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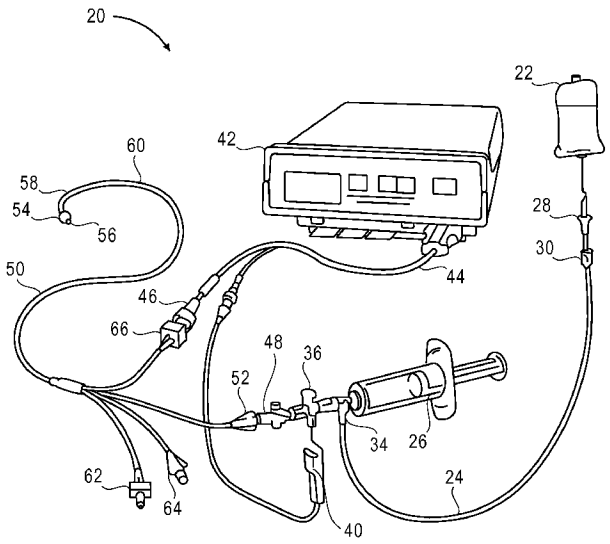

FIG. 1

(57) Abstract: Apparatus and methods for the measurement, control, or both, of thermodilution injectate flow for calculation of transpulmonary thermodilution parameters. An injectate delivery system includes a syringe for holding an injectate and a conduit configured at one end to be connected to a catheter. A flow measurement device is interposed in the conduit to generate a signal for determining the flow rate of the fluid from the syringe to the catheter. A processor receives the signal from the flow measurement device and calculates the injectate volume to be used as input for calculating a transpulmonary thermodilution parameter such as cardiac output. A GUI is provided to direct a user on whether the injection rate is too fast or too slow. Rather than measuring or calculating flow rate, a system may include a constant flow valve to provide a constant flow rate from the syringe.

WO 2017/069755 A1

THERMODILUTION INJECTATE MEASUREMENT AND CONTROL

FIELD

[0001] Aspects of the disclosure generally relate to apparatus and methods for measurement, control, or both, of fluid discharged from a syringe or other reservoir, and in particular may relate to accuracy of measured or calculated transpulmonary thermodilution parameters.

BACKGROUND

[0002] Thermodilution is the most widely used technique for determining cardiac output. The thermodilution method applies indicator dilution principles, using temperature change as the indicator.

[0003] A known amount of solution with a known temperature is injected rapidly into the right atrial lumen of a first catheter. This cooler solution mixes with and cools the surrounding blood, and the temperature is measured downstream in the pulmonary artery by a thermistor bead embedded in a second catheter. The resultant change in temperature is then plotted on a time-temperature curve. This curve is similar to the one produced by the indicator-dilution method.

[0004] A normal curve characteristically shows a sharp upstroke from rapid injection of the injectate. This is followed by a smooth curve and slightly prolonged downslope back to the baseline. Since this curve is representing a change from warmer temperature to cooler and then back to warmer temperature, the actual curve is in a negative direction. In many illustrative and display graphs, the curve is produced in an upright fashion, so that the area under the curve is inversely proportional to the cardiac output.

[0005] When cardiac output is low, more time is required for the temperature to return to baseline, producing a larger area under the curve. With high cardiac output, the cooler injectate is carried faster through the heart, and the temperature returns to baseline faster. This produces a smaller area under the curve.

[0006] Critical to the technique is the injectate temperature, volume, and flow rate. As the result of rates of injections differing between users who perform the procedure, however, actual volume and solution temperature of the injectate, or injected cold bolus, may vary considerably, with a loss of accuracy and precision of the cardiac output measurement. Some users apply extreme force to the syringe to inject the bolus as quickly as possible, while others inject at a slower rate. Mistakes may be made by the user when injecting the bolus, including injecting a different volume than the quantity that was entered into a monitoring device and on which calculations are based.

SUMMARY

[0007] In accordance with one embodiment of the concepts disclosed herein, an injectate delivery system is provided. The system includes a reservoir for holding a fluid injectate, a conduit in fluid communication with the reservoir and configured at one end to be connected to a catheter, and a manually or mechanically driven syringe, another form of injector, or other means for manually discharging the fluid from the reservoir to the conduit. A flow measurement device is interposed in the conduit, and the flow measurement device is configured for generating a signal used in determining the flow rate of the fluid from the reservoir to the catheter. A processing device is adapted to receive the signal from the flow measurement device and is configured to calculate injectate volume to be used as input for calculating at least one parameter. In some embodiments, the at least one parameter to be calculated is a transpulmonary

thermodilution parameter, and in some such embodiments, the transpulmonary thermodilution parameter is at least one of cardiac output, global end diastolic volume, and extra vascular lung water.

[0008] In some embodiments and in combination with any of the above embodiments, the reservoir is a syringe, and the means for manually discharging the fluid is a plunger of the syringe. In some such embodiments, the system further comprises a catheter in fluid communication with the reservoir, and in some of these embodiments, the catheter is a Swan-Ganz® catheter, manufactured and sold by Edwards Lifesciences.

[0009] In some embodiments and in combination with any of the above embodiments, the flow measurement device is configured to generate the signal to the processing device based on differential pressure. In some embodiments and in combination with any of the above embodiments, the flow measurement device comprises pressure sensors for measuring a pressure drop across an orifice. In some embodiments and in combination with any of the above embodiments, the flow measurement device defines an area of constricted flow and comprises pressure sensors for measuring vortex differential pressure. In some embodiments and in combination with any of the above embodiments, the flow measurement device comprises a Venturi tube. In some embodiments and in combination with any of the above embodiments, the flow measurement device comprises pitot tubes. In some embodiments and in combination with any of the above embodiments, the flow measurement device comprises a hot wire anemometer.

[0010] In some embodiments and in combination with any of the above embodiments, a sensor interposed in the conduit is configured to detect changes in

pressure or temperature of the injectate and to signal a timer to start at the beginning of the injection and stop at the end of the injection to measure elapsed time of an injection.

[0011] In accordance with another embodiment of the concepts disclosed herein, a method for determining injectate volume for use in the determining transpulmonary thermodilution parameters is provided. The method includes starting, by a processor, a timer upon receiving a signal of an increase in pressure at a pressure sensor indicating the start of an injection of a fluid injectate into a conduit from a syringe. A signal is received by a processor from a flow measurement device interposed in the conduit. A processor calculates a flow rate of the injectate. The timer is stopped to determine the elapsed time of the injection, and a processor calculates a volume of injectate that has been injected. The calculated volume is used in calculating at least one transpulmonary thermodilution parameter.

[0012] In some embodiments and in combination with the above embodiment, the transpulmonary thermodilution parameter is at least one of cardiac output, global end diastolic volume, and extra vascular lung water. In some embodiments and in combination with any of the above embodiments, the method further comprises graphically displaying a current flow rate of injectate. In some such embodiments, the method further comprises graphically displaying a predetermined minimum flow rate and a predetermined maximum flow rate that define limits within which the current flow rate is desired to appear.

[0013] In accordance with another embodiment of the concepts disclosed herein, an injectate delivery system is provided. The injectate delivery system includes a reservoir for holding a fluid injectate, a conduit in fluid communication with the reservoir and configured at one end to be connected to a catheter, and a syringe, an

injector, or another means for manually discharging the fluid injectate from the reservoir to the conduit during an injection. A constant flow control element is fluidically interposed in the conduit, and the constant flow control element is configured to maintain a substantially constant design flow rate for the duration of the injection for the flow of the fluid from the reservoir to the catheter. A sensor is interposed in the conduit configured to detect changes in pressure or temperature of the injectate and to signal a timer to start at the beginning of the injection and stop at the end of the injection. A processing device is adapted to receive a signal from a sensor, with the processing device being configured to calculate injectate volume based on the constant flow valve design flow rate and measured elapsed time of the injection. The volume is to be used as input for calculating at least one parameter. In some such embodiments, the at least one parameter to be calculated is a transpulmonary thermodilution parameter including at least one of cardiac output, global end diastolic volume, and extra vascular lung water.

[0014] In some embodiments and in combination with any of the above embodiments, the reservoir comprises a syringe and the constant flow control element comprises a constant flow valve fluidically interposed in the conduit. In other embodiments and in combination with any of the above embodiments, the reservoir comprises a syringe and the syringe comprises the constant flow control element as an integral feature of the syringe.

[0015] In accordance with another embodiment of the concepts disclosed herein, a method of displaying a relative flow rate for an injectate delivery system is provided. The method includes calculating, by a processor, a flow rate of a fluid injected into a conduit for a thermodilution procedure using parameters measured by a flow measurement device. The processor graphically displays on a display device an

indication of a predetermined minimum acceptable flow rate, a predetermined maximum acceptable flow rate, and the current flow rate relative to the minimum and maximum acceptable flow rates.

