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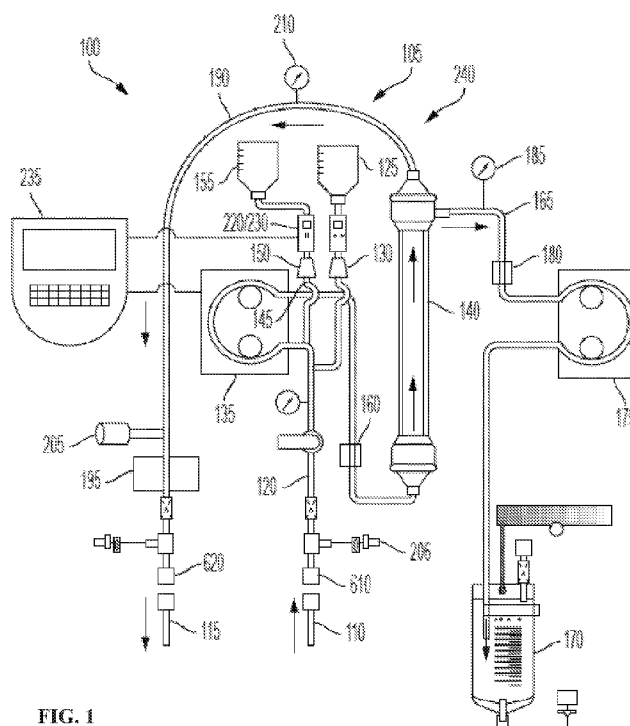


FIG. 1

(57) Abstract: Methods and systems for providing continuous renal replacement therapy (CRRT) to a patient are provided. The system includes a hemofiltration unit that provides continuous venovenous hemofiltration (CVVH), a replacement fluid flow regulator configured to regulate the flow of a replacement fluid, an anticoagulant flow regulator configured to pump an anticoagulant, and a blood warmer. The system provides enhanced communication between the hemofiltration unit and the replacement fluid flow regulator. The system may be used to treat patients having renal insufficiency, such as acute kidney injury.

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SYSTEM FOR CONTINUOUS RENAL REPLACEMENT THERAPY

[0001] CROSS-REFERENCE TO RELATED APPLICATIONS

[0002] This application claims the benefit of U.S. Provisional Application No. 62/783,345, filed December 21, 2018 under the laws of the United States of America and other countries.

[0003] BACKGROUND

[0004] FIELD OF THE DISCLOSURE

[0005] The present disclosure relates generally to continuous renal replacement therapy (CRRT). More particularly, this disclosure relates to an improved method and system for providing continuous venovenous hemofiltration (CVVH) to a pediatric patient.

[0006] BACKGROUND

[0007] Continuous renal replacement therapy (CRRT) is commonly used to provide renal support for critically ill patients with acute kidney injury. While neonates, infants, and small children experience higher rates of acute kidney injury than most critically ill populations, they receive renal support infrequently. The technical challenges of traditional machines make CRRT initiation in small children very difficult. For instance, most traditional machines are intended for use on adults and utilize a high extracorporeal volume (ECV). When these larger machines are used, the machines require that small children receive CRRT with proportionally larger ECV, filters, blood flows, clearance rates, and vascular catheters. This puts the infant or child at added risk of harm during the CRRT initiation process.

[0008] To mitigate concerns posed by CRRT machines with large ECV in relation to blood volume size, the AQUADEX™, a machine designed to perform ultrafiltration in adults with heart failure, has been adapted to provide pre-filter replacement fluids in order to perform CRRT in neonates and small children. The adapted machine maintains electrolyte and water homeostasis, clears waste products, and reduces the ECV, which improves the ability to initiate CRRT in small children who require renal support.

[0009] While this modified machine has greatly improved the ability to initiate therapy in neonates and small children, the modified machine does not operate without risk. For instance, the adapted system relies on a pre-replacement intravenous (IV) fluid flow regulator that does not communicate with the extracorporeal pump. If one stops, the other will continue to function absent human intervention. In addition, the current IV fluid delivery

systems are designed to operate under low pressure conditions. If the flow regulator delivers fluid into a high pressure system, the amount of delivered fluid can differ.

[0010] Thus, there is a need for improved communication between the fluid replacement flow regulator and the extracorporeal pump as well as a more precise fluid delivery calculation system.

[0011] **SUMMARY**

[0012] The following presents a simplified summary in order to provide a basic understanding of some aspects of the claimed subject matter. This summary is not an extensive overview. It is not intended to identify key or critical elements or to delineate the scope of the claimed subject matter. Its sole purpose is to present some concepts in a simplified form as a prelude to the more detailed description that is presented later.

[0013] In a first aspect, a system for providing continuous renal replacement therapy to a patient is provided, the system comprising a hemofiltration unit comprising a withdrawn blood line connecting a hemofilter to a first catheter connector; a blood pump positioned to propel blood in the withdrawn blood line from the first catheter connector to the hemofilter; a filtrate line connected to receive a filtrate from the hemofilter; an ultrafiltration pump configured to propel the filtrate from the filtrate line by exerting negative pressure on the hemofilter; a return line connected to receive a retentate from the hemofilter and terminating in a second catheter connector; a port for sampling or fluid infusion in at least one of the withdrawn blood line and the return line; and a hemofiltration control unit configured to control the blood pump and to measure the functioning of the blood pump; an anticoagulant flow regulator configured to pump anticoagulant from an anticoagulant source into the withdrawn blood line between the first catheter connector and the hemofilter; a replacement fluid flow regulator configured to regulate the flow of a replacement fluid from a replacement fluid source into one or both of the withdrawn blood line and the return line, and comprising a replacement fluid flow regulator control unit configured to control the replacement fluid flow regulator and to measure the functioning of the replacement fluid flow regulator; and a blood warmer positioned to warm the retentate prior to infusion into the patient; wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to modulate the functioning of the blood pump based on the functioning of the replacement fluid flow regulator, and to modulate the functioning of the replacement fluid flow regulator based on the functioning of the blood pump.

