generate warning or alarm signals (audible and/or visible), display messages with information or instructions for the operator, graphically indicate the location of connection errors, etc. The UI device 16 may also be operable by the control unit 15 to receive input from the operator. The UI device 16 may thus comprise one or more of a display, a touch panel, a loudspeaker, a

microphone, a keyboard, a mouse, an indicator lamp, etc. It is understood that the UI device 16 may be (part of) a conventional user interface on the machine 1.

The operation of the control unit 15 may be at least partly controlled by software instructions that are supplied on a computer-readable medium for execution by a processor 17 in conjunction with an electronic memory 18 in the control unit 15. In particular, the control unit 15 is configured to, by control signal C1, set the speed of the treatment fluid pump 7 and thus the flow rate of treatment fluid through the dialyzer 4. By control signal C2, the control unit 15 sets the speed of the blood pump 5 and thus the flow rate of blood in the EC circuit 1a. By control signal C4, the control unit 15 may set the temperature and/or composition of the treatment fluid provided by the source 6. By control signal C3, the control unit 15 sets the FSD 9 in either the first configuration (straight paths) or the second configuration (crossed paths). As indicated by a double-ended arrow, a switch of the FSD 9 between its first and second configurations causes a change of the flow direction in the treatment fluid compartment 4B. Thus, by switching the FSD 9, the machine 1 is switched between first and second operating states, which involve either co-current flow or counter-current flow in the dialyzer 4.

As noted above, the control unit 15 is configured to control the machine 1 to perform a test phase ("connection test") for the purpose of detecting connection errors. The connection test may be performed at startup of the machine, in advance of a treatment session. During the connection test, the treatment efficiency of the machine 1 is monitored while the machine 1 is switched between the first and second operating states. The treatment efficiency represents the in-vivo clearance and is computed based on the signals S1, S2 from the sensors 10A, 10B. The control unit 15 analyzes the resulting change in treatment efficiency to determine if the first operating state involves a counter-current flow in the dialyzer 4 or not.

As explained in the Background section, the current belief among persons skilled in the art is that the in-vivo clearance can only be monitored by generating a bolus change in a property of the treatment fluid that is supplied to the dialyzer and measuring the resulting change in the property upstream and downstream of the dialyzer. However, the present Applicant has found a clever way to compute an efficiency value, which is proportional to the in-vivo clearance, during each of the first and second operating states without generating such a bolus change. In embodiments of the invention, the efficiency value is computed as the difference between the property as measured by the sensors 10A, 10B, i.e. the difference between the measurement signals S1, S2. This difference is designated by ΔC in the following.

This "non-bolus technique" is only applicable if certain operating conditions of the machine 1 are fulfilled during the connection test, namely that the following

operating parameters are set to fixed values: the blood flow rate in the EC circuit 1a (i.e. through the dialyzer 4), the treatment fluid flow rate in the TF circuit 1b (i.e. through the dialyzer 4) and the measured property of the treatment fluid supplied to the dialyzer 4. In other words, these operating parameters should be the same before and after the switch between the first and second operating states. The non-bolus technique offers significant advantages over the conventional bolus technique, e.g. that disturbances of the source 6 are minimized and the detection time is shortened.

The non-bolus technique may operate on the same property as the conventional bolus technique. Thus, the sensors 10A, 10B may be dedicated concentration sensors that are configured to measure the concentration of a specific marker substance in the treatment fluid. The marker substance may be any substance that is present in the blood and is capable of exchanging across the semi-permeable membrane 4', such as urea, creatinine, vitamin B12, beta-two-microglobuline, NaCl, or any ion or combination of ions. Alternatively, the sensors 10A, 10B may be conductivity sensors, which are responsive to ions in the treatment fluid. In practice, conductivity sensors will effectively indicate the concentration of ionized sodium in the treatment fluid. In another alternative, the sensors 10A, 10B may be absorbance sensors configured to determine optical absorbance as a measure of concentration. In still another alternative, the sensors 10A, 10B may be polarimetry sensors configured to determine polarization as a measure of concentration of an optically active substance, such as glucose, that rotates the plane of linearly polarized light. In still another alternative, the sensors 10A, 10B may be density sensors configured to measure the density (mass per unit volume) of the treatment fluid. According to yet another alternative, the sensors 10A, 10B may be temperature sensors configured to measure the temperature of the treatment fluid.

The non-bolus technique will now be exemplified with reference to FIG. 4, which is a flow chart of a method executed by the control unit 15 (FIG. 3A) during the connection test 40 according to one embodiment. In step 41, the control unit 15 generates the control signals C1, C2 and C4 to set predefined values of the blood flow rate generated by the blood pump 5, the treatment fluid flow rate generated by the TF pump 7, and the property of the treatment fluid supplied by the source 6. These predefined values are then maintained (fixed) throughout subsequent steps 42-45. In step 42, the control unit 15 generates the control signal C3 to set the machine 1 in the first operating state (if not already in this state), by setting the FSD 9 in the first configuration (straight paths). While the machine 1 is in the first operating state, the control unit 15 acquires first sensor values from the sensors 10A, 10B (step 43). In step 44, the control unit 15 generates control signal C3 to set the machine 1 in a second operating state, by setting the FSD 9 in the second configuration (crossed paths). While

the machine 1 is in the second operating state, the control unit 15 acquires second sensor values from the sensors 10A, 10B (step 45). In step 46, first and second efficiency values are calculated as a function of the first and second sensor values to represent the in-vivo clearance in the first operating state and the second operating state, respectively. In step 47, first and second efficiency values are evaluated for detection of a connection error in the first operating state. In the example of FIG. 3A, the connection error corresponds a co-current configuration of the dialyzer 4.

To further explain step 47, reference will be given to FIG. 5 which is a plot of theoretically calculated efficiency values, given as a difference of conductivity measured by the sensors 10A, 10B, as a function of blood flow rate B for the different flow direction statuses of the machine 1 in FIG. 3A. The curves 50-53 in FIG. 5 have been calculated by use of equations that will be derived below with reference to FIGS 6A-6C, and by assuming a conductivity gradient between blood and treatment fluid of 1 mS/cm, a cardiac output of 5 l/min, a treatment fluid flow rate of 500 ml/min, a dialyzer permeability (k_0A) of 1500 ml/min, and no ultrafiltration. The calculations further presume that the access devices 2', 2" are correctly connected in a normal configuration (cf. FIG. 2A). Curves 50 and 51 are calculated for a counter-current configuration and an access flow rate of 1000 ml/min and 300 ml/min, respectively. Curves 52 and 53 are calculated for a co-current configuration, and an access flow rate of 1000 ml/min and 300 ml/min, respectively. The fall-off in curves 51 and 53 at $B \geq 300$ ml/min is caused, as noted above, by recirculation that occurs when the blood flow rate in the EC circuit 1a exceeds the access flow rate.

FIG. 5 indicates that there is a considerable difference in ΔC values between the counter-current and co-current configurations. This means that it is possible to allocate a respective flow direction status to the first and second operating conditions by computing a ΔC value for each of the first and second operating conditions, and comparing the ΔC values. The larger ΔC value is obtained for the counter-current configuration and the smaller ΔC value is obtained for the co-current configuration. The skilled person readily realizes that there are numerous ways of formalizing the foregoing analysis into an evaluation of the ΔC values in step 47. In one implementation, the ΔC values are simply compared to each other. In another implementation, an efficiency change parameter is computed as a (weighted) difference of the ΔC values, which may be analyzed with respect to sign. For example, if the sign is positive, the first operating state involves a counter-current configuration, otherwise a co-current configuration. In another implementation, the efficiency change parameter is computed as a ratio of the ΔC values, which may be analyzed with respect to magnitude

(irrespective of sign). For example if the ratio is larger than 1, the first operating state involves a counter-current configuration, otherwise a co-current configuration.

As indicated by step 48 in FIG. 4, the control unit 15 may generate feedback to the operator of the machine 1 based on the outcome of step 47, by controlling the UI device 16 via the control signal C5. In one example, if the first operating state is found to involve a counter-current configuration, the feedback may confirm to the operator that the machine 1 is correctly connected. Alternatively or additionally, the control unit 15 may be configured to selectively enable the machine 1 to start a blood treatment session if the machine 1 passes the connection test 40. In another example, if the first operating state is found to involve a co-current configuration, the feedback may explicitly or implicitly instruct the operator to check or change the connection of the dialyzer 4. Alternatively, the control unit 15 may, by the control signal C3, set the FSD 9 in its second configuration (crossed paths) so as to automatically achieve a counter-current configuration of the dialyzer 4. Furthermore, whenever the connection test 40 fails, the control unit 15 may be configured to block the machine 1 from initiating a blood treatment session until the connection error has been resolved, e.g. as verified by a further, subsequent connection test, or by the operator affirming via the UI device 16 that the connections have been checked and are correct.

The skilled person realizes that the connection test 40 in FIG. 4 may be modified so that the machine 1 is instead switched from the second operating state to the first operating state, by switching the FSD 9 from its second configuration to its first configuration.

FIG. 3B illustrates a variant of the machine 1. Compared to the machine 1 in FIG. 3A, the FSD 9 is instead placed in the EC circuit 1a, downstream of the blood pump 5. As indicated by a double-ended arrow, a switch of the FSD 9 between its first and second configurations causes a change of flow direction in the blood compartment 4A. Thus, like in Fig. 3A, the control unit 15 is operable, by the control signal C3, to switch the machine 1 between first and second operating states which involve either co-current flow or counter-current flow in the dialyzer 4. Clearly, the connection test 40 in FIG. 4 is equally applicable to the machine 1 in FIG. 3B. It should be noted that the FSD 9 in FIG. 3B is in contact with blood, which means that the FSD 9 may need to be discarded after each treatment session. The FSD 9 may e.g. be part of the above-mentioned disposable. In contrast, in FIG. 3A, the FSD 9 is only in contact with the treatment fluid and may be installed as a permanent component within the chassis of the machine 1.