[0016] In accordance with another embodiment of the concepts disclosed herein, a system for displaying a relative flow rate for an injectate delivery system is provided. The system includes a display device, a processor operably connected to the display device; and a memory. The memory is operably connected with the processor to store a predetermined minimum acceptable flow rate and a predetermined maximum acceptable flow rate, and is also operably connected to store computer program code which, when executed, causes the processor to calculate a flow rate of a fluid injected into a conduit for a thermodilution procedure using parameters measured by a flow measurement device, and graphically present, on the display device, an indication of the predetermined minimum acceptable flow rate, the predetermined maximum acceptable flow rate, and the current flow rate relative to the minimum and maximum acceptable flow rates.

[0017] In accordance with another embodiment of the concepts disclosed herein, an apparatus for displaying a relative flow rate for an injectate delivery system is provided. The apparatus includes means for storing a predetermined minimum acceptable flow rate and a predetermined maximum acceptable flow rate, means for calculating a flow rate of a fluid injected into a conduit for a thermodilution procedure using parameters measured by a flow measurement device, and means for graphically displaying an indication of the predetermined minimum acceptable flow rate, the predetermined maximum acceptable flow rate, and the current flow rate relative to the minimum and maximum acceptable flow rates.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] For a more complete understanding, reference should now be had to the embodiments shown in the accompanying drawings and described below. In the drawings;

[0019] FIG. 1 is a perspective view of a prior art injectate delivery system.

[0020] FIG. 2 is a schematic view of an injectate delivery system in accordance with example embodiments of the invention.

[0021] FIG. 3 is a flowchart illustrating a process that can be carried out with example embodiments of the invention.

[0022] FIG. 4 is a screenshot of a screen of the display device that is part of the system of FIG. 2. Such a screen may be produced by embodiments of the invention.

[0023] FIG. 5 is a block diagram of a system according to example embodiments of the invention.

[0024] FIG. 6 is a schematic view of another injectate delivery system in accordance with example embodiments of the invention.

[0025] FIGS. 7-9 are graphs representing the impact of incorrect injectate volume, either being injected or recorded, on transpulmonary thermodilution parameters.

DETAILED DESCRIPTION

[0026] The following detailed description of embodiments refers to the accompanying drawings, which illustrate specific embodiments. Other embodiments having different structures and operation do not depart from the scope of the present disclosure.

[0027] Embodiments of concepts disclosed herein are directed to apparatus and methods for measuring, controlling, or both, characteristics of an injected bolus. The characteristics may include, for example, pressure, temperature, and flow, and although the disclosed apparatus and methods may apply to automated devices such a syringe pumps, they are discussed herein with respect to manually operated syringes and reservoirs. In addition, real-time feedback may be provided to a user to help reduce variability in the injection technique as well as reduce the potential for user error in entering data into the monitoring device.

[0028] As will be appreciated by one of skill in the art, the present invention may be embodied as a method, device, article, system, computer program product, or a combination of the foregoing. Any suitable computer usable or computer readable medium may be utilized for a computer program product including non-transitory computer program code to implement all or part of an embodiment of the invention. The computer usable or computer readable medium may be, for example but not limited to, a tangible electronic, magnetic, optical, electromagnetic, or semiconductor system, apparatus or device.

[0029] There are two primary injectate delivery systems for thermodilution procedures. One is an open system that utilizes prefilled syringes, with injectate either iced or at room temperature. The other is a closed system, also either for iced or room temperature injectate, which is maintained in a closed-loop fashion to reduce multiple entries into a sterile system. Available data suggest that there will be less variability in cardiac output determinations if iced solution is used. Optionally, an injectate temperature that is warmer than body temperature could be used. A computer registers a change in temperature, which may be through a signal, from the patient's baseline, which

may be noise. In some conditions, a variation in temperature of 0.05°C may occur with respirations. This decreases the "signal-to-noise'' ratio and may produce an abnormally low cardiac output value. Other conditions where an increased signal-to-noise ratio may be beneficial include febrile patients, low cardiac output states, and patients with wide respiratory variations.

[0030] A modified Stewart-Hamilton equation is used to calculate the cardiac output, taking into consideration the change in temperature as the indicator. Modifications include the measured temperature of the injectate and the patient's blood temperature, along with the specific gravity of the solution injected. The Stewart-Hamilton equation is as follows:

[0031] $CO = (V \times (T_B - T_I)/A) \times (S_I \times C_I)/(S_B \times C_B) \times (60 \times C \times K)$

[0032] Where:

[0033] CO = cardiac output

[0034] V = Volume of injectate (mL)

[0035] A = area of thermodilution curve in square mm divided by paper speed (mm/sec)

[0036] T_B, T_I = temperature of blood (B) and injectate (I)

[0037] S_B, S_I = specific gravity of blood and injectate

[0038] C_B, C_I = specific heat of blood and injectate

[0039] $(S_I \times C_I)/(S_B \times C_B) = 1.08$ when 5% dextrose is used

[0040] 60 = 60 sec/min

[0041] C_T = correction factor for injectate warming

[0042] A dilution apparatus, method, and computer program applicable to thermodilution is disclosed in U.S. Patent No. 8,343,058, to Pfeiffer et al., issued January

1, 2013, and assigned to Edwards Lifesciences IPRM AG, the contents of which are hereby incorporated by reference in their entirety. At least three key transpulmonary thermodilution parameters may be impacted by injectate volume, being cardiac output, global end diastolic volume, and extra vascular lung water.

[0043] Referring to the drawings, where like reference numerals refer to the same or similar parts, FIG. 1 shows a prior art injectate delivery system 20, which in this embodiment is an open system. The system 20 includes a sterile injectate solution reservoir 22 connected with injectate delivery tubing 24 to an outlet or tubing connected to the outlet of a syringe 26. A non-vented IV spike 28 and a means of stopping flow from the tubing, such as a snap clamp 30, may be provided along the injectate delivery tubing 24. A check valve 34 may be provided proximate to the connection of the tubing 24 to the syringe outlet to allow flow from the reservoir 22 to the syringe 26, but not allow flow back to the reservoir 22.

[0044] Downstream of the connection of the check valve 34 to the syringe outlet, a flow-through housing 36 may be provided that receives a temperature probe 40. The temperature probe 40 is one of several features electrically connected to a computer 42, which may include an associated processor or processing device, CPU, monitor, and control unit, with electrical cables 44 and catheter connectors 46. A three-way stopcock and continuous flush device 48 may be connected downstream of the flow-through housing 36 for the temperature probe 40. The most downstream element may be a catheter 50, which may be, for example, a Swan-Ganz catheter. The catheter 50 may include a proximal injectate hub 52. At the distal end of the catheter 50 there may be a balloon 54 and a distal lumen 56, with a thermistor 58 proximate to the balloon 54 and spaced from a proximal injectate port 60. At the proximal end of the catheter 50, in

addition to the proximal injectate hub 52 there may be a balloon inflation valve 62, an IV/pressure monitoring line 64, and a thermistor connector 66, connected with a catheter connector 46 to the computer 42.

[0045] An example embodiment according to the invention of an injectate delivery system 70 is shown schematically in FIG. 2. In this embodiment, a flow measurement device may be provided. In the flow measurement device a pressure differential may measured across a pressure reducing feature, such as, for example, an orifice, a constricted flow area resulting in vortex differential pressure, a differential pressure transducer, or a Venturi tube, in order to calculate a flow rate of injectate. The flow measurement device may alternatively include pitot tubes or a hot wire anemometer-type device. Taken over a measured time, the flow rate may be used to calculate a volume of injectate, which in turn may be used in the Stewart-Hamilton equation and the equations of incorporated U.S. Patent No. 8,343,058, and may provide a more accurate result than might otherwise be reached.

[0046] The injectate delivery system 70 of FIG. 2 may include a reservoir such as a syringe 26 that may draw from an injectate reservoir 22, with a check valve 34 allowing flow from the reservoir 22 but preventing flow back to the reservoir 22. Alternatively, the reservoir 22, tubing 24, and check valve 34 may be omitted, leaving the system closed, with only the syringe 26 as the source of injectate; the syringe 26 may be pre-filled and itself cooled. Another check valve 72 may be provided that allows the flow of discharged injectate from the syringe 26, but prevents backflow into the syringe 26 from tubing 24 when the syringe 26 is aspirated to draw injectate from the reservoir 22. A flow measurement device 74, as described above, may be inserted in line with the tubing 24. Pressure sensors 78, 80 may be provided upstream and downstream of the

flow measurement device 74, and a temperature sensor 82, which may be a thermistor, may be provided as well, preferably downstream of the flow measurement device 74. The pressure sensors 78, 80 and temperature sensor 82 may be connected to the computer 42 with cables 44. A stopcock 84 or other valve may be provided and may be connected to a proximal injectate hub (not shown). The catheter 50 is represented by a single line in FIG. 2, but it should be understood that there may be multiple connection lines incorporated in the catheter that serve a variety of functions, as exemplified in FIG 1.

