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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 June 2020 (11.06.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/117340 A1

(51) International Patent Classification:
A61M 1/16 (2006.01) *A61M 1/34* (2006.01)
A61B 5/145 (2006.01) *A61M 1/36* (2006.01)

(21) International Application Number:
PCT/US2019/048980

(22) International Filing Date:
30 August 2019 (30.08.2019)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
16/207,980 03 December 2018 (03.12.2018) US

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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.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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

(54) **Title:** DETERMINATION OF PATIENT BLOOD VOLUME AT START OF A DIALYSIS TREATMENT

(57) **Abstract:** Embodiments of the disclosure provide a method for determining beginning blood volume of a patient during dialysis (e.g., hemodialysis). Ultrafiltration rates are determined at different time stamps during dialysis by obtaining a blood flowrate measurement and hematocrit measurements at input port and output port of a dialyzer connected to the patient. The flowrate and hematocrit measurements are used to determine fluid removed from the patient during dialysis. The ultrafiltration rates and fluid removed from the patient are used to determine the beginning blood volume of the patient.

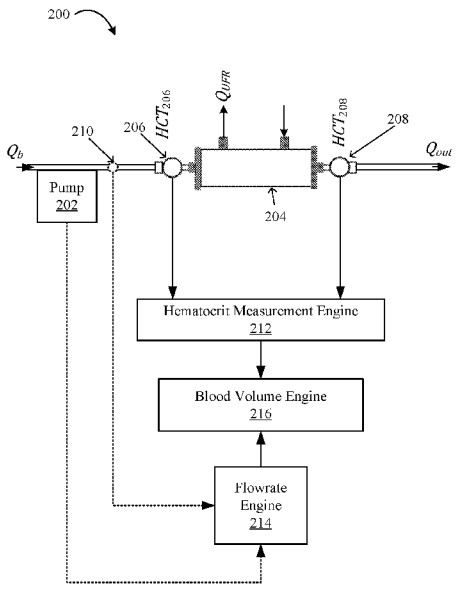

FIG. 2

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DETERMINATION OF PATIENT BLOOD VOLUME AT START OF A DIALYSIS TREATMENT

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] Priority is claimed to U.S. Patent Application No. 16/207,980, filed on December 3, 2018, the entire disclosure of which is hereby incorporated by reference herein.

BACKGROUND

[0002] Patients with kidney failure or partial kidney failure typically undergo hemodialysis treatment, often at a hemodialysis treatment center or clinic. When healthy, kidneys maintain the body's internal equilibrium of water and minerals (e.g., sodium, potassium, chloride, calcium, phosphorous, magnesium, and sulfate). The kidneys also function as part of the endocrine system to produce the hormone erythropoietin as well as other hormones. Hemodialysis is an imperfect treatment to replace kidney function, in part, because it does not correct the endocrine functions of the kidney. Conventional methods of performing dialysis are based on estimates of the amount of fluid which can be removed from a patient based on the patient's weight at the time of arrival for regular treatments. Rough estimates for a "target" weight are determined by algorithms using factors such as height, weight and other physiological conditions before a physician orders the dialysis treatment.

[0003] In hemodialysis, blood is taken from a patient through an intake needle (or catheter) which draws blood from an artery located in a specific accepted access location (arm, thigh, subclavian, etc.). The drawn blood is pumped through extracorporeal tubing via a peristaltic pump, and then through a special filter termed a "dialyzer." The dialyzer is intended to remove unwanted toxins such as blood urea, nitrogen, potassium, and excess water from the blood. As the blood passes through the dialyzer, it travels in straw-like tubes which serve as semi-permeable membrane passageways for the uncleaned blood. Fresh dialysate liquid, which is a solution of chemicals and water, flows through the dialyzer in the direction opposite the blood flow. As the dialysate flows through the dialyzer, it surrounds the straw-like membranes in the dialyzer. These membranes feature small holes which are large enough to pass liquid and liquid based impurities – but are not large enough to pass red blood cells. The fresh dialysate collects excess impurities passing through the straw-like tubes by diffusion, and also collects excess water through an ultrafiltration process due to a pressure drop across the membranes. During this process, the red cell volume is preserved

inside the straw-like tubes and recirculated back into the body. The used dialysate exits the dialyzer with the excess fluids and toxins via an output tube, thus cleansing the blood and red cell volume flowing through the dialyzer. The dialyzed blood then flows out of the dialyzer via tubing and a needle (or catheter) back into the patient. Sometimes, a heparin drip or pump is provided along the extracorporeal blood flow loop in order to prevent red cell clotting during the hemodialysis process. Several liters of excess fluid can be removed during a typical multi-hour treatment session. In the U.S., a chronic patient will normally undergo hemodialysis treatment in a dialysis center three times per week, either on Monday-Wednesday-Friday schedule or a Tuesday-Thursday-Saturday schedule. These in-center treatments are typically completed over 3 to 4 hours with blood flow rates typically above 300 ml/minute. In other countries, the flow rates and time for treatment are lower and longer, respectively.

[0004] Hemodialysis has an acute impact on the fluid balance of the body due in part to the rapid change in circulating blood volume. When the dialysis fluid removal rate is more rapid than the plasma refilling rate of the stored plasma held by the internal tissue of the body, intravascular blood volume decreases. The resulting imbalance has been linked to complications similar to conventional blood loss such as hypotension, loss of consciousness, headaches, vomiting, dizziness and cramps experienced by the patient, both during and after dialysis treatments. Continuous quantitative measurement of parameters relating to the processing of the blood volume (in real-time) during hemodialysis can reduce the chance of dialysis-induced hypotension, and otherwise optimize dialysis therapy regimens by controlling fluid balance and aiding in achieving the target dry weight for the patient.

[0005] Although dialysis involves fluid removal from a patient, there is no convenient way of obtaining an initial blood volume of the patient before treatment. A patient can go to a hospital or an in-patient facility to measure blood volume using dilution indicators. For example, a chemical sample is injected into the patient's blood and then a sample of the blood is extracted to determine concentration of the chemical sample in the blood using special equipment. Since dialysis clinics usually do not have a setup for using dilution indicators, blood volume obtained in this manner may be unhelpful because blood volume is a moving target. That is, before getting to a dialysis clinic, a patient that measured his blood volume beforehand may have lost blood volume from exercising or may have gained blood volume from eating lunch. Thus, the blood volume measurement obtained before reaching

the dialysis clinic can be drastically different from the patient's actual blood volume at start of dialysis.

SUMMARY

[0006] An embodiment of the disclosure provides a system for determining beginning blood volume of a patient undergoing dialysis treatment. The system comprises: a first portion of tubing, configured to connect a patient to an input of a dialyzer; a second portion of tubing, configured to connect the patient to an output of the dialyzer; a pump, configured to pump blood from the patient through the first portion of tubing into the dialyzer, and out of the dialyzer into the second portion of tubing; a first blood chamber, disposed along the first portion of tubing, and a second blood chamber, disposed along the second portion of tubing, wherein the first blood chamber and the second blood chamber are configured to facilitate hematocrit measurement; and a controller, configured to determine the beginning blood volume using hematocrit values associated with the input of the dialyzer, hematocrit values associated with the output of the dialyzer, and a flowrate of blood through the first portion of tubing.

[0007] An embodiment of the disclosure provides a method for determining beginning blood volume of a patient connected to a dialysis system. The method comprises: circulating, using a pump of the dialysis system, blood from the patient through a dialyzer; and determining, using the dialysis system, beginning blood volume of the patient. Determining the beginning blood volume includes: (a) determining a blood flowrate corresponding to an input side of the dialyzer; (b) determining a fluid removal rate at an initial time via the blood flowrate, hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the output side of the dialyzer at the initial time; (c) determining a fluid removal rate after a first measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the first measurement period and hematocrit corresponding to the output side of the dialyzer after the first measurement period; (d) determining volume of fluid removed for the first measurement period via the fluid removal rate at the initial time and the fluid removal rate after the first measurement period; (e) determining fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer after the first measurement period; and (f) determining the beginning blood volume

via the fractional blood volume change and the volume of fluid removed for the first measurement period.