[0014] In a second aspect, a system for providing continuous renal replacement therapy to a patient is provided, the system comprising a hemofiltration unit comprising a

withdrawn blood line connecting a hemofilter to a first catheter connector; a blood pump positioned to propel blood in the withdrawn blood line from the first catheter connector to the hemofilter; a filtrate line connected to receive a filtrate from the hemofilter; an ultrafiltration pump configured to propel the filtrate from the filtrate line by exerting negative pressure on the hemofilter; a return line connected to receive a retentate from the hemofilter and terminating in a second catheter connector; a sampling port in the return line; and a hemofiltration control unit configured to control the blood pump; an anticoagulant flow regulator configured to regulate the flow of an anticoagulant from an anticoagulant source into the withdrawn blood line between the first catheter connector and the hemofilter; a replacement fluid flow regulator configured to regulate the flow of a replacement fluid from a replacement fluid source into the withdrawn blood or the return line; a replacement fluid dose meter that measures the amount of replacement fluid delivered by at least one of weight and volume; and a blood warmer positioned to warm the retentate prior to infusion into the patient; wherein the hemofiltration control unit is in communication with the replacement fluid dose meter so as to modulate the functioning of the blood pump based on the dose of replacement fluid administered.

[0015] In a third aspect, a method for treating renal insufficiency in a patient in need thereof is provided. The method comprises withdrawing blood from the patient; processing the blood with the system described in the first aspect or the second aspect; and reinfusing the processed blood into the patient.

[0016] **BRIEF DESCRIPTION OF THE DRAWINGS**

[0017] Further features and advantages can be ascertained from the following detailed description that is provided in connection with the drawings described below:

[0018] FIG. 1 is a schematic diagram illustrating the operation and fluid path of the CRRT system according to one embodiment of the present disclosure.

[0019] FIG. 2 is a schematic diagram of an embodiment of a computing device for controlling the operation of the CRRT system associated with FIG. 1.

[0020] **DETAILED DESCRIPTION**

[0021] DEFINITIONS

[0022] Unless otherwise defined, all terms (including technical and scientific terms) used herein have the same meaning as commonly understood by one of ordinary skill in the art of this disclosure. It will be further understood that terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the specification and should not be interpreted in an idealized

or overly formal sense unless expressly so defined herein. Well known functions or constructions may not be described in detail for brevity or clarity.

[0023] The terms “about” and “approximately” shall generally mean an acceptable degree of error or variation for the quantity measured given the nature or precision of the measurements. Typical, exemplary degrees of error or variation are within 20 percent (%), preferably within 10%, and more preferably within 5% of a given value or range of values. Numerical quantities given herein are approximate unless stated otherwise, meaning that the term “about” or “approximately” can be inferred when not expressly stated.

[0024] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. As used herein, the singular forms “a,” “an,” and “the” are intended to include the plural forms as well (i.e., at least one of whatever the article modifies), unless the context clearly indicates otherwise.

[0025] With reference to the use of the word(s) “comprise” or “comprises” or “comprising” in the foregoing description and/or in the following claims, unless the context requires otherwise, those words are used on the basis and clear understanding that they are to be interpreted inclusively, rather than exclusively, and that each of those words is to be so interpreted in construing the foregoing description and/or the following claims.

[0026] The term “consisting essentially of” means that, in addition to the recited elements, what is claimed may also contain other elements (steps, structures, ingredients, components, etc.) that do not adversely affect the operability of what is claimed for its intended purpose. Such addition of other elements that do not adversely affect the operability of what is claimed for its intended purpose would not constitute a material change in the basic and novel characteristics of what is claimed.

[0027] Terms such as “at least one of A and B” should be understood to mean “only A, only B, or both A and B.” The same construction should be applied to a longer list (e.g., “at least one of A, B, and C”).

[0028] The terms “first”, “second”, “third,” and the like are used herein to describe various features or elements, but these features or elements should not be limited by these terms. These terms are only used to distinguish one feature or element from another feature or element. Thus, a first feature or element discussed below could be termed a second feature or element, and similarly, a second feature or element discussed below could be termed a first feature or element without departing from the teachings of the present disclosure.

[0029] The terms “treatment”, “treat” and “treating” as used herein refers a course of action initiated after the onset of a clinical manifestation of a disease state or condition so as

to eliminate or reduce such clinical manifestation of the disease state or condition. Such treating need not be absolute to be useful.

[0030] The term “in need of treatment” as used herein refers to a judgment made by a caregiver that a patient requires or will benefit from treatment. This judgment is made based on a variety of factors that are in the realm of a caregiver's expertise, but that includes the knowledge that the patient is ill, or will be ill, as the result of a condition that is treatable by a method or device of the present disclosure.

[0031] The term “individual”, “subject” or “patient” as used herein refers to any animal, including mammals, such as mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, and humans. The term may specify male or female or both, or exclude male or female.

[0032] In this disclosure terms such as “administering” or “administration” include acts such as prescribing, dispensing, giving, or taking a substance such that what is prescribed, dispensed, given, or taken is actually contacts the patient's body externally or internally (or both). It is specifically contemplated that instructions or a prescription by a medical professional to a subject or patient to take or otherwise self-administer a substance is an act of administration.

[0033] SYSTEM FOR CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)

[0034] Figure 1 illustrates the operation and fluid path of the CRRT system 100 according to an exemplary embodiment of the present disclosure. The CRRT system 100 of the present disclosure advantageously provides an extracorporeal circuit 105 having a low extracorporeal volume (ECV) that is particularly suitable for use with infants and small children (although suitable in some instances for larger children and adults). In one embodiment, the ECV of the present extracorporeal circuit 105 is about 20 mL to about 40 mL. In another embodiment, the ECV of the present extracorporeal circuit 105 is about 30 mL to about 40 mL. In still another embodiment, the ECV of the present extracorporeal circuit 105 is about 33 mL. Higher ECV may be used in some instances, for example for non-pediatric applications.

[0035] To initiate treatment, access points for the withdrawal and return of blood are inserted to suitable peripheral or central veins on a patient. Blood is withdrawn from the patient through a withdrawal access point 110 and returned to the patient through a return access point 115. The withdrawal access point 110 and the return access point 115 may include a needle, a central line, or a catheter. Once the blood is withdrawn from the patient,

the blood enters a withdrawn blood line 120 and into a hemofiltration unit 240. The withdrawn blood line 120 may be made of any type of suitable plastic tubing, such as polyvinyl chloride (PVC) tubing.

[0036] In some embodiments, the withdrawn blood line 120 is operatively connected to an anticoagulant source 125. “Anticoagulant” as used herein refers to any substance having the effect of inhibiting the coagulation of blood. Examples of anticoagulants include, but are not limited to, heparin, warfarin, rivaroxaban, dabigatran, apixaban, citrate, and edoxaban. The anticoagulant source 125 may be operatively connected to the withdrawn blood line 120 by any suitable connector to provide the anticoagulant. For instance, the anticoagulant source 125 may be operatively connected to the withdrawn blood line 120 by a Y-connector. In a preferred embodiment the anticoagulant source 125 infuses anticoagulant into the withdrawn blood line 120 upstream of the blood pump 136. In one embodiment, an anticoagulant flow regulator 130 is configured to pump the anticoagulant from the anticoagulant source 125 into the withdrawn blood line 120. Such flow regulators are generally referred to in the art as “pumps,” even when they merely control the rate of flow caused by gravity instead of actively pumping the anticoagulant. Suitable “pumps” are commercially available, such as the ALARIS family of pumps (Becton, Dickinson and Company Franklin Lakes, NJ).

