US009370324B2

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Barrett et al.

(10) **Patent No.: US 9,370,324 B2**
(45) **Date of Patent: Jun. 21, 2016**

(54) **HEMODIALYSIS PATIENT DATA ACQUISITION, MANAGEMENT AND ANALYSIS SYSTEM**

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(73) Assignee: **FRESENIUS MEDICAL CARE HOLDINGS, INC.**, Waltham, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 736 days.

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(51) **Int. Cl.**

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A61B 5/145	(2006.01)
A61B 5/1455	(2006.01)
A61M 1/16	(2006.01)
G06F 19/00	(2011.01)
G06Q 50/24	(2012.01)
A61M 1/36	(2006.01)
G06G 7/58	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/14535*** (2013.01); ***A61B 5/14557*** (2013.01); ***A61M 1/16*** (2013.01); ***A61M 1/361*** (2014.02); ***G06F 19/322*** (2013.01); ***G06F 19/3406*** (2013.01); ***G06F 19/3481*** (2013.01); ***G06Q 50/24*** (2013.01); *A61B 2562/08* (2013.01); *A61M 2205/3313* (2013.01); *A61M 2205/3553* (2013.01); *A61M 2205/3592* (2013.01); *A61M 2205/52* (2013.01)

(58) **Field of Classification Search**

CPC G06F 19/3481; G06F 19/3406
USPC 604/403, 408, 411, 412, 414, 415, 416
See application file for complete search history.

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Primary Examiner — Eric S Dejong
(74) *Attorney, Agent, or Firm* — Leydig, Voit & Mayer, Ltd.

(57) **ABSTRACT**

A hemodialysis patient data acquisition and management system resides on a host computer which receives information from one or more non-invasive, optical blood monitors associated with a hemodialysis system. When a patient is undergoing hemodialysis treatment, a sensor assembly monitors the patient's blood flowing through the hemodialysis system and a controller for the blood monitor generates data which includes at least an identification code for the patient undergoing the treatment on the respective system, and non-invasively determined blood data taken at the onset of the scheduled treatment, such as initial Hgb, HCT, and SAT values. A host computer communicates with the one or more optical blood monitors, preferably via a wireless network, and the patient's session commencement data is downloaded to the host computer. The host computer includes a patient database containing historical session commencement data for a plurality of patients, as well as screen displays for displaying historical data for individual patients, such as Hgb trends. The system also preferably provides a predictive algorithm for the patient's Hgb at the patient's next scheduled hemodialysis treatment session. The preferred system also includes software that provides a recommended dose of the anemia management drug for the patient.

7 Claims, 12 Drawing Sheets

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Petitioner Terumo Exhibit 1011-0001

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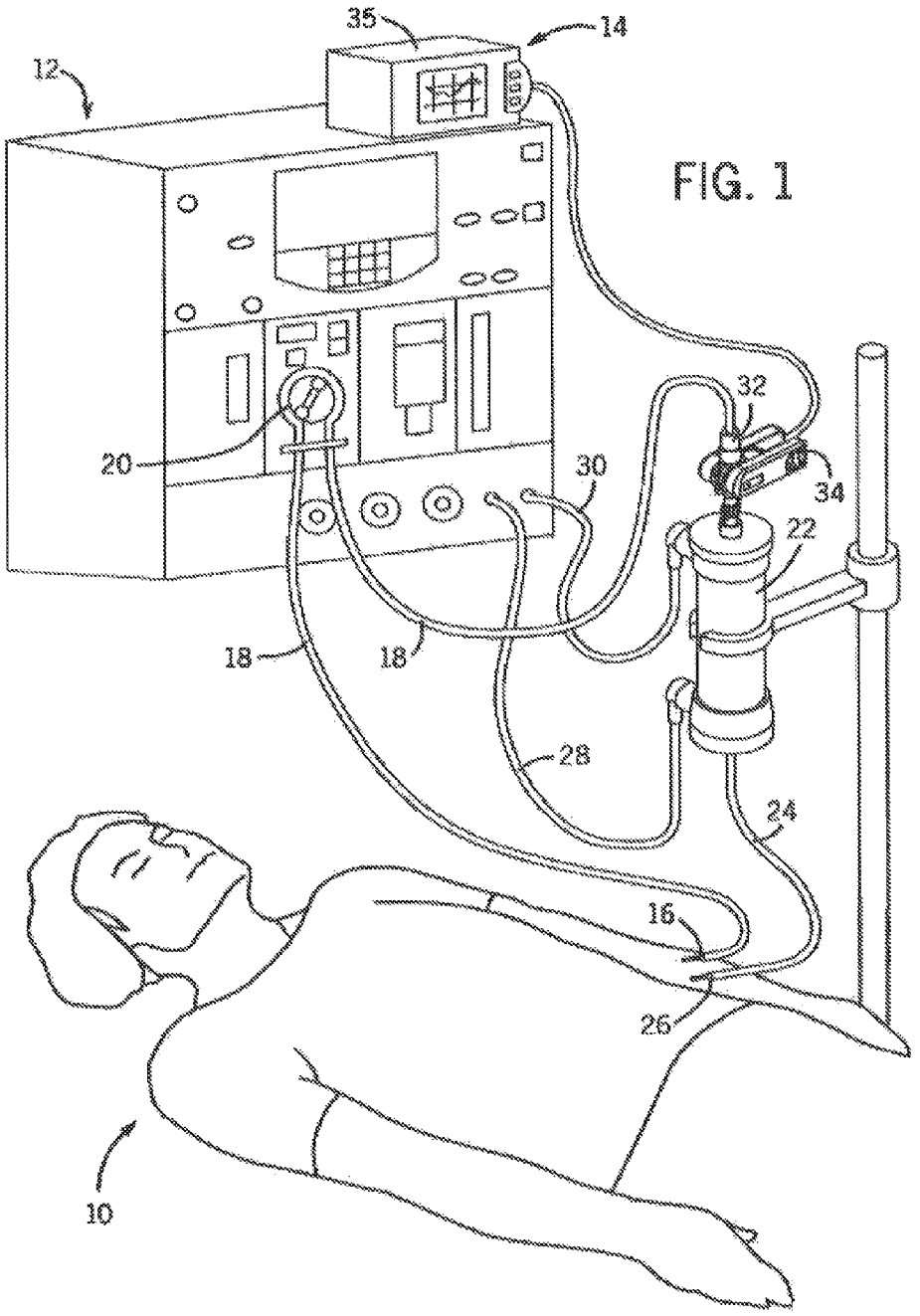


FIG. 1

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Petitioner Terumo Exhibit 1011-0004