As will be described below with reference to FIGS 8A-8D, the connection test 40 in FIG. 4 is also applicable to embodiments in which the machine 1 is controllable to switch flow direction through the access devices 2', 2" instead of the dialyzer 4, or

through both the dialyzer 4 and the access devices 2', 2". To generally explain and motivate the non-bolus technique for all connection tests 40, reference is made to FIGS 6A-6C, which illustrate a hydraulic model of a patient connected to a dialysis system for three different flow conditions in the vascular access. The aim of the following formal analysis of the hydraulic model is to derive expressions that represent the in-vivo clearance when the machine 1 in FIG. 1 is in each of four different flow direction statuses: "correct condition" (counter-current configuration of the dialyzer 4 and normal configuration of the access devices 2', 2"), "dialyzer fault condition" (co-current configuration of the dialyzer 4 and normal configuration of the access devices 2', 2"), "access fault condition" (counter-current configuration of the dialyzer 4 and reversed configuration of the access devices 2', 2") and "dual fault condition" (co-current configuration of the dialyzer 4 and reversed configuration of the access devices 2', 2"). The formal analysis considers both large and small access flow rates, to account for recirculation within the vascular access 3 also when the access devices 2', 2" are in the normal (correct) position. Although the following description refers to conductivity and conductivity sensors, it is equally applicable to other sensors, as explained above. Further, while the analysis assumes that the ultrafiltration rate is zero, the conclusions are sufficiently correct also in the presence of ultrafiltration. All flow rates below refer to blood water, which typically represents 85-90% of the total blood volume.

The following notation is used:

CO	Cardiac Output (water flow rate)
A	Access blood water flow rate
B	Blood water flow rate to dialyzer
D	Treatment fluid flow rate to dialyzer
k_0A	Mass transfer area coefficient of dialyzer (water value)
K	Dialyzer clearance
C_{bi}	Blood water conductivity at dialyzer inlet
C_{bo}	Blood water conductivity at dialyzer outlet
α	Donnan factor
C_A	Blood water conductivity in blood access
C_v	Blood water conductivity in venous blood from body
C_{di}	Treatment fluid conductivity at dialyzer inlet
C_{do}	Treatment fluid conductivity at dialyzer outlet

For simplicity, the ultrafiltration rate is assumed to be zero. In this case, the dialyzer clearance K in the counter-current configuration is:

$$K = \frac{B \cdot D \cdot (1 - f)}{D - f \cdot B} \quad (1)$$

with

$$f = \exp(k_0 A \cdot (1/D - 1/B)) \quad (2)$$

In the co-current configuration, the dialyzer clearance K is

$$K = \frac{B \cdot D \cdot (1 - f)}{B + D} \quad (3)$$

with

$$f = \exp(-k_0 A \cdot (1/D + 1/B)) \quad (4)$$

The transport from blood to treatment fluid can be expressed in three ways, looking at what leaves the blood side, enters the dialysis fluid side or crosses the membrane, respectively:

$$B \cdot (C_{bi} - C_{bo}) = D \cdot (C_{do} - C_{di}) = K \cdot (\alpha \cdot C_{bi} - C_{di}) \quad (5)$$

These expressions are independent of the flow direction status of the dialyzer as long as the correct value for clearance is used (counter-current or co-current). Eq. (5) provides an expression for the conductivity difference ΔC in the treatment fluid:

$$\Delta C = C_{do} - C_{di} = \frac{K}{D} \cdot (\alpha \cdot C_{bi} - C_{di}) \quad (6)$$

It is important to note that K designates the dialyzer clearance, not the in-vivo clearance. The following formal analysis will show that the conductivity difference ΔC is not only directly proportional to the dialyzer clearance K, as indicated by Eq. (6), but also to the in-vivo clearance. The formal analysis aims at expressing Eq. (6) as a function of C_v, which may be considered invariant during the switch of pumping direction, instead of C_{bi}, which is affected by recirculation in the blood vessel access.

A first part of the formal analysis is based on FIG. 6A, which illustrates fluid flows in the hydraulic model with the access devices in the normal position and with an access flow rate that exceeds the blood water flow rate in the EC circuit (i.e. $A > B$). In this case, C_{bi} is equal to C_A. A relation between C_A and C_v is given by a mass balance analysis at the joint before the heart-lung system, where the blood from the body with concentration C_v is mixed with cleaned blood returning from the vascular access:

$$CO \cdot C_A = (CO - A) \cdot C_v + A \cdot C_A - D \cdot \Delta C \quad (7)$$

where the mass in the cleaned blood from the vascular access is calculated by subtracting the mass removed in the dialyzer (expressed as $D \cdot \Delta C$) from the mass going to the access from the heart. Eq. (7) is valid for all configurations and yields:

$$C_A = C_v - \frac{D}{CO - A} \cdot \Delta C \quad (8)$$

Inserting Eq. (8) into Eq. (6), with $C_A = C_{bi}$, and solving for ΔC yields:

$$\Delta C = \frac{1}{1 + \frac{\alpha \cdot K}{CO - A}} \cdot \frac{K}{D} \cdot (\alpha \cdot C_v - C_{di}) \quad (9)$$

with K being given by Eq. (1) or Eq. (3) above, depending on configuration (counter-current or co-current).

A second part of the formal analysis is based on FIG. 6B, which illustrates fluid flows in the hydraulic model with the access devices in the normal position but with an access flow rate that is lower than the blood water flow rate in the EC circuit (i.e. $A < B$). This means that part of the treated blood that is returned to the vascular access will be recirculated back into EC circuit. In this case, a mass balance analysis yields:

$$B \cdot C_{bi} = A \cdot C_A + (B - A) \cdot C_{bo} \quad (10)$$

$$B \cdot C_{bo} = B \cdot C_{bi} - D \cdot \Delta C \quad (11)$$

Combining Eq. (10), Eq. (11), Eq. (6) and Eq. (8) yields:

$$\Delta C = \frac{\beta}{1 + \beta \cdot \frac{\alpha \cdot K}{CO - A}} \cdot \frac{K}{D} \cdot (\alpha \cdot C_v - C_{di}) \quad (12)$$

with

$$\beta = \frac{A \cdot B}{A \cdot B + \alpha \cdot K \cdot (B - A)} \quad (13)$$

Eq. (9) and Eq. (12) may be summarized in one equation covering all values of A:

$$\Delta C = min\left(\frac{1}{1 + 1 \cdot \frac{\alpha \cdot K}{CO - A}}, \frac{\beta}{1 + \beta \cdot \frac{\alpha \cdot K}{CO - A}}\right) \cdot \frac{K}{D} \cdot (\alpha \cdot C_v - C_{di}) \quad (14)$$

A third part of the formal analysis is based on FIG. 6C, which illustrates fluid flows in the hydraulic model with the access devices in reversed position. In this case, a mass balance analysis yields:

$$A \cdot C_{bi} = A \cdot C_A - D \cdot \Delta C \tag{15}$$

Combining Eq. (15), Eq. (6) and Eq. (8) yields:

$$\Delta C = \frac{A \cdot (CO - A)}{A \cdot (CO - A) + \alpha \cdot K \cdot CO} \cdot \frac{K}{D} \cdot (\alpha \cdot C_v - C_{di}) \tag{16}$$

Both Eq. (14) and Eq. (16) may be rewritten as:

$$\Delta C = \frac{K_{\text{eff}}}{D} \cdot (\alpha \cdot C_v - C_{di}) \tag{17}$$

where K_{eff} is the in-vivo clearance ("effective clearance"). Eq. (17) shows that changes in the conductivity difference ΔC may be used to analyze changes in the in-vivo clearance K_{eff}, provided that the dialysis fluid flow rate D, the inlet conductivity C_{di}, the Donnan factor α, and the blood concentration C_v are unchanged. The Donnan factor α may be regarded as a constant; in practice it is always close to 1, and any change will be very small and have a minute impact on the result. Further, a change of flow direction through the dialyzer 4 and/or the access devices 2', 2" will not affect C_v. However, it should be noted that the in-vivo clearance K_{eff} is affected by the blood flow rate B, see e.g. Equations (1), (3) and (13). Thus, to the extent that the conductivity difference ΔC is used to analyze the effect of a change of flow direction through the dialyzer and/or access devices 2', 2", the blood flow rate B should remain essentially invariant during the change.

In summary, the foregoing analysis indicates that the non-bolus technique is applicable for use in the connection test 40, provided that each of the following operational parameters is controlled to be essentially unchanged during and between steps 43 and 45 in FIG. 4: the blood flow rate B, the treatment fluid flow rate D and the conductivity C_{di} of treatment fluid at the inlet to the dialyzer 4. In this context, "essentially unchanged" means that slight variations in the respective operational parameter are allowed to the extent that the resulting change in ΔC is small compared to the change caused by the change of flow direction. Typically, a ΔC change of ±1%, ±2%, ±5% or ±10% caused by variations in these operational parameters is deemed small.

It should be noted that the change of flow direction will not cause a change in measured conductivity difference ΔC if the inlet conductivity is equal to the plasma conductivity of the patient, i.e. $C_{di} = \alpha \cdot C_v$ in Eq. (17). Thus, it may be preferable, before initiating the connection test 40, to verify that the measured conductivity difference ΔC exceeds a minimum value, which may be predefined to yield a sufficient accuracy of the connection test 40. For example, the control unit 15 may operate the machine 1 in the first or second operating state, using predefined values of B, D and C_{di}, compute a ΔC value based on the measurements signals S1, S2 and compare the ΔC value to the minimum value. If the ΔC value is less than the minimum value, the control unit 15 operates the source 6, by generating the control signal C4, to adjust the inlet conductivity C_{di} so that the ΔC value exceeds the minimum value. It is conceivable that this adjustment is made for ΔC values computed for both the first operating state and the second operating state. The verification is a preparatory procedure, which is completed in advance of the connection test 40 in FIG. 4. The connection test 40 is then conducted with the predefined values of B, D and with the inlet conductivity C_{di} given by the verification.