[0008] An embodiment of the disclosure provides a non-transitory computer readable medium for determining beginning blood volume of a patient connected to a dialysis system. The non-transitory computer readable medium includes instructions for causing a processor of the dialysis system to facilitate performing: blood circulation, using a pump of the dialysis system, blood from the patient through a dialyzer; and determining, using the dialysis system, beginning blood volume of the patient. Determining the beginning blood volume includes: (a) determining a blood flowrate corresponding to an input side of the dialyzer; (b) determining a fluid removal rate at an initial time via the blood flowrate, hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the output side of the dialyzer at the initial time; (c) determining a fluid removal rate after a first measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the first measurement period and hematocrit corresponding to the output side of the dialyzer after the first measurement period; (d) determining volume of fluid removed for the first measurement period via the fluid removal rate at the initial time and the fluid removal rate after the first measurement period; (e) determining fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer after the first measurement period; and (f) determining the beginning blood volume via the fractional blood volume change and the volume of fluid removed for the first measurement period.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] FIG. 1 is a perspective view of a typical patient undergoing hemodialysis treatment with a non-invasive, optical blood monitor monitoring the patient's blood in real-time as it passes through extracorporeal tubing in the hemodialysis system;

[0010] FIG. 2 illustrates an exemplary system for determining patient blood volume according to some embodiments of the disclosure;

[0011] FIG. 3 illustrates a view of a patient undergoing hemodialysis treatment with a system configuration that may be used to determine patient blood volume according to some embodiments of the disclosure; and

[0012] FIG. 4 illustrates a process for determining patient blood volume according to some embodiments of the disclosure.

DETAILED DESCRIPTION

[0013] Embodiments of the disclosure provide a non-invasive method for determining patient blood volume during dialysis. Knowing a patient's blood volume at the start of dialysis allows for better, more effective treatment of the patient compared to using estimated benchmarks based on weight and height of the patient. The patient's blood volume at the start of dialysis can be tracked through various treatments to determine how the blood volume fluctuates over time. Blood volume at start of dialysis can also inform how long the dialysis treatment should last.

[0014] Blood volume at start of a dialysis treatment is a parameter currently not available to physicians in dialysis clinics. Thus embodiments of the disclosure provide a method of benchmarking the condition of dialysis patients at the beginning of their dialysis sessions without resorting to invasive dye and/or isotope methods. Dyes and isotopes are not practical for use in a dialysis clinic. These systems are not readily available in the clinics and the patients have inadequate time in the clinic based on the time required for dialysis to perform these measurements. In addition, the cost of this type of measurement can be prohibitive and would not be available for every treatment. Yet, due to the success of a dialysis treatment a patient may feel good after it and eat or drink improperly before the next session. Therefore, the clinician and physician have no readily available benchmark of the patient's fluid condition at the beginning of a treatment to gauge what adjustments need to be made in the next session for best fluid management. The embodiments disclosed here provide for the important benchmark of the patient's starting fluid level volume. Before describing embodiments of the disclosure, FIG. 1 shows an example setup for a hemodialysis treatment.

[0015] FIG. 1 is a perspective view of an exemplary patient undergoing hemodialysis treatment with a non-invasive, optical blood monitor monitoring the patient's blood in real-time as it passes through extracorporeal tubing in the hemodialysis system. The environment illustrated in FIG. 1 is usable with exemplary embodiments of the present disclosure. Further, it will be appreciated that the environment shown in FIG. 1 is merely exemplary, and that the principles discussed herein with respect to exemplary embodiments of the present disclosure may be implemented in other environments as well.

[0016] FIG. 1 illustrates a patient 10 undergoing hemodialysis treatment using a hemodialysis system 12, as well as a non-invasive, optical blood monitor 14. A typical hemodialysis clinic will have several hemodialysis systems 12 for treating patients on a Monday-Wednesday-Friday schedule or a Tuesday-Thursday-Saturday schedule. While the invention is not limited to the number of hemodialysis systems located at a clinic, or the specific type of hemodialysis system, the general operation of the hemodialysis system 12 is helpful for understanding the environment in which the invention is intended to operate.

[0017] An input needle or catheter 16 is inserted into an access site of the patient 10, such as in the arm, and is connected to extracorporeal tubing 18 that leads to a peristaltic pump 20 and then to a dialyzer or blood filter 22. The dialyzer 22 removes toxins and excess fluid from the patient's blood. The dialyzed red cell blood volume is returned from the dialyzer 22 through extracorporeal tubing 24 and return needle or catheter 26. In some parts of the world (primarily the United States), the extracorporeal blood flow may additionally receive a heparin drip to prevent clotting. The excess fluids and toxins are removed by clean dialysate liquid, which is supplied to the dialyzer 22 via tube 28 and removed for disposal via tube 30. A typical hemodialysis treatment session takes about 3 to 5 hours in the United States.

[0018] In the exemplary environment depicted in FIG. 1, the optical blood monitor 14 includes a blood chamber 32, an optical blood sensor assembly 34, and a controller 35. The blood chamber 32 is preferably located in line with the extracorporeal tubing 18 upstream of the dialyzer 22. Blood from the peristaltic pump 20 flows through the tubing 18 into the blood chamber 32. The preferred sensor assembly 34 includes LED photo emitters that emit light optical wavelengths to measure oxyhemoglobin (HbO_2), hemoglobin (Hb), and H_2O. For example, an LED, at substantially 810 nm, is isobestic for red blood cell hemoglobin. The blood chamber 32 includes lenses so that the emitters and detectors of the sensor assembly 34 can view the blood flowing through the blood chamber 32, and determine the patient's real-time hematocrit value using ratiometric techniques generally known in the prior art.

[0019] FIG. 2 illustrates an exemplary system 200 for determining patient beginning blood volume at start of a dialysis treatment, according to some embodiments of the disclosure. The system 200 includes a hematocrit measurement engine 212, a flowrate measurement engine 214, and a blood volume engine 216.

[0020] The exemplary system 200 shows a generalized embodiment which may be incorporated in the hemodialysis system 12 provided, as outlined in FIGS. 1 and 3. The

hematocrit measurement engine 212, the flowrate measurement engine 214, and the blood volume engine 216 may be implemented in the hemodialysis system 12 and the non-invasive, optical blood monitor 14. In this example configuration, the flowrate measurement engine 214 may be included in the hemodialysis system 12, the hematocrit measurement engine 212 included in the optical blood monitor 14, and the blood volume engine 216 included in the optical blood monitor 14 and/or in the hemodialysis system 12. The hemodialysis system 12 and the optical blood monitor 14 can be communicably coupled to each other to realize the relationships provided in FIG. 2 for system 200, or the desired parameters can be measured independently with discrete calculations.

[0021] For an integrated embodiment, the hematocrit measurement engine 212, the flowrate measurement engine 214, and the blood volume engine 216 correspond to hardware that includes one or more processors, for example, microprocessors or microcontrollers. The hardware can also include a non-transitory computer-readable medium for temporary and/or permanent storage, for example, a read-only memory (ROM), a random access memory (RAM), a flash memory, and other computer memories and storage. Additionally, the hematocrit measurement engine 212 may utilize one or more optical blood sensor assemblies, for example, optical blood sensor assembly 34, to measure hematocrit values at both main blood flow ports of the dialyzer 204. The blood volume engine 216 may be a computing device, for example, the controller 35, that utilizes a processor and storage to determine the hematocrit values of the dialyzer 204, read the blood flowrate entering the dialyzer 204 from the processor in the dialysis machine 12, read the ultra-filtration pump rate of the dialysis machine 12 and then calculate beginning blood volume of the patient at the start of dialysis.

[0022] In the system 200 of FIG. 2, as applied to FIG 3, blood flows into an input port of the dialyzer 204 at a blood flowrate Q_b. The blood flowrate is determined by the pump 202, which may be peristaltic pump 20, which is part of the dialysis machine 12 of FIG. 3. In the treatment setting of FIG 3, blood enters the dialyzer 204, undergoes a filtration process, and filtered blood flows out of an output port of the dialyzer 204 at a blood flowrate Q_{out}. The difference between the blood flowrate at the input port of the dialyzer 204 and the blood flowrate at the output port of the dialyzer 204 is denoted in FIG. 2 as Q_{UFR}. In the treatment setting of FIG 3, the Q_{out} rate is the difference determined by the Q_b rate minus the Q_{UFR}. The pumps on the dialysis machine 12 are calibrated, and these calibrated values are readily available during measurements. These rates can be arbitrary, but should remain the same throughout the measurements.

[0023] Multiple methods may be used to determine the flowrate Q_b. As shown in FIG. 2, in one embodiment, a flowmeter 210 is provisioned in the extracorporeal tubing to measure Q_b. The measurements from the flowmeter 210 may be provided to the flowrate engine 214.