[0037] In some embodiments of the system, the withdrawn blood line 120 may be operatively connected to a hematocrit sensor 215. The hematocrit sensor 215 can be configured to measure the volume percentage of red blood cells in the blood in the withdrawn blood line 120. The hematocrit sensor 215 may also be controlled by software that can automatically stop the removal of fluid from the patient if the hematocrit hits a prescribed hematocrit limit.

[0038] Blood flow is controlled by a blood pump 135 that is positioned to propel blood in the withdrawn blood line 120 to a filter 140. In one embodiment, the blood pump 135 is a roller pump. In this aspect, as the blood pump 135 rotates, rollers compress a segment of the withdrawn blood line 120 to generate blood flow. The blood pump 135 provides negative pressure through the withdrawn blood line 120 to bring blood from the patient to the filter 140. The blood pump 135 may be rotated by a motor under microprocessor control. In one embodiment, the blood pump 135 may be designed to operate from about 10 mL/minute to about 40 mL/minute. In another embodiment, the blood pump 135 may be designed to operate from about 15 mL/minute to about 35 mL/minute. In still another embodiment, the

blood pump 135 may be designed to operate from about 20 mL/minute to about 30 mL/minute.

[0039] While blood is pumped through the withdrawn blood line 120, replacement fluid is infused into the withdrawn blood line 120 through a port 145, for instance, a pigtail. In one embodiment, a replacement fluid flow regulator 150 is configured to pump the replacement fluid into the withdrawn blood line 120. Again, such flow regulators are generally referred to in the art as “pumps,” even when they merely control the rate of flow caused by gravity instead of actively pumping the replacement fluid. For example, the replacement fluid flow regulator 150 may be a large volume infusion pump such as the ALARIS™ pump module. In another embodiment, the replacement fluid flow regulator 150 is configured to regulate the flow of the replacement fluid into the withdrawn blood line 120. The replacement fluid may be stored in a replacement fluid source 155 that is operatively connected to the port 145. The replacement fluid can be infused into the withdrawn blood line 120 at any point before the blood pump 135. In some embodiments of the system the replacement fluid is infused into the return line 190 post-filter 140 (in theory replacement fluid could be infused at multiple points in the extracorporeal circuit 105).

[0040] In some embodiments, as the blood travels from the blood pump 135 to the filter 140, the blood passes through an air detector 160. The air detector 160 can detect air in amounts exceeding about 50 microliters. If an air bubble is detected, the blood pump 135 is stopped instantaneously. In this embodiment, since air can only enter the extracorporeal circuit 105 from the pre-pump segment, the air detector 160 should be positioned before the filter 140. In another embodiment, the air detector 160 should be positioned after the filter 140.

[0041] As the blood travels from the blood pump 135, the blood passes through the filter 140. The infusion of replacement fluids allows for the use of continuous venovenous hemofiltration (CVVH). In this aspect, the filter 140 is a hemofilter having a semi-permeable membrane. In CVVH, a high rate of ultrafiltration across the semi-permeable hemofilter membrane is created by a hydrostatic gradient, and solute transport occurs by convection (in some cases by negative pressure exerted by an ultrafiltration pump 175). Small molecular weight solutes are entrained in the bulk flow of water across the membrane, while the membrane prevents red blood cells, proteins, and other high molecular weight blood components from passing through. In one embodiment, the hemofilter is not configured for countercurrent dialysis.

[0042] In some embodiments, the hemofilter has an effective filtration area of about 0.09 m² to about 0.3 m². In another embodiment, the hemofilter has an effective filtration area of about 0.1 m² to about 0.2 m². In still another embodiment, the hemofilter has an effective filtration area of about 0.12 m². Higher effective filtration areas may be used in some instances, for example for non-pediatric applications. The hemofilter may be composed of a porous material. For example, the hemofilter may be composed of polysulfone membranes.

[0043] The hemofilter has a sieving coefficient that allows for the passage of water and small solutes, such as urea, creatinine, and vitamin B12, but prevents the passage of larger components, such as red blood cells, proteins (such as albumin), and other blood components. As used herein, “sieving coefficient” refers to the ratio of solute filtrate concentration to the respective solute plasma concentration. A sieving coefficient of 1 indicates unrestricted transport while a sieving coefficient of zero indicates there is no transport. In one embodiment, the hemofilter has a sieving coefficient for urea of about 0.98. In another embodiment, the hemofilter has a sieving coefficient for creatinine of about 0.98. In still another embodiment, the hemofilter has a sieving coefficient for vitamin B12 of about 0.98. In yet another embodiment, the hemofilter has a sieving coefficient for albumin of less than about 0.02.

[0044] Upon completion of the hemofiltration, a filtrate (e.g., the filtered plasma and small solutes) exits the filter 140 and is pumped through a filtrate line 165 to a filtrate collection container 170, such as a collection bag. An ultrafiltration pump 175 may be used to propel the filtrate through the filtrate line 165 by exerting negative pressure on the filter 140. In one embodiment, the ultrafiltration pump 175 can perform ultrafiltration from about 10 mL/h to about 500 mL/h. In another embodiment, the ultrafiltration pump 175 can perform ultrafiltration from about 50 mL/h to about 450 mL/h. In still another embodiment, the ultrafiltration pump 175 can perform ultrafiltration from about 100 mL/h to about 400 mL/h. In some embodiments, ultrafiltration rates of up to 500 mL/h are ample for clearance of waste products in small children in CVVH mode. Higher pump rates may be used in some instances, for example for non-pediatric applications.

[0045] A blood leak detector 180 may be operatively connected to the filtrate line 165 and positioned adjacent to the ultrafiltration pump 175. The blood leak detector 180 is used to detect the leakage of red blood cells across the filter membrane if the membrane is damaged. In one embodiment, the blood leak detector 180 may be of a photometric type and respond to the change of color of the filtrate. An ultrafiltrate pressure sensor 185 may also be

operatively connected to the filtrate line 165. In one embodiment, the ultrafiltrate pressure sensor 185 is configured to measure pressure in the filtrate line 165. The ultrafiltrate pressure sensor 185 can also be used to monitor the transmembrane pressure (TMP) and to detect clotting or fouling of the filter 140. A withdrawal pressure sensor may also be present to monitor pressure in the withdrawn blood line 120.