It should also be understood that the upstream sensor 10A may be omitted if the inlet conductivity C_{di} is otherwise known to the control unit 15, e.g. from the settings of the TF circuit 1b (e.g. via control signal C4).

FIGS 7A-7B are plots of theoretically calculated ΔC values obtained based on Eq. (14) and Eq. (16), with K taken from Eq. (1) for a counter-current dialyzer configuration and from Eq. (3) for a co-current dialyzer configuration. FIG. 7A is generated for a conductivity gradient between blood and treatment fluid of 1 mS/cm, a cardiac output of 5 l/min, a treatment fluid flow rate of 500 ml/min, a dialyzer permeability (k_0A) of 1500 ml/min, an access flow rate of 1000 ml/min and no ultrafiltration. Curve 50 represents the correct condition, curve 52 represents the dialyzer fault condition, curve 54 represents the access fault condition, and curve 55 represents the dual fault condition. FIG. 7B is generated for the same set of input values, except that the access flow rate is 300 ml/min. Curve 51 represents the correct condition, curve 53 represents the dialyzer fault condition, curve 56 represents the access fault condition, and curve 57 represents the dual fault condition.

The curves in FIGS 7A-7B will now be used to explain and exemplify the connection test 40 for different embodiments shown in FIGS 8A-8D.

The embodiment in FIG. 8A differs from the embodiment in FIG. 1 by the provision of an FSD 9 in the EC circuit 1a adjacent to the access devices 2', 2". Specifically, the FSD 9 is connected to a blood line between the blood pump 5 and the access device 2' and to a blood line downstream of the dialyzer 4. As indicated by

double-ended arrows, a switch of the FSD 9 between its first and second configurations causes a change of flow direction through the access devices 2', 2", without affecting the flow direction of blood in the dialyzer 4. Thus, the control unit 15 (FIG. 3A) is operable, by the control signal C3, to switch the machine 1 between a correct condition and an access fault condition, assuming that all connections to the dialyzer 4 are correct. In FIG. 7A, the switch of the FSD 9 corresponds to a switch between curve 50 and curve 54. In FIG. 7B, the switch of the FSD 9 corresponds to a switch between curve 51 and curve 56. As seen, for most blood flow rates B, there will be a considerable difference in ΔC values between the correct condition and the access fault condition, where the larger ΔC value is obtained for the correct condition and the smaller ΔC value is obtained for the access fault condition. Clearly, the connection test 40 in FIG. 4 is equally applicable to the machine 1 in FIG. 8A, to determine if the first operating state is in the correct condition or the access fault condition. With respect to the examples given in relation to FIG. 3A, the feedback provided by step 47 if the first operating state is found to be in the access fault condition may be modified to explicitly or implicitly instruct the operator to check or change the connection of the access devices 2', 2".

It is conceivable that the operational parameters of the machine 1 are set in step 41 to values that are known to provide a sufficient difference between the ΔC values, irrespective of access flow rate A, cardiac output CO and dialyzer permeability k_0A, which are generally unknown to the control unit 15. Thus, the control unit 15 may be configured to, in step 41, obtain dedicated settings for the operational parameters D, B and C_{di} and then generate the control signals C1, C2, C4 to set the machine 1 accordingly. Simulations based on Equations (1), (3), (14) and (16) above indicate that a sufficient difference between ΔC values are ensured by setting the treatment fluid flow rate D in the range of 200-400 ml/min and the blood flow rate B in the range of 200-300 ml/min. These ranges are applicable to all embodiments disclosed herein.

It should be understood that step 41 may also include the above-described preparatory verification that ΔC exceeds a minimum value. Thus, even if dedicated settings indicate a desired value for the parameter C_{di}, the inlet conductivity C_{di} may be additionally adjusted before steps 42-45 to ensure that ΔC exceeds the above-mentioned minimum value.

The embodiment in FIG. 8B differs from the embodiment in FIG. 1 by the provision two FSDs 9, which are separately controlled by a respective control signal C3, and corresponds to a combination of the embodiments in FIGS 3A and 8A. Thus, a first FSD 9 is arranged in the TF circuit 1b, intermediate the sensors 10A, 10B and the inlet and outlet ports of the treatment fluid chamber 4B, and a second FSD 9 is arranged adjacent to the access devices 2', 2". The skilled person readily realizes that the

connection test 40 is equally applicable to the machine 1 in FIG. 8B, by executing at least steps 42-45 for each FSD 9 separately. Thus, in a first sequence of steps 42-45, the machine 1 is set in first and second operating states by switching the first (or second) FSD 9, and in a second sequence of steps 42-45, the machine 1 is set in first and second operating states by switching the second (or first) FSD 9. It should be noted that the operational parameters set in step 41 may but need not be the same in the first and second sequences of steps 42-45. As will be exemplified in the following with reference to FIGS 7A-7B, the ΔC resulting values may be analyzed to allocate a respective flow direction status to the first and second operating states.

In the example of FIG. 7A, a switch of the first FSD 9 corresponds to either a switch between curve 50 (correct condition) and curve 52 (dialyzer fault condition) or a switch between curve 54 (access fault condition) and curve 55 (dual fault condition). In the example of FIG. 7B, a switch of the first FSD 9 corresponds to either a switch between curve 51 (correct condition) and curve 53 (dialyzer fault condition) or a switch between curve 56 (access fault condition) and curve 57 (dual fault condition). In both examples, when switching the first FSD 9, the larger ΔC value corresponds to a counter-current configuration of the dialyzer 4. In the example of FIG. 7A, a switch of the second FSD 9 corresponds to either a switch between curve 50 (correct condition) and curve 54 (access fault condition) or a switch between curve 52 (dialyzer fault condition) and curve 55 (dual fault condition). In the example of FIG. 7B, a switch of the second FSD 9 corresponds to either a switch between curve 51 (correct condition) and curve 56 (access fault condition) or a switch between curve 53 (dialyzer fault condition) and curve 57 (dual fault condition). In both examples, when switching the second FSD 9, the larger ΔC value corresponds to a normal configuration of the access devices 2', 2".

Clearly, it is possible to allocate a respective flow direction status to the first and second operating states based on the ΔC values obtained in the embodiment in FIG. 8B. The skilled person can readily adapt steps 46-48 to the foregoing analysis to identify any connection errors, inform the operator accordingly and optionally correct these connection errors by switching one or more of the FSDs 9 accordingly.

The embodiment in FIG. 8C is a variant of the machine 1 in FIG. 8B and corresponds to a combination of the embodiments in FIGS 3B and 8A. It is realized that the connection test 40 may be executed in the same way as for the embodiment in FIG. 8B.

The embodiment in FIG. 8D differs from the embodiment in FIG. 1 by the provision of a reversible blood pump 5, which is thus operable in both a forward (default) direction and a reverse direction. As will be explained in the following, the blood pump 5 is operated as an FSD 9, and thus the control signal C3 is given by the

control signal C2. The embodiment in FIG. 8D reduces cost and complexity of the machine 1 compared to the embodiment in FIGS 3A-3B and 8A-8C, since it obviates the need for potentially complex and costly valve arrangements in the FSD 9. It also enables the connection test 40 to determine the flow direction status based on a single reversal of the blood pump 5.

As indicated by double-ended arrows in the dialyzer 4 and adjacent to the access devices 2', 2", a switching of the blood pump 5 between a first configuration (forward direction) and a second configuration (reverse direction) causes a simultaneous change of flow direction in the blood compartment 4A and through the access devices 2', 2". Thus, by switching the pumping direction of the blood pump 5, the machine 1 is switched between first and second operating states, which differ by the flow directions in the blood chamber 4A and through the access devices 2', 2". In the example of FIG. 7A, a switch of the pumping direction corresponds to either a switch between curve 50 (correct condition) and curve 55 (dual fault condition), or a switch between curve 52 (dialyzer fault condition) and 54 (access fault condition), depending on the flow direction status of the first operating state. In the example of FIG. 7B, a switch of the pumping direction corresponds to either a switch between curve 51 (correct condition) and curve 57 (dual fault condition), or a switch between curve 53 (dialyzer fault condition) and 56 (access fault condition), depending on the flow direction status of the first operating state.

The connection test 40 in FIG. 4 is equally applicable to the embodiment in FIG. 8D, although the analysis in step 47 and the feedback in step 48 may be modified to take into account the joint switching of flow directions in the dialyzer 4 and the access devices 2', 2".

FIGS 7A-7B show that there is a considerable difference in ΔC values between the different flow direction statuses. Arrow 77 indicates the change in ΔC value when switching, at a blood flow rate $B = 250$ ml/min, from the correct condition to the dual fault condition, or vice versa, and arrow 78 indicates the change in ΔC value when switching from the access fault condition to the dialyzer fault condition, or vice versa. As seen, the change 77 is much larger than the change 78 in both FIG. 7A and FIG. 7B. Thus, it is possible to discriminate between a switch between the correct condition and the dual fault condition, and a switch between the access fault condition and the dialyzer fault condition. Further, since the curves are well-separated, it may be possible to use the sign of the change to allocate a flow direction status to the first and second operating states, at least for blood flow rates B of about 100 ml/min or larger. However, as seen in FIGS 7A-7B, it may be difficult to generally discriminate between the dialyzer fault condition (curves 52, 53) and the access fault condition (curves 54, 56).

The skilled person readily realizes that there are numerous ways of formalizing the foregoing analysis into computation and evaluation of an efficiency change parameter in step 47 of FIG. 4. In one example, the efficiency change parameter is computed as a (weighted) difference of the ΔC values, which may be analyzed with respect to magnitude and sign. In another example, the efficiency change parameter is given by or computed as a function of a ratio R of the ΔC values, which may be analyzed with respect to magnitude.