[0024] In another exemplary embodiment, the flowmeter 210 may or may not be provided, and Q_b is determined from a calibrated pumping rate of the pump 202. The pump 202 may operate at a specific number of rotations per minute, which may be matched to a commanded flowrate of blood entering the dialyzer 204. The pump 202 may provide the number of rotations per minute to the flowrate engine 214, which then determines Q_b from the number of rotations per minute.

[0025] In addition to determining flowrates, the system 200 also determines hematocrit at the input port of the dialyzer 204 (HCT_{206}) and the output port of the dialyzer 204 (HCT_{208}). In one embodiment, a ratiometric technique, as disclosed in U.S. Pat. No. 5,372,136 entitled, "System and Method for Non-Invasive Hematocrit Monitoring," which is incorporated by reference in its entirety, can be used to determine hematocrit values at locations 206 and 208 in FIG 2. If one optical blood sensor assembly 34 is used, then after measuring hematocrit at the input port of the dialyzer 204 (HCT_{206}), the optical blood assembly 34 is moved to measure hematocrit at the output port of the dialyzer 204 (HCT_{208}). If two optical blood sensor assemblies are used, then one can measure HCT_{206} while the other measures HCT_{208}. In some embodiments, non-invasive (not requiring the pulling of samples) hematocrit measurements, for example, measurements made with the Crit-Line® system, may be used to obtain hematocrit values.

[0026] The blood volume engine 216 receives hematocrit measurements from the hematocrit measurement engine 212 and receives flowrate measurements from the flowrate engine 214. Using the hematocrit and the flowrate measurements, the blood volume engine 216 determines the total blood volume of the patient at the start of the dialysis treatment. The total blood volume of the patient at the start of dialysis treatment is determined by dividing the total blood volume of the patient removed during a treatment time by a fractional blood volume change during the same treatment time. The total blood volume removed and the fractional blood volume change are determined using the measured hematocrit values HCT_{206} and HCT_{208} and the blood flow rate Q_b.

[0027] Determination of a patient's total blood volume at time zero (TBV_0), at the commencement of a dialysis treatment, involves two sets of measurements since there are two unknowns, i.e., TBV_0 and instantaneous total blood volume at time T into the treatment,

$TBV(\mathrm{T})$. For performing these measurements, it is assumed that the dialysis access is viable and there is no recirculation from the venous to the arterial needles due to stenosis in or after the access.

[0028] For the first set of mearsurements, the fractional change in blood volume (ΔBV) measured by a device such as the Crit-Line® or the Crit-Line® clip monitor (CLiC™) device must be based on calibrated blood parameters. For example, the ΔBV must be based on calibrated hematocrit values being accurate or traceable to any standard calibrated measurement of the hematocrit blood parameter.

[0029] In an embodiment, the measurement of ΔBV can be made using the CLiC™ device at location 206. A blood chamber can be placed at 206 to facilitate the measurement with the CLiC™ device. When the CLiC™ device is manufactured, each is measured on a matching blood chamber to verify accuracy of hematocrit measurements made by the device through use of human blood in the production facility's blood lab. The CLiC™ device is used here as an example of the hematocrit measurement engine 212. Since the hematocrit values measured are equivalent to laboratory hematocrit accuracy, the calibrated state of the device can be used to make a viable measurement of ΔBV at any point in time during a dialysis treatment. Hematocrit (HCT) can be defined as Eq. 1.

$$HCT = \frac{RBV}{TBV} \qquad \text{Eq. 1}$$

Where HCT is hematocrit, RBV is red blood cell volume, and TBV is total blood volume. Based on the mass balance condition where no red blood cell volume is lost in the dialyzer (only fluid is removed from the blood), calculations can be performed based on HCT_{206} measured at location 206.

[0030] An initial HCT_{206} can be measured at the beginning of treatment (at time T=0) before being influenced by fluid removal. The initial HCT_{206} is referred to as HCT_0 from here on to distinguish from subsequent HCT_{206} measurements. From Eq. 1, HCT_0 can be written as Eq. 2.

$$HCT_0 = \frac{RBV}{TBV_0} \qquad \text{Eq. 2}$$

Where HCT_0 is the initial hematocrit HCT_{206} measured at the beginning of treatment, RBV is red blood cell volume, and TBV_0 is the initial total blood volume at the beginning of treatment (at time T=0).

[0031] At time duration T, a subsequent hematocrit can be measured. Hematocrit HCT_{206} measured at time duration T can be defined as Eq. 3.

$$HCT(\mathrm{T}) = \frac{RBV}{TBV(\mathrm{T})} \qquad \text{Eq. 3}$$

Where $HCT(\mathrm{T})$ is the hematocrit HCT_{206} measured at time T into the treatment, RBV is red blood cell volume, and $TBV(\mathrm{T})$ is total blood volume at time T into the treatment.

[0032] Eq. 2 and Eq. 3 can be rearranged to produce Eq. 4 and Eq. 5, respectively.

$$TBV_0 = \frac{RBV}{HCT_0} \qquad \text{Eq. 4}$$

$$TBV(\mathrm{T}) = \frac{RBV}{HCT(\mathrm{T})} \qquad \text{Eq. 5}$$

[0033] Since RBV is constant, Eq. 4 and Eq. 5 can be combined to calculate fractional change in blood volume ΔBV as indicated in Eq. 6.

$$\Delta\mathrm{BV} = \frac{TBV(\mathrm{T}) - TBV_0}{TBV_0} = \left[\frac{HCT_0}{HCT(\mathrm{T})} - 1\right] \qquad \text{Eq. 6}$$

The ΔBV is based on calibrated hematocrit values and is bounded by the accuracy of the hematocrit measurements. Rearranging Eq. 6 provides Eq. 7.

$$\Delta\mathrm{BV} \times TBV_0 = TBV(\mathrm{T}) - TBV_0$$
$$TBV(\mathrm{T}) = TBV_0 \times (\Delta\mathrm{BV} + 1) \qquad \text{Eq. 7}$$

[0034] Eq. 7 provides a relationship for the first set of measurements and provides a first equation involving two unknowns, both the original patient blood volume TBV_0 at the beginning of treatment and the patient blood volume $TBV(\mathrm{T})$ at some time T into the treatment. To solve Eq. 7, a second set of measurements is determined.

[0035] The second relationship between TBV_0 and $TBV(\mathrm{T})$ involves an approximate integration of the blood volume fluid amount removed from time zero (i.e., from time T=0). That is, the total blood removed through ultrafiltration from time zero (e.g., the start of treatment) until time T can be written as Eq. 8. Eq. 8 presents fluid removal volume based on a sampled integration technique based on timed samples.

$$TBV(\mathrm{T}) - TBV_0 = \sum_{n=1\ (Step\ \Delta t)}^{\mathrm{T}/\Delta t} \left(\frac{Q_{UFR}(n) + Q_{UFR}(n-1)}{2}\right) \times \Delta t \qquad \text{Eq. 8}$$

[0036] In Eq. 8, Q_{UFR} is actual fluid removal rate in the dialysis circuit based on ultrafiltration mechanisms. Q_{UFR} is not the ultrafiltration rate of an ultrafiltration pump. Δt is time between measurements of Q_{UFR} along the $TBV(\mathrm{T})$ history curve. The smaller Δt becomes, the more data is processed by the blood volume engine 216 and the more accurate the integration estimation of Eq. 8 becomes. Time T is total time into the treatment in which Q_{UFR} has been active. For use of Eq. 8, ultrafiltration pump rate and blood pump rate should remain at steady-state from an initial time T=0 until time T. To enhance readability, the initial time T=0 will be referred to as initial time t_0. In an embodiment, the floor of $\mathrm{T}/\Delta t$ can be seen as number of measurement periods from the initial time t_0.

[0037] The Q_{UFR} volume change is the rate of removing fluid from the blood (in the dialyzer 204) into the dialysate. This should not be confused with pump ultrafiltration rate value set for an ultrafiltration pump for circulating dialysate through the dialyzer 204. Because the fluid removal from the patient's blood is accomplished by osmosis using the dialysate liquid passing through the dialyzer 204, external to the dialyzer fibers, while blood flow is confined within the dialyzer fibers, the actual fluid volume transfer Q_{UFR} is not equal to the flowrate of dialysate (ultrafiltration pump rate) passing outside the dialyzer fibers. The fluid volume transfer is dependent not only on the ultrafiltration pump rate but also on factors such as, efficiency of the dialyzer construction, chemistry makeup of the dialysate, and so on. The fluid volume rate removed from the blood Q_{UFR} is an additive component to the spent dialysate volume as it passes out of the dialyzer.