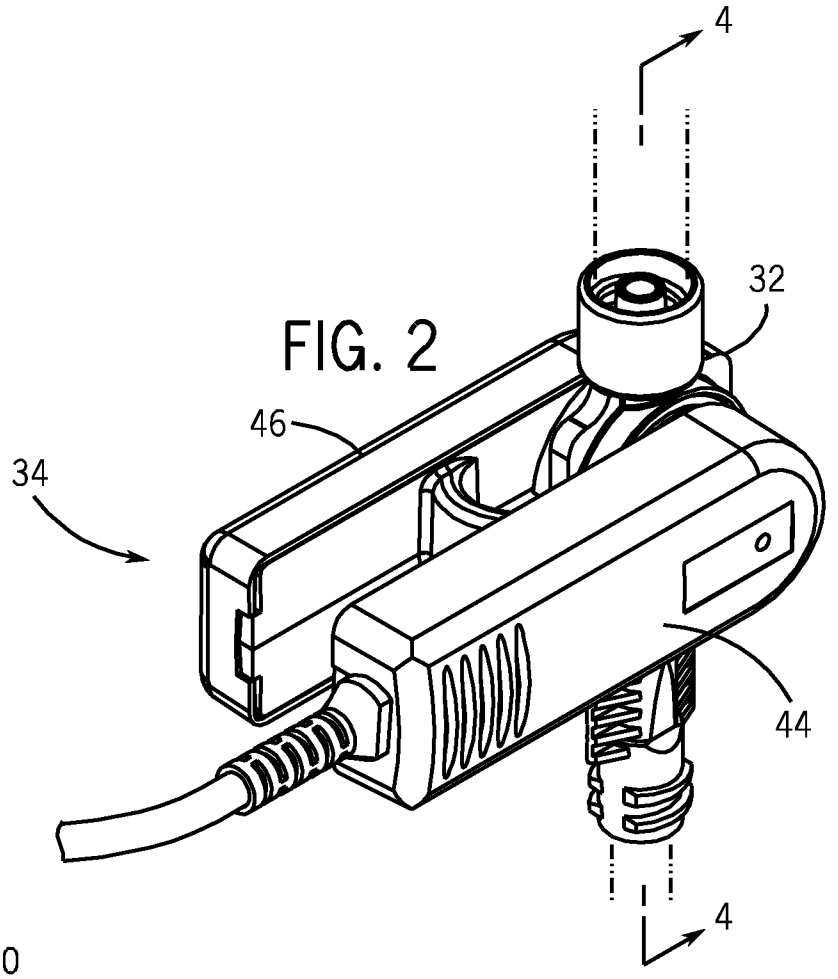


FIG. 2

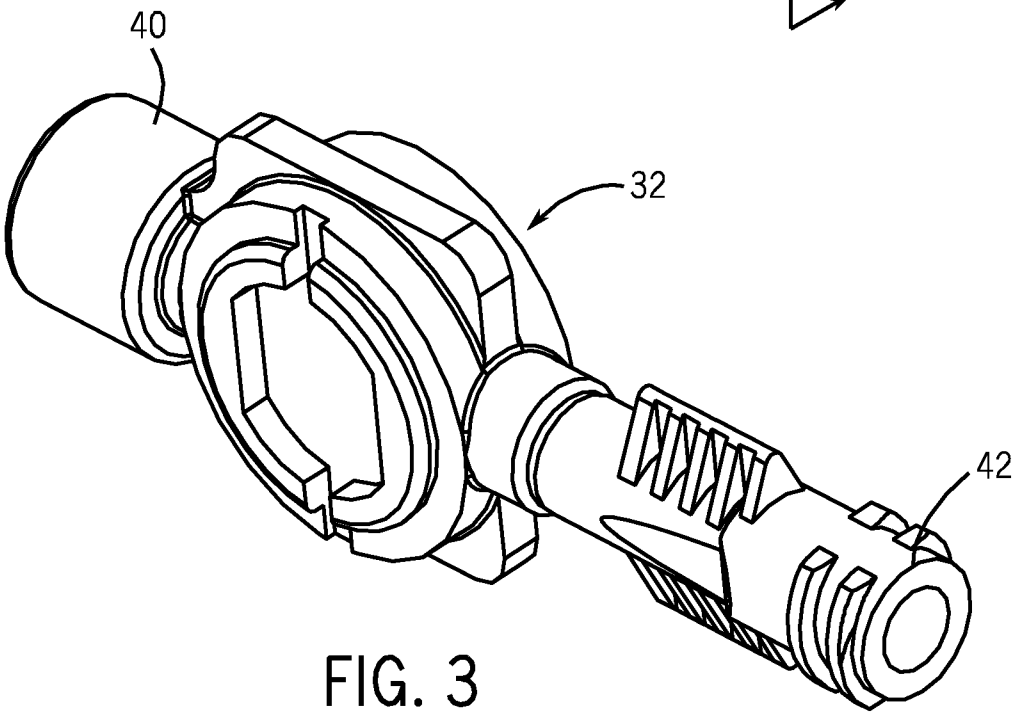


FIG. 3

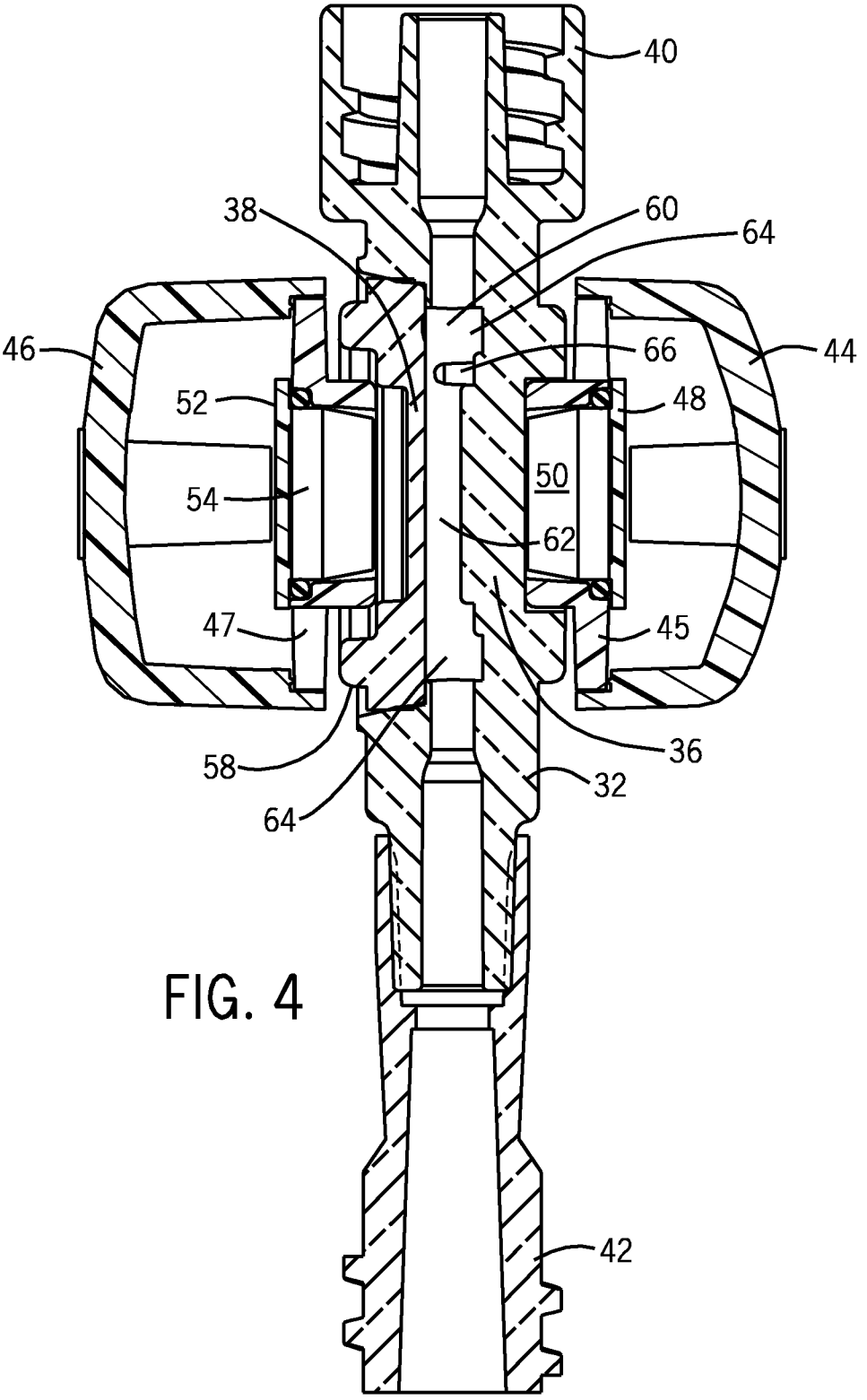


FIG. 4

Terumo v. Haemonetics - IPR2025-01470
Petitioner Terumo Exhibit 1011-0006

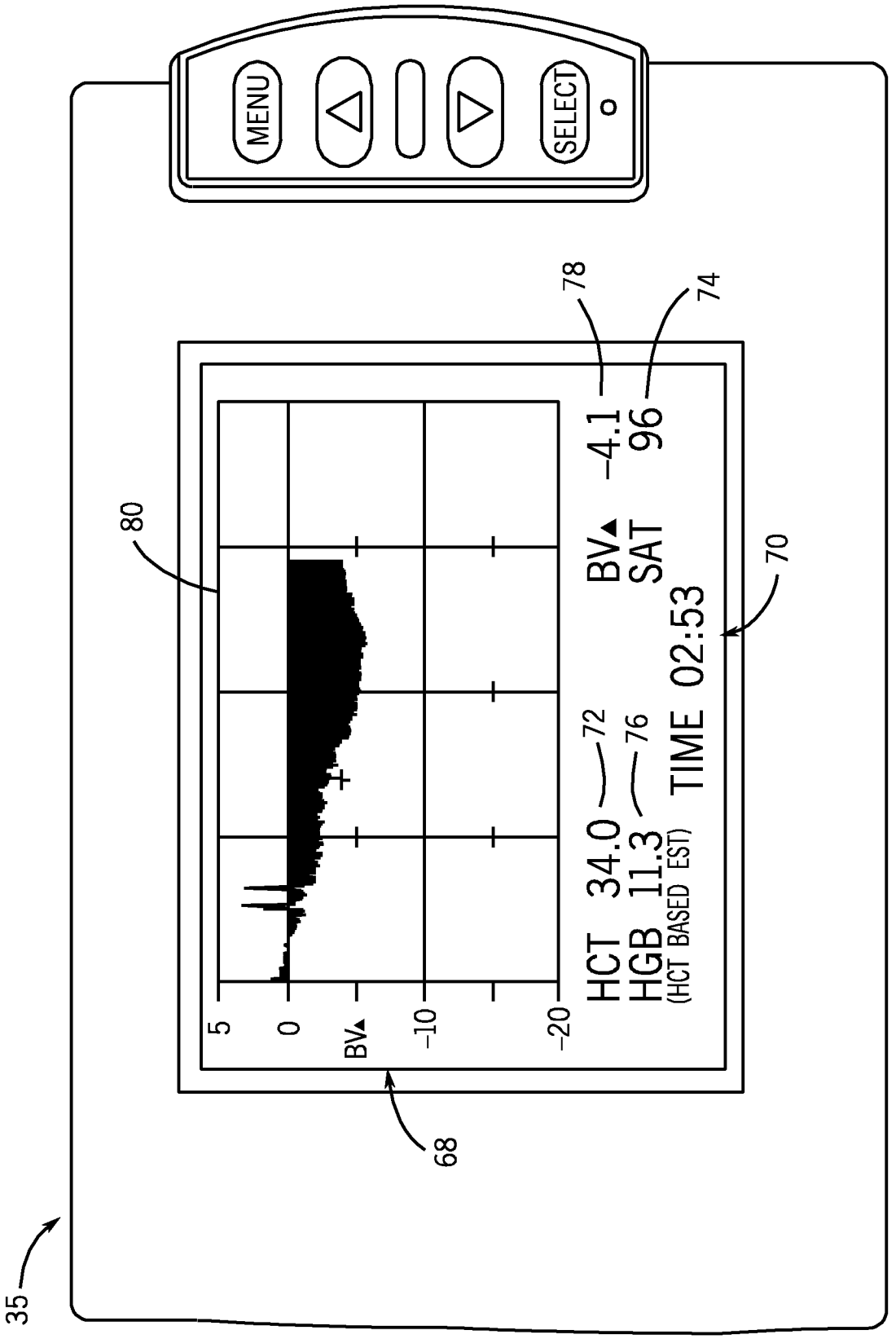

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SELECT
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74
80
70
BV▲ −4.1
SAT 96
TIME 02:53
72
76
HCT 34.0
HGB 11.3
(HCT BASED EST)
5
0
BV▲
−10
−20
68
35

FIG. 5

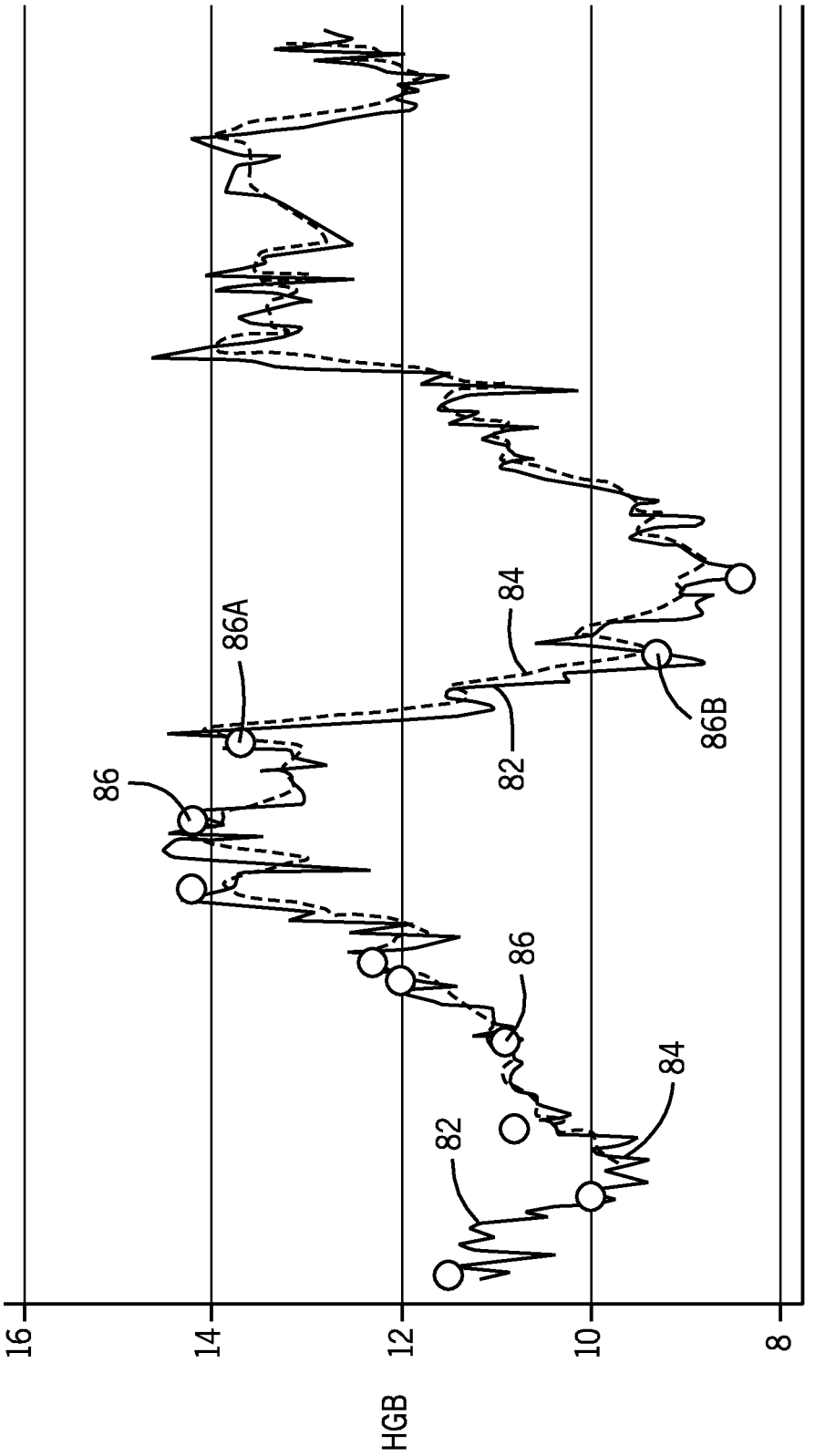

HGB
16
14
12
10
8
86
86A
84
82
86B
86
84
82
TIME SERIES FROM MARCH, 2007 TO MAY, 2008
REGRESSION MODEL
OPTICAL HGB VALUE
LAB HGB VALUE

FIG. 6

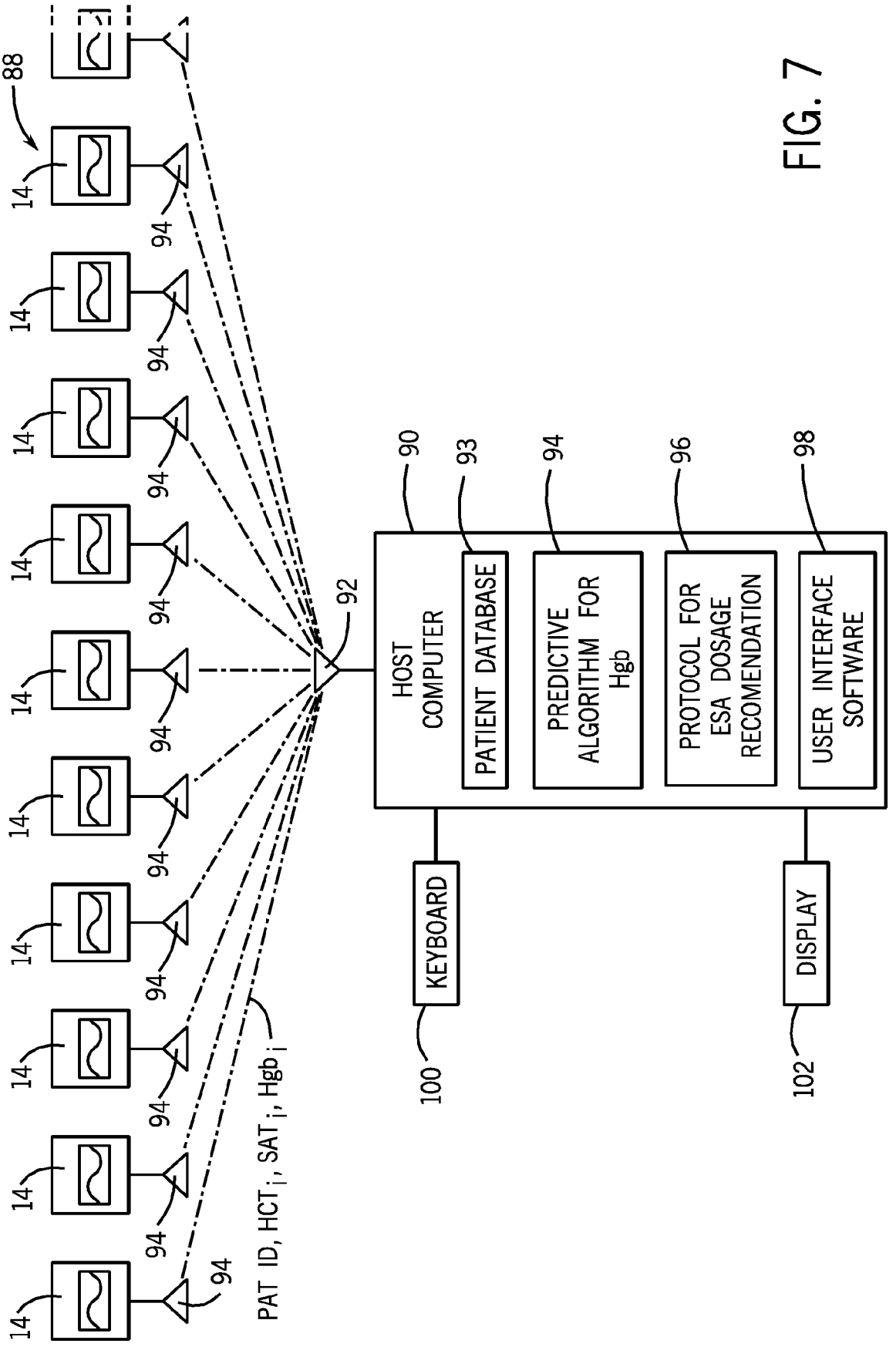

88
14
94
92
90
HOST COMPUTER
93
PATIENT DATABASE
94
PREDICTIVE ALGORITHM FOR Hgb
96
PROTOCOL FOR ESA DOSAGE RECOMENDATION
98
USER INTERFACE SOFTWARE
KEYBOARD
100
DISPLAY
102
PAT ID, HCT$_i$, SAT$_i$, Hgb$_i$