FIGS 9A-9C illustrate different combinations of ranges that may be applied by the control unit 15 in step 47 when evaluating the ratio R, which is computed by dividing the ΔC values obtained in the first and second operating states of the machine 1 in FIG. 8D. Each range is associated with a respective flow direction status of the machine 1 in the first operating state. Thus, in step 47, the control unit 15 may simply compare the R value to the different ranges to determine the flow direction status of the first operating state. The ranges may be identified to the control unit 15 by a range definition stored in the memory 18 (FIG. 3A) for retrieval in step 47. The range definition may identify the respective range by an upper limit value and a lower limit value. It is also possible that one or more ranges are defined by either an upper limit value or a lower limit value, e.g. if the range is open-ended. Thus, as used herein, a "range" includes both closed and open-ended ranges. Depending on implementation, the range definition may be given for different combinations of operational and/or system parameters. Such a range definition may be implemented by one or more look-up tables and/or one or more functions for computing a respective range based on one or more current values of the operational and/or system parameters. Thus, in step 47, the control unit 15 may dynamically obtain the ranges by accessing the range definition based on current values of the operational and/or system parameters.

FIG. 9A illustrates ranges $\Delta R1$-$\Delta R3$ that are set to be applicable irrespective of the permeability k_0A of the dialyzer, and also irrespective of A and CO, where $\Delta R1$ corresponds to the correct condition, $\Delta R2$ corresponds to the dual fault condition, and $\Delta R3$ corresponds to a "single fault condition" (i.e. in any of the access fault condition and the dialyzer fault condition). Depending on implementation, the definition in FIG. 9A may only be valid if the machine 1 is operated within a predefined interval of blood flow rates B and/or treatment fluid flow rates D. The definition may even be limited to a specific combination of values for B and D. It should also be understood that a corresponding definition of $\Delta R1$-$\Delta R3$ may be used in step 47 even if one or more system parameters are known.

FIG. 9B illustrates variant of the definition in FIG. 9A, in which additional ranges $\Delta R4'$, $\Delta R4''$ are defined on both sides of $\Delta R3$, adjacent to $\Delta R2$ and $\Delta R1$, respectively.

The ranges $\Delta R4'$, $\Delta R4''$ are both associated with a "potential fault condition", which deemed to potentially involve a fault condition.

FIG. 9C illustrates a range definition capable of identifying all possible flow direction statuses of the first operating state, where range $\Delta R1$ corresponds to the correct condition, $\Delta R2$ corresponds to the dual fault condition, $\Delta R3'$ corresponds to the access fault condition, and $\Delta R3''$ corresponds to the dialyzer fault condition. The range definition in FIG. 9C is typically valid for a specific combination of specific values or limited intervals of at least some of the operational parameters and system parameters. For example, the ranges may be defined based on FIG. 7A or FIG. 7B, to be valid only for a specific combination of values/ranges of B, D, k_0A and A, as indicated in FIG. 9C.

It is realized from FIGS 9A-9C that step 47 may result in different levels of detail regarding the connection errors. In a first example, the control unit 15 is configured to discriminate between all of the different flow direction statuses and thus determines if the first operating state is in the correct condition, the dual fault condition, the access fault condition or the dialyzer fault condition. In a second example, the control unit 15 is configured to determine if the first operating state is in the correct condition, the dual fault condition or the single fault condition. In both of the first and second examples, the control unit 15 may additionally determine a "potential fault condition", which deemed to potentially involve a fault condition.

Clearly, the feedback generated by step 48 depends on the implementation of step 47. In one example, if the first operating state is found to be in the dual fault condition, the single fault condition, the access fault condition or the dialyzer fault condition, the feedback may indicate to the operator that the connection test has failed. In another example, if the first operating state is found to be in the dual fault condition, the feedback may explicitly or implicitly instruct the operator to change the connection of the dialyzer 4 and the connection of the access devices 2', 2''. Alternatively, if the first operating state is found to be in the dual fault condition, the control unit 15 may automatically correct the error by operating the blood pump 5 in the reverse direction during blood treatment. In another example, if the first operating state is found to be in the correct condition or, equivalently, if the second operating state is found to be in the dual fault condition, the feedback may confirm to the operator that the machine 1 is correctly connected. In yet another example, if the first operating state is found to be in the single fault condition, the feedback may explicitly or implicitly instruct the operator to check both the connection of the dialyzer 4 and the connection of the access devices 2', 2''. In yet another example, if the first operating state is found to be in the access fault condition, the feedback may explicitly or implicitly instruct the operator to change the connection of the access devices 2', 2''. In yet another example, if the first operating

state is found to be in the dialyzer fault condition, the feedback may explicitly or implicitly instruct the operator to change the connection of the dialyzer 4. In still another example, if the first operating state is found to be in the potential fault condition, the feedback may inform the operator about a possible connection error and instruct the operator to check both the connection of the dialyzer 4 and the connection of the access devices 2', 2".

The control unit 15 as described herein may be implemented by special-purpose software (or firmware) run on one or more general-purpose or special-purpose computing devices. In this context, it is to be understood that an "element" or "means" of such a computing device refers to a conceptual equivalent of a method step; there is not always a one-to-one correspondence between elements/means and particular pieces of hardware or software routines. One piece of hardware sometimes comprises different means/elements. For example, a processor serves as one element/means when executing one instruction, but serves as another element/means when executing another instruction. In addition, one element/means may be implemented by one instruction in some cases, but by a plurality of instructions in some other cases. Such a software controlled computing device may include one or more processors (cf. 17 in FIG. 3A), e.g. a CPU ("Central Processing Unit"), a DSP ("Digital Signal Processor"), an ASIC ("Application-Specific Integrated Circuit"), discrete analog and/or digital components, or some other programmable logical device, such as an FPGA ("Field Programmable Gate Array"). The control unit 15 may further include a system memory and a system bus that couples various system components including the system memory (cf. 18 in FIG. 3A) to the processor. The system bus may be any of several types of bus structures including a memory bus or memory controller, a peripheral bus, and a local bus using any of a variety of bus architectures. The system memory may include computer storage media in the form of volatile and/or non-volatile memory such as read only memory (ROM), random access memory (RAM) and flash memory. The special-purpose software may be stored in the system memory, or on other removable/non-removable volatile/non-volatile computer storage media which is included in or accessible to the computing device, such as magnetic media, optical media, flash memory cards, digital tape, solid state RAM, solid state ROM, etc. The control unit 15 may include one or more communication interfaces, such as a serial interface, a parallel interface, a USB interface, a wireless interface, a network adapter, etc, as well as one or more data acquisition devices, such as an A/D converter. The special-purpose software may be provided to the control unit 15 on any suitable computer-readable medium, transitory or non-transitory, including a record medium or a read-only memory. It is also conceivable that some (or all) elements/means are fully or partially implemented by dedicated

hardware, such as an FPGA, an ASIC, or an assembly of discrete electronic components (resistors, capacitors, operational amplifier, transistors, filters, etc), as is well-known in the art. It should be emphasized that the invention is not limited to digital signal processing, but could be fully implemented by a combination of analog devices.

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, it is conceivable that the machine 1 is switched between the first and second operating states by manual intervention, instead of by control signal C3. For example, the control unit 15 may instruct the operator, via the UI device 16 and before step 44, to manually change the FSD 9 from its first configuration to its second configuration, or vice versa.

Further, it should be understood that the definition and use of ranges as described with reference to FIGS 9A-9C are equally applicable to other definitions of the efficiency change parameter, including the above-mentioned difference of ΔC values.

Even if the foregoing embodiments give the control unit 15 the ability to set the measured property of the treatment fluid, by the control signal C4, the connection test 40 may be implemented also for embodiments that lack this ability, e.g. if the source 6 is configured to supply a ready-made treatment fluid of predefined composition.

CLAIMS

1. A control device for a blood treatment machine (1) comprising an extracorporeal blood flow circuit (1a) with first and second access devices (2', 2") for connection to upstream and downstream portions, respectively, of a vascular access (3) of a patient and having a blood pump (5) operable to generate a flow of blood in the extracorporeal blood flow circuit (1a) from one of the first and second access devices (2', 2") through a blood compartment (4A) of a dialyzer (4) and to another of the first and second access devices (2', 2"), and a treatment fluid flow circuit (1b) configured to generate a flow of treatment fluid through a treatment fluid compartment (4B) of the dialyzer (4), said treatment fluid compartment (4B) being separated from the blood compartment by a semi-permeable membrane (4'), said control device being configured to, during a connection test:

cause the blood treatment machine (1) to operate in a first operating state with fixed values of the flow rate of blood, the flow rate of treatment fluid and a fluid property of the treatment fluid,

cause the blood treatment machine (1) to operate in a second operating state with said fixed values, the second operating state differing from the first operating state by a change of flow direction in at least one of the dialyzer (4) and the first and second access devices (2', 2"),

acquire an output signal (S1, S2) of at least one sensor (10A, 10B) which is arranged in the blood treatment machine (1) to measure the fluid property of the treatment fluid,

compute, based on the output signal (S1, S2), a first efficiency value that represents the in-vivo clearance of the blood treatment machine (1) in the first operating state,

compute, based on the output signal (S1, S2), a second efficiency value that represents the in-vivo clearance of the blood treatment machine (1) in the second operating state, and

evaluate the first and second efficiency values for detection of a connection error at the dialyzer (4) and/or the access devices (2', 2") when the blood treatment machine is operated in the first operating state.

2. The control unit of claim 1, which is configured to compute each of the first and second efficiency values to represent a difference in the fluid property between an inlet and an outlet of the treatment fluid chamber (4B).

3. The control unit of any preceding claim, wherein the connection error causes a detectable reduction in the in-vivo clearance compared to a correct operating state of the blood treatment machine (1), in which the blood pump (5) is operated to generate the flow of blood from the upstream portion of the vascular access (3), via the first access device (2'), through the blood compartment (4A) and via the second access device (2") to the downstream portion of the vascular access (3), and in which the treatment fluid flow circuit (1b) is operated to generate the flow of treatment fluid through the treatment fluid compartment (4B) along the semipermeable membrane (4') in opposite direction to the flow of blood through the blood compartment (4A) along the semipermeable membrane (4').

