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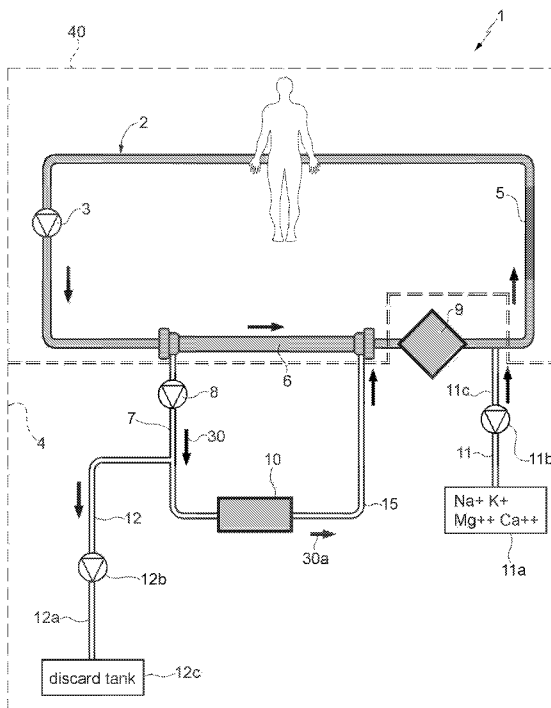


FIG. 1

(57) Abstract: The present invention concerns an extracorporeal circuit (1, 100, 200, 300, 400, 500) for removing CO₂ from blood comprising a blood withdrawal line (2) for withdrawing blood from the patient, a filtration unit (6) for producing plasma water (30) and a line for returning the blood (5) to the patient, defining a main circuit (40); the extracorporeal circuit further comprises a decarbonating group (4) comprising a secondary circuit (7) for the recirculation of plasma water, means (12) for removing a fraction of said plasma water (30), a CO₂ exchanger (9), a cationic resin charged with H⁺ ions (10) set upstream of the CO₂ exchanger (9) and adapted to generate acid plasma water (30a), means (15) for the infusion of the acid plasma water (30a) upstream of the CO₂ exchanger (9) and means (11) for the infusion of ions in a solution downstream of the CO₂ exchanger (9).



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"EXTRACORPOREAL CIRCUIT FOR REMOVAL OF CO₂ FROM BLOOD"

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application claims priority from Italian patent application no. 102018000005641 filed on 23/05/2018, the entire disclosure of which is incorporated herein by reference.

TECHNICAL FIELD

10 The present invention relates to an extracorporeal circuit for removing CO₂ from blood.

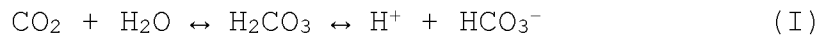
The extracorporeal removal of CO₂ from blood is necessary when the pulmonary function has to be supplemented, even only partially, when said function is compromised due to various pathologies.

BACKGROUND ART

In general, extracorporeal circuits for removing CO₂ from blood entail drainage of the patient's blood into an extracorporeal circuit to be artificially oxygenated and decarbonated by means of a gas exchanger, such as an oxygenator. More specifically, in a veno-venous extracorporeal system, part of the venous blood which returns towards the right atrium of the heart is collected in the extracorporeal circuit and pumped into the oxygenator, from which it is then reinfused into the venous system.

The most commonly used oxygenator devices are membrane oxygenators in which the blood and the oxygen (or an oxygen-rich mixture) are made to flow on opposite sides of a membrane. This type of apparatus therefore acts on the quantity of CO₂ dissolved in the blood which is actually a limited portion of the total CO₂ content. In fact, it is known that 90% of the CO₂ transported in the blood is in the form of bicarbonate ions according to the chemical balance (I) shown

below.



5 A solution for increasing removal of CO₂ from blood by means of membrane oxygenators is that of intervening on the chemical balance (I) inducing an increase in the percentage of gaseous CO₂. This increase in the concentration of gaseous CO₂ subject to removal by the oxygenator favours removal of the total CO₂.

10

One of the ways of intervening on the chemical balance (I) in favour of the gaseous CO₂ is exogenous acidification. Said acidification is achieved by adding an acid substance in the extracorporeal circuit upstream of the oxygenator.

15

By converting the bicarbonate ions into dissolved CO₂, the acidification increases the transmembrane pCO₂ gradient, and therefore increases the transfer of CO₂ through the oxygenator membrane. Exogenous acidification of the blood allows removal
20 of the equivalent of 50% of the total production of CO₂ of an adult male from extracorporeal blood at a rate of 250 ml/min.

Alternatively, a technique based on ventilation of the acidified dialysate has also been developed, which has shown a
25 slightly lower efficiency (10-15%) compared to direct ventilation of the blood, but reduces the exogenous contact surface with the blood and can therefore offer possible advantages.

30 In both cases, the acidification is obtained by infusion of a concentrated solution of metabolizable organic acids, for example lactic acid. However, when infused exogenously, despite their high clearance, said acids can cause a certain level of metabolic acidosis and an increase in the production
35 of total corporeal CO₂, thus reducing the effectiveness of the extracorporeal removal of CO₂ in reducing the minute

ventilation of the patient.

Therefore, as will be obvious to a person skilled in the art, said addition of acid can reduce the effectiveness of the extracorporeal technique of CO₂ removal and can entail a series of drawbacks that must be dealt with in order not to alter the patient's homeostasis.