[0038] Solving Eq. 8 for $TBV(\mathrm{T})$ provides Eq. 9, and setting Eq. 7 equal to Eq. 9 provides Eq. 10.

$$TBV(\mathrm{T}) = \left[\sum_{n=1\ (Step\ \Delta t)}^{\mathrm{T}/\Delta t} \left(\frac{Q_{UFR}(n) + Q_{UFR}(n-1)}{2} \right) \times \Delta t \right] + TBV_0 \qquad \text{Eq. 9}$$

$$TBV_0 = \frac{\left[\sum_{n=1\ (Step\ \Delta t)}^{\mathrm{T}/\Delta t} \left(\frac{Q_{UFR}(n) + Q_{UFR}(n-1)}{2} \right) \times \Delta t \right]}{\Delta \mathrm{BV}} \qquad \text{Eq. 10}$$

[0039] Thus, to determine an accurate TBV_0 by solving Eq. 10, actual Q_{UFR} must be determined. Q_{UFR} can be measured from the following outlined process:

[0040] Dialysis blood pump is calibrated and accurate in its settings for moving blood through the dialyzer blood circuit. That is, pump 202 should provide a calibrated pump volume flow Q_b. Commonly, pumps used in dialysis are calibrated at their factories.

[0041] During the measurement period, pump volme flow Q_b should remain constant from time t_0 to time T.

[0042] Calibrated hematocrit sensors, e.g., Crit-Line® or CLiC™ devices, are used to measure HCT_{206} and HCT_{208}. As previously discussed, one sensor can be used measure HCT_{206} and afterwards used to measure HCT_{208} for a setup in FIG. 1, or two sensors can be used to simultaneously measure both HCT_{206} and HCT_{208} for a setup in FIG. 3. Δt can be used to gauge whether one sensor or two sensors will suffice. If Δt is reasonably large, e.g., 1 sample per minute or more, a single sensor can be used to measure hematocrit at both points because dialysis parameters do not change quickly.

[0043] At a periodic time interval Δt, with the dialysis pump set to a constant and known Q_b, HCT_{206} and HCT_{208} are measured simultaneously (or near simultaneously if the hematocrit values are not changing rapidly). At the same time hematocrit measurements are made, fractional change in blood volume ΔBV is calculated using Eq. 6 and HCT_{206}.

[0044] Using mass balance of the red blood cell volume flowing through the dialyzer (assuming no loss of red blood cell volume during time T), the following relationships can be derived to solve for Q_{UFR}. Beginning at location 206:

$$HCT_{206} = \frac{RBVR}{Q_b} \qquad \text{Eq. 11}$$

Where HCT_{206} is calibrated measured hematocrit at location 206, $RBVR$ is red blood cell volume rate flowing through the dialyzer, and Q_b is blood flow rate dictated by a calibrated blood pump. A similar relationship can be written at location 208 as:

$$HCT_{208} = \frac{RBVR}{Q_b - Q_{UFR}} \qquad \text{Eq. 12}$$

Where HCT_{208} is calibrated measured hematocrit at location 208, $RBVR$ is red blood cell volume rate flowing through the dialyzer, Q_b is calibrated blood flowrate, and Q_{UFR} is true fluid removal volume rate.

[0045] Embodiments of the disclosure use the hematocrit monitoring engine 212 to measure the hematocrit of the blood entering the dialyzer 204 and then the HCT blood exiting the dialyzer 204. Due to the nature of the dialyzer 204, no red blood cells are lost across dialyzer membranes within the dialyzer 204 – only fluid, for example, urea, passes through into the waste collecting dialysate. Since red blood cells do not cross the dialyzer membranes

into the waste, mass balance analysis of the red blood cell volume is applicable. Assuming red blood cell volume is constant (i.e., no red blood cell volume is lost during time T), then Eqs. 11 and 12 can be combined to provide Eq. 13:

$$HCT_{206} \times Q_b = HCT_{208} \times (Q_b - Q_{UFR}) \quad \text{Eq. 13}$$

[0046] Eq. 13 can be rearranged as Eq. 14.

$$Q_{UFR} = \left(\frac{HCT_{208} - HCT_{206}}{HCT_{208}}\right) \times Q_b \quad \text{Eq. 14}$$

[0047] Since HCT_{208} and HCT_{206} are calibrated hematocrit values and Q_b is a calibrated flow rate of the blood pump 202, Q_{UFR}, which is derived from the calibrated values of HCT_{208}, HCT_{206}, and Q_b, is also a calibrated value. Values of Q_{UFR} obtained and used at samples $n = 0$ through $n = \lfloor T/\Delta t \rfloor$ with sampling rate of Δt, can be used in Eq. 10 to calculate a number of solutions for TBV_0. Successive values of calculated TBV_0 at each measurement time $n\Delta t$ can be averaged to improve accuracy of TBV_0 obtained.

[0048] The blood volume engine 216 determines TBV_0 using relationships shown in Eq. 10 and Eq. 14, depending on information received from the hematocrit measurement engine 212 and the flowrate engine 214. Note that in FIG. 2, dotted lines represent potential alternative inputs for determining flowrate, some or all of which may be used in different exemplary embodiments. For example, the blood flowrate at the input of the dialyzer 204 is desired, but this flowrate can be determined from either the calibrated pump 202 or the flowmeter 210, thus one of these measurement paths may be active and the other inactive.

[0049] FIG. 4 illustrates a process 400 for determining patient blood volume, according to some embodiments of the disclosure. At step 402, the system 200 determines Q_{UFR} (actual fluid removal rate) at an initial time t_0 using Q_b (calibrated blood flowrate) and hematocrit measurements HCT_{206} and HCT_{208} at the time t_0. The blood volume engine 216 determines Q_{UFR} at time t_0 according to Eq. 14 using HCT_{206} and HCT_{208} at the time t_0 from the hematocrit measurement engine 212 and Q_b from the flowrate engine 214. The Q_{UFR} measured is associated with time t_0, and a temporary variable $i = \lfloor T/\Delta t \rfloor$ is used to keep track of total number of measurement periods, a current or most recent measurement period, or a total number of TBV_0 measurements taken. Initially, at time T=0, i is 0, and i only becomes 1 after a time period Δt has passed. That is, once T reaches Δt.

[0050] At step 404, after an elapsed time Δt, the blood volume engine 216 automatically increments i, based on the mathematical relationship above, and determines Q_{UFR} in a similar manner as already discussed with respect to step 402. The Q_{UFR} determined at 404 is Q_{UFR} for the measurement period i.

[0051] At step 406, the blood volume engine 216 determines difference in total blood volume for cumulative measurement periods between time t_0 (T=0) and time T. That is, the blood volume engine 216 determines fluid removed during a total number of elapsed measurement periods in the time T. Referring to Eq. 8, volume removed during a single measurement period involves adding a previous Q_{UFR} and a current Q_{UFR}, dividing the result of the addition by 2, and then multiplying the result by the duration Δt between the Q_{UFR} measurements. That is, volume removed in measurement period i is determined using Q_{UFR} for measurement period i-1, Q_{UFR} for measurement period i, and Δt, time duration between Q_{UFR} measurements for periods i-1 and i. The volume removed in measurement period i is then added to total volume removed from time t_0 until measurement period i-1 to obtain total blood volume removed for cumulative measurement periods between time t_0 and T.

[0052] For illustrative purposes, an example is provided. At time t_0, total volume removed is 0. At measurement period 1, volume removed is calculated to be $TBV(1\Delta t) - TBV_0$. This value, $TBV(1\Delta t) - TBV_0$, is added to the previous total volume removed, 0, to obtain current total volume removed, $TBV(1\Delta t) - TBV_0$. At measurement period 2, volume removed is calculated to be $TBV(2\Delta t) - TBV(1\Delta t)$. This value, $TBV(2\Delta t) - TBV(1\Delta t)$, is added to the previous total volume removed, $TBV(1\Delta t) - TBV_0$, to obtain the current total volume removed $TBV(2\Delta t) - TBV_0$. In this manner, through every successive measurement period, a difference of volume removed for a most recent measurement period is contiunually calculated and added to a running total of blood volume removed. At 406, the blood volume engine 216 thus determines fluid removed for cumulative measurement periods from initial time t_0 until a most recent time T.

[0053] At step 408, the blood volume engine 216 determines percentage change in blood volume or fractional change in blood volume ΔBV for the cumulative measurement periods. The ΔBV is determined according to Eq. 6, with HCT_0 being HCT_{206} at initial time t_0 and $HCT(\mathrm{T})$ being HCT_{206} for the most recent measurement period i. Since measurements are made at sample intervals Δt, note that $HCT(\mathrm{T})$ for the most recent measurement period i corresponds to $HCT(i\Delta t)$.