4. The control unit of any preceding claim, wherein the connection error results in at least one of a co-current dialyzer configuration, in which the flow of blood through the blood compartment (4A) and the flow of treatment fluid through the treatment fluid compartment (4B) are in a common direction along the semi-permeable membrane (4'), and a reversed access device configuration, in which the first and second access devices (2', 2") are connected to the downstream and upstream portions, respectively, of the vascular access (3).

5. The control unit of claim 4, wherein the second operating state differs from the first operating state by the flow direction in the dialyzer (4), and wherein the connection error results in the co-current dialyzer configuration.

6. The control unit of claim 4 or 5, wherein the second operating state differs from the first operating state by the flow direction in the first and second access devices (2', 2"), and wherein the connection error results in the reversed access device configuration.

7. The control unit of claim 5 or 6, which is configured to detect the connection error when the first efficiency value is smaller than the second efficiency value.

8. The control unit of any preceding claim, which is operatively associated with an interface device (16) configured to output instructions for an operator of the blood treatment machine (1), wherein the control device is configured to, when detecting the connection error, operate the interface device (16) to inform the operator that the connection test has failed, and optionally to instruct the operator on how to correct the connection error.

9. The control device of any preceding claim, which is further configured to obtain at least the fixed values of the flow rate of blood and the flow rate of treatment fluid from an electronic memory (18).

10. The control device of any preceding claim, wherein the fixed values define the flow rate of blood to a value in the approximate range of 200-300 ml/min.

11. The control device of any preceding claim, wherein the fixed values define the flow rate of treatment fluid to a value in the approximate range of 200-400 ml/min.

12. The control device of any preceding claim, which is further configured to, in advance of the connection test, compute at least one of the first and second efficiency values and, if said at least one of the first and second efficiency values is lower than a predefined minimum value, control a source (6) of treatment fluid in the treatment fluid flow circuit (1b) to adjust the fluid property of the treatment fluid so that said at least one of the first and second efficiency values exceeds the predefined minimum value.

13. The control unit of any preceding claim, which is configured to cause the blood treatment machine (1) to be switched between the first and second operating states by causing at least one flow switching device (9) in the blood treatment machine (1) to change the flow direction in at least one of the dialyzer (4) and the first and second access devices (2', 2").

14. The control unit of claim 13, which is configured to generate a control signal (C3) for the at least one flow switching device (9) to switch the blood treatment machine (1) between the first and second operating states.

15. The control unit of claim 13 or 14, wherein the at least one flow switching device (9) comprises the blood pump (5), and wherein the blood pump (5) is set to operate in a forward pumping direction in the first operating state of the blood treatment machine (1) and in a reverse pumping direction in the second operating state of the blood treatment machine (1).

16. The control unit of any one of claims 13-15, which is further configured to correct the connection error by selectively operating the at least one flow switching

device (9) to change the flow direction in at least one of the dialyzer (4) and the first and second access devices (2', 2") in the first operating state.

17. The control unit of any preceding claims, wherein the fluid property is a physical and/or chemical property of the treatment fluid.

18. The control unit of any preceding claim, wherein the fluid property is one of a temperature and a concentration of a substance that is present in the blood and is capable of exchanging across the semi-permeable membrane (4').

19. The control unit of any preceding claim, wherein said at least one sensor (10A, 10B) is one of a concentration sensor, a temperature sensor, a conductivity sensor, an optical absorbance sensor, a polarimetry sensor and a density sensor.

20. A blood treatment machine, comprising an extracorporeal blood flow circuit (1a) with first and second access devices (2', 2") for connection to upstream and downstream portions, respectively, of a vascular access (3) of a patient and having a blood pump (5) operable to generate a flow of blood from one of the first and second access devices (2', 2") through a blood compartment (4A) of a dialyzer (4) and to another of the first and second access devices (2', 2"), a treatment fluid flow circuit (1b) configured to generate a flow of treatment fluid through a treatment fluid compartment (4B) of the dialyzer (4), said treatment fluid compartment (4B) being separated from the blood compartment by a semi-permeable membrane (4'), and the control device according to any preceding claim.

21. A method of performing a connection test of a blood treatment machine (1) comprising an extracorporeal blood flow circuit (1a) with first and second access devices (2', 2") for connection to upstream and downstream portions, respectively, of a vascular access (3) of a patient and having a blood pump (5) operable to generate a flow of blood in the extracorporeal blood flow circuit (1a) from one of the first and second access devices (2', 2") through a blood compartment (4A) of a dialyzer (4) and to another of the first and second access devices (2', 2"), and a treatment fluid flow circuit (1b) configured to generate a flow of treatment fluid through a treatment fluid compartment (4B) of the dialyzer (4), said treatment fluid compartment (4B) being separated from the blood compartment by a semi-permeable membrane (4'), said method comprising the steps of:

causing the blood treatment machine (1) to operate in a first operating state with fixed values of the flow rate of blood, the flow rate of treatment fluid and a fluid property of the treatment fluid,

causing the blood treatment machine (1) to operate in a second operating state with said fixed values, the second operating state differing from the first operating state by a change of flow direction in at least one of the dialyzer (4) and the first and second access devices (2', 2"),

acquiring an output signal (S1, S2) of at least one sensor (10A, 10B) which is arranged in the blood treatment machine (1) to measure the fluid property of the treatment fluid,

computing, based on the output signal (S1, S2), a first efficiency value that represents the in-vivo clearance of the blood treatment machine (1) in the first operating state,

computing, based on the output signal (S1, S2), a second efficiency value that represents the in-vivo clearance of the blood treatment machine (1) in the second operating state, and

evaluating the first and second efficiency values for detection of a connection error at the dialyzer (4) and/or the access devices (2', 2") when the blood treatment machine is operated in the first operating state.

22. A computer-readable medium comprising computer instructions which, when executed by a processor (17), cause the processor (17) to perform the method of claim 21.