[0047] The flow measurement device 74 may have known flow characteristics and flow area that provide a relationship between pressure loss and velocity of the injectate, such that when the pressure loss is known, the velocity may be determined. In addition, the initial change in pressure, or if desired, temperature, when the bolus discharge from the syringe 26 begins may trigger a timer to start in the computer 42. With the velocity and the fluid characteristics of the injectate known, and the elapsed time being measured, the volume of the injectate may be calculated.

[0048] An embodiment of a process 88 for determining injectate volume for use in the determining transpulmonary thermodilution parameters is shown in FIG. 3. First, discharge of injectate from a syringe begins 90. A timer starts upon receiving a signal of an increase in pressure at a pressure sensor 92, for example, at a pressure sensor in the line from the syringe; which pressure sensor to use, or both, may be selected as desired to suit the application and apparatus. A signal is received from a flow measurement device in the line from the syringe 94, which may be on both sides of a pressure reducing device (upstream and downstream), or alternatively from flow that cools a hot wire anemometer to generate a signal. Then the flow rate may be calculated 96, from, for

example, pressure differential across a pressure reducing device, pitot tubes, or from a hot wire anemometer.

[0049] Optionally, a graphical user interface (GUI) may be provided that graphically displays the real-time flow rate of injectate 98. The display may include limits within which the flow rate should appear. The timer may be stopped 100 upon receiving a signal of a drop in the pressure at a selected one or both of the pressure sensors. Volume is calculated 102 using the flow rate and the measured elapsed time. A signal from a temperature sensor is received to indicate the temperature of the injectate 104, and the volume and temperature are used in the calculation of at least one transpulmonary thermodilution parameter 106.

[0050] FIG. 4 shows a monitor 120 associated with a computer 42 (FIGS. 1 and 2). The monitor 120 may display a GUI of the flow rate of injectate from the syringe 26 into the catheter 50. The flow rate may be displayed in real time, as represented in this embodiment by a bubble 122a. The flow rate increases from left to right in FIG. 3. A minimum limit 124 and a maximum limit 126 of flow rate may be displayed on the monitor 120. The target 130 may be centrally located, and various example positions of the bubble being shown in dashed lines. A second bubble 122b shows that the flow rate is too slow, as it is outside the acceptable range and below the minimum limit 124. A third bubble 122c shows that the flow rate is acceptable but should be increased, as it is just within the acceptable range and above the minimum limit 124. A fourth bubble 122d shows that the flow rate is too fast, as it is outside the acceptable range and above the maximum limit 126. A fifth bubble 122e shows that the flow rate is acceptable but should be decreased, as it is just within the acceptable range and below the maximum limit 124. The user applying force to the syringe 26 may watch the monitor 120 for

direction regarding how fast the plunger of the syringe 26 should be depressed and accordingly what force should be applied to result in an acceptable flow rate.

[0051] FIG. 5 schematically illustrates detail of the computer 42 with associated CPU, monitor, and control unit of FIG. 1, also showing selected other features of an injectate delivery system as well as a patient 200. The system includes I/O interface 202, which may in turn include an appropriate connector, and circuitry to monitor signals from the sensor system. This circuitry may include analog-to-digital converters, encoders, decoders, and the like. I/O interface 202 is coupled to a central processing unit (CPU) 204, which controls the operation of the entire system.

[0052] The I/O interface receives sensor signals from pressure sensors, temperature sensors, and/or flow rate detectors 205, and the like. CPU 204 is further operatively connected to memory 206. Memory 206 stores all of the information needed for the system to operate. Such information may be stored in a temporary fashion, or may be stored more permanently. This memory may include a single, or multiple types of memory. For example, a portion of the memory connected with CPU 204 may be “flash” memory which stores information semi-permanently for use by the system. In either event memory 206 of FIG. 5 in this example embodiment includes computer program code 208 which, when executed by CPU 204, causes the system to carry out the various processes to graphically display information according to example embodiments disclosed herein. Memory 206 also stores data 210, which in example embodiments includes historical numerical values for the pressures, temperatures, times, flow rates, and injectate volumes.

[0053] Still referring to FIG. 5, monitoring and control unit 12 may also include a network interface 213. This network interface can allow the system to be connected to a

wired or wireless network to allow monitoring on a remote display (not shown). For example, the remote display could duplicate, or be used in place of the local display panel. In the embodiment of FIG. 5, a local display device, 217 (which may be the same as monitor 120 of FIG. 4), is connected with CPU 204 via a graphics engine 224. The local display device may be an LCD panel, plasma panel, or any other type of display component and accompanying circuitry to interface the display device to graphics engine 224. Graphics engine 224 may be on its own chip, or in some embodiments it may be on the same chip as CPU 204. Note that display device 217 may include user input functionality, for example an optical or capacitive touchscreen over the display screen. In such a case, monitoring control unit 42 may include additional circuitry to process such input. Alternatively, such circuitry may be included in the display device itself, the graphics engine, or the CPU 204.

[0054] FIG. 6 schematically shows another example embodiment according to the invention of an injectate delivery system 300. Similarly to the injectate delivery system 70 of FIG. 2, the injectate delivery system 300 of FIG. 6 may include a reservoir such as a syringe 26 that may draw from an injectate reservoir 22, with a check valve 34 allowing flow from the reservoir 22 but preventing flow back to the reservoir 22. Alternatively, the reservoir 22, tubing 24, and check valve 34 may be omitted, leaving the system closed, with only the syringe 26 as the source of injectate; the syringe 26 may be pre-filled and itself cooled. Another check valve 72 may be provided that allows the flow of discharged injectate from the syringe 26, but prevents backflow into the syringe 26 from tubing 24 when the syringe 26 is aspirated to draw injectate from the reservoir 22. In this embodiment, however, a constant flow valve 302 may be inserted in line with the tubing 24. The constant flow valve 302 will remain closed until a “cracking pressure”

is reached from actuating the plunger of the syringe 26, at which time the seal will open and flow will begin, being maintained at the same constant flow rate based on the design of the valve. The pressure required to break the seal may be on the order of, for example, one pound. Alternatively, a constant flow syringe may be provided, combining the syringe and the constant flow valve.

[0055] A pressure sensor 306, and a temperature sensor 308, which may be a thermistor, may be provided in line with and preferably downstream of the constant flow valve 302. The pressure sensor 306 and temperature sensor 308 may be connected to the computer 42 with cables 44. The pressure sensor 306 may be useful to initiate and stop the timer to allow volume calculation based on the flow rate of the valve multiplied by the elapsed time, while the temperature sensor 308 is needed for the thermodilution calculation. A stopcock 84 or other valve may be provided and may be connected to a proximal injectate hub (not shown). The catheter 50 is represented by a single line in FIG. 6, but it should be understood that there may be multiple connection lines incorporated in the catheter that serve a variety of functions, as exemplified in FIG 1.

[0056] The materials of components of the apparatus disclosed herein may be as selected by one of ordinary skill in the medical equipment design arts.

[0057] As discussed above, the thermodilution algorithm is sensitive to the injectate volume that is applied to the patient. If the injectate volume is incorrectly input into the system, or the volume applied to the patient is different, then the computational values are not accurate. To demonstrate the influence of the injectate volume on the results of key transpulmonary thermodilution parameters, an analysis was performed. Using a thermodilution bolus from a clinical study, the output parameters using a range of injectate volumes between 10 mL to 20 mL were recalculated to allow review of the

range and error of the parameter values resulting from incorrect injectate volumes. The impact of injectate volume on the three primary transpulmonary thermodilution parameters of cardiac output, global end diastolic volume, and extra vascular lung water was considered.

[0058] The procedure used a thermodilution bolus from a clinical study to recalculate the output parameters using a range of injectate volumes between 10 mL to 20 mL, then to study the range and error of the parameter values resulting from incorrect injectate volumes. The results were as follows:

Injection Volume (mL)	CO (L/min)	GEDV (mL)	EVLW (mL)
10	3.28	1005.7	304.2
11	3.64	1105.6	332.7
12	4	1205.4	316.3
13	4.35	1305.2	389.8
14	4.71	1405.1	418.4
15	5.07	1504.9	447
16	5.43	1604.7	475.5
17	5.79	1704.6	504.1
18	6.15	1804.4	532.6
19	6.51	1904.3	561.2
20	7.01	2004.1	589.7

[0059] FIGS. 7-9 show the results plotted with the parameters each as a function of injectate volume. The graphs and the table above show that assuming the original 10 mL value is correct, in this particular example, if 20 mL is incorrectly injected rather than the intended 10 mL, there can be an error of up to 114% with respect to CO (FIG. 7), an error of up to 99% with respect to GEDV (FIG. 8), and an error of up to 94% with respect to EVLW (FIG. 9).