[0046] Blood exits the filter 140 through a return line 190 and is continuously returned to the patient through the return line 190 that is terminated at the return access point 115. In one embodiment, a blood warmer 195 may be operatively connected to the return line 190. The blood warmer 195 can heat the blood prior to transfusion back into the patient. Thermal management of the extracorporeal circuit 105 is of increased importance in pediatric patients and neonates.

[0047] In another embodiment, a sampling port 205 may also be operatively connected to the return line 190. The sampling port 205 can be used to monitor the anticoagulation of the blood that is returned to the patient. In some embodiments, an infusion pressure sensor 210 is operatively connected to the return line 190. The infusion pressure sensor 210 may be configured to measure the pressure in the return line 190.

[0048] The CRRT system 100 of the present disclosure advantageously provides enhanced communication between the replacement fluid flow regulator 150 and the blood pump 135. For example, the CRRT system 100 of the present disclosure allows for the replacement fluid flow regulator 150 to communicate its functioning status to the blood pump 135 and vice versa. This enhanced communication not only prevents fluid from being removed in the filter 140 in the case the replacement fluid flow regulator 150 fails to deliver replacement fluid, but also prevents the replacement fluid flow regulator 150 from delivering fluid in the event the blood pump 135 or filter 140 fails to function properly, stops, pauses or reverses due to triggered alarms.

[0049] In one embodiment, the replacement fluid flow regulator 150 includes a replacement fluid flow regulator control unit 220. The replacement fluid flow regulator control unit 220 is operatively connected to the replacement fluid flow regulator 150 and is configured to control and measure the functioning of the replacement fluid flow regulator 150. The replacement fluid flow regulator control unit 220 may be configured to determine and communicate the functioning status of the replacement fluid flow regulator 150. For instance, the replacement fluid flow regulator control unit 220 can determine whether the replacement fluid flow regulator 150 is operable, inoperable, or in an off mode.

[0050] In another embodiment, the disclosed CRRT system 100 may include a replacement fluid dose meter 230. The replacement fluid dose meter 230 provides increased accuracy over conventional pumps. In one embodiment, the replacement fluid dose meter 230 is configured to measure the amount of replacement fluid being delivered to the patient. A weight scale (not shown) can be operatively connected to or incorporated in the replacement fluid dose meter 230 to provide control and monitoring of the weight of the fluid being delivered to the patient. In one embodiment, the weight scale is a hanging scale having a load cell or weight sensor. In another embodiment, a volumetric-based scale (not shown) can be operatively connected to the replacement fluid dose meter 230 to provide control and monitoring of the volume of the fluid being delivered to the patient. For instance, a syringe pump may be operatively connected to the replacement fluid dose meter 230 to monitor the volume of fluid. In these embodiments, the replacement fluid dose meter 230 can monitor fluid dosing data and communicate changes in the dosing data to other components of the system.

[0051] The meter 230 may output a signal that is representative of the rate of infusion. The meter 230 can measure the rate of infusion of the replacement fluid in terms of volume per unit time or weight per unit time. In some embodiments, the replacement fluid infusion rate is from about 100 mL/hour to about 500 mL/hour. In another embodiment, the replacement fluid infusion rate is from about 200 mL/hour to about 400 mL/hour. In still another embodiment, the replacement fluid infusion rate is about 300 mL/hour.

[0052] The replacement fluid flow regulator control unit 220 and the replacement fluid dose meter 230 may be operatively connected to a hemofiltration control unit 235. The hemofiltration control unit 235 is configured to control and/or measure the functioning of the blood pump 135. In one embodiment, the hemofiltration control unit 235 is in communication with the replacement fluid flow regulator control unit 220. In this embodiment, the hemofiltration control unit 235 can modulate the functioning of the blood pump 135 based on the functioning of the replacement fluid flow regulator 150. For instance, the hemofiltration control unit 235 can shut down the blood pump 135 if the replacement fluid flow regulator 150 ceases to function. The hemofiltration control unit 235 can also shut down the replacement fluid flow regulator 150 if the blood pump 135 ceases to function.

[0053] In another embodiment, the hemofiltration control unit 235 is in communication with the replacement fluid dose meter 230. In this embodiment, the hemofiltration control unit 235 can modulate the functioning of the blood pump 135 based on the dose of replacement fluid measured by the replacement fluid dose meter 230. For

instance, the hemofiltration control unit 235 can receive replacement fluid dosing data from the replacement fluid dose meter 230 and modulate the speed of the blood pump 135 in response to the replacement dosing data.

[0054] FIG. 2 is a schematic diagram of a computer system 500 of a kind that may be used as the control unit for either or both of the replacement fluid flow regulator 220 and the hemofiltration control unit 235. Through the use of computer system 500, the hemofiltration control unit 235 can provide an enhanced communication interface for the components of the CRRT system 100.

[0055] Computer system 500 may typically be implemented using one or more programmed general-purpose computer systems, such as embedded processors, systems on a chip, personal computers, workstations, server systems, and minicomputers or mainframe computers, or in distributed, networked computing environments. Computer system 500 may include one or more processors (CPUs) 502A-502N, input/output circuitry 504, network adapter 506, and memory 508. CPUs 502A-502N execute program instructions to carry out the functions of the present systems and methods. Typically, CPUs 502A-502N are one or more microprocessors, such as an INTEL CORE® processor.

[0056] Input/output circuitry 504 provides the capability to input data to, or output data from, computer system 500. For example, input/output circuitry 504 may include input devices, such as keyboards, mice, touchpads, trackballs, scanners, analog to digital converters, etc., output devices, such as video adapters, monitors, printers, etc., and input/output devices, such as, modems, etc. Network adapter 506 interfaces computer system 500 with a network 510. Network 510 may be any public or proprietary LAN or WAN, including, but not limited to, the Internet.

[0057] Memory 508 stores program instructions that are executed by, and data that are used and processed by, CPU 502 to perform the functions of computer system 500. Memory 508 may include, for example, electronic memory devices, such as random-access memory (RAM), read-only memory (ROM), programmable read-only memory (PROM), electrically erasable programmable read-only memory (EEPROM), flash memory, etc., and electro-mechanical memory, such as magnetic disk drives, tape drives, optical disk drives, etc., which may use an integrated drive electronics (IDE) interface, or a variation or enhancement thereof, such as enhanced IDE (EIDE) or ultra-direct memory access (UDMA), or a small computer system interface (SCSI) based interface, or a variation or enhancement thereof, such as fast-SCSI, wide-SCSI, fast and wide-SCSI, etc., or Serial Advanced Technology

Attachment (SATA), or a variation or enhancement thereof, or a fiber channel-arbitrated loop (FC-AL) interface.