[0054] At step 410, the blood volume engine 216 determines and stores TBV_0 solution for the current measurement period i. The blood volume engine 216 determines the beginning blood volume of the patient TBV_0, as defined in Eq. 10, using the ΔBV from step 408 and the difference in total blood volume from step 406.

[0055] At step 412, the blood volume engine 216 displays stored TBV_0 for measurement period i and current time T and/or time when the measurement was taken $i\Delta t$.

[0056] At step 414, the blood volume engine 216 determines whether there are more measurement periods. If there are more measurements to be made, then a new Q_{UFR} measurement is made at step 404 and i is incremented, otherwise the blood volume engine 216 determines, at step 416, an average of the stored TBV_0 solutions for measurement period 1 through measurement period i.

[0057] At step 418, the blood volume engine 216 displays data summary of all measurements made during the process 400.

[0058] Based on the value that a user obtains from the output of the hemodialysis system 12, the user may determine a treatment plan for the patient or know how aggressive the dialysis treatment should be. If the patient's beginning blood volume differs signigicantly from previous visits, the user (physician) can further provide additional tips to the patient on managing the total blood volume.

[0059] In an exemplary embodiment, the invention provides a system for determining beginning blood volume of a patient undergoing dialysis treatment, the system comprising: a first portion of tubing, configured to connect a patient to an input of a dialyzer; a second portion of tubing, configured to connect the patient to an output of the dialyzer; a pump, configured to pump blood from the patient through the first portion of tubing into the dialyzer, and out of the dialyzer into the second portion of tubing; a first blood chamber, disposed along the first portion of tubing, and a second blood chamber, disposed along the second portion of tubing, wherein the first blood chamber and the second blood chamber are configured to facilitate hematocrit measurement; and a controller, configured to determine the beginning blood volume using hematocrit values associated with the input of the dialyzer, hematocrit values associated with the output of the dialyzer, and a flowrate of blood through the first portion of tubing.

[0060] In a further exemplary embodiment, the controller determines the flowrate of blood through the first portion of tubing through a calibrated pumping rate of the pump.

[0061] In a further exemplary embodiment, the system further comprises at least one of: a flowmeter coupled to the first portion of tubing, the flowmeter configured to determine the flowrate of blood through the first portion of tubing.

[0062] In a further exemplary embodiment, the system further comprises a first sensor assembly coupled to the first blood chamber, the first sensor assembly configured to measure hematocrit values associated with the input of the dialyzer; and a second sensor assembly coupled to the second blood chamber, the second sensor assembly configured to measure hematocrit values associated with the output of the dialyzer.

[0063] In a further exemplary embodiment, the controller is further configured to: determine a fractional change in patient blood volume using a hematocrit value associated with the input of the dialyzer at the beginning of the dialysis treatment and a hematocrit value associated with the input of the dialyzer at an end of a measurement session; determine a plurality of fluid removal volume rates during the measurement session using the hematocrit values associated with the input of the dialyzer, the hematocrit values associated with the output of the dialyzer, and the flowrate of blood through the first portion of tubing; and determine the beginning blood volume based on the fractional change in patient blood volume and the plurality of fluid removal volume rates.

[0064] In a further exemplary embodiment, the controller is further configured to: determine an initial fluid removal volume rate in the plurality of fluid removal volume rates; and determine each successive fluid removal volume rates in the plurality of fluid removal volume rates at a sample interval.

[0065] In a further exemplary embodiment, the sample interval is 1 minute or longer.

[0066] In a further exemplary embodiment, the controller is further configured to: determine that the beginning blood volume is an average of a plurality of beginning blood volumes corresponding to the plurality of fluid removal volume rates; wherein a number of the plurality of beginning blood volumes is at least 2 and a number of the plurality of fluid removal volume rates is at least 3.

[0067] In an exemplary embodiment, the invention provides a method for determining beginning blood volume of a patient connected to a dialysis system, the method comprising: circulating, using a pump of the dialysis system, blood from the patient through a dialyzer; and determining, using the dialysis system, beginning blood volume of the patient, wherein determining the beginning blood volume includes: determining a blood flowrate

corresponding to an input side of the dialyzer; determining a fluid removal rate at an initial time via the blood flowrate, hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the output side of the dialyzer at the initial time; determining a fluid removal rate after a first measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the first measurement period and hematocrit corresponding to the output side of the dialyzer after the first measurement period; determining volume of fluid removed for the first measurement period via the fluid removal rate at the initial time and the fluid removal rate after the first measurement period; determining fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer after the first measurement period; and determining the beginning blood volume via the fractional blood volume change and the volume of fluid removed for the first measurement period.

[0068] In a further exemplary embodiment, determining the beginning blood volume further includes: displaying the beginning blood volume on a screen of the dialysis system.

[0069] In a further exemplary embodiment, determining the beginning blood volume further includes: determining whether there are more measurement periods; and in response to the determining that there are more measurement periods, performing by the dialysis system: determining a fluid removal rate for a next measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the next measurement period and hematocrit corresponding to the output side of the dialyzer after the next measurement period; determining cumulative volume of fluid removed via two most recent fluid removal rates determined and volume of fluid removed for a previous measurement period; determining the fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer for the next measurement period; and determining the beginning blood volume via the fractional blood volume change and the cumulative volume of fluid removed.

[0070] In a further exemplary embodiment, in response to the determining that there are more measurement periods, the dialysis system further performs: determining average beginning blood volume for all measurement periods; and displaying the average of the multiple beginning blood volumes on the screen of the dialysis system.

[0071] In a further exemplary embodiment, the blood flowrate corresponding to the input side of the dialyzer is determined via a calibrated pumping rate of the pump or an input flowmeter of the dialysis system.

[0072] In a further exemplary embodiment, hematocrit corresponding to the input side of the dialyzer and hematocrit corresponding to the output side of the dialyzer are measured via a first sensor assembly of the dialysis system and a second sensor assembly of the dialysis system, respectively.

[0073] In a further exemplary embodiment, hematocrit corresponding to the input side of the dialyzer is measured via a sensor assembly of the dialysis system, and after a time period, hematocrit corresponding to the output side of the dialyzer is measured via the sensor assembly of the dialysis system.

[0074] In a further exemplary embodiment, each measurement period has a duration of 1 minute.

[0075] In an exemplary embodiment, the invention provides a non-transitory computer readable medium for determining beginning blood volume of a patient connected to a dialysis system, the non-transitory computer readable medium including instructions for causing a processor of the dialysis system to facilitate performing: circulating, using a pump of the dialysis system, blood from the patient through a dialyzer; and determining, using the dialysis system, beginning blood volume of the patient, wherein determining the beginning blood volume includes: determining a blood flowrate corresponding to an input side of the dialyzer; determining a fluid removal rate at an initial time via the blood flowrate, hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the output side of the dialyzer at the initial time; determining a fluid removal rate after a first measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the first measurement period and hematocrit corresponding to the output side of the dialyzer after the first measurement period; determining volume of fluid removed for the first measurement period via the fluid removal rate at the initial time and the fluid removal rate after the first measurement period; determining fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer after the first measurement period; and determining the beginning blood volume via the

fractional blood volume change and the volume of fluid removed for the first measurement period.

[0076] In a further exemplary embodiment, determining the beginning blood volume further includes: displaying the beginning blood volume on a screen of the dialysis system.

[0077] In a further exemplary embodiment, determining the beginning blood volume further includes: determining whether there are more measurement periods; and in response to the determining that there are more measurement periods, performing by the dialysis system: determining a fluid removal rate for a next measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the next measurement period and hematocrit corresponding to the output side of the dialyzer after the next measurement period; determining cumulative volume of fluid removed via two most recent fluid removal rates determined and volume of fluid removed for a previous measurement period; determining the fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer for the next measurement period; and determining the beginning blood volume via the fractional blood volume change and the cumulative volume of fluid removed.

[0078] In a further exemplary embodiment, in response to the determining that there are more measurement periods, the dialysis system further performs: determining average beginning blood volume for all measurement periods; and displaying the average of the multiple beginning blood volumes on the screen of the dialysis system.