FIG. 7

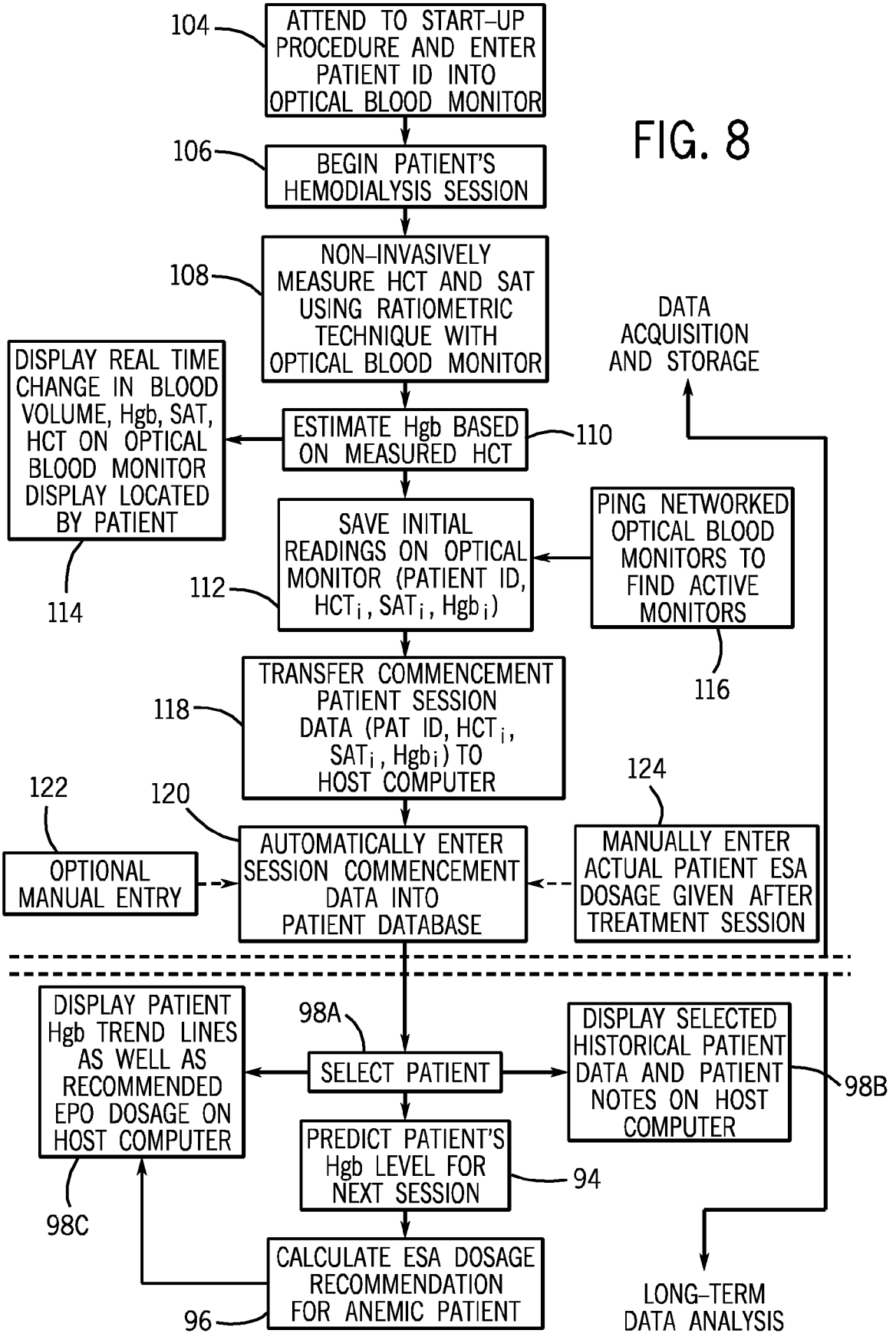

104
ATTEND TO START-UP PROCEDURE AND ENTER PATIENT ID INTO OPTICAL BLOOD MONITOR
106
BEGIN PATIENT'S HEMODIALYSIS SESSION
108
NON-INVASIVELY MEASURE HCT AND SAT USING RATIOMETRIC TECHNIQUE WITH OPTICAL BLOOD MONITOR
DATA ACQUISITION AND STORAGE
DISPLAY REAL TIME CHANGE IN BLOOD VOLUME, Hgb, SAT, HCT ON OPTICAL BLOOD MONITOR DISPLAY LOCATED BY PATIENT
ESTIMATE Hgb BASED ON MEASURED HCT
110
114
SAVE INITIAL READINGS ON OPTICAL MONITOR (PATIENT ID, HCT_i, SAT_i, Hgb_i)
PING NETWORKED OPTICAL BLOOD MONITORS TO FIND ACTIVE MONITORS
112
116
TRANSFER COMMENCEMENT PATIENT SESSION DATA (PAT ID, HCT_i, SAT_i, Hgb_i) TO HOST COMPUTER
118
122
120
124
OPTIONAL MANUAL ENTRY
AUTOMATICALLY ENTER SESSION COMMENCEMENT DATA INTO PATIENT DATABASE
MANUALLY ENTER ACTUAL PATIENT ESA DOSAGE GIVEN AFTER TREATMENT SESSION
DISPLAY PATIENT Hgb TREND LINES AS WELL AS RECOMMENDED EPO DOSAGE ON HOST COMPUTER
98A
SELECT PATIENT
DISPLAY SELECTED HISTORICAL PATIENT DATA AND PATIENT NOTES ON HOST COMPUTER
98B
PREDICT PATIENT'S Hgb LEVEL FOR NEXT SESSION
94
98C
CALCULATE ESA DOSAGE RECOMMENDATION FOR ANEMIC PATIENT
96
LONG-TERM DATA ANALYSIS