DISCLOSURE OF INVENTION

10 The object of the present invention is therefore to produce an extracorporeal circuit for removing CO₂ from blood, able to increase removal of the CO₂ by intervening on the chemical balance (I) without recourse to the administration of an exogenous acid, while at the same time guaranteeing high
15 safety levels.

Said object is achieved by the present invention relative to an extracorporeal circuit for removing CO₂ from blood, the essential characteristics of which are described in claim 1,
20 and the preferred and/or auxiliary characteristics of which are described in the dependent claims.

In particular, an extracorporeal circuit is provided for removing CO₂ from blood comprising a withdrawal line for withdrawing blood from the patient, a filtration unit for the production of plasma water and a line for returning the blood to the patient defining a main circuit. The extracorporeal circuit further comprises a decarbonation group comprising means for removal of a fraction of said plasma water, a
30 cationic resin charged with H⁺ ions adapted to generate acid plasma water, a CO₂ exchanger, means for infusion of the acid plasma water upstream of the CO₂ exchanger and means for the infusion of a solution of electrolytes downstream of said CO₂ exchanger.

35

Advantageously, the use of a cationic resin charged with H⁺

ions to treat the plasma water, for example a dialysate or an ultrafiltrate, allows replacement, in a controlled manner, of the positively charged ions present in said solution, without the addition of exogenous acids.

5

In particular, the H⁺ charged cationic resin is able to replace the calcium, sodium, potassium and magnesium ions present in the plasma water with hydrogen ions, leading to a regional acidification of this solution forming an acid solution.

10

The regional acidification allows improvement in the extracorporeal removal of carbon dioxide, acting on the chemical balance (I) shown above.

15 Furthermore, the H⁺ charged cationic resin, by removing sodium ions above all, since they are present in greater quantities in the blood, allows greater acidification of the plasma water than the systems known in the art with the same volume of liquid treated. A further advantage of the use of an H⁺
20 charged cationic resin consists in the fact that said resin works without the addition of exogenous liquids, simplifying the hydroelectrolytic balance of the blood after the treatment before reinfusion in the patient.

25 The device of the invention, acting on the concentration of cations in the blood, can furthermore be used not only for removing CO₂ but also to simultaneously carry out a continuous renal replacement therapy.

30 Continuous renal replacement therapy (CRRT) is an extracorporeal support technique widely used in the treatment of patients affected by acute kidney failure and other pathological conditions like sepsis and multi-organ dysfunction. During CRRT the patient's blood is treated
35 through diffusion, conduction and absorption mechanisms.

In one embodiment, the filtration unit is a filter selected from the group consisting of a haemodialysis filter, a haemofilter and a dialyser.

- 5 Preferably the cationic resin is a resin provided with sulphonic groups or carboxylic groups.

BRIEF DESCRIPTION OF THE DRAWINGS

10 For a better understanding of the invention, it will now be described in detail for purely illustrative non-limiting purposes with the help of the figures of the attached drawings, in which:

- Figure 1 illustrates a first embodiment of the invention;
- Figure 2 illustrates a second embodiment of the invention;
- 15 - Figure 3 illustrates a third embodiment of the invention;
- Figure 4 illustrates a fourth embodiment of the invention;
- Figure 5 illustrates a fifth embodiment of the invention;
- Figure 6 illustrates a sixth embodiment of the invention.

20 BEST MODE FOR CARRYING OUT THE INVENTION

In figure 1 an extracorporeal circuit for removing blood according to a first embodiment of the present invention is indicated overall by 1.

25 The circuit 1 comprises a withdrawal line for withdrawing blood 2 from the patient, on which a pump 3 acts, for example a peristaltic pump, a filtration unit 6, for example a haemodialysis filter, a decarbonating group 4 and a line for returning the blood 5 to the patient. The withdrawal line for
30 withdrawing blood 2 from the patient, the filtration unit 6, and the line for returning the blood 5 to the patient define a main circuit 40.

The haemodialysis filter 6 is connected to a secondary circuit
35 7 for recirculation of the plasma water 30, in this case dialysate, on which a pump 8 acts.

The decarbonating group 4 comprises a cationic resin charged with H⁺ ions 10 adapted to generate acid plasma water 30a positioned downstream of the pump 8 on the secondary circuit 7
5 of the plasma water 30.

The decarbonating group 4 further comprises an oxygenator 9 arranged on the main circuit 40 downstream of the haemodialysis filter 6 along the return line 5 for returning
10 the blood to the patient.

Advantageously the cationic resin 10 is able to retain the calcium, potassium and magnesium ions but above all the sodium ions, present in large quantities in the plasma water 30,
15 replacing them with H⁺ ions and generating acid plasma water 30a at the resin outlet.

Advantageously the acidification of the plasma water 30 causes a shift in the chemical balance (I) in favour of the gaseous
20 CO₂ in the acid plasma water 30a in recirculation. The gaseous CO₂ is then removed by the action of the oxygenator 9, for example a bubble oxygenator. In this way, it is possible to improve removal of the CO₂ from the plasma water 30a.