[0079] All references, including publications, patent applications, and patents, cited herein are hereby incorporated by reference to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

[0080] The use of the terms “a” and “an” and “the” and “at least one” and similar referents in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The use of the term “at least one” followed by a list of one or more items (for example, “at least one of A and B”) is to be construed to mean one item selected from the listed items (A or B) or any combination of two or more of the listed items (A and B), unless otherwise indicated herein or clearly

contradicted by context. The terms "comprising," "having," "including," and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to,") unless otherwise noted. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

[0081] Preferred embodiments of this invention are described herein, including the best mode known to the inventors for carrying out the invention. Variations of those preferred embodiments may become apparent to those of ordinary skill in the art upon reading the foregoing description. The inventors expect skilled artisans to employ such variations as appropriate, and the inventors intend for the invention to be practiced otherwise than as specifically described herein. Accordingly, this invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the invention unless otherwise indicated herein or otherwise clearly contradicted by context.

CLAIMS:

1. A system for determining beginning blood volume of a patient undergoing dialysis treatment, the system comprising:

a first portion of tubing, configured to connect a patient to an input of a dialyzer;

a second portion of tubing, configured to connect the patient to an output of the dialyzer;

a pump, configured to pump blood from the patient through the first portion of tubing into the dialyzer, and out of the dialyzer into the second portion of tubing;

a first blood chamber, disposed along the first portion of tubing, and a second blood chamber, disposed along the second portion of tubing, wherein the first blood chamber and the second blood chamber are configured to facilitate hematocrit measurement; and

a controller, configured to determine the beginning blood volume using hematocrit values associated with the input of the dialyzer, hematocrit values associated with the output of the dialyzer, and a flowrate of blood through the first portion of tubing.

2. The system according to claim 1, wherein the controller determines the flowrate of blood through the first portion of tubing through a calibrated pumping rate of the pump.

3. The system according to claim 1, further comprising at least one of:

a flowmeter coupled to the first portion of tubing, the flowmeter configured to determine the flowrate of blood through the first portion of tubing.

4. The system according to claim 1, further comprising:

a first sensor assembly coupled to the first blood chamber, the first sensor assembly configured to measure hematocrit values associated with the input of the dialyzer; and

a second sensor assembly coupled to the second blood chamber, the second sensor assembly configured to measure hematocrit values associated with the output of the dialyzer.

5. The system according to claim 1, wherein the controller is further configured to:

determine a fractional change in patient blood volume using a hematocrit value associated with the input of the dialyzer at the beginning of the dialysis treatment and a hematocrit value associated with the input of the dialyzer at an end of a measurement session;

determine a plurality of fluid removal volume rates during the measurement session using the hematocrit values associated with the input of the dialyzer, the hematocrit values associated with the output of the dialyzer, and the flowrate of blood through the first portion of tubing; and

determine the beginning blood volume based on the fractional change in patient blood volume and the plurality of fluid removal volume rates.

6. The system according to claim 5, wherein the controller is further configured to:

determine an initial fluid removal volume rate in the plurality of fluid removal volume rates; and

determine each successive fluid removal volume rates in the plurality of fluid removal volume rates at a sample interval.

7. The system according to claim 6, wherein the sample interval is 1 minute or longer.

8. The system according to claim 5, wherein the controller is further configured to:

determine that the beginning blood volume is an average of a plurality of beginning blood volumes corresponding to the plurality of fluid removal volume rates;

wherein a number of the plurality of beginning blood volumes is at least 2 and a number of the plurality of fluid removal volume rates is at least 3.

9. A method for determining beginning blood volume of a patient connected to a dialysis system, the method comprising:

circulating, using a pump of the dialysis system, blood from the patient through a dialyzer; and

determining, using the dialysis system, beginning blood volume of the patient, wherein determining the beginning blood volume includes:

determining a blood flowrate corresponding to an input side of the dialyzer;

determining a fluid removal rate at an initial time via the blood flowrate, hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the output side of the dialyzer at the initial time;

determining a fluid removal rate after a first measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the first measurement period and hematocrit corresponding to the output side of the dialyzer after the first measurement period;

determining volume of fluid removed for the first measurement period via the fluid removal rate at the initial time and the fluid removal rate after the first measurement period;

determining fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer after the first measurement period; and

determining the beginning blood volume via the fractional blood volume change and the volume of fluid removed for the first measurement period.

10. The method according to claim 9, wherein determining the beginning blood volume further includes:

displaying the beginning blood volume on a screen of the dialysis system.

11. The method according to claim 9, wherein determining the beginning blood volume further includes:

determining whether there are more measurement periods; and

in response to the determining that there are more measurement periods, performing by the dialysis system:

determining a fluid removal rate for a next measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the next measurement period and hematocrit corresponding to the output side of the dialyzer after the next measurement period;

determining cumulative volume of fluid removed via two most recent fluid removal rates determined and volume of fluid removed for a previous measurement period;

determining the fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer for the next measurement period; and

determining the beginning blood volume via the fractional blood volume change and the cumulative volume of fluid removed.

12. The method according to claim 11, wherein in response to the determining that there are more measurement periods, the dialysis system further performs:

determining average beginning blood volume for all measurement periods; and

displaying the average of the multiple beginning blood volumes on the screen of the dialysis system.

13. The method according to claim 11, wherein the blood flowrate corresponding to the input side of the dialyzer is determined via a calibrated pumping rate of the pump or an input flowmeter of the dialysis system.

14. The method according to claim 11, wherein hematocrit corresponding to the input side of the dialyzer and hematocrit corresponding to the output side of the dialyzer are measured via a first sensor assembly of the dialysis system and a second sensor assembly of the dialysis system, respectively.

15. The method according to claim 11, wherein hematocrit corresponding to the input side of the dialyzer is measured via a sensor assembly of the dialysis system, and after a time period, hematocrit corresponding to the output side of the dialyzer is measured via the sensor assembly of the dialysis system.

16. The method according to claim 11, wherein each measurement period has a duration of 1 minute.

17. A non-transitory computer readable medium for determining beginning blood volume of a patient connected to a dialysis system, the non-transitory computer readable medium including instructions for causing a processor of the dialysis system to facilitate performing:

circulating, using a pump of the dialysis system, blood from the patient through a dialyzer; and

determining, using the dialysis system, beginning blood volume of the patient, wherein determining the beginning blood volume includes:

determining a blood flowrate corresponding to an input side of the dialyzer;

determining a fluid removal rate at an initial time via the blood flowrate, hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the output side of the dialyzer at the initial time;

determining a fluid removal rate after a first measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the first measurement period and hematocrit corresponding to the output side of the dialyzer after the first measurement period;

determining volume of fluid removed for the first measurement period via the fluid removal rate at the initial time and the fluid removal rate after the first measurement period;

determining fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer after the first measurement period; and

determining the beginning blood volume via the fractional blood volume change and the volume of fluid removed for the first measurement period.

18. The non-transitory computer readable medium according to claim 17, wherein determining the beginning blood volume further includes:

displaying the beginning blood volume on a screen of the dialysis system.

19. The non-transitory computer readable medium according to claim 17, wherein determining the beginning blood volume further includes:

determining whether there are more measurement periods; and

in response to the determining that there are more measurement periods, performing by the dialysis system:

determining a fluid removal rate for a next measurement period via the blood flowrate, hematocrit corresponding to the input side of the dialyzer after the next measurement period and hematocrit corresponding to the output side of the dialyzer after the next measurement period;

determining cumulative volume of fluid removed via two most recent fluid removal rates determined and volume of fluid removed for a previous measurement period;

determining the fractional blood volume change via hematocrit corresponding to the input side of the dialyzer at the initial time and hematocrit corresponding to the input side of the dialyzer for the next measurement period; and

determining the beginning blood volume via the fractional blood volume change and the cumulative volume of fluid removed.

20. The non-transitory computer readable medium according to claim 19, wherein in response to the determining that there are more measurement periods, the dialysis system further performs:

determining average beginning blood volume for all measurement periods; and

displaying the average of the multiple beginning blood volumes on the screen of the dialysis system.