FIG. 8

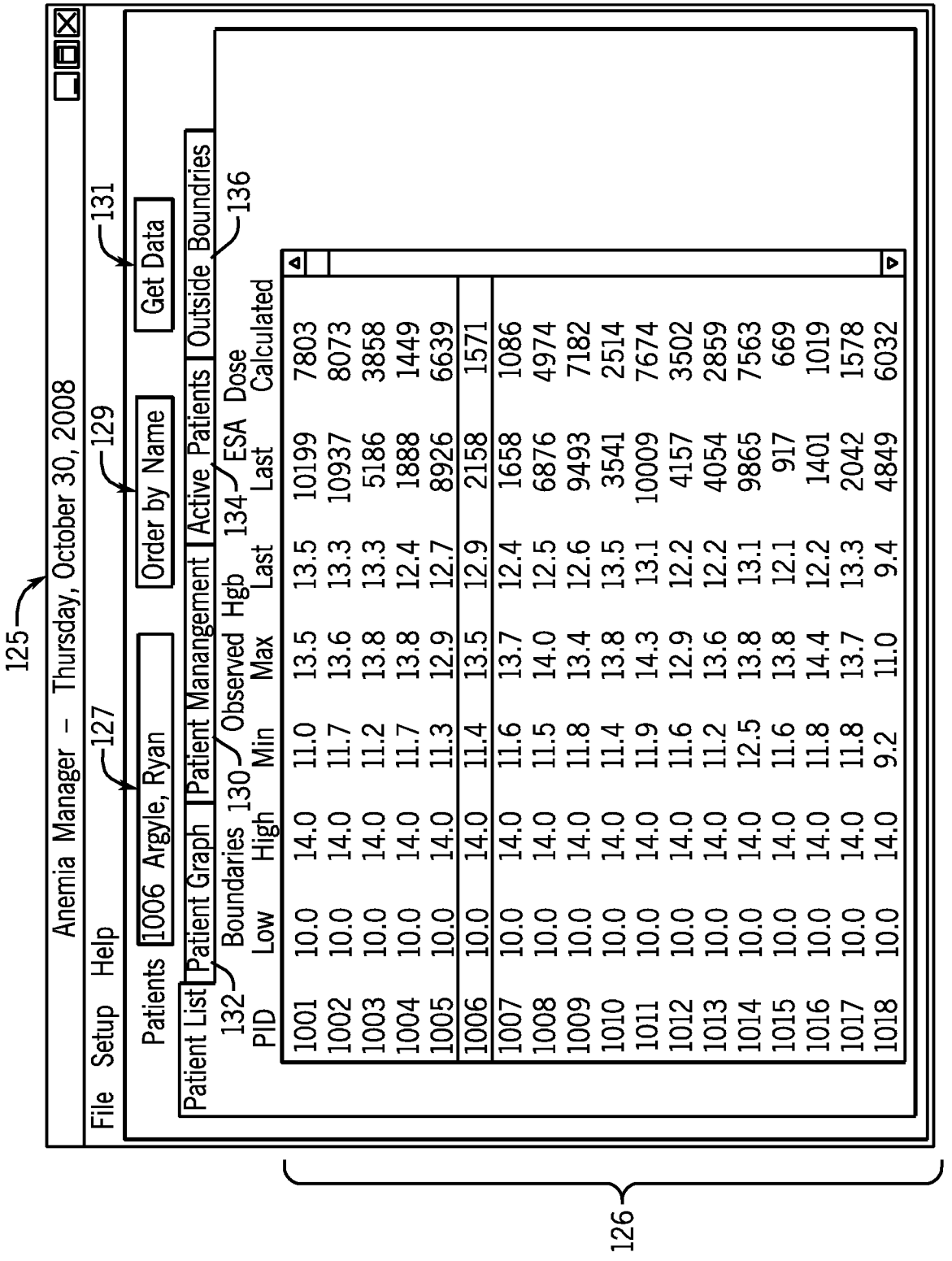


FIG. 9

Terumo v. Haemonetics - IPR2025-01470
Petitioner Terumo Exhibit 1011-0011

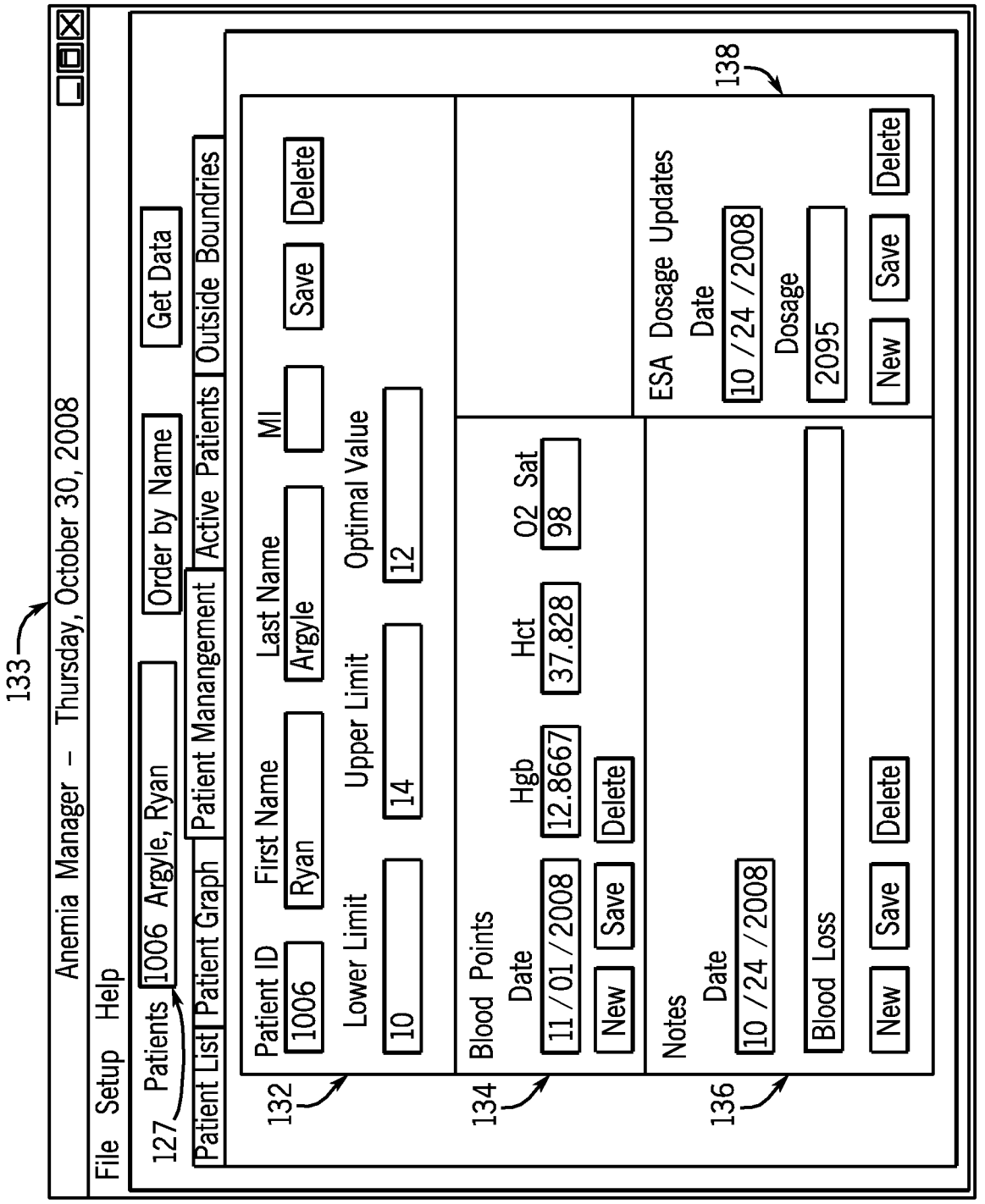

133
Anemia Manager – Thursday, October 30, 2008
File Setup Help
127
Patients 1006 Argyle, Ryan
Order by Name
Get Data
Patient List
Patient Graph
Patient Manangement
Active Patients
Outside Boundries
132
Patient ID
1006
First Name
Ryan
Last Name
Argyle
MI
Save
Delete
Lower Limit
10
Upper Limit
14
Optimal Value
12
134
Blood Points
Date
11/01/2008
Hgb
12.8667
Hct
37.828
O2 Sat
98
New
Save
Delete
136
Notes
Date
10/24/2008
Blood Loss
New
Save
Delete
138
ESA Dosage Updates
Date
10/24/2008
Dosage
2095
New
Save
Delete

FIG. 10

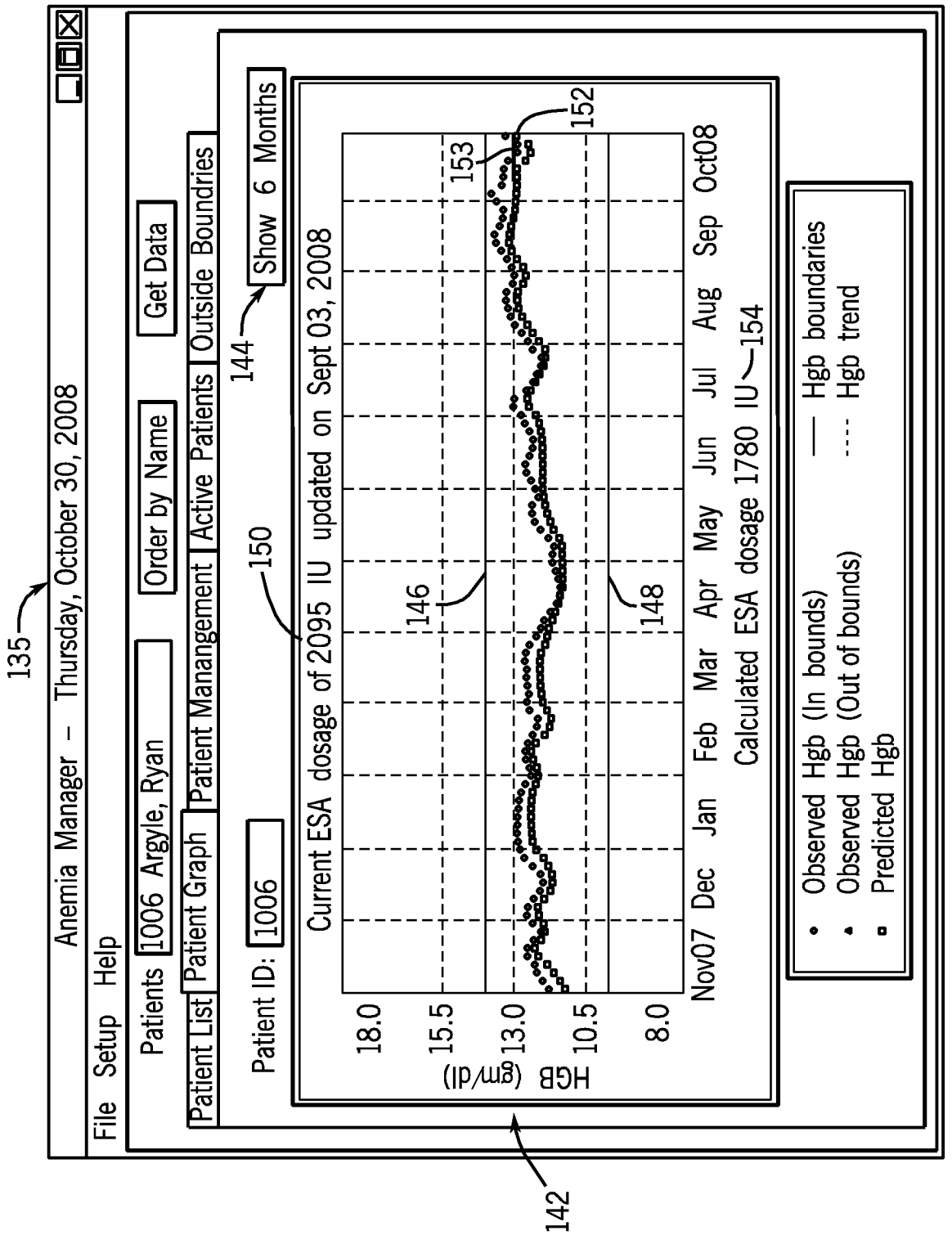

135
Anemia Manager – Thursday, October 30, 2008
File Setup Help
Patients 1006 Argyle, Ryan
Order by Name
Get Data
Patient List
Patient Graph
Patient Manangement
Active Patients
Outside Boundries
Patient ID: 1006
150
144
Show 6 Months
Current ESA dosage of 2095 IU updated on Sept 03, 2008
HGB (gm/dl)
18.0
15.5
13.0
10.5
8.0
146
148
153
152
Nov07 Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct08
Calculated ESA dosage 1780 IU
154
Observed Hgb (In bounds)
Observed Hgb (Out of bounds)
Predicted Hgb
Hgb boundaries
Hgb trend
142

FIG. 11

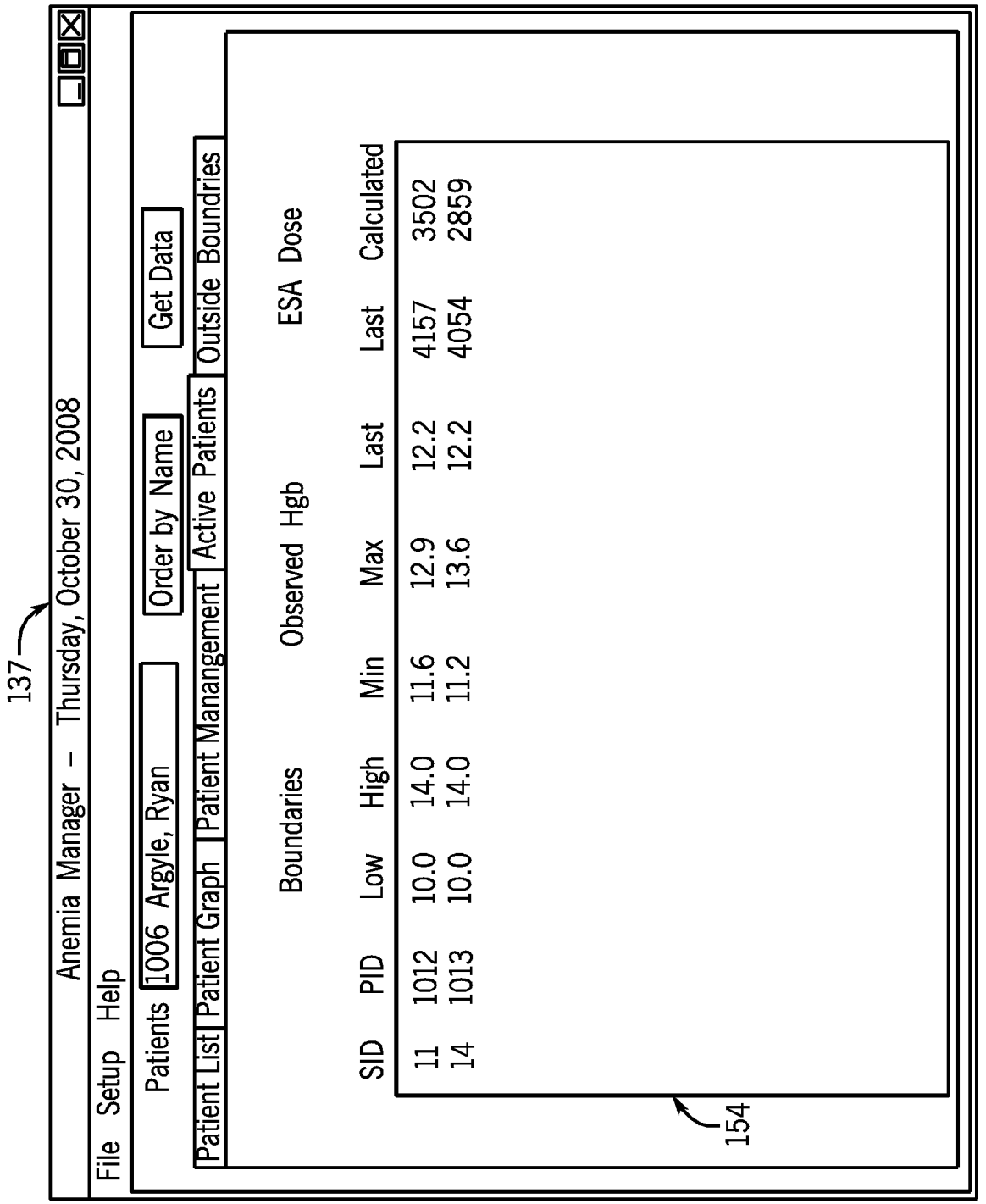

137
Anemia Manager – Thursday, October 30, 2008
File Setup Help
Patients
1006 Argyle, Ryan
Order by Name
Get Data
Patient List
Patient Graph
Patient Manangement
Active Patients
Outside Boundries
Boundaries
Observed Hgb
ESA Dose
SID PID Low High Min Max Last Last Calculated
11 1012 10.0 14.0 11.6 12.9 12.2 4157 3502
14 1013 10.0 14.0 11.2 13.6 12.2 4054 2859
154

FIG. 12

139
Anemia Manager – Thursday, October 30, 2008
File Setup Help
Patients
1006 Argyle, Ryan
Order by Name
Get Data
Patient List
Patient Graph
Patient Manangement
Active Patients
Outside Boundries
Boundaries
Observed Hgb
ESA Dose
PID Low High Min Max Last Last Calculated
1018 10.0 14.0 9.2 11.0 9.4 4849 6032
1056 10.0 14.0 9.2 11.1 9.7 815 1001
1073 10.0 14.0 9.1 11.4 9.4 8705 10842
1076 10.0 14.0 9.2 11.0 9.7 4252 5556
1077 10.0 14.0 9.2 11.2 9.4 4381 5327
1108 10.0 14.0 9.2 11.0 9.4 1581 2272
1122 10.0 14.0 11.6 14.2 14.2 7924 3913
1144 10.0 14.0 9.1 11.0 9.6 4164 4963
1157 10.0 14.0 9.1 11.2 9.7 9487 11978
1166 10.0 14.0 9.3 11.3 9.3 7900 9898
1169 10.0 14.0 9.1 11.2 9.6 8437 10316
1177 10.0 14.0 9.2 11.0 9.6 800 1152
1183 10.0 14.0 9.2 11.1 9.7 4449 5500
1202 10.0 14.0 9.2 12.2 9.6 4529 5468
1208 10.0 14.0 9.2 11.1 9.3 808 1052

FIG. 13

HEMODIALYSIS PATIENT DATA ACQUISITION, MANAGEMENT AND ANALYSIS SYSTEM

FIELD OF THE INVENTION

The invention relates to data acquisition for hemodialysis patients, and the management and analysis of that data. In particular, it relates to the use of data taken at the onset of a series of scheduled hemodialysis treatment sessions for the patient, preferably gathered via a non-invasive, optical blood monitor. The invention enables the practical use of predictive algorithms to forecast an individual patient's blood condition in the future, e.g. a prediction of patient's hemoglobin level at next treatment session. Such prognostic data can be used to recommended therapeutic care, such as medication dosing. The invention is particularly useful for dosing anemia medication in hemodialysis patients, such as erythropoiesis stimulating agents (ESAs).