[0060] Although specific embodiments have been illustrated and described herein, those of ordinary skill in the art appreciate that any arrangement which is calculated to achieve the same purpose may be substituted for the specific embodiments shown and that the embodiments herein have other applications in other environments. This application is intended to cover any adaptations or variations of the present disclosure. The following claims are in no way intended to limit the scope of the disclosure to the specific embodiments described herein. While the foregoing is directed to embodiments of thermodilution injectate measurement and control, other and further embodiments may be devised without departing from the basic scope thereof, and the scope thereof is determined by the claims that follow.

What is claimed is:

1. An injectate delivery system, comprising:

a reservoir for holding a fluid injectate;

a conduit in fluid communication with the reservoir and configured at one end to be connected to a catheter;

an injector configured to discharge the fluid from the reservoir to the conduit;

a flow measurement device interposed in the conduit, wherein the flow measurement device is configured for generating a signal used in determining the flow rate of the fluid from the reservoir to the catheter; and

a processing device adapted to receive the signal from the flow measurement device and configured to calculate injectate volume to be used as input for calculating at least one parameter.

2. The system of claim 3, wherein the at least one parameter to be calculated is a transpulmonary thermodilution parameter.

3. The system of claim 4, wherein the transpulmonary thermodilution parameter is at least one of cardiac output, global end diastolic volume, and extra vascular lung water.

4. The system of claim 1, wherein the reservoir is a reservoir of a syringe that includes a manually operable plunger as the injector.

5. The system of claim 4, further comprising a catheter in fluid communication with the reservoir.

6. The system of claim 5, wherein the catheter is a Swan-Ganz catheter.

7. The system of claim 1, wherein the flow measurement device is configured to generate the signal to the processing device based on differential pressure.

8. The system of claim 1, wherein the flow measurement device comprises pressure sensors for measuring a pressure drop across an orifice.

9. The system of claim 1, wherein the flow measurement device defines an area of constricted flow and comprises pressure sensors for measuring vortex differential pressure.

10. The system of claim 1, wherein the flow measurement device comprises a Venturi tube.

11. The system of claim 1, wherein the flow measurement device comprises pitot tubes.

12. The system of claim 1, wherein the flow measurement device comprises a hot wire anemometer.

13. The system of claim 1, wherein a sensor interposed in the conduit is configured to detect changes in pressure or temperature of the injectate and to signal a timer to start at the beginning of the injection and stop at the end of the injection to measure elapsed time of an injection.

14. A method for determining injectate volume for use in the determining transpulmonary thermodilution parameters, comprising:

starting, by a processor, a timer upon receiving a signal of an increase in pressure at a pressure sensor indicating the start of an injection of a fluid injectate into a conduit from a syringe;

receiving, by a processor, a signal from a flow measurement device interposed in the conduit;

calculating, by a processor, a flow rate of the injectate;

stopping the timer to determine the elapsed time of the injection;

calculating, by a processor, a volume of injectate that has been injected; and

using the calculated volume in calculating at least one transpulmonary thermodilution parameter.

15. The method of claim 14, wherein the transpulmonary thermodilution parameter is at least one of cardiac output, global end diastolic volume, and extra vascular lung water.

16. The method of claim 14, further comprising graphically displaying a current flow rate of injectate.

17. The method of claim 16, wherein further comprising graphically displaying a predetermined minimum flow rate and a predetermined maximum flow rate that define limits within which the current flow rate is desired to appear.

18. An injectate delivery system, comprising:

a reservoir for holding a fluid injectate;

a conduit in fluid communication with the reservoir and configured at one end to be connected to a catheter;

an injector operable to discharge the fluid injectate from the reservoir to the conduit during an injection; and

a constant flow control element fluidically interposed between the reservoir and the end of the conduit that is configured to be connected to the catheter, wherein the constant flow control element is configured to maintain a substantially constant design flow rate for the duration of the injection for the flow of the fluid from the reservoir to the catheter;

a sensor interposed in the conduit configured to detect changes in pressure or temperature of the injectate and to signal a timer to start at the beginning of the injection and stop at the end of the injection; and

a processing device adapted to receive a signal from a sensor, the processing device being configured to calculate injectate volume based on the constant flow control element design flow rate and measured elapsed time of the injection, the volume to be used as input for calculating at least one parameter.

19. The system of claim 18, wherein the at least one parameter to be calculated is a transpulmonary thermodilution parameter including at least one of cardiac output, global end diastolic volume, and extra vascular lung water.

20. The system of claim 18, wherein the reservoir comprises a syringe and the constant flow control element comprises a constant flow valve fluidically interposed in the conduit.

21. The system of claim 18, wherein the reservoir comprises a syringe and the syringe comprises the constant flow control element as an integral feature of the syringe.

22. A method of displaying a relative flow rate for an injectate delivery system, the method comprising:

calculating, by a processor, a flow rate of a fluid injected into a conduit for a thermodilution procedure using parameters measured by a flow measurement device; and

graphically displaying, by the processor on a display device, an indication of a predetermined minimum acceptable flow rate, a predetermined maximum acceptable flow rate, and the current flow rate relative to the minimum and maximum acceptable flow rates.

23. A system for displaying a relative flow rate for an injectate delivery system, the system comprising:

a display device;

a processor operably connected to the display device; and

a memory operably connected with the processor to store a predetermined minimum acceptable flow rate and a predetermined maximum acceptable flow rate, and also operably connected with the processor to store computer program code which, when executed, causes the processor to determine, to calculate a flow rate of a fluid injected into a conduit for a thermodilution procedure using parameters measured by a flow measurement device, and graphically present, on the display device, an indication of the predetermined minimum acceptable flow rate, the predetermined maximum acceptable flow rate, and the current flow rate relative to the minimum and maximum acceptable flow rates.

24. Apparatus for displaying a relative flow rate for an injectate delivery system, comprising:

means for storing a predetermined minimum acceptable flow rate and a predetermined maximum acceptable flow rate;

means for calculating, a flow rate of a fluid injected into a conduit for a thermodilution procedure using parameters measured by a flow measurement device; and means for graphically displaying an indication of the predetermined minimum acceptable flow rate, the predetermined maximum acceptable flow rate, and the current flow rate relative to the minimum and maximum acceptable flow rates.