25 The acid plasma water 30a is returned to the haemodialysis filter 6, inside which it will function as a dialysis liquid, by means of the line 15. The blood flowing out of the haemodialysis filter 6 is then deprived of the CO₂ by the oxygenator 9. The blood flowing out of the oxygenator 9 will
30 therefore have an electrolytic imbalance due to the removal of cations by the cationic resin 10. To re-balance the concentration of the electrolytes in the blood before reinfusion to the patient, downstream of the oxygenator 9, along the line 5, means 11 are provided for the reinfusion of
35 sodium, potassium, calcium and magnesium ions in solution to re-balance the quantity of cations lost at the level of the

cationic resin 10. Said means 11 for the reinfusion of ions consist for example in one or more sacs 11a each containing an electrolytic solution, a pump 11b and an infusion line 11c. For example, an electrolytic solution comprising NaOH, KOH, 5 NaCl or NaHCO₃ can be infused and, separately, a solution comprising calcium ions and magnesium ions. Said solutions can also include glucose if CRRT is also performed.

The circuit 1 further comprises, upstream of the cationic 10 resin 10, means 12 for removing part of the plasma water. Said means 12 for removing part of the plasma water consist, for example, of a removal line 12a, a peristaltic pump 12b and a discard tank 12c.

15 The removal of part of the plasma water is necessary to compensate for the increase in volume of the plasma water, which occurs following addition of the electrolytic solution through the means 11. Therefore, to respect the hydroelectric balance of the system, the quantity of water removed by the 20 means 12 must be equal to the quantity of water reinfused with the electrolytic solution through the means 11.

Likewise, the electrolytic solution reinfused with the means 11 must contain a quantity of sodium, potassium, calcium and 25 magnesium equal to that removed with the cationic resin 10 plus that removed with the means 12 for removing part of the plasma water.

Alternatively, when the circuit of the invention is used, not 30 only for removing the CO₂ but also for renal therapy, the quantity of water and electrolytes removed by the means 12 can be different from that reinfused with the means 11.

Lastly, the blood flowing out of the haemodialysis filter 6 is 35 returned to the patient by means of a line for returning the blood 5.

In the circuit of figure 1, for example, the blood flowing out of the patient can be set to 200 ml/min, the flow of the plasma water through the cationic resin is therefore 10-25
5 ml/min.

Figures 2 to 6 illustrate alternative embodiments of the circuit of figure 1 according to the present invention; the details similar or equal to those already described are
10 indicated for the sake of simplicity by the same reference numbers.

In particular, figure 2 illustrates a second embodiment of the invention which represents a variation 100 of the circuit
15 illustrated in figure 1. In this case, the plasma water 30 flowing out of the haemodialysis filter is split into two flows, 30b and 30c respectively, at the connection point 14. Then part of the plasma water, indicated by 30c, is treated by the cationic resin 10, while the remaining part of the plasma
20 water 30b is sent back to the connection point 17.

The acid plasma water 30a flowing out of the cationic resin 10 is recombined by means of the line 18 with the plasma water 30b and then conveyed along the line 15 to the oxygenator 9
25 which, in this embodiment, is on the secondary circuit 7.

Advantageously, this embodiment reduces the exogenous contact surface between the blood and the extracorporeal circulation system and reduces the pH variations to which the blood is
30 exposed.

In this embodiment, for example, the blood flow leaving the patient can be set to 200 ml/min and the flow of the ultrafiltrate from the haemodialysis filter can be set to 400-
35 1000 ml/min.

In figure 3 a third embodiment of the invention is illustrated which represents a variation 200 of the circuit illustrated in figure 1. In this case, the oxygenator 9 is positioned downstream of the haemodialysis filter 6 on the main circuit 40 on the line for return of the blood 5 to the patient and the plasma water flowing out of the cationic resin is returned to the main circuit of the blood on line 5 upstream of the oxygenator 9. In this embodiment, the oxygenator 9 is a membrane oxygenator. In this embodiment, for example, the blood flowing out of the patient can be set to 200 ml/min and the flow of the ultrafiltrate from the haemodialysis filter can be set to 10-25 ml/min.

In all the embodiments of the present invention, a gas trap can also be inserted downstream of the cationic resin 10 but upstream of the oxygenator 9 to further favour elimination of the carbon dioxide and prevent the accumulation of gas.

All the embodiments of the present invention can furthermore include a regional blood anticoagulation system. For example, the circuit of Figure 1 can be modified as illustrated in Figure 4. In particular, in the circuit 300, the plasma water flowing out of the haemodialysis filter 6 is split into two flows at the connection point 13. A part of the flow is directed to the cationic resin 10 while the remaining part is treated with a group for removal of the calcium, such as, for example, a cationic exchange resin 16 charged with sodium and potassium ions. Said resin 16 charged with sodium ions retains calcium ions, releasing sodium ions. The plasma water flowing out of the resin 16 charged with sodium ions is partly recombined with the acid plasma water 30a on the line downstream of the cationic resin 10 and partly sent back on the line 2 upstream of the haemodialysis filter by means of the line 20 to carry out regional anticoagulation of the blood in the circuit. Restoration of the correct hydro-electrolytic balance in the blood is then carried out by the means 11 for

the reinfusion of ions and the means 12 for removal of the plasma water.

The circuit of Figure 2 can be modified as in Figures 5 and 6.