BACKGROUND OF THE INVENTION

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.

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 dialyzer which removes 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. 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. The used dialysate exits the dialyzer with the excess fluids and toxins via an output tube, thus cleansing the blood 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 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.

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 fluid removal rate is more rapid than the plasma refilling rate of the body, intravascular blood volume decreases. The resulting imbalance has been linked to complications 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 circulating blood volume (in real-time) during hemodialysis reduces the chance of dialysis-induced hypotension, and otherwise optimizes dialysis therapy regimes by controlling fluid balance and aiding in achieving the appropriate dry weight for the patient.

In the art, it is known that, during a hemodialysis treatment session, the change in hematocrit value is inversely proportional to the change in blood volume. For example, see U.S. Pat. No. 5,351,686 entitled "Disposable Extracorporeal Conduit For Blood Constituent Monitoring", assigned to the assignee of the present application and issuing on Oct. 4, 1994. The hematocrit value is the percentage of blood volume occupied by red blood cells. Since the number of red blood cells remains substantially constant during dialysis treatments that do not include bleeding or transfusions, the hematocrit will change only as a result of changing blood volume. Therefore, the change in blood volume during hemodialysis can be monitored by measuring hematocrit during the hemodialysis session.

There are several techniques to monitor hematocrit, although many are not practical for real-time monitoring during hemodialysis. The most common technique is a manual method in which a syringe is used to extract blood from the patient. The extracted blood is then put into a capillary device which is placed in a microcentrifuge. Because of the blood draw, this manual process is inadequate for monitoring real-time changes in blood volume during a hemodialysis treatment session. It has also been found to be somewhat inaccurate in practice. In addition, even if blood is drawn only a few times per week each blood draw lowers the patient iron level and induces further anemia. Therefore, in practice, hemodialysis patients normally have manual blood work done to determine hematocrit, as well as other blood abnormalities, about once a month.

Another device for measuring hematocrit is called a cell counter or Coulter counter. In a cell counter, a metered volume of blood is tested. The red blood cells are literally counted as they drop through a small diameter pipette within the cell counter. The mean cell volume of the red blood cells is measured via an electrical current that passes through a designated area of the pipette. The size of the blood cell correlates to the amount of electrical current passed. The volume of red blood cells is found by multiplying the red blood cell count times the mean cell volume. The hematocrit is determined by dividing the calculated red blood cell volume over the total volume of the sample. This method is assumed in the art to be more accurate than the microcentrifuge method. However, this method again requires that a blood sample be taken from the patient.

Another way to monitor hematocrit is to use a non-invasive, real-time optical blood monitor. The assignee of the present application manufactures such an optical blood monitoring system marketed under the name CRIT-LINE®. The CRIT-LINE® system continuously monitors the change in hematocrit over a dialysis session, and uses this information to calculate and display accurate percent blood volume change. It can also determine and display oxygen saturation levels and hemoglobin levels. The dynamic display of blood data during a hemodialysis session, including the display of change in blood volume, is quite helpful to attending staff administering the treatment to the patient.

To use the CRIT-LINE® system, a sterile, single-use blood chamber is attached, prior to hemodialysis treatment, inline in extracorporeal tubing on the arterial side of the dialyzer. The

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blood chamber provides a viewing point for optical sensors during the hemodialysis procedure. Multiple wavelengths of light are directed through the blood chamber and the patient's blood flowing therethrough, and photo detectors detect the resulting intensity of each wavelength. The preferred wavelengths are about 810 nanometers, which is substantially isobectic for red blood cells containing hemoglobin, and about 1300 nanometers, which is substantially isobectic for water. A ratiometric technique implemented in the CRIT-LINE® controller, as substantially disclosed in U.S. Pat. No. 5,372,136 entitled "System And Method For Non-invasive Hematocrit Monitoring", which issued on Dec. 13, 1999 and is also assigned to the assignee of the present application, uses this information to calculate the patient's hematocrit value (HCT) in real-time, which as mentioned is the percentage of blood volume that is occupied by red blood cells. The CRIT-LINE® monitor provides an absolute measurement of hematocrit in real-time that is independent of other blood analytes. One of the advantages of monitoring the patient's blood non-invasively is that it is not necessary to take a blood draw, and therefore the anemic condition is not exacerbated.

The CRIT-LINE® monitor estimates patient hemoglobin levels (Hgb) from the measured hematocrit value. Hemoglobin levels are expressed as the amount of hemoglobin in grams (gm) per deciliter (dl) of whole blood. The most common direct method of measuring hemoglobin requires the extraction of a blood sample from the patient, and then treating the blood with a lysing agent in the laboratory in order to rupture the red blood cell membranes and release the hemoglobin into solution so that its concentration can be measured. Obviously, this technique cannot be implemented in real-time in the CRIT-LINE® monitor. Rather, the CRIT-LINE® system estimates real-time hemoglobin level based on the measured real-time hematocrit level (e.g. HCT=2.941 Hgb).

Oxygen saturation (SAT) measures the percentage of hemoglobin binding sites occupied by oxygen. Hematocrit independent oxygen saturation is measured in the CRIT-LINE® monitor using a photo emitter having a wavelength of about 660 nanometers. The photo detector monitors the intensity of 660 nm light after it passes through the blood chamber and the blood flowing through the blood chamber. A ratiometric model using the intensity of detected light at 660 nm and at substantially 810 nm is used to determine the real-time oxygen saturation level in the CRIT-LINE® monitor.

The CRIT-LINE® monitor is thus able to non-invasively monitor in real-time during hemodialysis the patient's hematocrit (HCT), change in blood volume (BVΔ), oxygen saturation (SAT), and calculated hemoglobin (Hgb) levels.

Hemodialysis centers normally include several hemodialysis systems so that multiple patients can be treated contemporaneously. In many centers, a dedicated CRIT-LINE® monitor is used in connection with each individual hemodialysis system. The display on the CRIT-LINE® monitor (which is normally located next to the patient) helps the attending nurses insure that hematocrit, oxygen saturation, and blood volume levels, as well as calculated hemoglobin levels, remain within the accepted tolerances for the treated patient. The patient data, such as hematocrit, oxygen saturation, and calculated hemoglobin values, is often downloaded to a host computer for patient records.

As kidney function decreases, one of the side effects is that erythropoietin synthesis decreases, which can potentially lead to anemia, causing fatigue in the patient. Hemoglobin variability is common in patients with End Stage Renal Disease (ESRD) on hemodialysis. Erythropoiesis stimulating agents (e.g., recombinant erythropoietin), commonly known as ESAs, are pharmaceutically produced and administered by physicians to hemodialysis patients in order to manage anemia when present. Recombinant ESA can be administered either subcutaneously via syringe, or via a drip in the extracorporeal tubing of the hemodialysis loop, normally at the end of a hemodialysis treatment session. The purpose of administering ESA is to maintain the patient's hemoglobin levels within a healthy range. Under dosing ESA results in low hemoglobin levels. On the other hand, overuse of ESA can result in excessive cost, as well as undesirable side effects.

SUMMARY OF THE INVENTION

In one aspect, the invention is a hemodialysis patient data acquisition and management system that receives data collected by one or more non-invasive, optical hemodialysis blood monitors, and in particular, downloads data collected at the onset of a patient's hemodialysis treatment sessions to a host computer.

A database on the host computer contains historical session commencement data for a large number of patients (e.g. 250 patients). Software on the host computer displays historical data for a selected patient. It is preferred that at least some of the data be displayed graphically, perhaps using trend lines as well as clear indications of maximum and minimum desired values of monitored data, such as Hgb_i, HCT_i, SAT_i. The purpose of the database is to provide the attending physician and/or nurse with historical information on the patient to facilitate therapeutic care for the patient.

It is notable that the downloaded data relates to the blood characteristics taken at the onset of the hemodialysis treatment session before the dynamics of the hemodialysis treatment begins to affect the patient. Once the hemodialysis treatment begins, blood data changes significantly. The purpose of this aspect of the invention is to collect blood data on the patient, during the stable regime of the blood reflecting the patient's true fluid condition, on a recurring basis in order to facilitate long-term analysis of the patient.

The preferred non-invasive, optical blood monitor includes an optical sensor assembly that monitors the patient's blood flowing through extracorporeal tubing in a hemodialysis system. The sensor assembly comprises a blood chamber connected in-line in the extracorporeal tubing, and a plurality of photo emitters emitting light at various wavelengths as well as one or more photo detectors for sensing the intensity of the light at each wavelength after it passes through the blood chamber and the patient's blood flowing through the blood chamber. The optical blood monitor also includes a controller that receives data signals from the one or more photo detectors, and also generates commencement session data for the patient undergoing hemodialysis treatment. The commencement session data includes at least an identification code for the patient, and measured blood data taken at the onset of the treatment session, such as initial values for hematocrit (HCT_i); hemoglobin (Hgb_i); oxygen saturation (SAT_i). In accordance with this aspect of the invention, the controller for each blood monitor communicates with a host computer, preferably via a wireless network. Whenever a blood monitor in the network becomes active, session commencement data from the blood monitor is automatically downloaded along with corresponding patient identification code from the respective blood monitor to the host computer. In this manner, the system is able to collect patient data taken at the onset of treatment sessions automatically. Ongoing data is collected on a recurring basis every two to three days as each patient is treated.

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The system also allows data to be entered manually. This may be useful in situations where one or more hemodialysis systems in a clinic are not set up with an optical blood monitor or when the communication block to a monitor is inoperative. In such situations, a blood sample may be taken from the patient before selected treatment sessions (e.g., on a monthly basis). Information such as hematocrit and hemoglobin levels determined from blood work done on the sample may be entered manually into the host computer. Of course, data automatically downloaded from an optical blood monitor every two to three days taken at the onset of each treatment session provides much more complete historical information than monthly data taken manually, thereby allowing for earlier detection of the trends and alerting attending medical staff to changes in a patient's condition sooner.

In another aspect of the invention, the host computer contains software implementing a predictive algorithm for predicting the patient's hemoglobin level at the start of his or her next scheduled treatment session. Such a predictive algorithm is particularly useful for managing therapeutic care for patients with anemia. The preferred predictive algorithm for Hgb is as follows:

Predicted Hgb Value=0.4784356 (Hgb of Last Period)+0.2042212 (Hgb of Second to Last Period)+0.222685 (Hgb of Third to Last Period)+ 0.0000396 (Last ESA Dose value)+0.9627966

where Hgb of last period, Hgb of second to last period and Hgb of the third to last period represent the patient's hemoglobin levels monitored at the previous three hemodialysis treatment sessions, the last ESA dose value represents the ESA dose administered to the patient at the patient's last treatment session, and the predicted Hgb value represents the predicted value of the patient's hemoglobin level at the start of the next treatment session.

The predictive algorithm provides the attending physician with a statistically accurate prediction of the patient's hemoglobin level at the start of the patient's next scheduled treatment session, based on data collected for the previous and current treatment sessions along with the corresponding ESA dosing in place. The algorithm is quite robust when the data is collected on an every two to three day period, which is possible with the automatic collection of session commencement data using an optical blood monitor as described above.

As mentioned, it is preferred that the predicted hemoglobin level be used by the system to determine a recommended dosage for an anemia management drug. For example, in a particularly preferred embodiment of the invention, the software on the host computer also includes protocol for calculating an ESA dosage recommendation, based at least in part on historical hemoglobin values for the patient stored in the patient database, and in part on the predicted hemoglobin value for the patient at the next treatment session.

The invention thus provides a number of tools for improving the probability that hemodialysis patients attain Hgb levels within their target hemoglobin range at the start of the next scheduled treatment session.

Other features and objects of the invention may be apparent to those skilled in the art upon reviewing the following drawings and description thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

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.

FIG. **2** is a perspective view showing an optical sensor assembly for the blood monitor positioned to sense blood flowing through a blood chamber connected in the extracorporeal tubing of the hemodialysis system.

FIG. **3** is a detailed view of the blood chamber shown in FIG. **2**.

FIG. **4** is a cross-sectional view taken along line **4-4** in FIG. **2**.

FIG. **5** is a front elevational view of the controller for the optical blood monitor illustrating displayed data including real-time hematocrit (HCT), change in blood volume (BVΔ), hemoglobin (HGB), and oxygen saturation (SAT) levels, as well as the amount of time into the hemodialysis treatment session and a graphical representation of the change in blood volume during the course of the hemodialysis treatment session.

FIG. **6** is a time series plot of data for a representative patient taken at the onset of a series of reoccurring hemodialysis treatment sessions by an optical blood monitor, which also shows monthly hemoglobin data from manual lab work for the representative patient, as well as historical results of a predictive algorithm for estimating the patient's hemoglobin level at the next treatment session.

FIG. **7** is a schematic drawing illustrating a hemodialysis patient data acquisition and management system operating in accordance with a preferred embodiment of the invention and being implemented in a hemodialysis center having a plurality of hemodialysis systems for which a non-invasive optical blood monitor is used to monitor the blood of the patient during the treatment session.

FIG. **8** is a block diagram illustrating the operation of the preferred embodiment of the invention.

FIGS. **9-13** depict the preferred graphical user interface appearing on a host computer running software to implement the preferred embodiment of the invention.