[0058] Memory 508 may include controller routines 512, controller data 514, and operating system 520. Controller routines 512 may include software routines to perform processing to implement one or more controllers. Controller data 514 may include data needed by controller routines 512 to perform processing. In one embodiment, controller routines 512 may include software for analyzing and communicating incoming data from the hemofiltration control unit 235 (e.g., measurements related to the functioning and speed of the blood pump 135) and/or from the replacement fluid flow regulator control unit 220 (e.g., measurements related to the functioning of the replacement fluid flow regulator 150). In another embodiment, controller routines 512 may include software for analyzing and communicating incoming data from the replacement fluid dose meter 230 (e.g., measurements related to replacement fluid dosing and the rate of infusion).

[0059] METHODS OF USE

[0060] The CRRT system 100 described herein can be used, for instance, to treat or support a patient with renal insufficiency by providing one or more kidney functions. The renal insufficiency could have various causes, such as one or more of acute injury, congenital defect, acute kidney disease, intrinsic renal disease, and chronic kidney disease. In some embodiments, the CRRT system 100 described herein may be used to treat acute intrinsic renal disease. In a further embodiment the CRRT system 100 is used to acute toxic renal injury.

[0061] In one embodiment, a method for treating or supporting a patient with renal insufficiency in need thereof is provided. In this embodiment, the method includes withdrawing blood from the patient and processing the blood with the CRRT system 100 described herein such that the blood undergoes CVVH. The processed blood (i.e., having passed through the filter 140 of the disclosed CRRT system 100) may then be reinfused into the patient. The disclosed method may be administered to any patient in need of medical care to treat renal insufficiency. In a preferred embodiment the patient is a pediatric patient. A “pediatric patient,” as used herein, refers to a patient less than 18 years of age. In another embodiment, the patient is an infant. An “infant,” as used herein, refers to a patient less than 1 year old. In another embodiment, the patient is a neonate. A “neonate,” as used herein, refers to a patient less than four weeks old.

[0062] EXEMPLARY EMBODIMENTS

[0063] In addition to anything described above or currently claimed, it is specifically contemplated that any of the following embodiments may be claimed:

[0064] Embodiment 1: A system for providing continuous renal replacement therapy to a patient, the system comprising: a hemofiltration unit comprising a withdrawn blood line connecting a hemofilter to a first catheter connector 610; a blood pump positioned to propel blood in the withdrawn blood line from the first catheter connector 610 to the hemofilter; a filtrate line connected to receive a filtrate from the hemofilter; an ultrafiltration pump configured to propel the filtrate from the filtrate line by exerting negative pressure on the hemofilter; a return line connected to receive a retentate from the hemofilter and terminating in a first catheter connector 620; a port for sampling or fluid infusion in at least one of the withdrawn blood line and the return line; and a hemofiltration control unit configured to control the blood pump and to measure the functioning of the blood pump; an anticoagulant flow regulator configured to pump anticoagulant from an anticoagulant source into the withdrawn blood line between the first catheter connector 610 and the hemofilter; a replacement fluid flow regulator configured to regulate the flow of a replacement fluid from a replacement fluid source into the withdrawn blood line or the return line, and comprising a replacement fluid flow regulator control unit configured to control the replacement fluid flow regulator and to measure the functioning of the replacement fluid flow regulator; and a blood warmer positioned to warm the retentate prior to infusion into the patient; wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to modulate the functioning of the blood pump based on the functioning of the replacement fluid flow regulator, and to modulate the functioning of the replacement fluid flow regulator based on the functioning of the blood pump.

[0065] Embodiment 2: The system of embodiment 1, wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to shut down the blood pump if the replacement fluid flow regulator ceases to function.

[0066] Embodiment 3: The system of any one of embodiments 1-2, wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to shut down the replacement fluid flow regulator if one or more of the following occur: the blood pump ceases to function, stops, pauses, or reverses.

[0067] Embodiment 4: A system for providing continuous renal replacement therapy to a patient, the system comprising: a hemofiltration unit comprising a withdrawn blood line connecting a hemofilter to a first catheter connector 610; a blood pump positioned to propel blood in the withdrawn blood line from the first catheter connector 610 to the hemofilter; a

filtrate line connected to receive a filtrate from the hemofilter; an ultrafiltration pump configured to propel the filtrate from the filtrate line by exerting negative pressure on the hemofilter; a return line connected to receive a retentate from the hemofilter and terminating in a first catheter connector 620; a sampling port in the return line; and a hemofiltration control unit configured to control the blood pump; an anticoagulant flow regulator configured to regulate the flow of an anticoagulant from an anticoagulant source into the withdrawn blood line between the first catheter connector 610 and the hemofilter; a replacement fluid flow regulator configured to regulate the flow of a replacement fluid from a replacement fluid source into the withdrawn blood line or the return line; a replacement fluid dose meter that measures the amount of replacement fluid delivered by at least one of weight and volume; and a blood warmer positioned to warm the retentate prior to infusion into the patient; wherein the hemofiltration control unit is in communication with the replacement fluid dose meter so as to modulate the functioning of the blood pump based on the dose of replacement fluid administered.

[0068] Embodiment 5: The system of embodiment 4, wherein the hemofiltration control unit is in communication with the replacement fluid dose meter to receive replacement fluid dosing data.

[0069] Embodiment 6: The system of any one of embodiments 4-5, wherein the hemofiltration control unit is in communication with the replacement fluid dose meter to receive replacement fluid dosing data, and wherein the hemofiltration control unit is configured to modulate the speed of the blood pump in response to the replacement fluid dosing data.

[0070] Embodiment 7: The system of any one of embodiments 4-6, wherein the replacement fluid dose meter measures the rate of infusion of the replacement fluid.

[0071] Embodiment 8: The system of any one of embodiments 4-7, wherein the replacement fluid dose meter measures the rate of infusion of the replacement fluid in terms of volume per unit time.

[0072] Embodiment 9: The system of any one of embodiments 4-8, wherein the replacement fluid dose meter measures the rate of infusion of the replacement fluid in terms of weight per unit time.

[0073] Embodiment 10: The system of any one of embodiments 1-9, wherein the anticoagulant flow regulator is not integral with the hemofiltration unit.