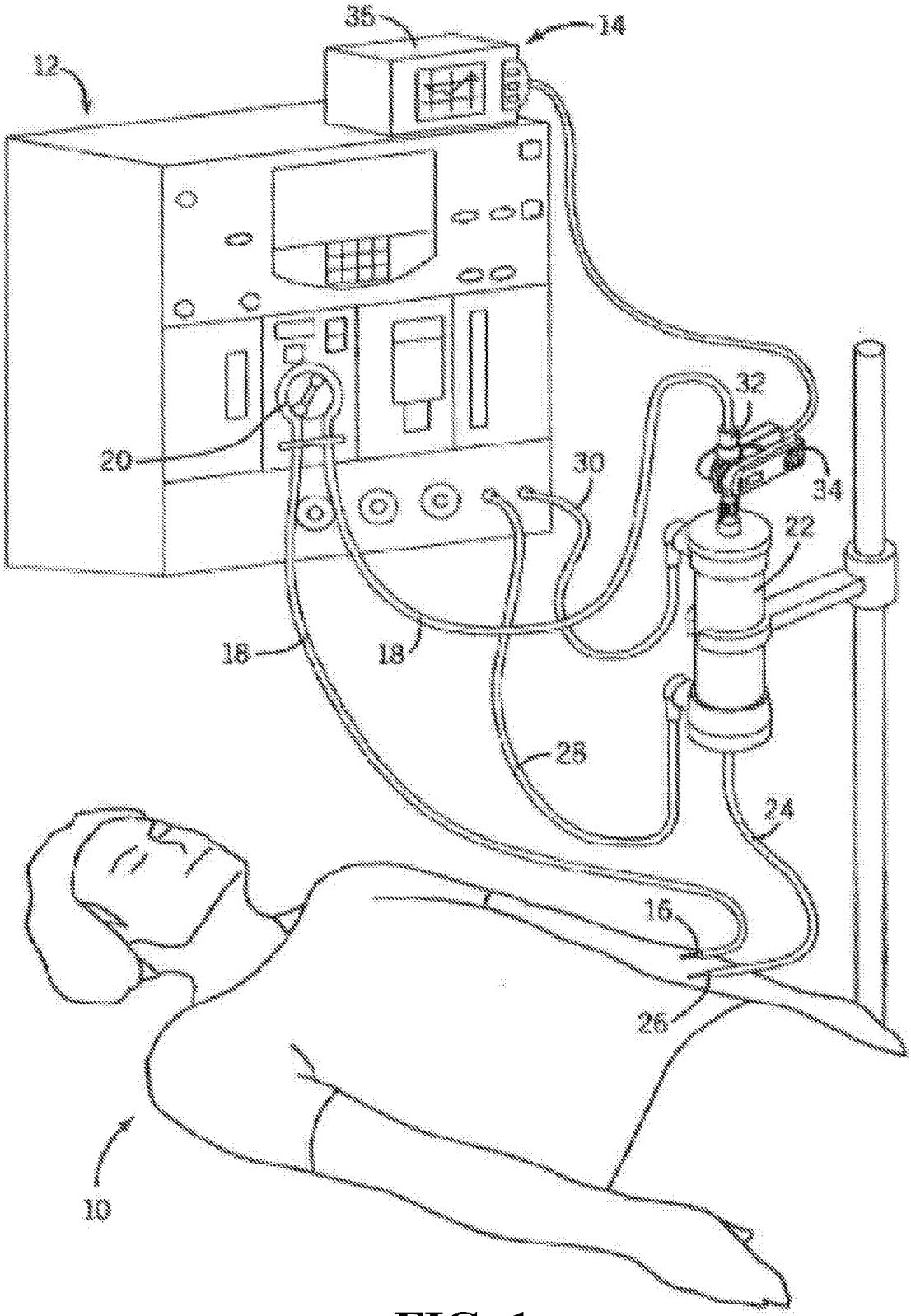

FIG. 1

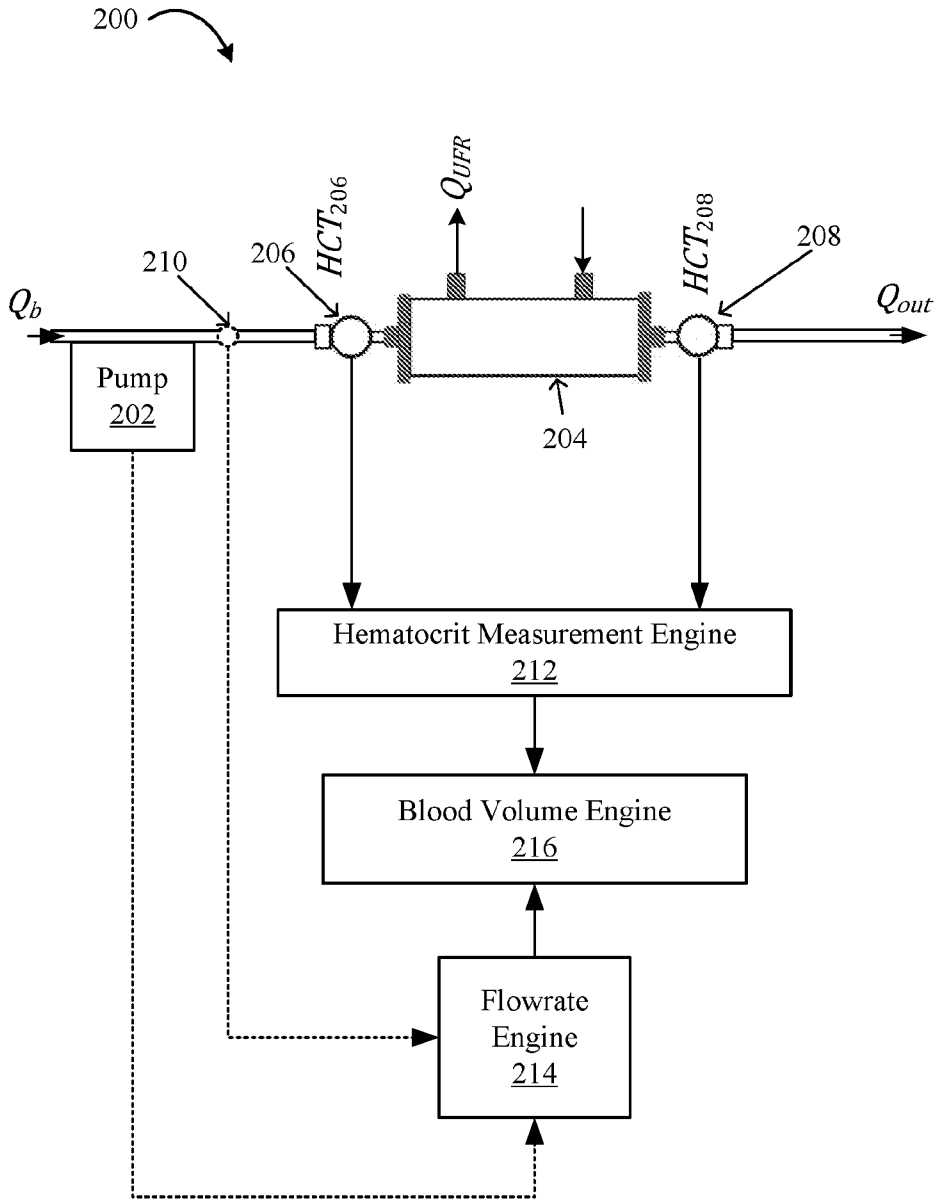
200
Q_{UFR}
HCT_{206}
HCT_{208}
208
210
206
Q_b
Q_{out}
Pump
202
204
Hematocrit Measurement Engine
212
Blood Volume Engine
216
Flowrate
Engine
214