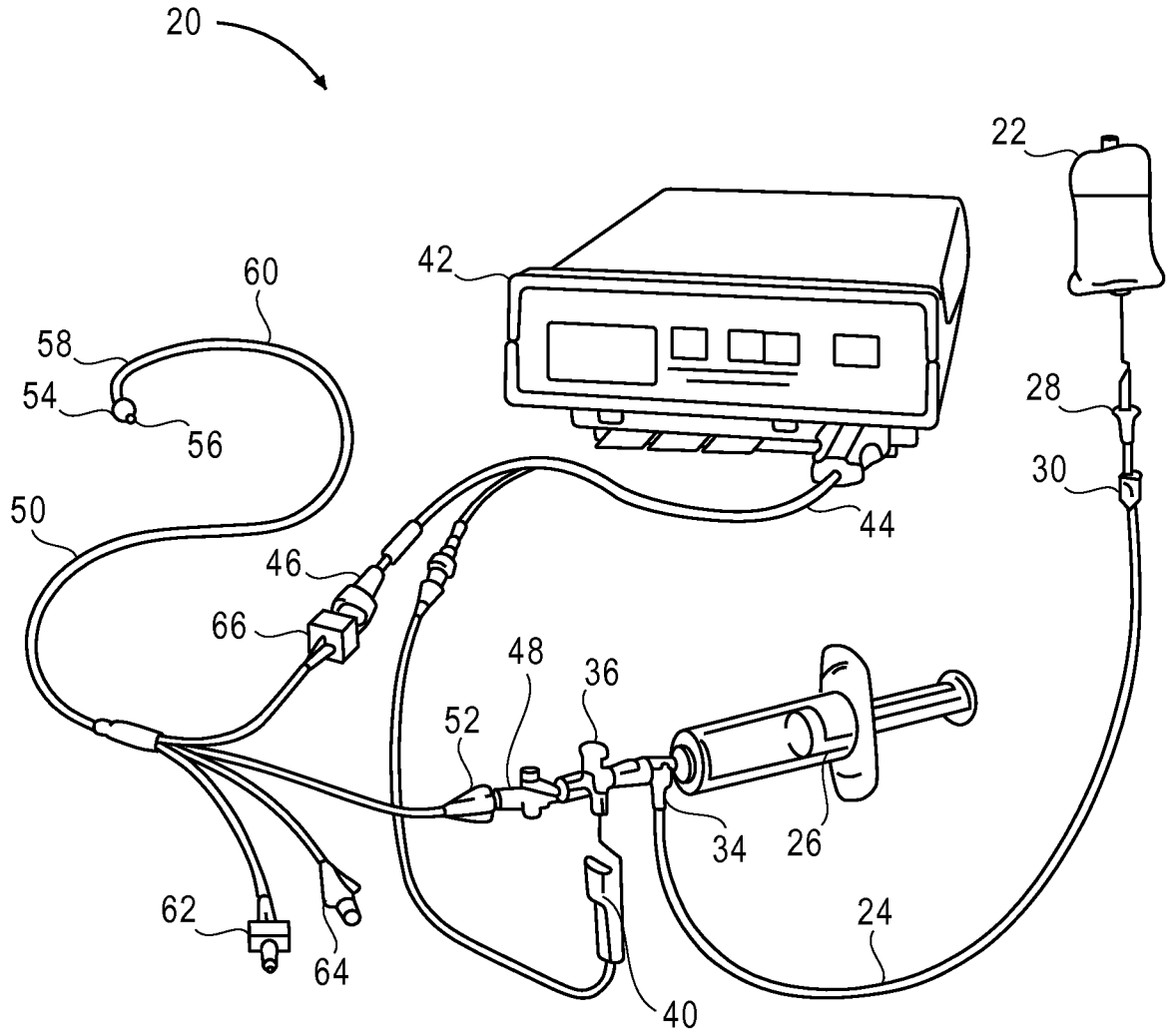

FIG. 1

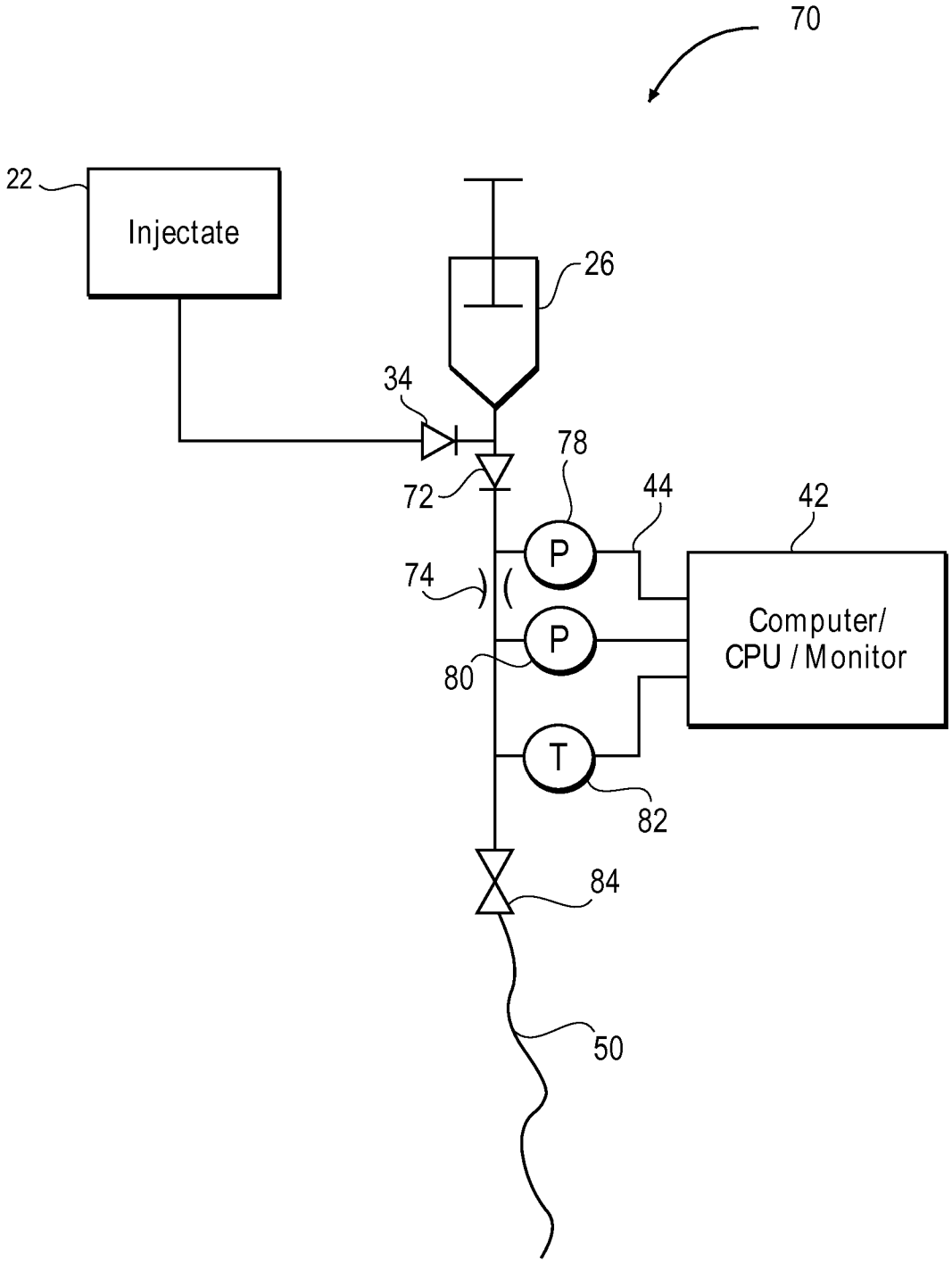
70
22
Injectate
26
34
78
72
44
42
P
74
P
Computer/
CPU / Monitor
80
T
82
84
50

FIG. 2

88

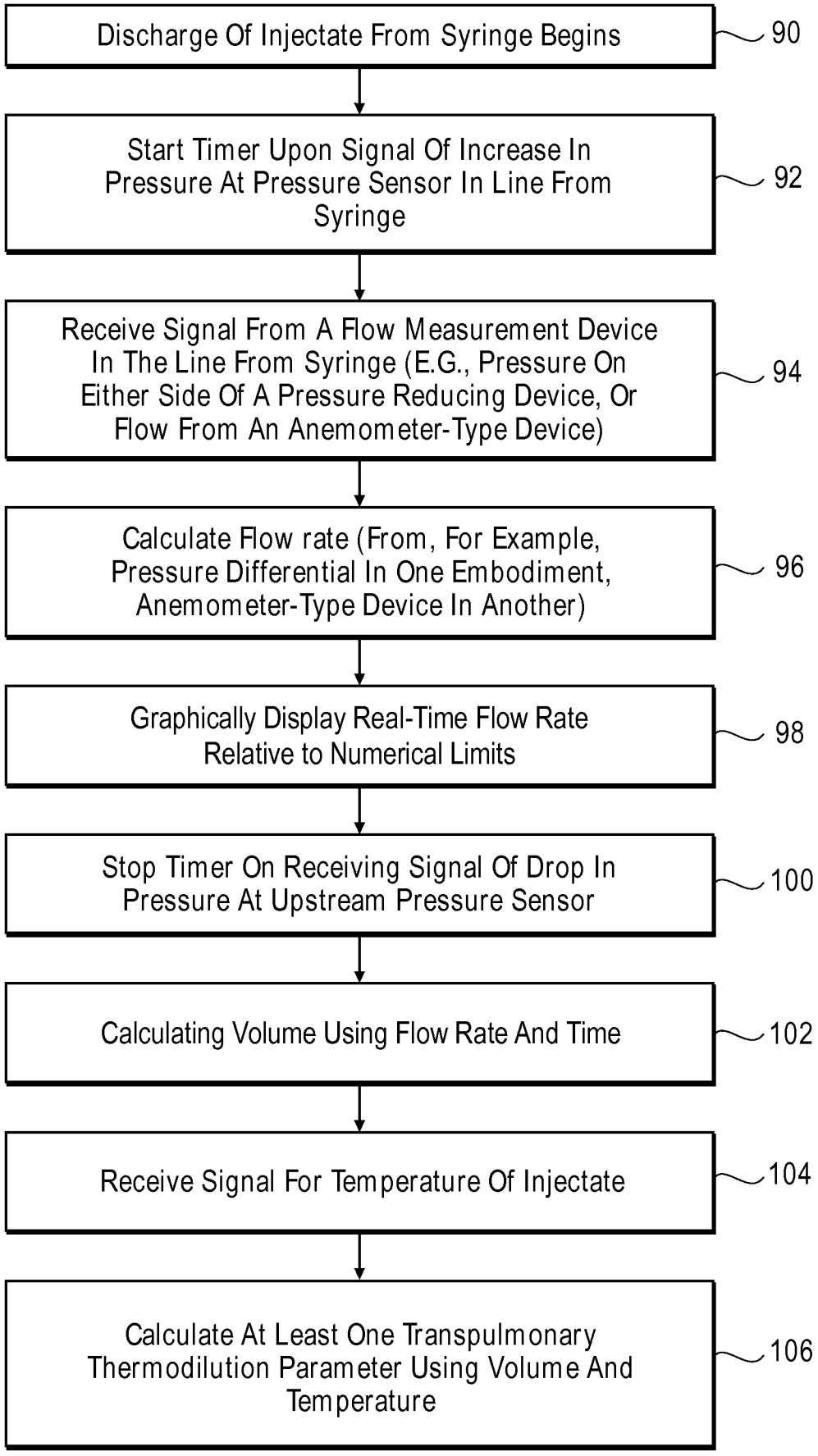
Discharge Of Injectate From Syringe Begins
90
Start Timer Upon Signal Of Increase In Pressure At Pressure Sensor In Line From Syringe
92
Receive Signal From A Flow Measurement Device In The Line From Syringe (E.G., Pressure On Either Side Of A Pressure Reducing Device, Or Flow From An Anemometer-Type Device)
94
Calculate Flow rate (From, For Example, Pressure Differential In One Embodiment, Anemometer-Type Device In Another)
96
Graphically Display Real-Time Flow Rate Relative to Numerical Limits
98
Stop Timer On Receiving Signal Of Drop In Pressure At Upstream Pressure Sensor
100
Calculating Volume Using Flow Rate And Time
102
Receive Signal For Temperature Of Injectate
104
Calculate At Least One Transpulmonary Thermodilution Parameter Using Volume And Temperature
106