[0074] Embodiment 11: The system of any one of embodiments 1-10, wherein said replacement fluid flow regulator is not integral with the hemofiltration unit.

[0075] Embodiment 12: The system of any one of embodiments 1-11, wherein said blood warmer is not integral with the hemofiltration unit.

[0076] Embodiment 13: The system of any one of embodiments 1-12, wherein the hemofiltration unit has an extracorporeal circuit volume of about 33 mL.

[0077] Embodiment 14: The system of any one of embodiments 1-13, wherein the hemofilter has an effective filtration area of about 0.09 to about 0.3 m², about 0.12 m², 0.1 to about 0.2 m², or about 0.12 m².

[0078] Embodiment 15: The system of any one of embodiments 1-14, wherein the hemofilter comprises a multiplicity of polysulfone membranes.

[0079] Embodiment 16: The system of any one of embodiments 1-15, wherein the hemofilter has a sieving coefficient for urea of about 0.98.

[0080] Embodiment 17: The system of any one of embodiments 1-16, wherein the hemofilter has a sieving coefficient for creatinine of about 0.98.

[0081] Embodiment 18: The system of any one of embodiments 1-17, wherein the hemofilter has a sieving coefficient for vitamin B12 of about 0.98.

[0082] Embodiment 19: The system of any one of embodiments 1-18, wherein the hemofilter achieves solute transfer by convection when in use with the system.

[0083] Embodiment 20: The system of any one of embodiments 1-19, wherein the hemofiltration unit comprises at least one of: an infusion pressure sensor positioned to measure pressure in the return line, an ultrafiltrate pressure sensor positioned to measure pressure in the filtrate line, and a hematocrit sensor positioned to measure hematocrit in the return line.

[0084] Embodiment 21: The system of any one of embodiments 1-20, wherein the blood pump is capable of operating over a range of about 10-40, 15-35, 20-30, 20, or 30 mL min⁻¹.

[0085] Embodiment 22: The system of any one of embodiments 1-21, wherein the ultrafiltration pump is capable of operating over a range of about 0-500 mL h⁻¹.

[0086] Embodiment 23: The system of any one of embodiments 1-22, wherein the hemofiltration unit is not configured for countercurrent dialysis.

[0087] Embodiment 24: The system of any one of embodiments 1-23, comprising a Y-connector connected to the anticoagulant source and the withdrawn blood line to provide the anticoagulant to the withdrawn blood line.

[0088] Embodiment 25: The system of any one of embodiments 1-24, wherein the anticoagulant regulator infuses anticoagulant upstream of the blood pump.

[0089] Embodiment 26: A method for treating a renal insufficiency in a patient in need thereof, comprising: withdrawing blood from the patient; processing the blood with the system of any one of embodiments 1-24; and reinfusing the processed blood into the patient.

[0090] Embodiment 27: The method of embodiment 26, wherein the renal insufficiency is one or more of: acute injury, congenital defect, acute kidney disease, intrinsic renal disease, and chronic kidney disease.

[0091] Embodiment 28: The method of any one of embodiments 26-27, wherein the patient is a pediatric patient.

[0092] Embodiment 29: The method of any one of embodiments 26-28, wherein the patient is a neonate.

[0093] Embodiment 30: The method of any one of embodiments 26-29, wherein the patient is an infant.

[0094] CONCLUSIONS

[0095] It is to be understood that any given elements of the disclosed embodiments of the invention may be embodied in a single structure, a single step, a single substance, or the like. Similarly, a given element of the disclosed embodiment may be embodied in multiple structures, steps, substances, or the like.

[0096] The foregoing description illustrates and describes the processes, machines, manufactures, compositions of matter, and other teachings of the present disclosure. Additionally, the disclosure shows and describes only certain embodiments of the processes, machines, manufactures, compositions of matter, and other teachings disclosed, but, as mentioned above, it is to be understood that the teachings of the present disclosure are capable of use in various other combinations, modifications, and environments and is capable of changes or modifications within the scope of the teachings as expressed herein, commensurate with the skill and/or knowledge of a person having ordinary skill in the relevant art. The embodiments described hereinabove are further intended to explain certain best modes known of practicing the processes, machines, manufactures, compositions of matter, and other teachings of the present disclosure and to enable others skilled in the art to utilize the teachings of the present disclosure in such, or other, embodiments and with the various modifications required by the particular applications or uses. Accordingly, the processes, machines, manufactures, compositions of matter, and other teachings of the present disclosure are not intended to limit the exact embodiments and examples disclosed herein. Any section headings herein are provided only for consistency with the suggestions

of 37 C.F.R. § 1.77 or otherwise to provide organizational queues. These headings shall not limit or characterize the invention(s) set forth herein.

CLAIMS

What is claimed is:

1. A system for providing continuous renal replacement therapy to a patient in need thereof, the system comprising:
 - (a) a hemofiltration unit comprising
 - (i) a withdrawn blood line connecting a hemofilter to a first catheter connector;
 - (ii) a blood pump positioned to propel blood in the withdrawn blood line from the first catheter connector to the hemofilter;
 - (iii) a filtrate line connected to receive a filtrate from the hemofilter;
 - (iv) an ultrafiltration pump configured to propel the filtrate from the filtrate line by exerting negative pressure on the hemofilter;
 - (v) a return line connected to receive a retentate from the hemofilter and terminating in a second catheter connector;
 - (vi) a port for sampling or fluid infusion in at least one of the withdrawn blood line and the return line; and
 - (vii) a hemofiltration control unit configured to control the blood pump and to measure the functioning of the blood pump;
 - (b) an anticoagulant flow regulator configured to pump anticoagulant from an anticoagulant source into the withdrawn blood line between the first catheter connector and the hemofilter;
 - (c) a replacement fluid flow regulator configured to regulate the flow of a replacement fluid from a replacement fluid source into one or both of the withdrawn blood line and the return line, and comprising a replacement fluid flow regulator control unit configured to control the replacement fluid flow regulator and to measure the functioning of the replacement fluid flow regulator; and
 - (d) a blood warmer positioned to warm the retentate prior to infusion into the patient;

wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to modulate the functioning of the blood pump based on the functioning of the replacement fluid flow regulator, and to modulate the functioning of the replacement fluid flow regulator based on the functioning of the blood pump.