FIG. 2

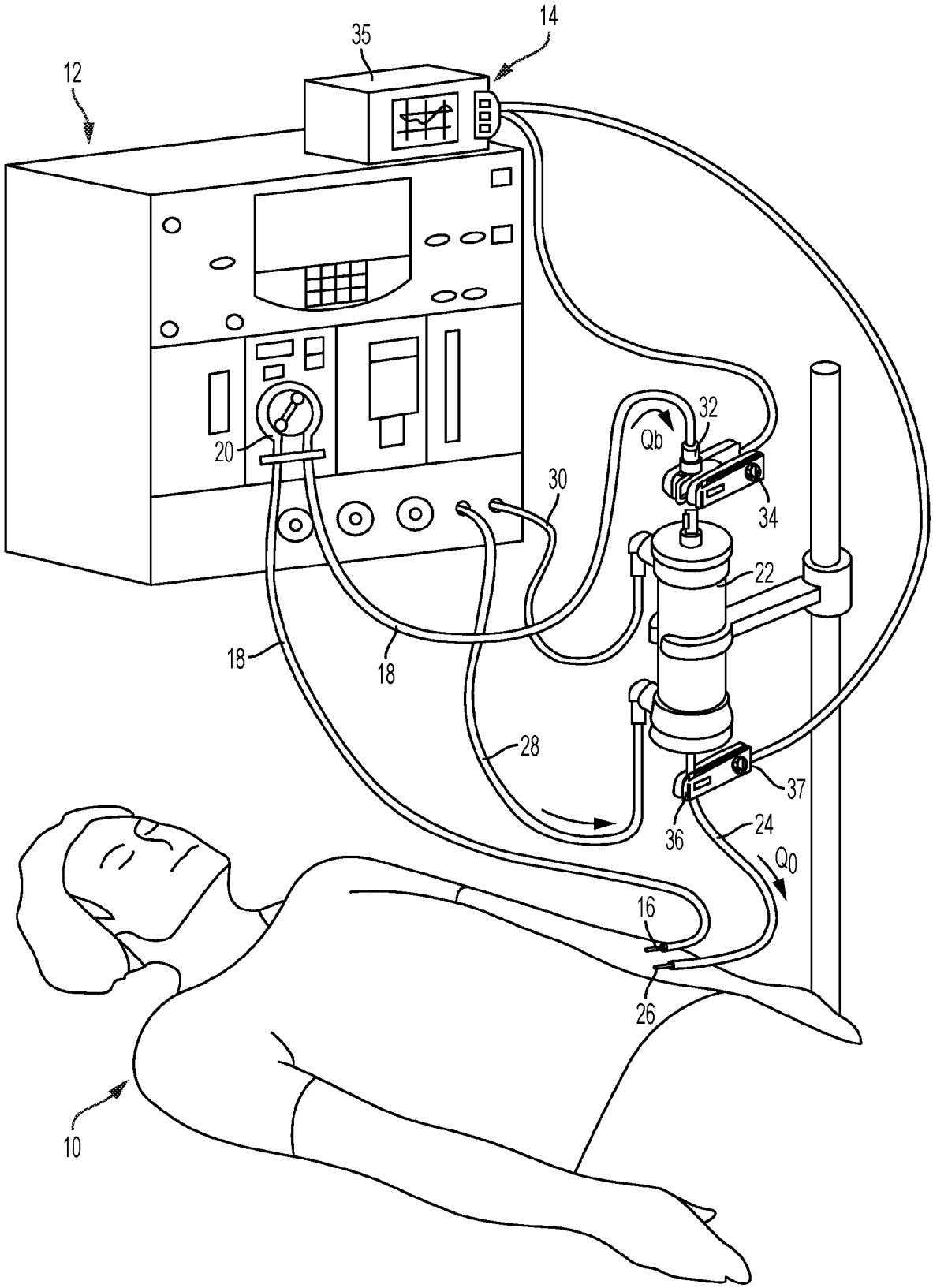

FIG. 3

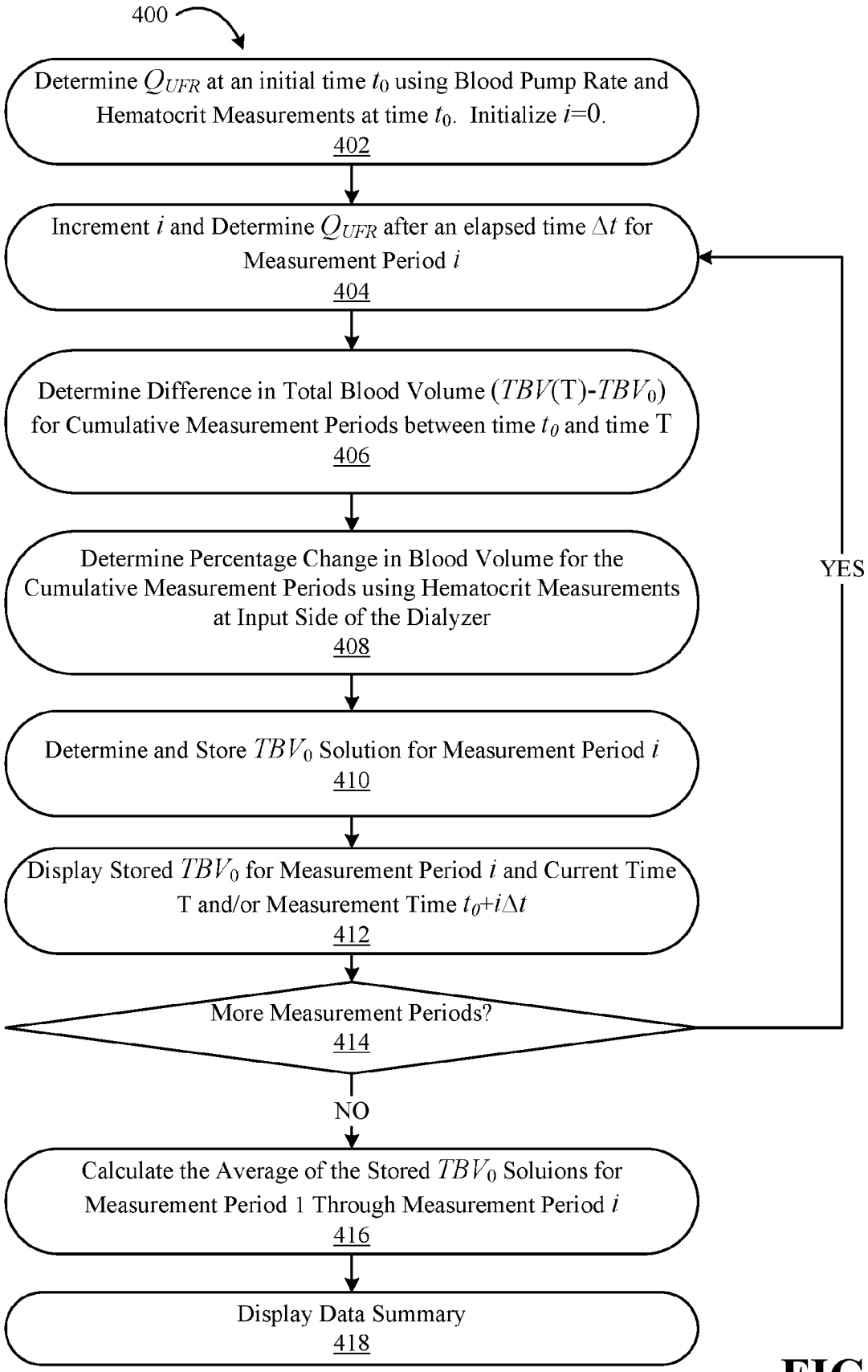
400
Determine Q_{UFR} at an initial time t_0 using Blood Pump Rate and Hematocrit Measurements at time t_0. Initialize i=0.
402
Increment i and Determine Q_{UFR} after an elapsed time Δt for Measurement Period i
404
Determine Difference in Total Blood Volume (TBV(T)-TBV_0) for Cumulative Measurement Periods between time t_0 and time T
406
Determine Percentage Change in Blood Volume for the Cumulative Measurement Periods using Hematocrit Measurements at Input Side of the Dialyzer
408
Determine and Store TBV_0 Solution for Measurement Period i
410
Display Stored TBV_0 for Measurement Period i and Current Time T and/or Measurement Time t_0+$i\Delta t$
412
More Measurement Periods?
414
YES
NO
Calculate the Average of the Stored TBV_0 Soluions for Measurement Period 1 Through Measurement Period i
416
Display Data Summary
418

FIG. 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/048980

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M1/16 A61B5/145 A61M1/34 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 A61B

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.
A	CA 2 949 679 A1 (FRESENIUS MEDICAL CARE HOLDINGS INC [US]) 26 November 2015 (2015-11-26) paragraphs [0016] - [0017], [0047] - [0078]; figures 1-6	1-8, 17-20
A	WO 2015/179523 A1 (FRESENIUS MED CARE HLDG INC [US]) 26 November 2015 (2015-11-26) paragraphs [0014] - [0026]; figures 1-5	1-8, 17-20
A	US 2008/103427 A1 (TOYODA MASAHIRO [JP] ET AL) 1 May 2008 (2008-05-01) paragraphs [0034] - [0065]; figures 1-8	1,17

☐ 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

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 November 2019	20/11/2019

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	Schlaug, Martin

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/048980

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 9-16
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Continuation of Box II.1

Claims Nos.: 9-16

Claims 9-16 define methods for determining beginning blood volume of a patient connected to a dialysis system and all comprise the step of circulating, using a pump of the dialysis system, blood from the patient through a dialyzer. This step thus encompasses extracting the living organ blood from a patient, treating it in a dialyzer and returning it to the patient. Those methods thus encompass methods of treating a human being i.e. a patient by therapy and surgery. The subject matter of claims 6-16 was therefore not searched (Article 17(2)(a)(i) /(ii) and Rule 39.1 (iv) PCT) and consequently no opinion will be formulated on the subject matter of those claims (Article 34(4)(a)(i) and Rule 67.1(iv) PCT).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/048980

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