DETAILED DESCRIPTION OF THE DRAWINGS

FIG. **1** illustrates a patient **10** undergoing hemodialysis treatment using a conventional 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.

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 dialysized blood is returned from the dialyzer through extracorporeal tubing **24** and return needle or catheter **26**. In some parts of the world, the extracorporeal blood flow may receive a heparin drip to prevent clotting although that is not shown in FIG. **1**. 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.

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

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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 at substantially 810 nm, which is isobestic for red blood cell hemoglobin, substantially 1300 nm, which is isobestic for water, and at substantially 660 nm, which is sensitive for oxygenated hemoglobin. The blood chamber **32** includes lenses so that the sensor emitters and detectors can view the blood flowing through the blood chamber **32**, and determine the patient's real-time hematocrit value and oxygen saturation value using ratiometric techniques generally known in the prior art. The preferred ratiometric model is described in more detail in copending patent application entitled "Measuring Hematocrit And Estimating Hemoglobin Values With An Optical Blood Monitoring System", filed on even date herewith by Louis Barrett, David Peterson, Kristian Sammann, this co-pending patent application being incorporated in its entirety herein. The incorporated copending patent application also describes a method of scaling output values for hematocrit (HCT) to account for differences in preservatives used to calibrate optical monitoring equipment and other equipment typically used in the clinic when taking blood samples from patients. It is contemplated that the preferred embodiment of the invention utilize the method of scaling hematocrit values, as discussed in the above-incorporated patent application.

Referring to now FIGS. **2-4**, the body of the blood chamber **32** is preferably made of molded polycarbonate. It includes two viewing windows **36**, **38** (see FIG. **4**). The inlet **40** and outlet **42** are designed to be compatible with standard medical industry connecting devices, conventionally known as Luer locks. In the blood chamber **32** shown in the drawings, the inlet **40** is integrally molded with the blood chamber **32**, whereas the outlet **42** consists of a suitable off-the-shelf connection adapter glued to the body of the blood chamber **32**. The sensor assembly **34** includes an emitter subassembly **44** and a detector subassembly **46**. As best shown in FIG. **4**, an emitter circuit board **48** containing LEDs emitting light at substantially 660 nm, 810 nm and 1300 nm, is mounted within the housing for the sensor subassembly **44**. The LED circuit board **48** emits light through a lens **50** that is mounted between the circuit board **48** and the viewing window **36** for the blood chamber **32**. The controller **35** controls the operation of each of the respective LED emitters and/or detectors so as to de-commutate the independent wavelength measurements. Another circuit board **52** containing light detectors, one made of silicon to detect light intensity at 810 nm and 660 nm, and the other made of InGaAs to detect light intensity at 1300 nm. The detector circuit board **52** is mounted within the housing for the detector subassembly **46**. A lens **54** is mounted between the detector circuit board **52** and the viewing window **38** in the blood chamber **32** in order to facilitate transmission of light at the respective wavelengths to the detectors on the circuit board **52**. Note that the viewing window **38** is molded into a separate insert **58** that is sonically welded to the body of the blood chamber **32**. As in the prior art, the blood flows from the inlet **40** through the passageway **60** to a central viewing region **62**. The light at the three selected wavelengths, namely 810 nm, 1300 nm and 660 nm, are transmitted through the blood flowing through this portion **62** of the blood flow path, as well as the viewing windows **36**, **38** in the chamber **32**. The viewing region **62** provides a substantially flat, thin (e.g. less than 0.1 inches) viewing region for the blood flowing through the blood chamber **36**. A moat **64** surrounds the flat viewing region **62**. The moat **64** is somewhat deeper than the flat viewing region **62**, and serves to distribute the flow evenly and steadily through the viewing region. It also serves to reduce errant light piping through the polycarbonate blood chamber **32** from the emitters **48** to the detectors **52** due to the higher concentration of blood surrounding the viewing area **62**. One or more protrusions **66** are located immediately upstream of the viewing region **62** so that the flow across the viewing region **62** is at least somewhat turbulent. While the flow across the viewing region **62** is preferably somewhat turbulent, the configuration of the blood chamber **32** shown in FIG. **4** results in a steady state flow through the viewing region **62** in terms of pressure and flow rate.

The housings **44** and **46** for the sensor assembly **34** include an inner housing piece **45**, **47** which connects to the outer shells **44**, **46**. The inner housing components **45**, **47** provide an opening into which the lenses **50**, **54** are mounted. The sensor assembly **34** is preferably a spring loaded clip that can be mounted to the blood chamber **32**, as shown in FIG. **2**. Both sides of the blood chamber **32** are molded such that the clip **34** will reside in a predetermined position when mounted to the blood chamber **32**. As mentioned, blood chamber **32** is a single use, reusable polycarbonate component. Between patients, the blood chamber **32** is replaced as is the extracorporeal tubing **18**, **24**, and blood filter **22**.

FIG. **5** is a front elevational view of the preferred controller **35** for the optical blood monitor **14**. The controller **35** includes a display **68** which provides real-time blood monitoring data for the patient undergoing hemodialysis. The display in FIG. **5** illustrates the amount of time **70** that the patient **10** has been monitored while undergoing hemodialysis for the current treatment session. The time **70** displayed on the screen **68** in FIG. **5** is 2 hours and 53 minutes. The display **68** also illustrates real-time values for the optically monitored hematocrit (HCT) **72** and oxygen saturation (SAT) level **74**, as well as the calculated values for hemoglobin (HGB) **76** and change in blood volume (BVΔ) during the treatment session **78**. The graph **80** on the display **68** illustrates the change in the patient's blood volume, HCT, or O_2SAT (as selected by Menu option) over the course of the 2 hour and 53 minute monitoring session. This data is displayed, as shown in FIG. **1**, in a location that is located within the vicinity of the patient **10**.

The preferred controller **35** for the optical blood monitor **14** contains an internal real-time clock that continuously registers time and date, and includes battery backup when it is off. The clock is preferably set at the factory, although it may be desirable to correct the time upon initial installation or for daylight savings time changes, etc. Periodically, the calibration and accuracy of the optical blood monitor **14** should be checked. In the art, this is normally done by placing the sensor clip **34** onto a verification filter (made of layered plastic having known optical qualities) that is mounted to the side of the monitor **14**. Calibration software within the controller **35** will verify the calibration of the unit, or allow the user to field calibrate the unit within specified limits to bring it back to factory calibration settings. If the specified adjustment limits are exceeded, it is necessary to return the unit to the factory for calibration.

For purposes of background, when a typical patient **10** arrives at a hemodialysis clinic, the patient is first checked in and then weighed on a scale at the clinic. The patient then is seated in an assigned hemodialysis chair where a clinician inserts an arterial and venous needle into the patient's access. The access may be an artificial shunt or a natural fistula that has been surgically tied from an artery to a vein. Alternatively, as mentioned previously, the connection might be through a catheter. Next, the dialysis lines **18**, **24** are prefilled with normal saline and connected to the patient. The peristaltic pump **20** is started slowly and the normal saline is flushed through the lines **18**, **24** as well as the dialyzer **22** into the

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patient **10**, as arterial blood is pulled into the dialysis circuit. The normal saline tends to lubricate or prime the system for blood passage. Also, since saline is less dense than blood, any leaks in the system will be immediately apparent.

The clinician then waits approximately 5 minutes for the hematocrit (HCT) of the patient's body to stabilize after the saline has been infused. The saline must mix out in the patient's body in order to obtain a stable reading for the initial hematocrit (HCT) at the onset of the hemodialysis process. During this wait time, the clinician presses the menu button on the monitor **14** and enters the patient ID number. While it would be technically possible to enter the patient's name in lieu of a patient ID number, it is preferable to enter a patient ID number in order to accommodate patient privacy laws. Once approximately 5 minutes have passed after the saline prime is flushed into the body, the patient's data run begins. The optical blood monitor **14** is turned on to measure and store in memory initial values for hematocrit (HCT_i), hemoglobin (Hgb_i), and oxygen saturation (SAT_i) levels. As mentioned, the hemoglobin level is estimated from the measured hematocrit (HCT=2.941*Hgb at sea level). As also mentioned, the hemoglobin level is preferably scaled according to the disclosure in the above mentioned copending patent application which has been incorporated herein by reference.

After the initial levels for hematocrit, hemoglobin and oxygen saturation are measured and stored in the controller **35**, the ultra filtration rate (UFR) on the dialysis machine is advanced, causing an osmosis vacuum to form across the dialyzer **22**. From that point on, fluid is removed from the blood, but red blood cells are preserved within the body. In the controller **35** for the blood monitor, the real-time data is updated in the memory and on the screen at a rate of one sample per minute for each of the displayed parameters. Real-time data is available at the serial port at a regular sample rate for external data collection use.

At the end of treatment, the menu button on the controller **35** is pressed and an option to stop the treatment session is selected. A printer can be connected to the monitor for printing graphs of HCT, BVΔ, and SAT.

The hemodialysis system **12** is stopped after the blood is drained from the lines into the venous needle **26** of the patient **10**. The patient is allowed to sit for a while, and the clinical staff assesses the patient's conditions while they remove the needles and bandage the patient. The patient is then weighed again at the end of the treatment, and perhaps a physician prescribes the administration of an ESA dose. The patient **10** then receives their prescribed dose and is released to go.

Preferably, the controller **35** is set up so that the memory of the patients'data for the day's treatment sessions are protected and must be deliberately cleared before the controller **35** is ready to monitor subsequent treatments on the hemodialysis system **12**. Also held in memory in the controller **35** are the initial values HCT_i, Hgb_i, SAT_i and a time and date stamp, for the commencement of the patient's treatment session. This set of session commencement data (HCT_i, Hgb_i, SAT_i, time and date stamp) is the subject of one aspect of the present invention, which is described in more detail below with respect to FIGS. **7** through **10**.

Another aspect of the invention involves the use of a predictive algorithm for estimating the patient's hemoglobin level at his or her next treatment session. Data was collected from 43 hemodialysis patients over the course of 15 months. The data collected included optically detected hemoglobin levels (Hgb) collected at the beginning of each patient's treatment session. In addition, from time to time, blood samples were taken, and hemoglobin levels for the patients were taken based on ordinary lab work. The optical blood monitor in the test estimated hemoglobin levels based on optically measured HCT.

While 43 different patients were monitored at the beginning of their scheduled hemodialysis treatment sessions, not all of the patients attended each of their scheduled hemodialysis sessions. The average number of treatment sessions being monitored per patient was 151.7, with the minimum number of observations being 119 per patient and the maximum being 188 per patient. The data were fit with a cross-sectional regression model, having the following format:

$$\text{Predicted Hgb Value} = 0.4784356\ (\text{Hgb of Last Period}) + 0.2042212\ (\text{Hgb of Second to Last Period}) + 0.222685\ (\text{Hgb of Third to Last Period}) + 0.0000396\ (\text{Last ESA Dose value}) + 0.9627966 \quad \text{Eq. (1)}$$

where Hgb of last period, Hgb of second to last period and Hgb of the third to last period represent the patient's hemoglobin levels (gm/dl) monitored at the previous three treatment sessions, and the last ESA dose value represents the ESA dose (International Units) administered to the patient at the patient's last treatment session, and the predicted Hgb value represents the predicted value of the patient's hemoglobin level at the start of the next scheduled treatment session. The inventors have found that three lag periods provides the best fit for the cross-sectional regression model. Of course, the coefficients in the cross-sectional regression model would likely change at least somewhat depending on the number of observations and the condition of the various patients in the test pool. It should be noted that other factors were monitored during the test, but no significant statistical correlation appeared to exist, for example, with the patient's MAP, average trans SAT, or Ferritin levels and or the patient's dry weight.

A cross-sectional regression model was chosen to model the collected data, in contrast to a regulated linear regression, because the data was expected to be statistically correlated. In other words, data points relating to a particular patient were not expected to be independent of other data points for that patient. Due to this expected correlation, a cross-sectional regression model is preferred with respect to a linear regression in a model. Nevertheless, collected data is likely to be adequately fit by other types of statistical models as well, such as a time series model like a constant coefficient single exponential smoothing model. Broadly speaking, this aspect of the invention may be implemented using a variety of statistical models.

Table 1 illustrates the statistical accuracy of the cross-sectional regression model of Eq. (1) to the data collected.