2. The system of claim 1, wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to shut down the blood pump if the replacement fluid flow regulator ceases to function, stops, pauses, or reverses.
3. The system of claim 1, wherein the hemofiltration control unit is in communication with the replacement fluid flow regulator control unit so as to shut down the replacement fluid flow regulator if the blood pump ceases to function, stops, pauses, or reverses.
4. A system for providing continuous renal replacement therapy to a patient in need thereof, the system comprising:
 - (a) a hemofiltration unit comprising
 - (i) a withdrawn blood line connecting a hemofilter to a first catheter connector;
 - (ii) a blood pump positioned to propel blood in the withdrawn blood line from the first catheter connector to the hemofilter;
 - (iii) a filtrate line connected to receive a filtrate from the hemofilter;
 - (iv) an ultrafiltration pump configured to propel the filtrate from the filtrate line by exerting negative pressure on the hemofilter;
 - (v) a return line connected to receive a retentate from the hemofilter and terminating in a second catheter connector;
 - (vi) a sampling port in the return line; and
 - (vii) a hemofiltration control unit configured to control the blood pump;
 - (b) an anticoagulant flow regulator configured to regulate the flow of an anticoagulant from an anticoagulant source into the withdrawn blood line between the first catheter connector and the hemofilter;
 - (c) a replacement fluid flow regulator configured to regulate the flow of a replacement fluid from a replacement fluid source into one or both of the withdrawn blood line and the return blood line;
 - (d) a replacement fluid dose meter that measures the amount of replacement fluid delivered by at least one of weight and volume; and
 - (e) a blood warmer positioned to warm the retentate prior to infusion into the patient;

wherein the hemofiltration control unit is in communication with the replacement fluid dose meter so as to modulate the functioning of the blood pump based on the dose of replacement fluid administered.

5. The system of claim 4, wherein the hemofiltration control unit is in communication with the replacement fluid dose meter to receive replacement fluid dosing data.
6. The system of claim 4, wherein the hemofiltration control unit is in communication with the replacement fluid dose meter to receive replacement fluid dosing data, and wherein the hemofiltration control unit is configured to modulate the speed of the blood pump in response to the replacement fluid dosing data.
7. The system of claim 4, wherein the replacement fluid dose meter measures the rate of infusion of the replacement fluid.
8. The system of claim 4, wherein the replacement fluid dose meter measures the rate of infusion of the replacement fluid in terms of volume per unit time.
9. The system of claim 4, wherein the replacement fluid dose meter measures the rate of infusion of the replacement fluid in terms of weight per unit time.
10. The system of any one of claims 1-9, wherein the anticoagulant flow regulator is not integral with the hemofiltration unit.
11. The system of any one of claims 1-9, wherein said replacement fluid flow regulator is not integral with the hemofiltration unit.
12. The system of any one of claims 1-9, wherein said blood warmer is not integral with the hemofiltration unit.
13. The system of any one of claims 1-9, wherein the hemofiltration unit has an extracorporeal circuit volume of about 33 mL.
14. The system of any one of claims 1-9, wherein the hemofilter has an effective filtration area of about 0.09 to about 0.3 m².
15. The system of any one of claims 1-9, wherein the hemofilter has an effective filtration area of about 0.1 to about 0.2 m².
16. The system of any one of claims 1-9, wherein the hemofilter has an effective filtration area of about 0.12 m².
17. The system of any one of claims 1-9, wherein the hemofilter comprises a multiplicity of polysulfone membranes.
18. The system of any one of claims 1-9, wherein the hemofilter has a sieving coefficient for urea of about 0.98.

19. The system of any one of claims 1-9, wherein the hemofilter has a sieving coefficient for creatinine of about 0.98.
20. The system of any one of claims 1-9, wherein the hemofilter has a sieving coefficient for vitamin B12 of about 0.98.
21. The system of any one of claims 1-9, wherein the hemofilter achieves solute transfer by convection when in use with the system.
22. The system of any one of claims 1-9, wherein the hemofiltration unit comprises at least one of: an infusion pressure sensor positioned to measure pressure in the return line, an ultrafiltrate pressure sensor positioned to measure pressure in the filtrate line, and a hematocrit sensor positioned to measure hematocrit in the withdraw line.
23. The system of any one of claims 1-9, wherein the blood pump is capable of operating over a range of about 10-40 mL min⁻¹.
24. The system of any one of claims 1-9, wherein the ultrafiltration pump is capable of operating over a range of up to about 500 mL h⁻¹.
25. The system of any one of claims 1-9, wherein the ultrafiltration pump is capable of operating over a range of about 10-500 mL h⁻¹.
26. The system of any one of claims 1-9, wherein the ultrafiltration pump is capable of operating over a range of about 50-450 mL h⁻¹.
27. The system of any one of claims 1-9, wherein the ultrafiltration pump is capable of operating over a range of about 100-400 mL h⁻¹.
28. The system of any one of claims 1-9, wherein the hemofiltration unit is not configured for countercurrent dialysis.
29. The system of any one of claims 1-9, comprising a Y-connector connected to the anticoagulant source and the withdrawn blood line to provide the anticoagulant to the withdrawn blood line.
30. The system of any one of claims 1-9, wherein the blood pump is capable of operating at about 10 to about 40 mL/min.
31. The system of any one of claims 1-9, wherein the blood pump is capable of operating at about 15 to about 35 mL/min.
32. The system of any one of claims 1-9, wherein the blood pump is capable of operating at about 20 to about 30 mL/min.
33. The system of any one of claims 1-9, wherein the blood pump is capable of operating at about 20 mL/min.

34. The system of any one of claims 1-9, wherein the blood pump is capable of operating at about 30 mL/min.
35. The system of any one of claims 1-9, wherein the anticoagulant regulator infuses the anticoagulant upstream of the blood pump.
36. A method for treating a renal insufficiency in a patient in need thereof, comprising:
 - withdrawing blood from the patient;
 - processing the blood with the system of any one of claims 1-9; and
 - reinfusing the processed blood into the patient.
37. The method of claim 36, wherein the renal insufficiency is one or more of: acute injury, congenital defect, acute kidney disease, intrinsic renal disease, and chronic kidney disease.
38. The method of claim 25, wherein the patient is a pediatric patient.
39. The method of claim 25, wherein the patient is an infant.
40. The method of claim 25, wherein the patient is a neonate.