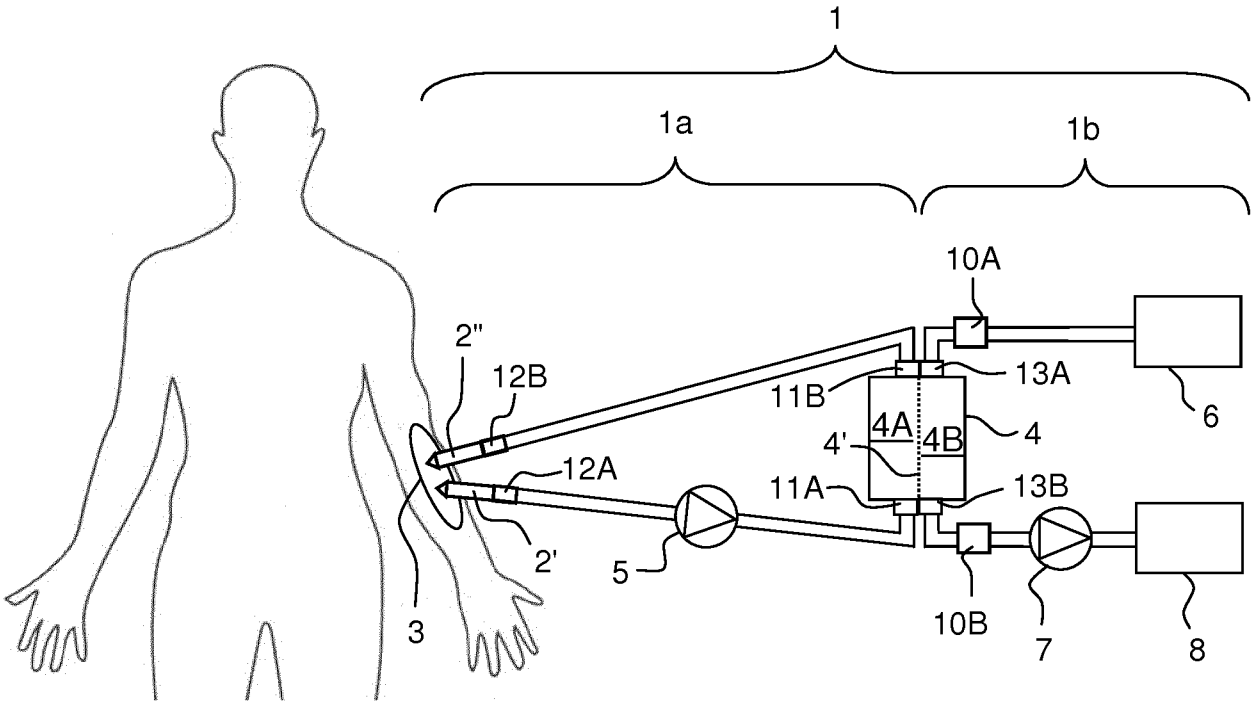

FIG. 1

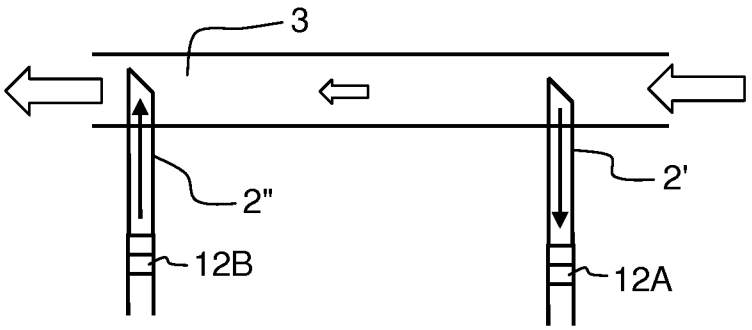

FIG. 2A

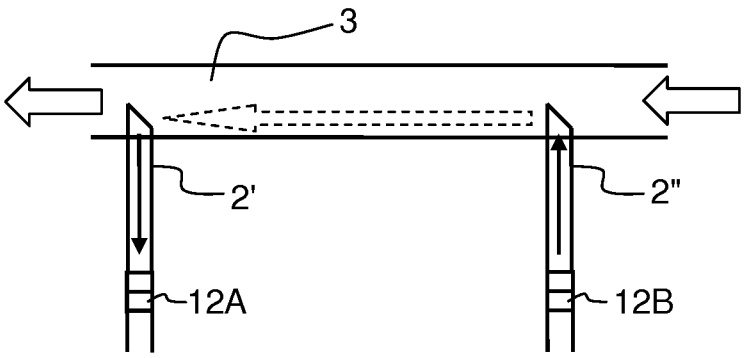

FIG. 2B

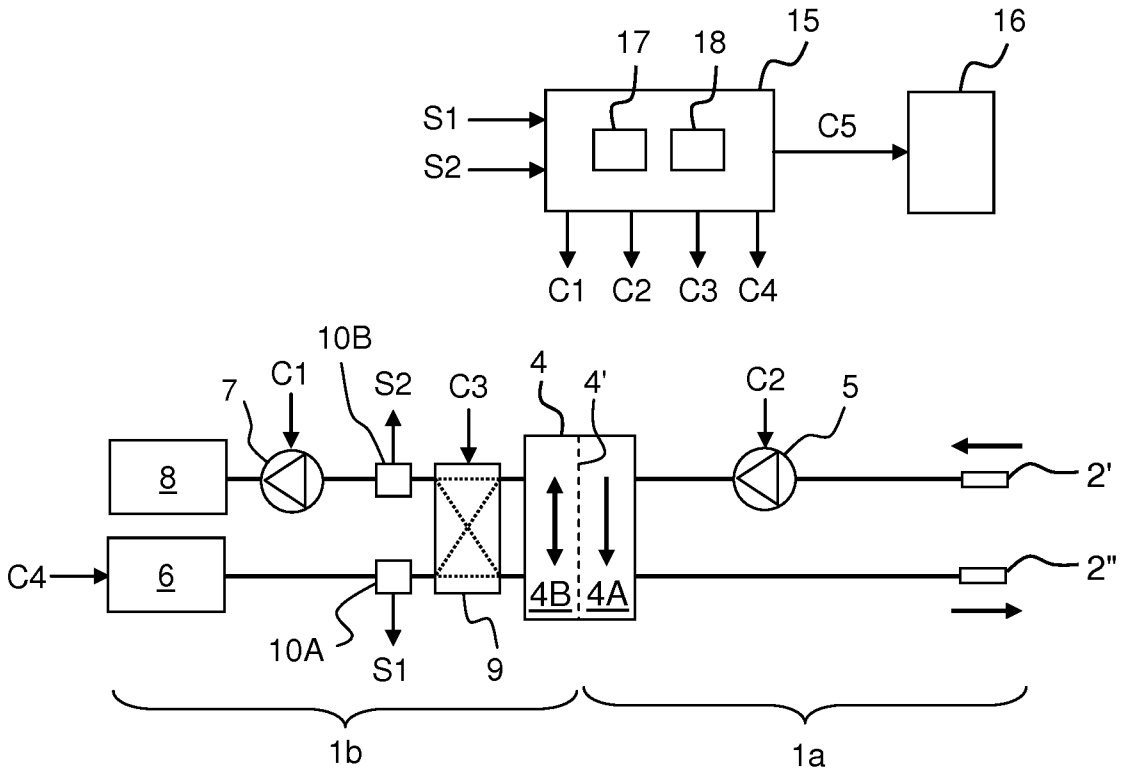
17
18
15
16
S1
S2
C5
C1
C2
C3
C4
10B
7
C1
S2
C3
4
4'
C2
5
8
2'
C4
6
2"
4B
4A
10A
S1
9
1b
1a

FIG. 3A

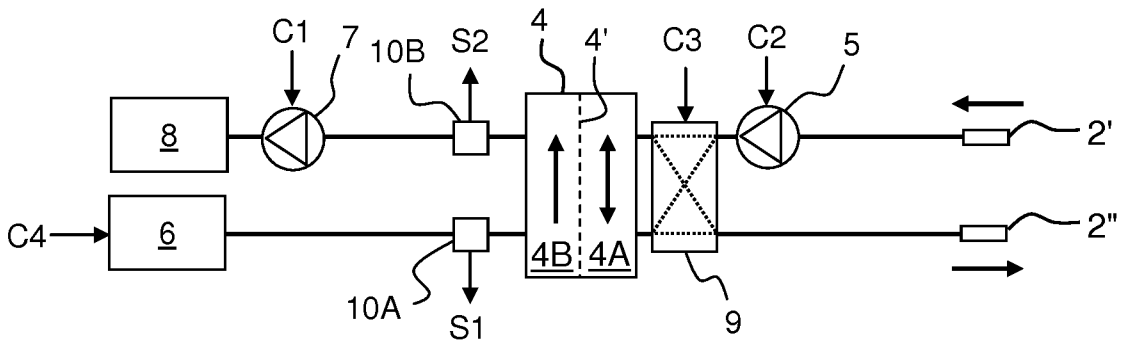
C1
7
10B
S2
4
4'
C3
C2
5
8
2'
C4
6
2"
4B
4A
10A
S1
9

FIG. 3B

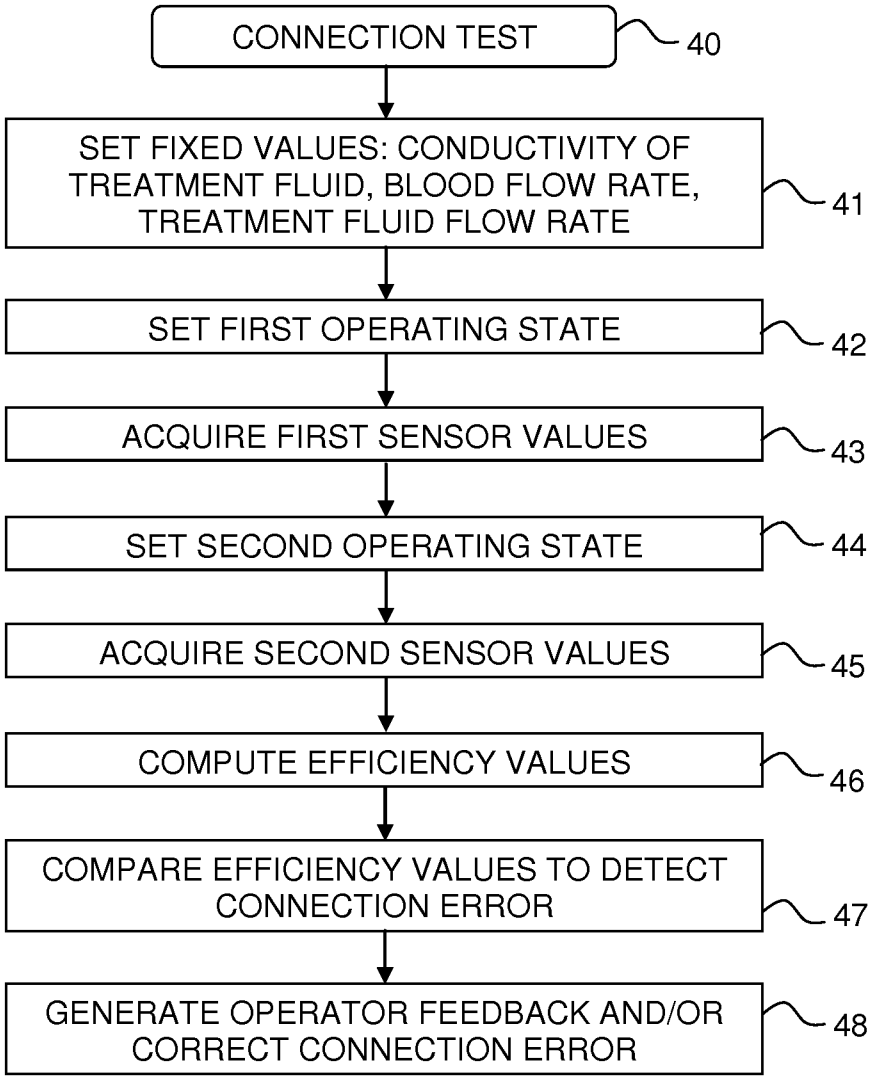
CONNECTION TEST
40
SET FIXED VALUES: CONDUCTIVITY OF TREATMENT FLUID, BLOOD FLOW RATE, TREATMENT FLUID FLOW RATE
41
SET FIRST OPERATING STATE
42
ACQUIRE FIRST SENSOR VALUES
43
SET SECOND OPERATING STATE
44
ACQUIRE SECOND SENSOR VALUES
45
COMPUTE EFFICIENCY VALUES
46
COMPARE EFFICIENCY VALUES TO DETECT CONNECTION ERROR
47
GENERATE OPERATOR FEEDBACK AND/OR CORRECT CONNECTION ERROR
48

FIG. 4

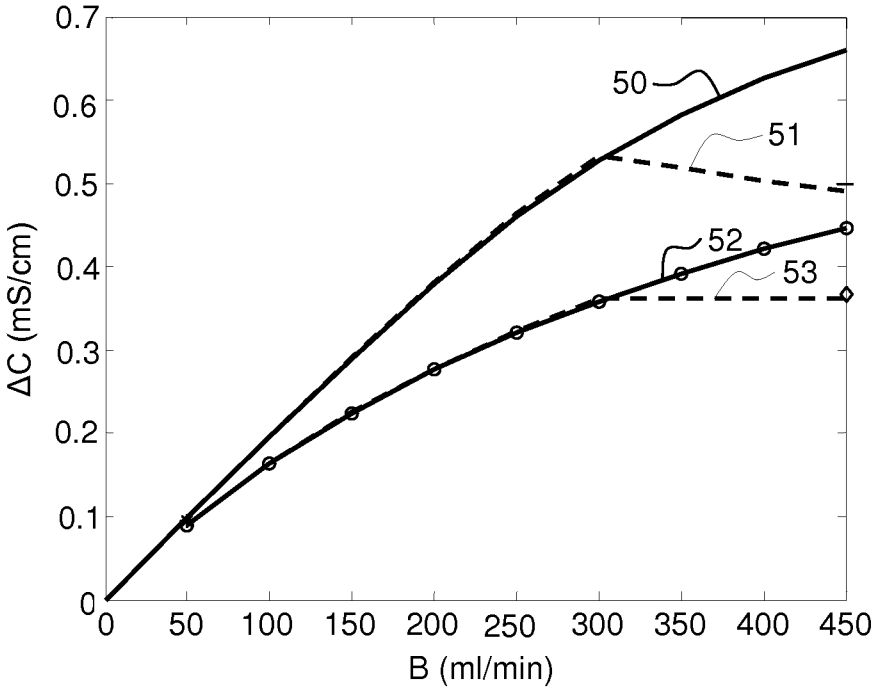
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
ΔC (mS/cm)
0
50
100
150
200
250
300
350
400
450
B (ml/min)
50
51
52
53