FIG. 3

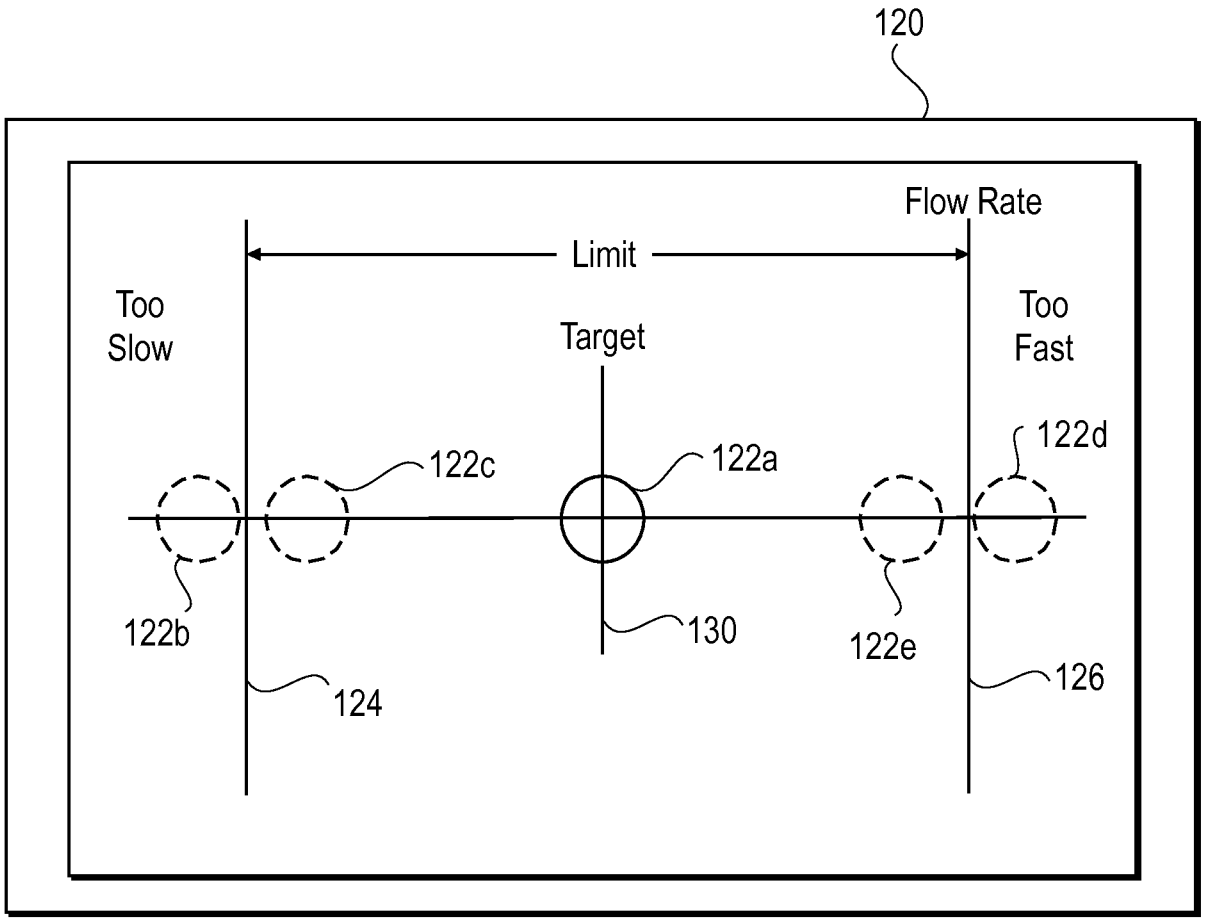
120
Flow Rate
Limit
Too
Slow
Target
Too
Fast
122d
122c
122a
122b
130
122e
126
124

FIG. 4

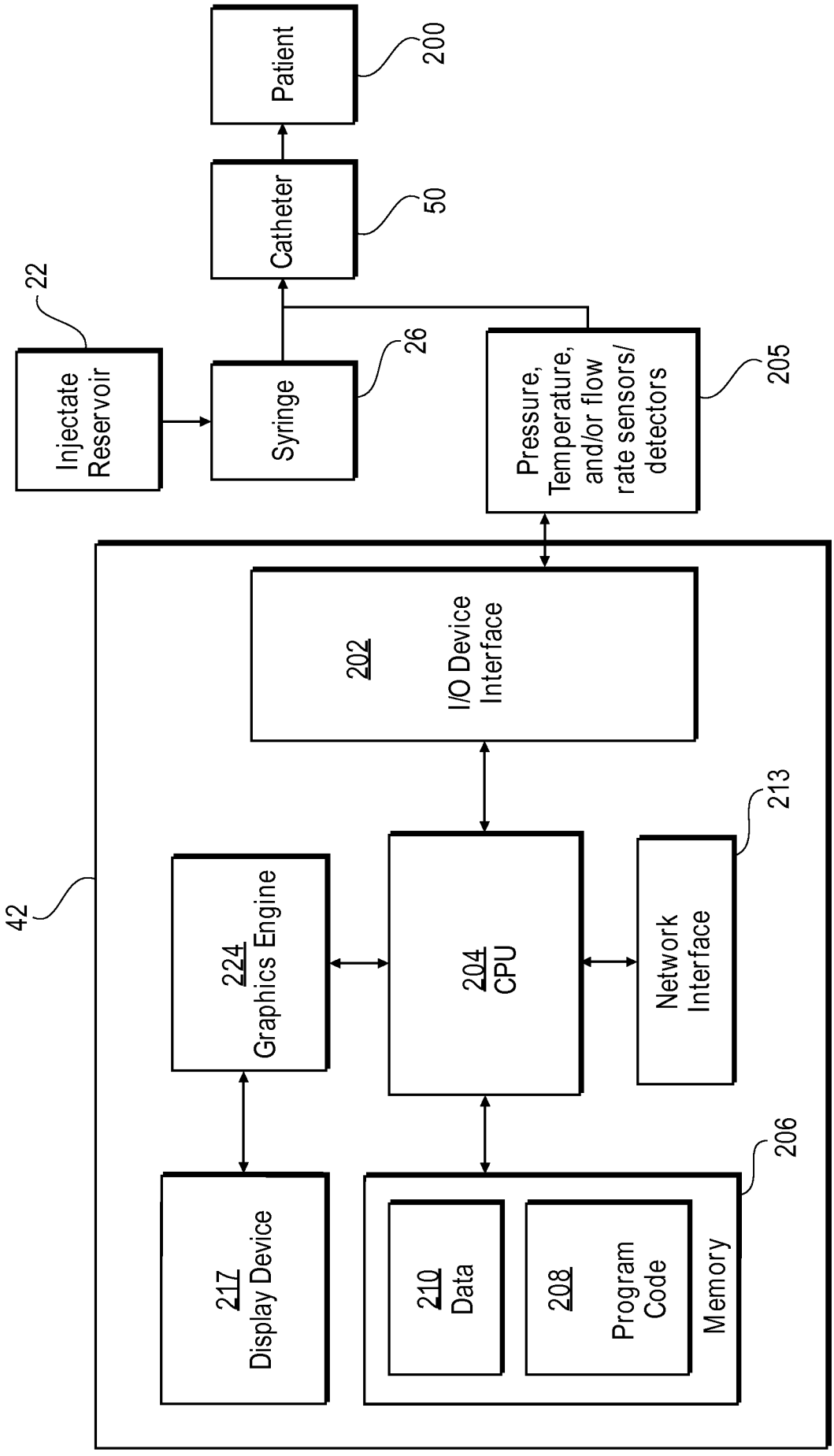
Patient
200
Catheter
50
22
Injectate Reservoir
Syringe
26
Pressure, Temperature, and/or flow rate sensors/ detectors
205
42
202 I/O Device Interface
224 Graphics Engine
204 CPU
Network Interface
213
217 Display Device
210 Data
208 Program Code
Memory
206