TABLE 1

Variable; Based on 43 Patients, 6537 observations (mean of 152 observations per patient)	Coefficient	Standard Error	95% Confidence Interval	P-Value
Optical Hgb of last time period	0.4784356	0.0120666	(0.455, 0.502)	<0.001
Optical Hgb of second to last time period	0.2042212	0.0131147	(0.179, 0.230)	<0.001
Optical Hgb of third to last time period	0.222685	0.0120086	(0.199, 0.246)	<0.001

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TABLE 1-continued

Variable; Based on 43 Patients, 6537 observations (mean of 152 observations per patient)	Coefficient	Standard Error	95% Confidence Interval	P-Value
ESA Dose (In international units) of last time period	0.0000396	3.58e−06	(3.260E−05, 4.670E−05)	<0.001
Constant	0.9627966	0.0777629	(0.810, 1.115)	<0.001

FIG. **6** is a plot of data from a representative patient, showing the patient's hemoglobin level at the onset of hemodialysis treatment sessions over a 15 month period. The solid line **82** in FIG. **6** tracks optically monitored hemoglobin values (HCT_i) which are collected by an optical blood monitor **14** monitoring the patient during a series of scheduled hemodialysis treatment sessions. The hemodialysis treatment sessions were scheduled to occur three times a week. The dashed line **84** plots the predicted values from the cross-sectional regression model. Note that the dashed line **84** does not begin until several optically measured data points are available (i.e. line **82**). The circles **86** identify the patient's hemoglobin data as taken from a blood sample and determined in a laboratory. Referring to reference numbers **86***a* and **86***b*, it is important to note that a patient's hemoglobin values can change substantially between the time that a patient normally obtains blood work from a laboratory (e.g. on a monthly basis). The difference between data point **86***a* and data point **86***b* is over three grams per deciliter. On the other hand, the optical blood monitor **14** is able to monitor the patient's hemoglobin level on a more frequent basis. As shown in FIG. **6**, the regression model **84** closely tracks the actual data **82** collected by the optical blood monitor. Of course, the regression model **84** is somewhat smoothing, and therefore its forecast is resistant to noise in the data signal. In any event, the hemoglobin values predicted by the regression model **84** are quite consistently accurate, as shown in FIG. **6**, with both the optically monitored hemoglobin levels and the hemoglobin levels determined via lab work. Further, use of the predictive hemoglobin algorithm helps staff to maintain a more constant hemoglobin level for the patient.

FIG. **7** illustrates a wireless example of a hemodialysis patient data acquisition, management and analysis systems **88** implemented in accordance with a preferred embodiment of the invention. In FIG. **7**, a host computer **90** has a wireless communication device **92** that communicates with a wireless communication device **94** associated with each of several optical blood monitors **14** located within a hemodialysis clinic. While FIG. **7** illustrates a wireless communication network, the invention could of course be implemented using another type of network. As mentioned, the optical blood monitor **14** stores in memory the session commencement data, Pat. ID, HCT_i, SAT_i Hgb_i, and time and date stamp for each respective patient taken at the onset of each respective hemodialysis treatment session. This data (Pat. ID, HCT_i, SAT_i Hgb_i, and time and date stamp) is downloaded via the wireless network from the optical blood monitor **14** to the host computer **90** and entered into a patient database **93** on the host computer.

In accordance with the invention, the host computer **90** contains software which implements a patient database **93**, the predictive algorithm for hemoglobin **94**, protocol for ESA dosage recommendations **96**, and user interface software **98**. A keyboard **100** and display **102** are also provided with the host computer **90**, as is well known. While the display **68** on the respective optical monitors **14** are each located near the patient **10**, the host computer **90** is located in a central location and is not specific to any particular patient or hemodialysis station.

The patient database **93** preferably contains session commencement data for each of the patients that are treated at the hemodialysis center. The patient database **93** can be programmed using any suitable database package, such as Microsoft Access™. The software modules for the predictive algorithm, the ESA protocol and user interface screens are custom programmed. The user interface software **98** on the host computer enables an attending physician or nurse to observe and analyze the patient's trends in hemoglobin, or hematocrit and oxygen saturation values over the long-term. The data in the patient database **93** is also used as input to the predictive algorithm for estimating the patient's hemoglobin level at his her next visit, see block **94**. The result of the predictive algorithm **94** is then used in connection with historical records of the patient's session commencement data, by software, block **96**, and implementing protocol for ESA dosage recommendations, as will be described in more detail below.

FIG. **8** is a flow diagram illustrating the operations of various aspects of the invention in more detail. Referring to block **104**, when the patient arrives at the clinic, the clinician attends to the appropriate hemodialysis startup procedures, and enters the patient ID number into the optical blood monitor **14** associated with the respective hemodialysis system, as described above. Once the startup procedure is complete, the patient's hemodialysis session begins, block **106**. As soon as the patient's blood is believed to be stable, the user starts the blood monitor **14** to non-invasively measure the patient's hematocrit and oxygen saturation levels using ratiometric techniques, as explained in the above incorporated, co-pending patent application. Once the hematocrit and oxygen saturation values are measured and calculated in the optical blood monitor, see block **108**, the controller **35** for the optical blood monitor estimates the hemoglobin level based on the measured hematocrit level, see block **110**. The preferred method for estimating hemoglobin based on the measured hematocrit level is disclosed in the above-noted incorporated patent application. Block **112** shows that the initial readings on the optical blood monitor taken at the onset of the patient's hemodialysis treatment session, namely the patient ID, HCT_i, SAT_i Hgb_i, and a time and date stamp are saved in memory on the optical monitor **14**. In addition, as described in block **114**, real-time data representing the change in blood volume, hematocrit, hemoglobin and oxygen saturation levels are displayed on the display **68** for the optical blood monitor **14** in accordance with the prior art.

Referring now to blocks **116** and **118** in FIG. **8**, the preferred controller **35** for the optical blood monitors **14** includes a commercially available interface for passing data from the controller **35** to a host computer. In the preferred embodiment of the invention, this interface is custom configured to store the session commencement data (patient ID, HCT_i, SAT_i Hgb_i, and time and date stamp) at the beginning of the patient's hemodialysis session. The preferred patient data collection system inside the controller **35** uses a circular or "round robin" buffer, which is continually reloaded with the latest sample data as well as monitor status and the treatment commencement data information of interest. When data is requested, the controller **35** for the optical blood monitor **14** downloads the next message in the queue. Preferably, the controller **35** for the optical blood monitor interfaces by serial hub with the host computer **90**, although the use of a network

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adapter or variety of other radio-linking equipment should be suitable. For example, a wireless radio link from Aerocom operating at 2.4 GHz is suitable. Each radio **94** connected to an optical blood monitor **14** is configured at the factory to operate as an end user, and the radio **92** for the host computer is designated as a hub radio. One suitable method of modulation for the radio system is a spread spectrum method in which the bit patterns change by a pseudo random algorithm or where the frequency of the radio system varies based on a similar pseudo random basis. The use of such a spread spectrum technique allows for multiple radios **94** to operate using the same modulation category on the same frequency without interference.

Once the wireless radio system is set up, the hub radio **92** associated with the host computer **90**, passes broadcast messages from the host computer **90** to the end user radios **94**. If the host computer **90** calls out a message to a particular blood monitor **14** through the hub radio **92**, all end user radios **94** receive that message and pass the message to their associated blood monitor **14**. Only the controller **35** for the blood monitor **14** for which the message is intended, i.e. the message includes the appropriate serial number for the respective blood monitor, will respond via its end user radio **94**. The host computer **90** preferably includes software that polls or pings the blood monitor network periodically (for example every five minutes) to determine which blood monitors **14** are active, see block **116** in FIG. **8**. If a newly identified blood monitor **14** is online, the monitor **14** is prompted to transfer the session commencement data (patient ID, HCT_i, SAT_i Hgb_i, and time and date stamp) to the host computer **90**, see block **118** in FIG. **8**. As mentioned, this data is taken in the beginning minutes of the treatment which is the most representative of the patient's true condition, because the body has established equilibrium since the previous treatment, typically two or three days prior. Once ultra filtration of the patient's blood begins, then the body fluids are dynamic and are no longer useful to characterize a patient's steady state fluid or anemia condition.

Referring still to FIG. **8**, the patient data transferred to the host computer, block **118**, is automatically entered into a patient database **93**, see block **120**. Blocks **122** and **124** indicate that data may also be entered manually into the patient database **93**. Block **122** indicates that optional manual entries may be made, for example, hemoglobin values measured on a monthly basis with standard laboratory blood work. Block **124** indicates that the attending staff manually enters the patient's ESA dosage.

Once the session commencement data is loaded into the patient database **93**, it is available to be used for long-term data analysis. The preferred user interface screens are shown in FIGS. **9** through **13**. Briefly, the user of the software on the host computer **90** first selects a patient, blocks **98**A. Block **98**B in FIG. **8** corresponds to the computer interface screen shown in FIG. **11**. Block **98**C shown in FIG. **8** corresponds to the screen shown in FIG. **10**. All of the user interface screens will be discussed in more detail below with respect to FIGS. **9-13**. Once the user selects the patient, the software predicts the patient's hemoglobin level for the next session, block **94**, using the regression model discussed earlier. The preferred system also calculates an ESA dosage recommendation for anemic patients, block **96**. The preferred ESA protocol is put forth below in Tables 2A and 2B.

TABLE 2A

HD: ESA Protocol

Rising Hemoglobin	Falling Hemoglobin or Constant Hemoglobin
Observed Hgb <10 g/dl If Predicted or Observed (P/O) Hgb rising by <0.4 g/dl/2 wks: Increase ESA dose by 25% If P/O Hgb rising by 0.4-0.7 g/dl/2 wks: No dose change If P/O Hgb rising by >0.7 g/dl/2 wks: Decrease ESA dose by 10%	Observed Hgb <10 g/dl Increase ESA dose 50%
Observed Hgb <11 g/dl If Predicted/Observed Hgb rising by <0.4 g/dl/2 wks: Increase ESA dose 25% If P/O Hgb rising by 0.4-0.7 g/dl/2 wks: No dose change If P/O Hgb rising by >0.7 g/dl/2 wks: Decrease ESA dose 10%	Observed Hgb 10.0-10.9 g/dl If Predicted/Observed Hgb decreasing >0.7% g/dl/2 wks: Increase ESA dose 50% If P/O Hgb decreasing 0.4-0.7 g/dl/2 wks: Increase ESA dose 25% If P/O Hgb decreasing <0.4 g/dl/2 wks: Increase ESA dose by 15%
Observed Hgb <11-12 g/dl If Predicted/Observed Hgb rising by >0.7 g/dl/2 wks. Decrease ESA dose 50% If P/O Hgb rising 0.4-0.-0.7 g/dl/2 wks: Decrease ESA dose 25% If P/O Hgb rising <0.4 g/dl/2 wks: No dose change	Observed Hgb 11-12 g/dl If Predicted/Observed Hgb decreasing <0.4 g/dl/2 wks. No dose change If P/O Hgb decreasing by 0.4-0.7 g/dl/2 wks: Increase ESA dose 25% If P/O Hgb decreasing by >0.7 g/dl/2 wks: Increase ESA dose 50%
Observed Hgb <12.1-13 g/dl If Predicted/Observed Hgb rising by >0.7 g/dl/2 wks. Decrease ESA dose 50% If P/O Hgb rising 0.4-0.7 g/dl/2 wks: Decrease ESA dose 25% If P/O Hgb rising <0.4 g/dl/2 wks: Decrease ESA dose 15%	Observed Hgb >12 g/dl If Predicted/Observed Hgb decreasing <0.4 g/dl/2 wks. Decrease ESA dose by 15% If P/O Hgb decreasing by 0.4 g/dl/2 wks: No dose change If P/O Hgb decreasing by >0.4-0.7 g/dl/2 wks: Increase ESA dose 25% If P/O Hgb decreasing by >0.7 g/dl/2 wks: Increase ESA dose 50%

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TABLE 2A-continued

HD: ESA Protocol	
Rising Hemoglobin	Falling Hemoglobin or Constant Hemoglobin
Observed Hgb <13.1-14 g/dl If Predicted/Observed Hgb rising by >0.4 g/dl/2 wks. Decrease ESA dose 50% If P/O Hgb rising by <0.4 g/dl/2 wks: Decrease ESA dose 25% If Observed Hgb >13 g/dl for 3 consecutive months: Hold ESA dose	Observed Hgb >13.1-14 g/dl Decrease ESA by 25% then If Predicted/Observed Hgb decrease by <0.4 g/dl/2 wks. Decrease ESA dose by another 15% If P/O Hgb decreases by 0.4 g/dl/2 wks: No further ESA dose change If P/O Hgb decreases by >0.4-0.7 g/dl/2 wks: Increase ESA dose by 15% If P/O Hgb decrease by >0.7 g/dl/2 wks: Increase ESA dose by 25%
Observed Hgb >14 g/dl Hold ESA dose, then When Observed Hgb <13 g/dl Restart ESA at 50% dose reduction	Observed Hgb >14 g/dl Hold ESA dose, then When P/O Hgb <13 g/dl Restart ESA at 50% dose reduction

TABLE 2B

Constant Hemoglobin
Observed Hgb <10 g/dl Increase ESA dose 50% Observed Hgb 10.0-10.9 g/dl Increase ESA dose 25% Observed Hgb 11-12 g/dl No dose change Observed Hgb 12.1-13 g/dl Decrease ESA dose by 25% Observed Hgb 13.1-14 g/dl Decrease ESA by 25%, then If Predicted Hgb decrease by <0.4 g/dl/2 wks. Decrease ESA dose by another 15% If Predicted Hgb decreases by 0.4-0.7 g/dl/2 wks. No further ESA dose change If Predicted Hgb decreases by >0.7 g/dl/2 wks. Increase ESA dose by 15% Observed Hgb >14 g/dl Hold ESA dose, the When Observed Hgb <13 g/dl Restart ESA at 50% dose reduction

In Tables 2A and 2B, the preferred protocol bases the percentage change in ESA dosage from the previous treatment session on several factors, including the observed patient hemoglobin level taken at the onset of the current hemodialysis treatment session (i.e., observed Hgb), as well as two-week trending of the predicted and observed hemoglobin level (i.e. P/O, gm/dl/2 wks). More specifically, the preferred protocol subtracts the mean of the three second-most recently observed Hgb levels for the patient from the mean of the three most recently observed Hgb levels to determine an observed two-week ΔHgb. The preferred protocol also subtracts the mean of the three second-most recently predicted Hgb levels for the patient from the mean of the three most recently predicted Hgb levels to determine a predicted two-week ΔHgb. The values (P/O) in Table 2A is the minimum (in terms of magnitude) of the observed two-week ΔHgb and the predicted two-week ΔHgb. The Rising Hemoglobin column in Table 2A is selected if the P/O is a positive value, and the Falling Hemoglobin column is selected if the P/O is a negative value. The Constant Hemoglobin Table 2B is chosen if P/O is equal to zero within one significant figure. The preferred protocol and the use of two-week trending are desirable in order to lessen short term data effects on recommended dosing. In general, it is desirable to maintain each patient's Hgb levels over the long term within a narrow preferred range, e.g., Hgb between 11-12 gm/dl, while at the same time maintaining the patient's ESA dosage at an appropriate and relatively constant level over the long term.