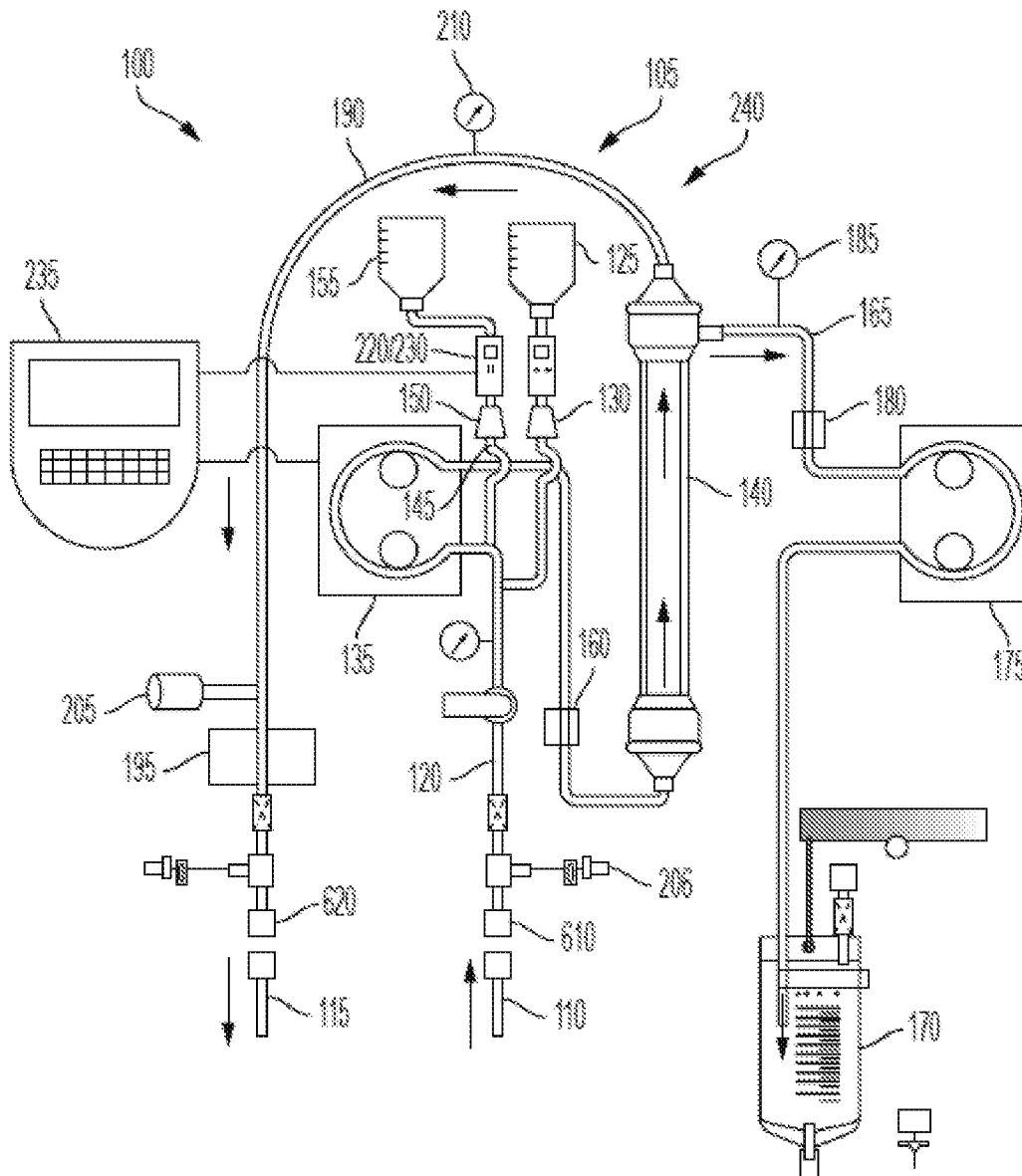


FIG. 1

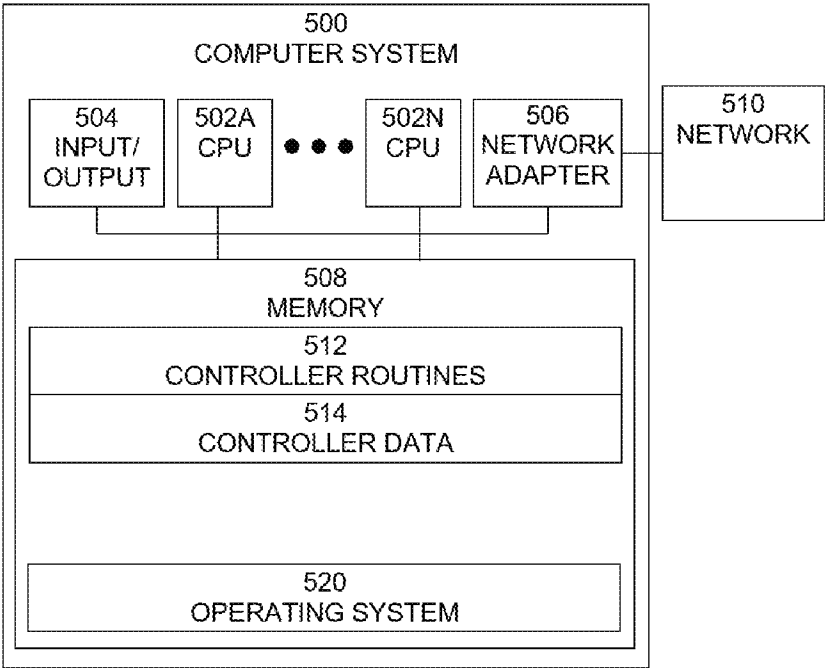


FIG. 2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/68381

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61M 1/14, 1/34, 1/36, 37/00, 39/10 (2020.01)

CPC - A61M 1/16, 1/1696, 1/341, 1/3621

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)

See Search History document

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

See Search History document

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2010/0038317 A1 (BISSLER, J. J. et al.) 18 February 2010, figure 2, paragraphs [0067], [0077]-[0078]	1-40
Y	US 2015/0114891 A1 (MEDTRONIC, INC.) 30 April 2015, figure 1D, paragraphs [0370], [0374]	1-40
Y	US 6,533,747 B1 (POLASCHEGG, H-D. et al.) 18 March 2003, column 7, lines 29-31	13
Y	US 2009/0131858 A1 (FISSELL, W. H. et al.) 21 May 2009, paragraph [0196]	14-16
Y	"The Diafilter Hemoconcentrator/Hemofilter" (MINNTECH CORPORATION) 2009, page 2, table: ultrafiltration rates, column 1	18-20
Y	US 6,299,589 B1 (UTTERBERG, D. S.) 9 October 2001, figure 2, column 6, lines 49-53	29
Y	US 2004/0024342 A1 (WEITZEL, W. F. et al.) 5 February 2004, paragraph [0037]	31-34

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

23 February 2020 (23.02.2020)

Date of mailing of the international search report

18 MAR 2020

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