FIG.5

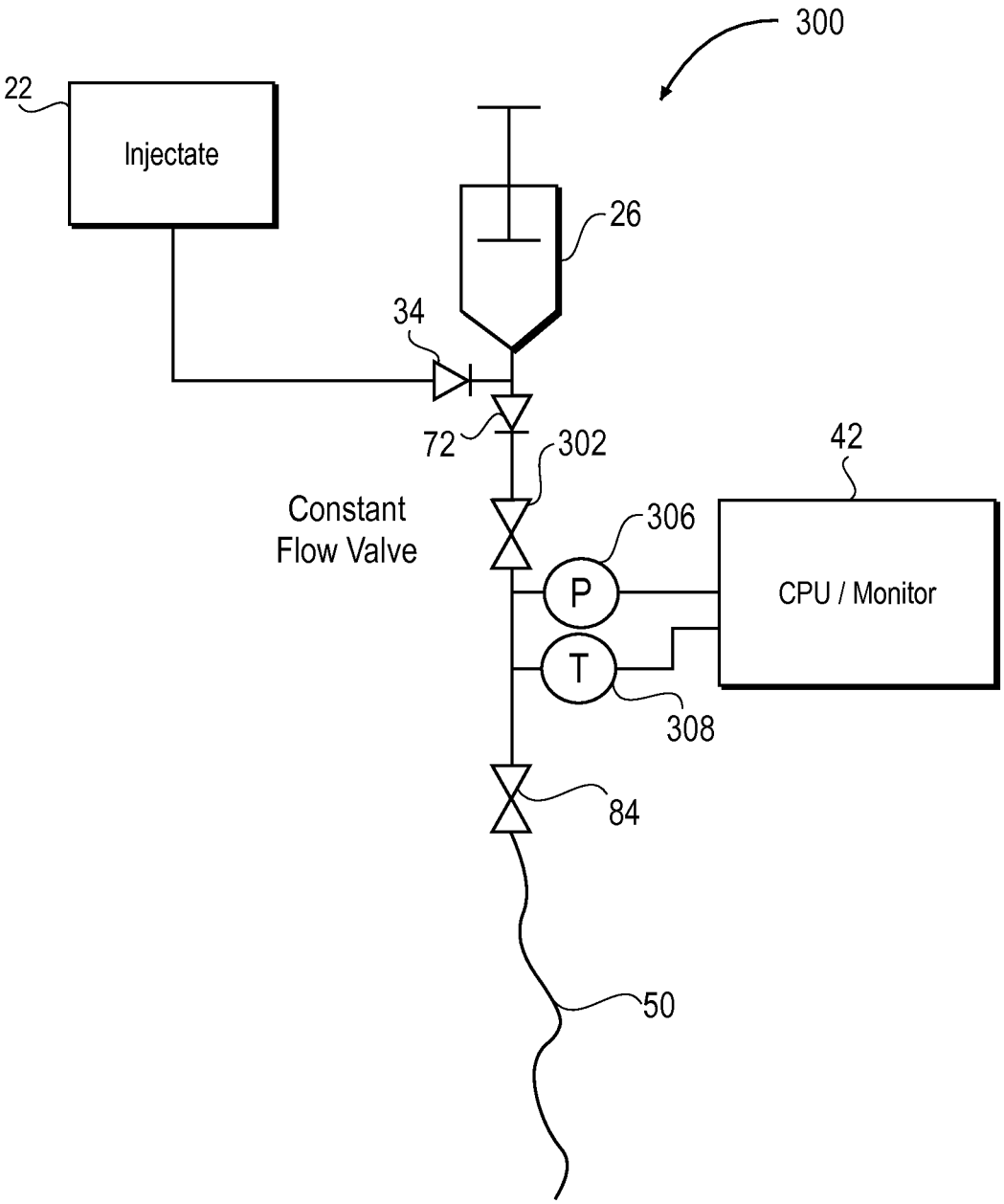
300
22
Injectate
26
34
72
302
42
Constant
Flow Valve
306
P
CPU / Monitor
T
308
84
50

FIG. 6

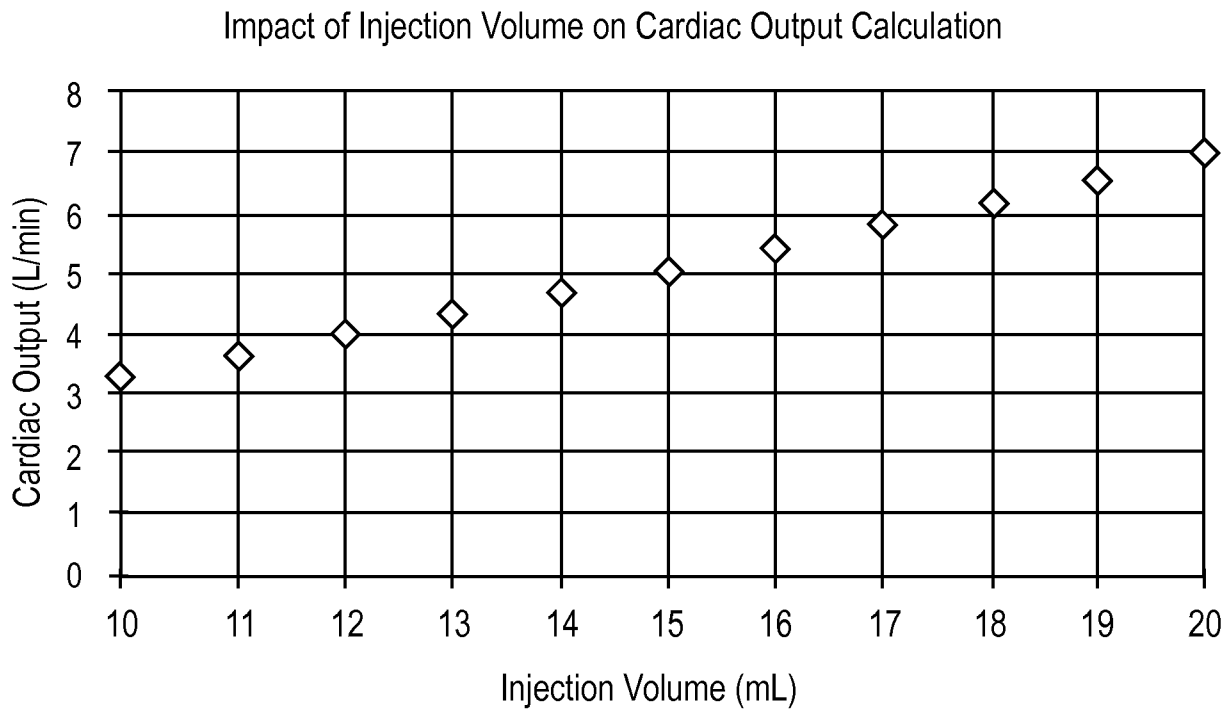
Impact of Injection Volume on Cardiac Output Calculation
Cardiac Output (L/min)
0
1
2
3
4
5
6
7
8
10
11
12
13
14
15
16
17
18
19
20
Injection Volume (mL)