- 5 In particular, in the circuit 400 of figure 5, a cationic exchange resin 16 charged with sodium and potassium ions is arranged upstream of the connection point 14 on the secondary circuit 7.
- 10 Alternatively, in the circuit 500 of figure 6, the cationic exchange resin 16 charged with sodium and potassium ions is present downstream of the oxygenator 9. In both cases part of the plasma water flowing out of the resin 16 is re-introduced into the circuit at the height of the withdrawal line for
- 15 withdrawing blood from the patient 2 by means of the line 20 so as to cause regional anticoagulation of the blood.

CLAIMS

1. An extracorporeal circuit (1, 100, 200, 300, 400, 500) for removing CO₂ from blood comprising a blood withdrawal line (2) for withdrawing blood from the patient, a filtration unit (6) for producing plasma water (30) and a line for returning the blood (5) to the patient, defining a main circuit (40); said extracorporeal circuit being characterised in that it comprises a decarbonating group (4) comprising a secondary circuit (7) for the recirculation of plasma water, means (12) for removing a fraction of said plasma water (30), a CO₂ exchanger (9), a cationic resin charged with H⁺ ions (10) set upstream of said CO₂ exchanger (9) and adapted to generate acid plasma water (30a), means (15) for the infusion of said acid plasma water (30a) upstream of said CO₂ exchanger (9) and means (11) for the infusion of ions in a solution downstream of said CO₂ exchanger (9).

2. The extracorporeal circuit according to claim 1, characterised in that said filtration unit (6) is a filter selected from the group consisting of a haemodialysis filter, a haemofilter and a dialyser.

3. The extracorporeal circuit according to claim 1, characterised in that said cationic resin charged with H⁺ ions is selected from the group consisting of a cationic resin provided with sulphonic group and cationic resin provided with carboxylic groups.

4. The extracorporeal circuit according to claim 1, characterised in that said CO₂ exchanger (9) is present on the main circuit (40) on said line for returning the blood (5) to the patient downstream of said filtration unit (6).

5. The extracorporeal circuit according to claim 1, characterised in that said CO₂ exchanger (9) is present on said secondary circuit (7) downstream of said cationic resin

charged with H⁺ ions (10).

6. The extracorporeal circuit according to any one of the preceding claims, characterised in that it further comprises a
5 gas trap arranged upstream of said CO₂ exchanger (9) and downstream of said cationic resin charged with H⁺ ions (10).

7. The extracorporeal circuit according to any one of the preceding claims, characterised in that it further comprises a
10 group for removing calcium (16) arranged on the secondary circuit (7) for the recirculation of plasma water.

8. The extracorporeal circuit according to the preceding claim, characterised in that said group for removing calcium
15 is a cationic exchange resin (16) charged with sodium and potassium ions.

9. The extracorporeal circuit according to the preceding claim, characterised in that said group for removing calcium
20 (16) is positioned in parallel to said cationic resin charged with H⁺ ions (10).

10. The extracorporeal circuit according to the preceding claim, characterised in that said group for removing calcium
25 (16) is positioned in series to said cationic resin charged with H⁺ ions (10).