Preferably, the protocol outputs a recommended ESA dosage based on the rules in the tables above. However, in the preferred embodiment of the invention, if the observed or predicted hemoglobin level drops below a predetermined level (for example 7 gm/dl) or if the observed or predicted hemoglobin level rises above a predetermined value (for example 17 gm/dl), the system sets an alarm or an alert to seek medical help. Also, while the above ESA protocol does not account for the effects of intravenous iron therapy, such therapy typically increases the hemoglobin level and therefore a decrease in the ESA dosage of 25% beyond what is called for by the protocol in the above table is likely appropriate.

Those skilled in the art will recognize that modifications can be made to the ESA protocol without departing from the spirit of the invention. For example, the protocol can be modified to compare data trends for shorter or longer time periods than two weeks, or it can be modified to be based solely on observed values, solely on predicted values or on a different combination of observed and predicted values than are presented specifically in Tables 2A and 2B. Further, amount of the percentage ESA dosage change can be modified depending, for example, on the specific medication.

Once a patient has ended his or her treatment session, the attending staff prescribes an ESA dosage which is administered to the patient. At that point, the staff should enter the actual ESA dosage manually into the patient database, box **124** in FIG. **8**. The patient is then weighed and released, and the database **93** is loaded with data for the next treatment session for the patient.

Referring now to FIG. **9**, the Patient List screen **98**A includes a listing of patient identification numbers **126**. A patient identification number **126** is set up for each hemodialysis patient that is serviced by the clinic. If desirable and appropriate, each patient ID is associated with a patient's name, see drop-down box **127**, although as mentioned before, care must be taken to respect patient privacy laws. For example, it may be necessary to provide accessibility to the database software only by user name and password in order to protect the patient's privacy. For each patient in the database, the Patient List screen **125** lists a desired minimum hemoglobin level and a desired maximum hemoglobin level which had been entered into the system by the clinician, nurse or physician. The Patient List screen **125** also lists observed hemoglobin levels for the patient (i.e. optically observed Hgb_i), and

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in particular, the minimum value for that patient in the database, the maximum value for that patient in the database, and the patient's last observed Hgb_i value. Further, the Patient List screen lists the last ESA dose for the patient, as well as the calculated ESA dose for the current treatment session. Once a patient has been released, the calculated ESA dosage listed in the Patient List screen **125** does not change until the patient's next treatment session. The "Order by Name" button **129** rearranges the list by patient name, rather than patient identification number. The "Get Data" button **131** allows the user to manually prompt the system so that the host computer interrogates the network of optical blood monitors to download additional data. In order to view additional data for any given patient, the user selects a patient number on screen **125** and then selects one of tab **130** for a "Patient Management" screen (FIG. **10**) or tab **132** for a "Patient Graph" screen. Tab **134** redirects the user to an "Active Patients" screen (FIG. **12**) and tab **136** directs the user to an "Outside Boundaries" screen (FIG. **13**).

The Patient Management screen **133** is shown in FIG. **10**. Window **132** provides prompts for adding new patient information or editing patient information. The fields in window **132** are patient ID, patient Name, Lower limit which is the desired minimum hemoglobin value for the patient, Upper limit which is the desired maximum hemoglobin level for the patient, and Optimal Value which is the desired hemoglobin level for the patient. These values, as mentioned before, are entered by staff. When the values in window **132** or the patient identification number are changed, the user selects the "Save" button in window **132** to add the new patient or edit the values for an existing patient. The "Delete" button is used to remove the patient from the database.

The "Blood Points" window **134** lists session commencement data stored in the patient database on the date selected. The prompt label date includes a dropdown listing of all the dates in which blood data has been entered for the patient, normally automatically (see, box **120** in FIG. **8**). However, data for any particular date can be entered manually as well, see box **122** in FIG. **8**. The "Save" button in the "Blood Points" window **134** is used to edit the values for Hgb, HCT and oxygen saturation for a particular date. The "New" button is used to add blood data for a new date. The "Delete" button in the "Blood Points" window **134** can be used to remove data for the identified patient on the particular listed date.

The Patient Management screen **133** also preferably includes a "Notes" window **136** in which staff can enter and store notes on a particular date for a particular patient. The Patient Management screen **133** also includes an "ESA Dosage" window **138** in which staff manually enters, edits or deletes a dosage that has been administered to the patient on a given date. All of the information entered in the Patient Management screen **133** is stored in the patient database **93**. The user of the software can access the data for a given patient in windows **134**, **136** and **138** on various dates by merely selecting a different date under the date prompt. The user can change the identified patient using the patient ID prompt in window **132**.

Turning now to the Patient Graph screen in FIG. **11**, the Patient Graph screen **135** includes a graph **142** which displays a trend of the patient's (patient ID #**1006**) hemoglobin levels, both measured (open circles) and predicted (open squares). The graph **142** preferably includes horizontal lines **146** and **148** which correspond to the maximum desired hemoglobin level (**146**) and the minimum desired hemoglobin level (**148**) for the patient. It can be seen on the graph **142** in FIG. **11** that the patient's measured hemoglobin levels, as well as the predicted hemoglobin levels, are trending slightly upward, yet still between the maximum desired level **146** and the minimum desired level **148**.

Above the graph **142**, the software lists the current ESA dosage for the patient **150** (meaning the last dosage prescribed). The predicted hemoglobin level for the patient's next visit is plotted on the graph **142**, see reference number **152**. The Patient Graph display screen **135** also indicates the calculated ESA dose for the patient (per the ESA protocol) at the end of the current treatment session, see reference number **154**. The graph **142** in FIG. **11** also shows a trend line **153** which is a linear regression through the last six data points. Other information can be displayed on the Patient Graph screen **135**, as desired. For example, it may be desirable to display the predicted hemoglobin value numerically on the screen **135**, or it may be desired to provide an alert in case the trend line **153** is too steep, or the predicted or observed hemoglobin values fall beyond the desired minimum and maximum levels **148** and **146**, respectively. The software also preferably provides a "Show 6 Months" button **144** which adjusts the time scale in the graph **142** at a six month time period.

As can be seen in FIG. **11**, use of the system allows the attending staff to easily analyze the long-term trend of the patient and facilitate informed decision making. Use of the system promotes more frequent hemoglobin monitoring for each individual patient, which in turn should reduce undesirable fluctuations in patient hemoglobin levels. Frequent hemoglobin monitoring allows early detection of trends in the hemoglobin slope lines, and also early evidence of the patient's response to ESA dosages and perhaps alert the staff that more appropriate anemia management tools may be needed.

The "Active Patients" screen **137** is shown in FIG. **12**. Screen **137** lists each of the active optical monitors **14** in the main window **154**. The first column labeled "SID" lists the Station ID, for example hemodialysis station #**11** or #**14**, as shown in FIG. **12**. The second column lists the patient ID number for the active stations as well as the same information that was listed for that patient in the Patient List screen **125** shown in FIG. **9**.

The "Outside Boundaries" screen **139** is shown in FIG. **13**. The purpose of this screen is to list all patients whose initial hemoglobin readings (Hgb_i) are out of bounds. The data listed for each patient is again similar to that shown in the Patient List screen **125**, however, in the Outside Boundaries screen **139**, only patients whose hemoglobin level is currently out of bounds are listed.

The described embodiment of the invention should be considered in all respects as illustrative and not restrictive. For example, as mentioned above, the preferred means for communicating data between the controller for the blood monitor and the host computer is a wireless communication device, although other means of data communication may be used. In addition, various aspects of the system can be implemented without implementing other aspects of the system. For example, the system can be implemented with the predictive algorithm for the hemoglobin without implementing the protocol for ESA dosage recommendations. Also, the system can be implemented with the patient database and the user software interface screens without using either the predictive algorithm for the hemoglobin level or the software for the ESA protocol dosage recommendations. Even in such a system, the patient management **133**, patient graph **135** and outside boundaries **137** screens can be quite useful to attending staff for following trends of a patient's hemoglobin levels. On the other hand, it would be quite possible to implement the

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predictive hemoglobin algorithm and/or the protocol for the ESA dosage recommendations, in environments other than one in which optically monitored hemoglobin levels are downloaded automatically from the optical blood monitors to the host computer. For example, the data could be entered in a manual form into a patient database.

We claim:

1. An anemia management system for hemodialysis patients comprising:

at least one hemodialysis system for drawing blood from a patient, passing the drawn blood through extracorporeal tubing and through a dialyzer, and returning the dialyzed blood through extracorporeal tubing to the patient, the hemodialysis system comprising:

a blood chamber having an inlet and an outlet which are connected in line with the extracorporeal tubing of the hemodialysis system and a fluid passageway through which the drawn blood flows;

a first photo emitter for emitting light at a first wavelength through the blood chamber and the drawn blood flowing through the blood chamber;

a second photo emitter for emitting light at a second wavelength through the blood chamber and the drawn blood flowing through the blood chamber; and

at least one photo detector for detecting the intensity of light at the first and second wavelength after it passes through the blood chamber and the drawn blood flowing through the blood chamber;

a computing system, connected to the at least one hemodialysis system, the computing system comprising processor-executable instructions, stored on one or more non-transitory processor-readable media, and one or more processors for executing the processor-executable instructions, wherein the processor-executable instructions include instructions for:

receiving a signal representing the detected light intensity levels from the at least one hemodialysis system;

determining a value representing the patient's hemoglobin level based on the received signal;

storing the determined value in a patient database of the computing system;

determining, based on information stored in the patient database, a predicted value for the patient's hemoglobin level at the onset of a next treatment session by applying a statistical model to stored patient data, where the predicted value is based on multiple instances of the patient's previous hemoglobin levels corresponding to measurements taken at the onset of a series of treatment sessions, multiple coefficients determined based on the statistical model with each coefficient corresponding to one of the multiple instances of the patient's previous hemoglobin levels, and at least one previously administered dosage of an erythropoiesis stimulating agent (ESA);

determining a recommended ESA dosage for the patient based on the predicted value; and

outputting the recommended ESA dosage via an output interface of the computing system.

2. The anemia management system as recited in claim **1**, wherein the first photo emitter emits light at a wavelength of substantially 800 nm, and the second photo emitter emits light at a wavelength of substantially 1300 nm.

3. The anemia management system as recited in claim **1**, wherein the computing system is further configured to determine a hematocrit value and an oxygen saturation value for the patient, as well as time and date information at the onset of the patient's hemoglobin treatment session.

4. The anemia management system as recited in claim **3**, wherein the at least the first and second photo emitters of the non-invasive blood monitor emit light at a wavelength of substantially 800 nm and substantially 1300 nm, respectively, and a third photo emitter emits light at a wavelength of substantially 660 nm.

5. The anemia management system as recited in claim **1**, wherein determining the statistical model is a cross-sectional regression model based on statistical analysis of data collected from a plurality of hemodialysis patients over a number of hemodialysis treatment sessions being monitored by a non-invasive blood monitor.

6. The anemia management system as recited in claim **1**, wherein determining the predicted value is based on the following equation:

$$\text{Predicted Hgb Value} = A^*(\text{Hgb of Last Period}) + B^*(\text{Hgb of Second to Last Period}) + C^*(\text{Hgb of Third to Last Period}) + D^*(\text{Last ESA Dose value}) + E$$

where Hgb of last period, Hgb of second to last period and Hgb of the third to last period represent the patients hemoglobin levels monitored at the previous three hemodialysis treatment sessions, the last ESA dose value represents the ESA dose administered to the patient at the patient's last treatment session, the values A through E are statistical regression coefficients, and the predicted Hgb value represents the predicted value of the patient's hemoglobin level at the start of the next treatment session.

7. The anemia management system as recited in claim **6**, wherein the ESA is recombinant erythropoietin, and the regression coefficient A is substantially equal to 0.4784356, the regression coefficient B is substantially equal to 0.2042212, the regression coefficient C is substantially equal to 0.222685, the regression coefficient D is substantially equal to 0.0000396, and the regression coefficient E is substantially equal to 0.9627966.

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