FIG. 7

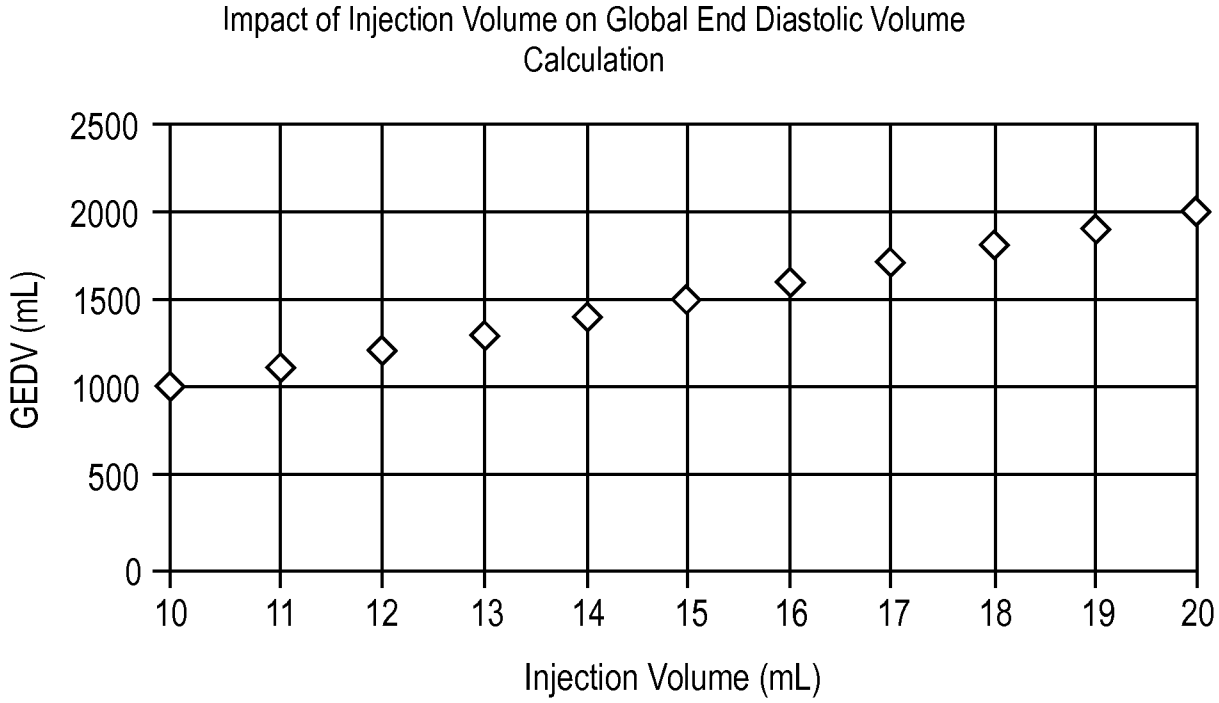
Impact of Injection Volume on Global End Diastolic Volume Calculation
GEDV (mL)
0
500
1000
1500
2000
2500
10
11
12
13
14
15
16
17
18
19
20
Injection Volume (mL)

FIG. 8

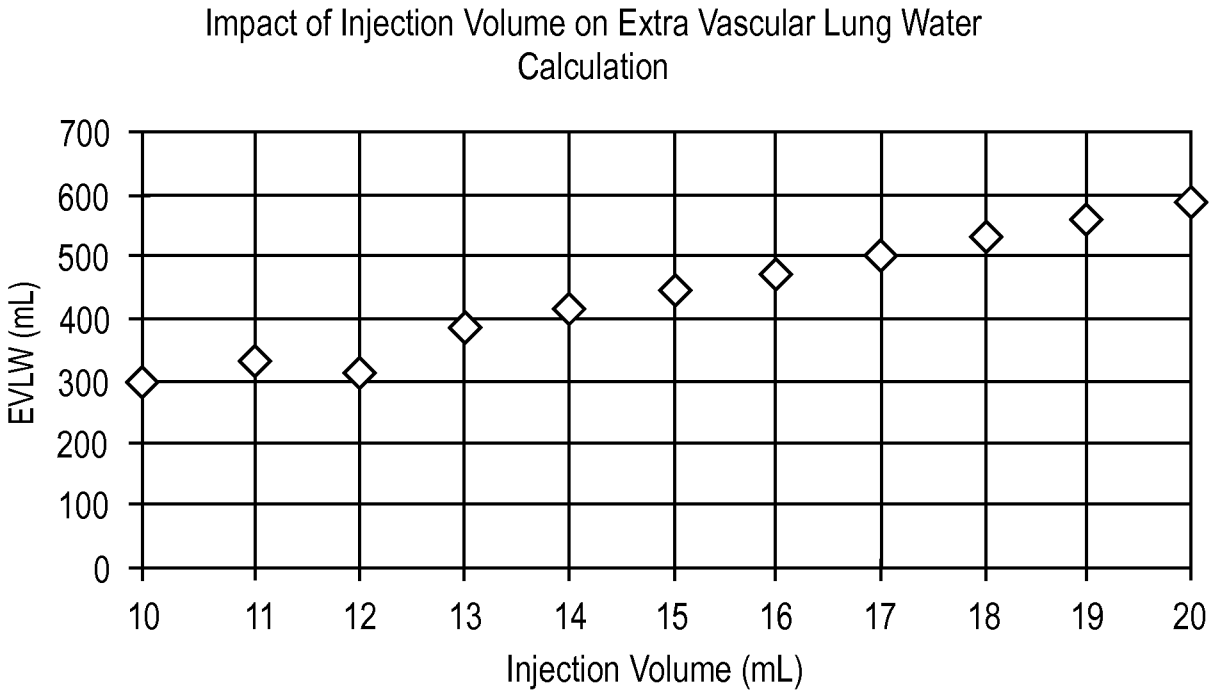
Impact of Injection Volume on Extra Vascular Lung Water Calculation
EVLW (mL)
700
600
500
400
300
200
100
0
10
11
12
13
14
15
16
17
18
19
20
Injection Volume (mL)

FIG. 9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/056765

A. CLASSIFICATION OF SUBJECT MATTER

A61B 5/028(2006.01)i, A61B 5/00(2006.01)i

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)
A61B 5/028; A61M 5/145; A61B 5/05; A61M 5/142; A61M 5/00; A61B 17/34; A61B 5/03; A61M 5/172; A61B 5/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: injectate, delivery, flow, measurement, transpulmonary, thermodilution

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2009-049252 A1 (OPTISCAN BIOMEDICAL CORPORATION) 16 April 2009 See abstract, paragraphs [62]-[74],[243], claim 1 and figures 3,4,24.	1-24
Y	WO 2012-071307 A2 (MALLINCKRODT LLC) 31 May 2012 See abstract, page 13, lines 30-32, claim 1 and figure 1.	1-24
A	WO 2011-096421 A1 (NEMOTO KYORINDO CO., LTD.) 11 August 2011 See abstract, claims 1-9 and figure 2.	1-24
A	WO 92-15256 A1 (INDUSTRIAS PALEX, S.A.) 17 September 1992 See abstract, claim 1 and figures 1-3.	1-24
A	US 2005-0107697 A1 (RALPH BERKE) 19 May 2005 See abstract, claim 1 and figure 1.	1-24

☐ 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
29 June 2016 (29.06.2016)	**05 July 2016 (05.07.2016)**

Name and mailing address of the ISA/KR
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2015/056765

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009-049252 A1	16/04/2009	CA 2702116 A1	16/04/2009
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		EP 1758416 A1	28/02/2007
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		EP 0536138 A1	14/04/1993
		EP 0538259 A1	28/04/1993
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		DE19859811 C2	10/05/2001
		EP 1140258 A1	10/10/2001
		JP 2002-533172 A	08/10/2002
		WO 00-38764 A1	06/07/2000

专利名称(译)	热稀释进样的测量和控制		
公开(公告)号	EP3364867A4	公开(公告)日	2019-10-02
申请号	EP2015895855	申请日	2015-10-21
[标]申请(专利权)人(译)	爱德华兹生命科学公司		
申请(专利权)人(译)	爱德华生命科学公司		
当前申请(专利权)人(译)	爱德华生命科学公司		
[标]发明人	SIEMONS ALEXANDER H LIU WEI JIUN		
发明人	SIEMONS, ALEXANDER, H. LIU, WEI-JIUN		
IPC分类号	A61B5/028 A61B5/00		
CPC分类号	A61B5/028 A61B5/029 A61B5/6852 A61B5/7275 A61B5/7285 A61B5/742 A61B5/0295		
其他公开文献	EP3364867A1		
外部链接	Espacenet		

摘要(译)

用于计算，控制或同时测量热稀释注入流量以计算经肺热稀释参数的装置和方法。一种注射输送系统，包括用于保持注射的注射器和配置在一端以连接至导管的导管。流量测量装置插入导管中，以产生用于确定从注射器到导管的流体流速的信号。处理器从流量测量设备接收信号，并计算要用作输入的注射量，以计算经肺热稀释参数（例如心输出量）。提供GUI来指导用户喷射速率是太快还是太慢。除了测量或计算流速之外，系统还可以包括恒定流量阀，以提供来自注射器的恒定流量。