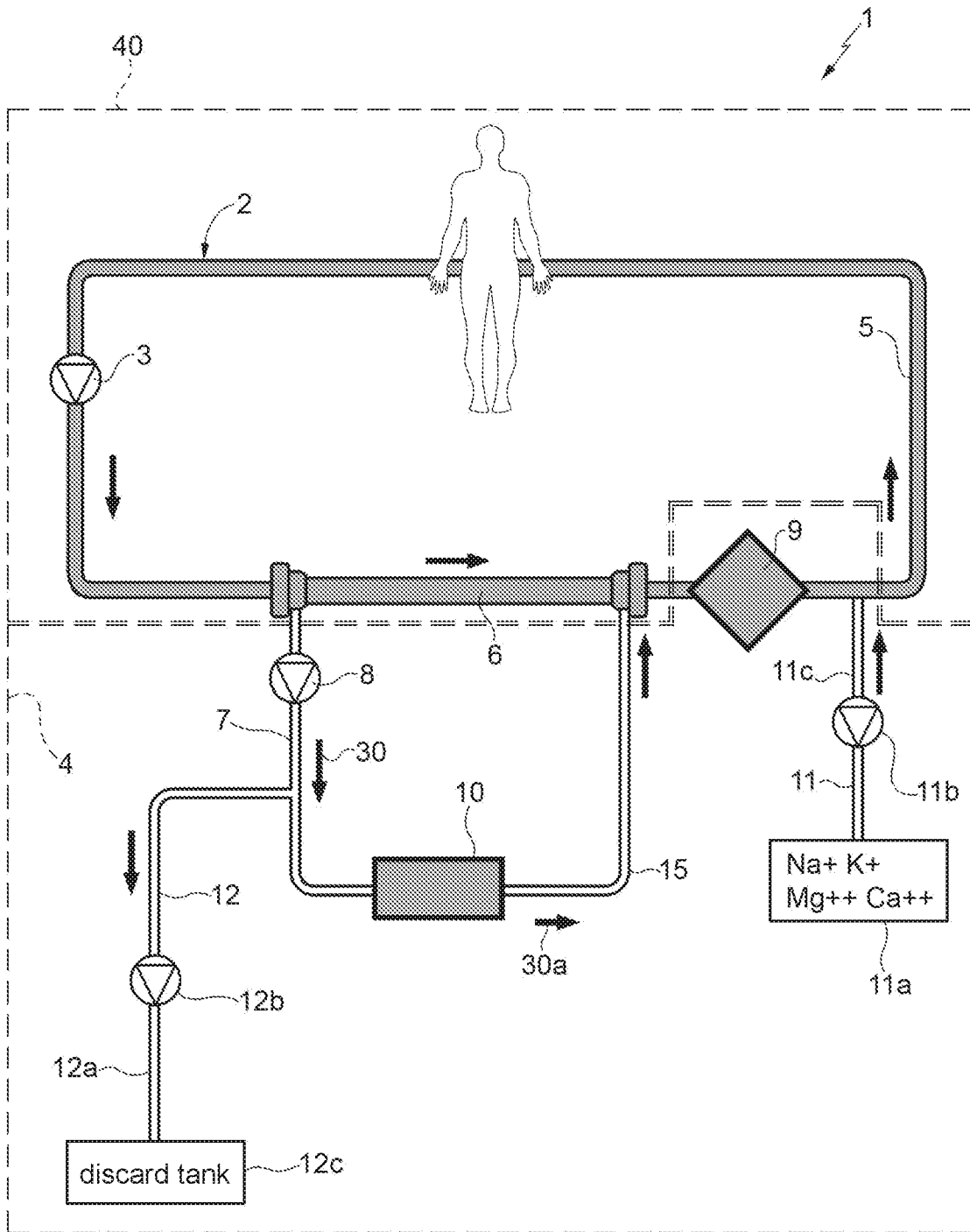


FIG. 1

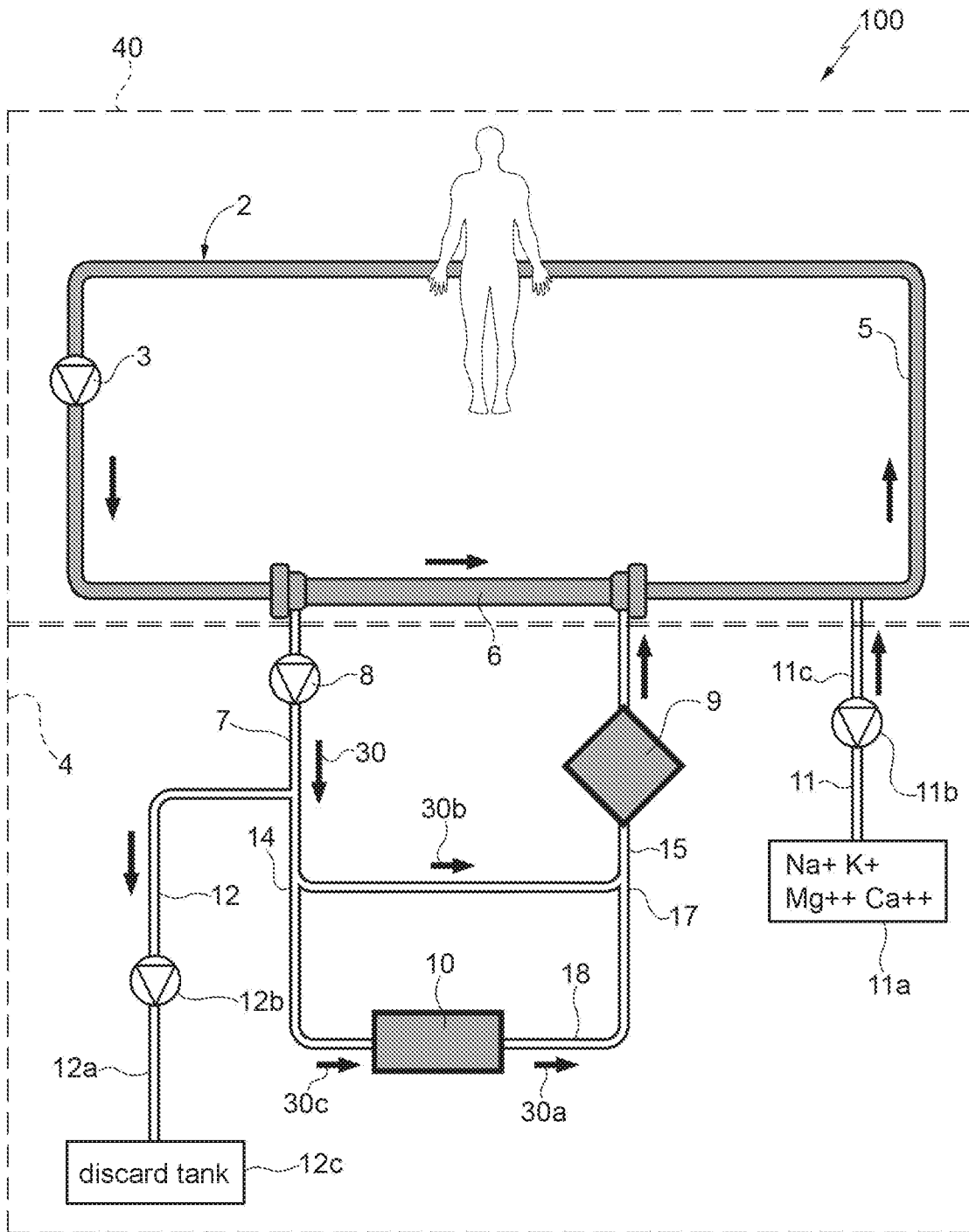


FIG. 2

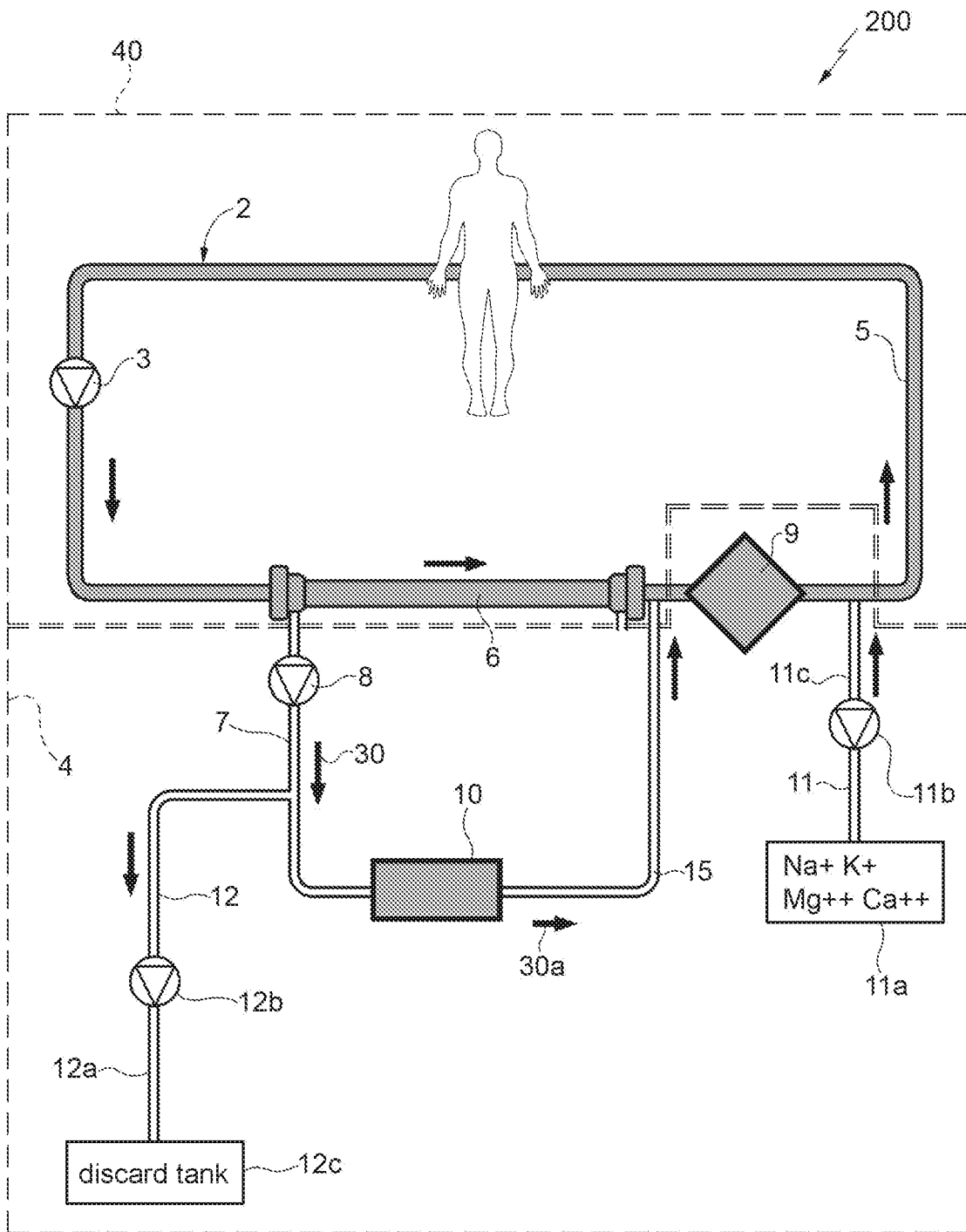


FIG. 3

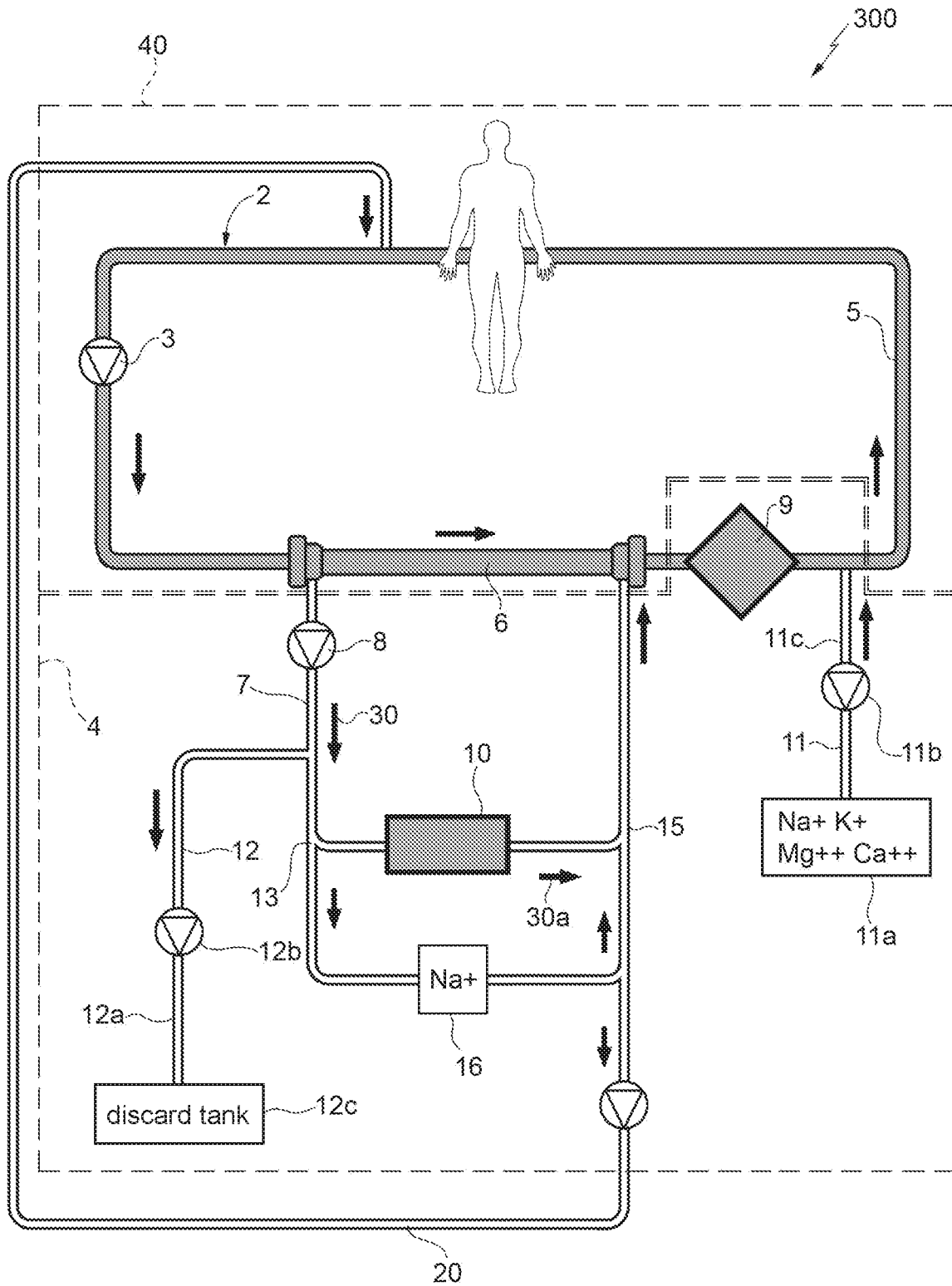


FIG. 4

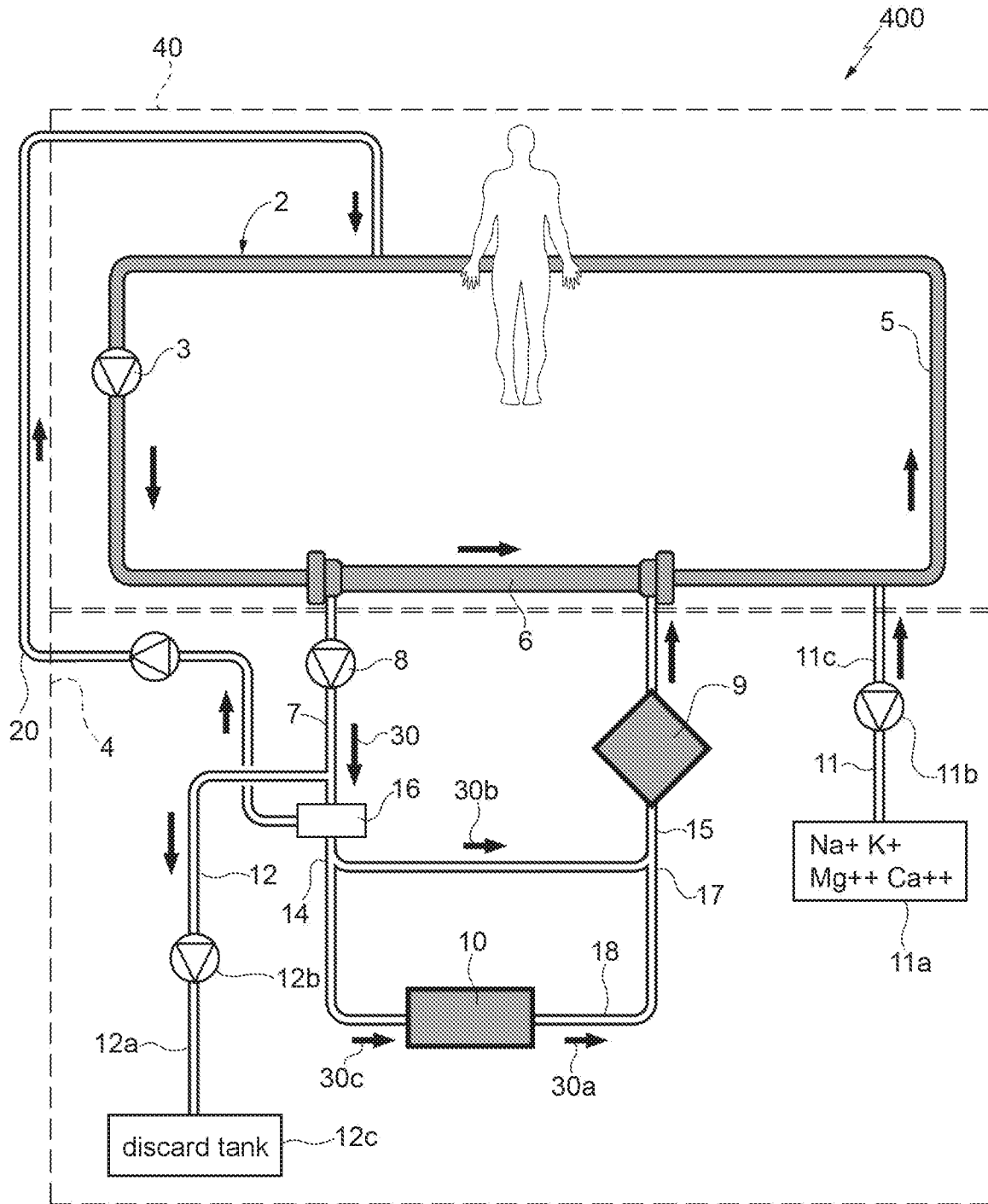


FIG. 5