FIG. 5

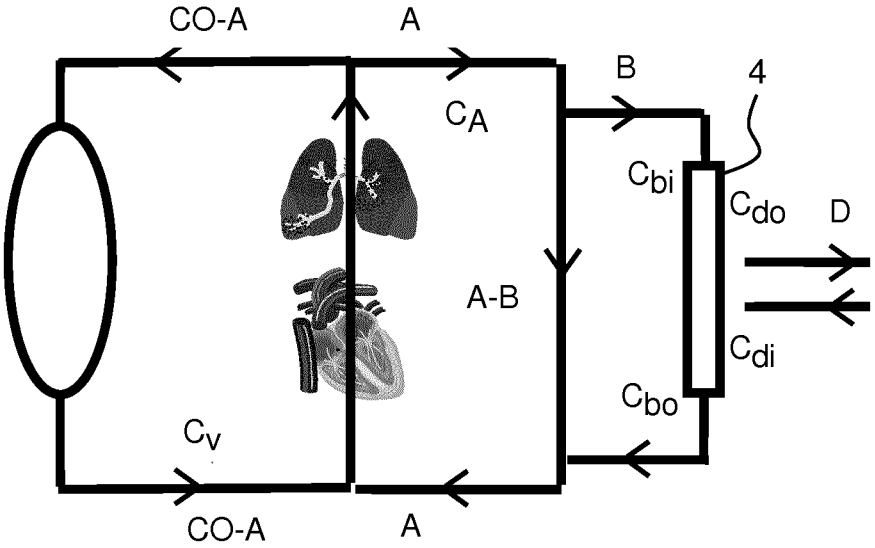

FIG. 6A

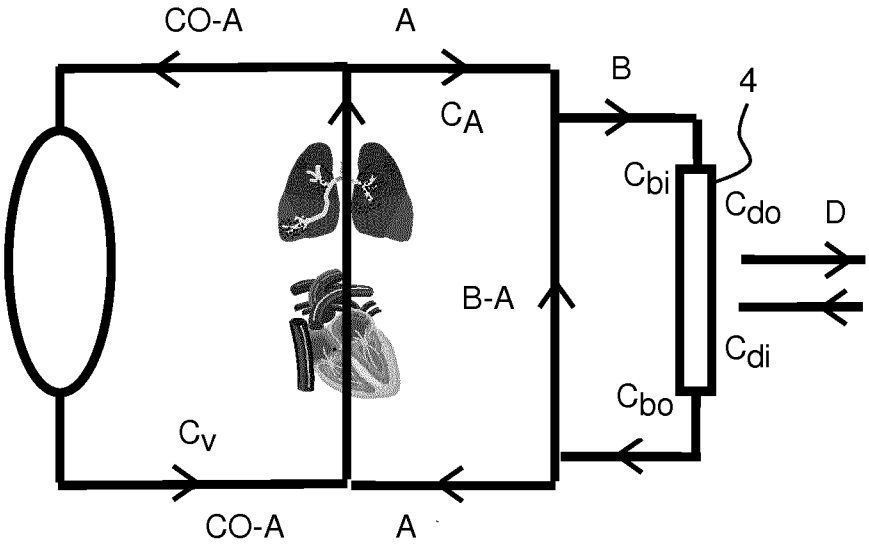

FIG. 6B

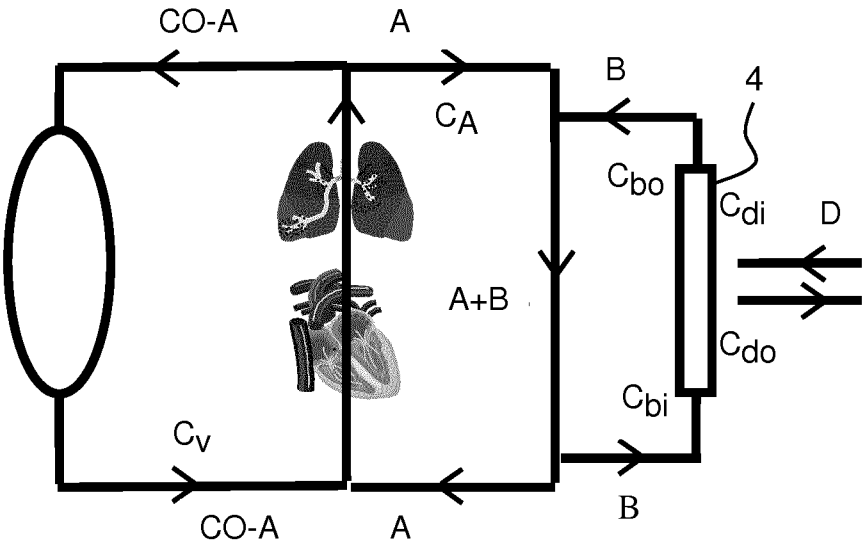

FIG. 6C

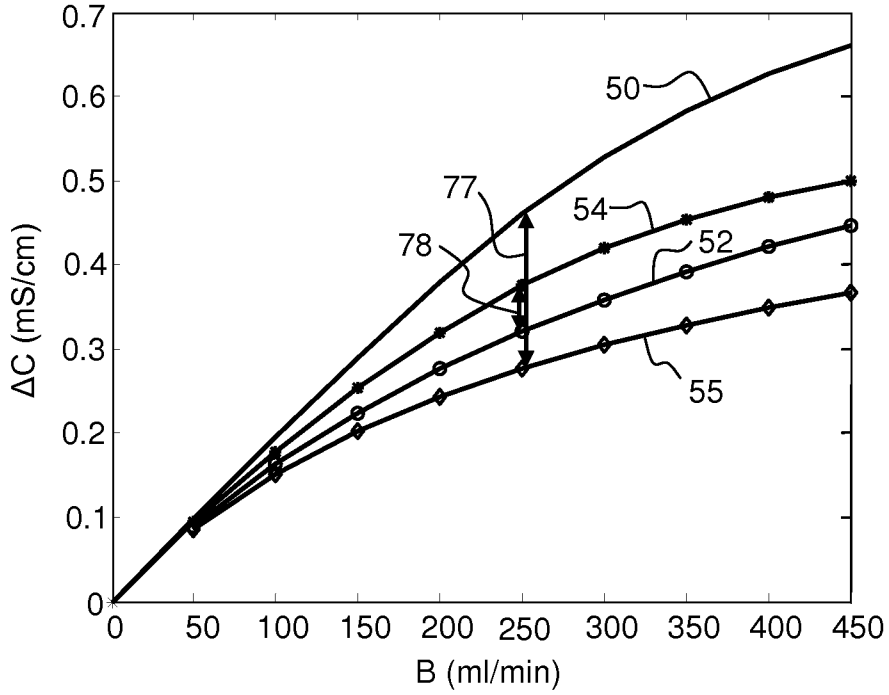

FIG. 7A

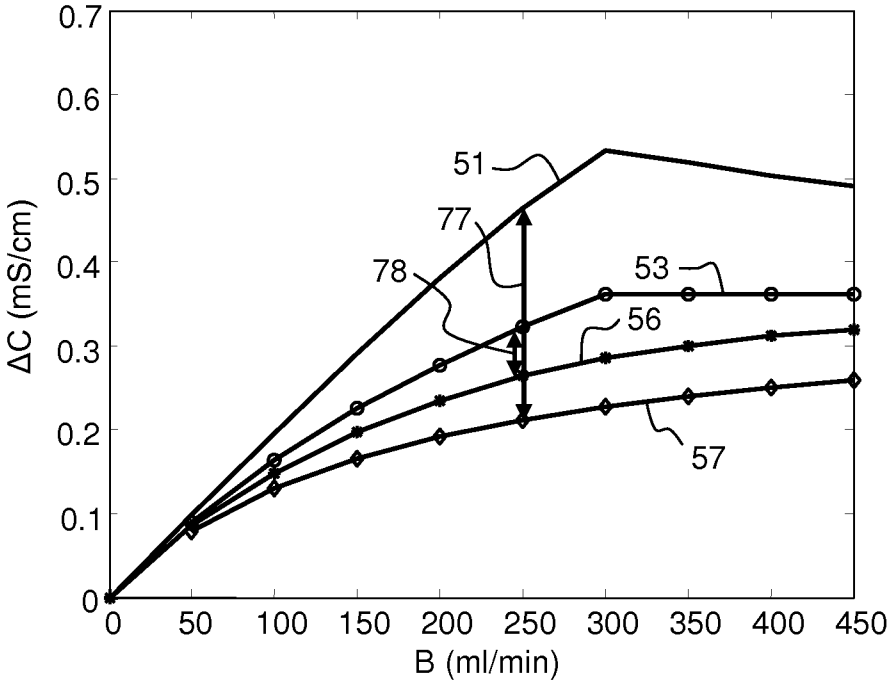

FIG. 7B

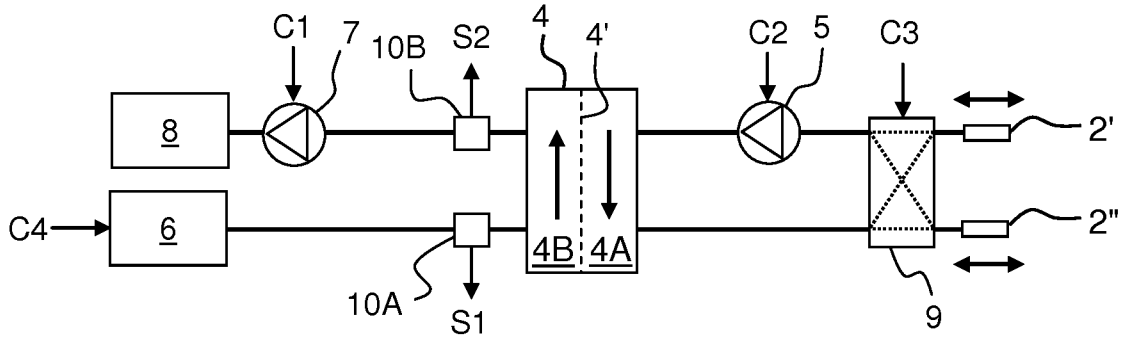

FIG. 8A

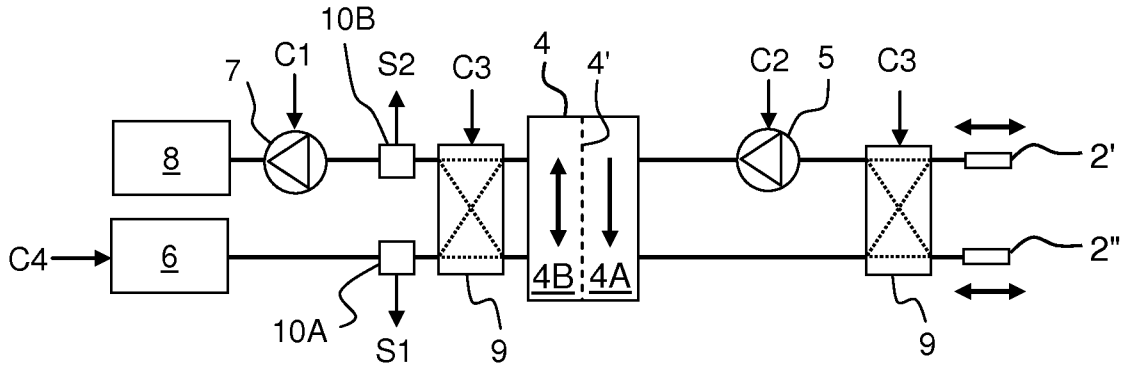

FIG. 8B

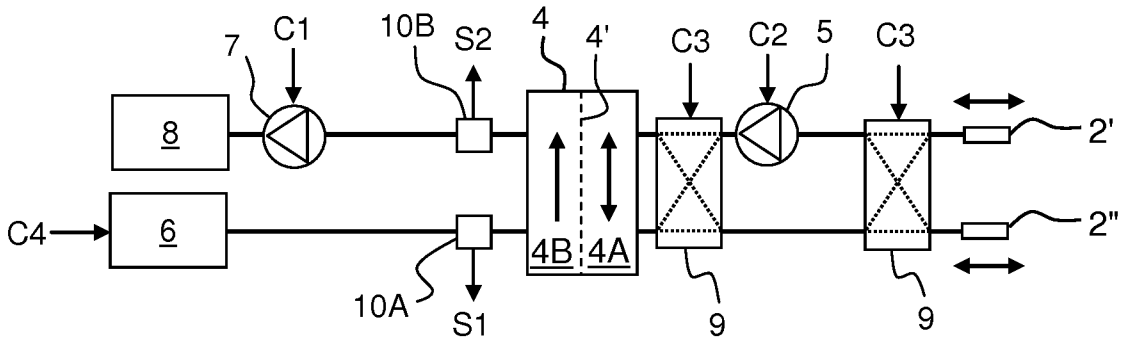

FIG. 8C

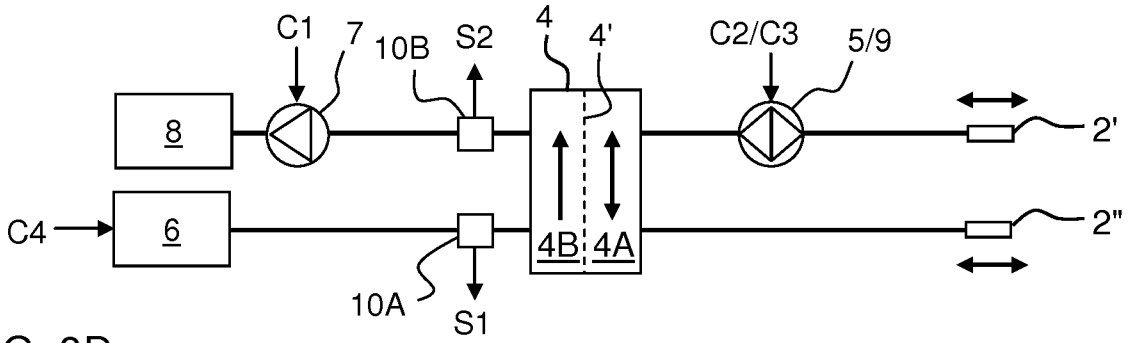

FIG. 8D

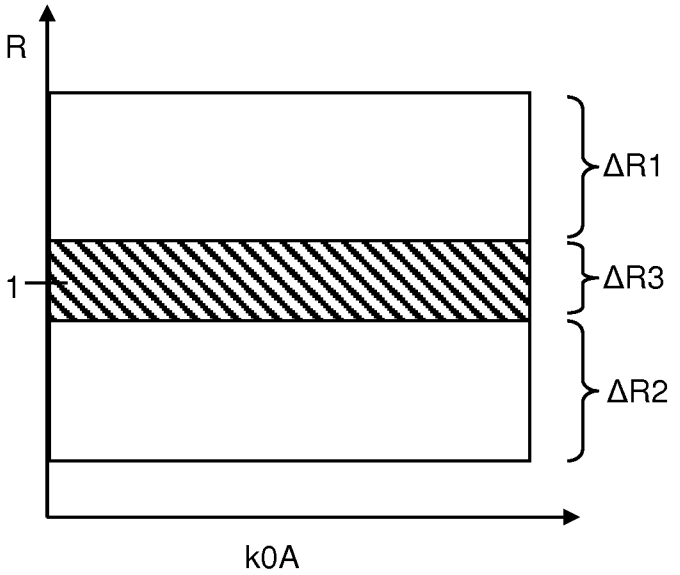

FIG. 9A

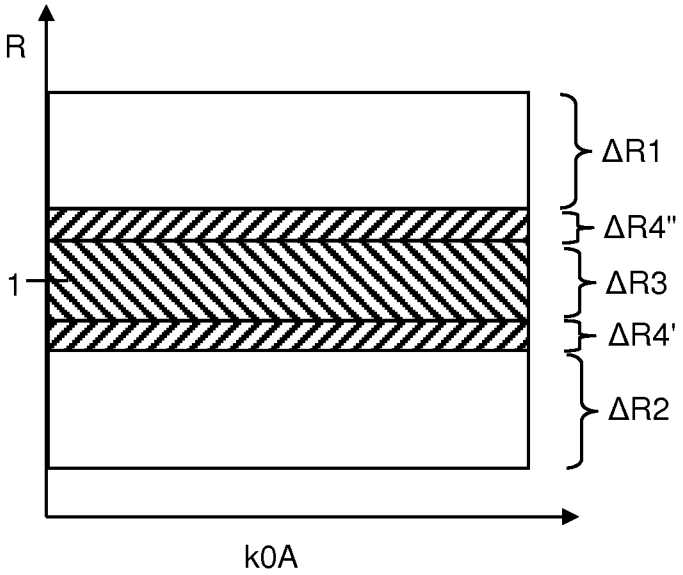

FIG. 9B

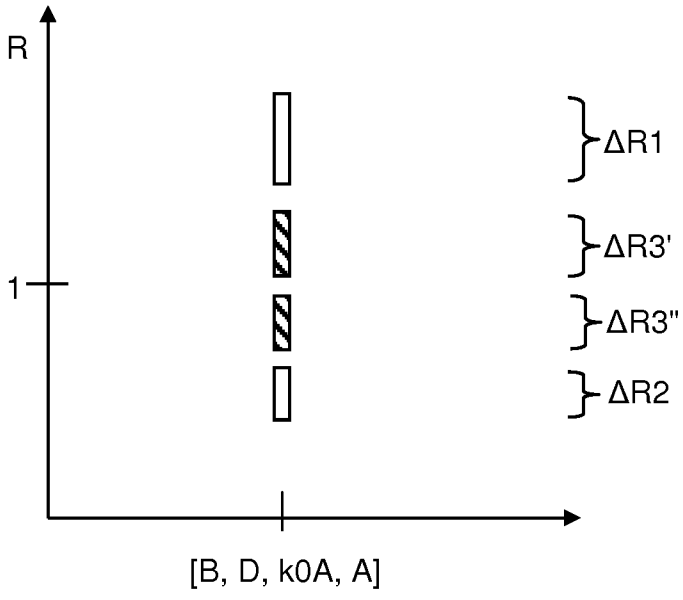

FIG. 9C

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/065768

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M1/16 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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 938 847 B1 (GAMBRO LUNDIA AB [SE]) 11 June 2014 (2014-06-11) paragraphs [0003], [0010] - [0016], [0023], [0025], [0049]; claims 4,5; figure 2	1-4,6-22
X	WO 2016/016039 A1 (FRESENIUS MEDICAL CARE DE GMBH [DE]) 4 February 2016 (2016-02-04) figure 1 page 3, paragraph 2-4 page 5, paragraph 2 - page 7, paragraph 3 page 12, paragraph 2 - page 13, paragraph 3 page 19, paragraph 2-4	1-22
A	US 2013/026098 A1 (HAECKER JUERGEN [DE] ET AL) 31 January 2013 (2013-01-31) paragraphs [0005] - [0021]; figures 1,5	1-22

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 August 2017	31/08/2017

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	Nurmi, Jussi

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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