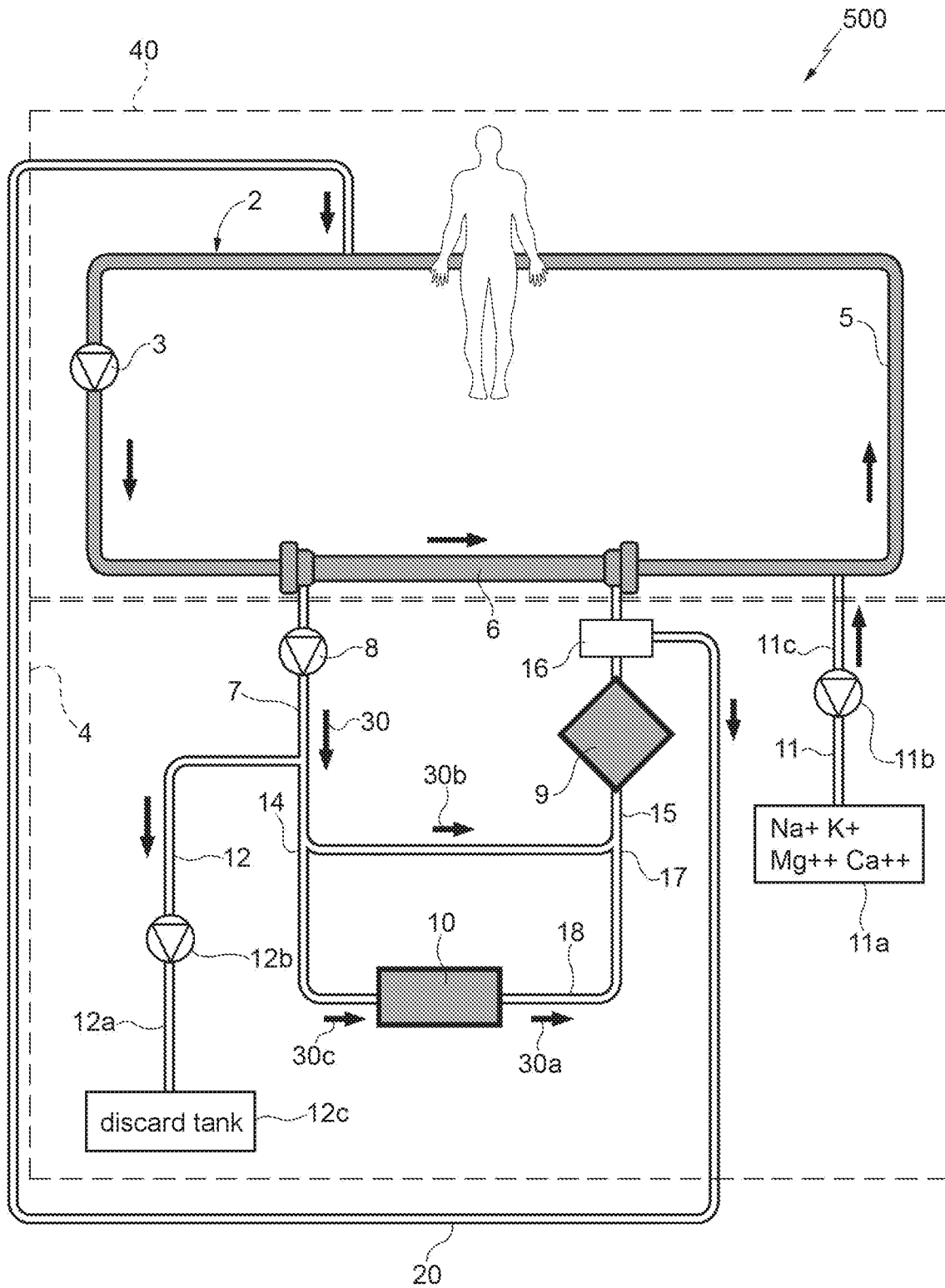


FIG. 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2019/054288

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61M1/34 A61M1/36 B01D15/36 A61M1/16
 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 B01D

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	US 2012/035523 A1 (FARNIKOVA HELENA [DE]) 9 February 2012 (2012-02-09) page 1, paragraph 23 - page 2, paragraph 34 page 2, paragraph 36 - page 2, paragraph 49 figure 2	1
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Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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

International application No
PCT/IB2019/054288

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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