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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 October 2008 (16.10.2008)

PCT

(10) International Publication Number
WO 2008/124644 A1

(51) International Patent Classification:
A61M 5/172 (2006.01)

(21) International Application Number:
PCT/US2008/059496

(22) International Filing Date: 4 April 2008 (04.04.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/921,974 5 April 2007 (05.04.2007) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,

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(54) Title: AUTOMATED THERAPY SYSTEM AND METHOD

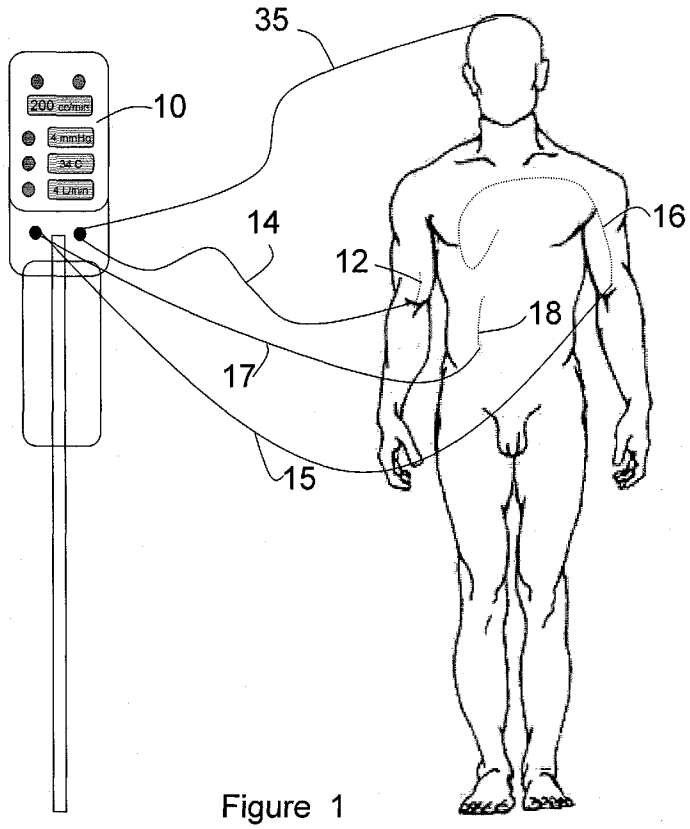

Figure 1

(57) Abstract: An automated therapy system having an infusion catheter; a sensor adapted to sense a patient parameter; and a controller communicating with the sensor and programmed to control flow output from the infusion catheter into a patient based on the patient parameter without removing fluid from the patient. The invention also includes a method of controlling infusion of a fluid to a patient. The method includes the following steps: monitoring a patient parameter with a sensor to generate a sensor signal; providing the sensor signal to a controller; and adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient.

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FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

AUTOMATED THERAPY SYSTEM AND METHOD

INCORPORATION BY REFERENCE

[0001] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] Fluids and other substances are infused into patients for a variety of reasons. For example, fluids may be given to a patient intravenously to hydrate the patient or to control overall blood volume.

[0003] It is often important to control infusion of fluid into patients in order to optimize the therapy being provided. Monitoring of patient parameters can consume precious health care time and resources, however. Fluid infusion into patients is therefore not always optimized.

[0004] Mantle US 2006/0161107 describes a system that extracts fluid from a body cavity, processes the fluid and then recirculates fluid back into the cavity. Mantle does not describe infusion of a fluid into a patient without extraction of the fluid from the patient, however. In addition, the parameters on which the Mantle system is controlled are limited.

SUMMARY OF THE INVENTION

[0005] One aspect of the invention provides an automated therapy system having an infusion catheter; a sensor adapted to sense a patient parameter; and a controller communicating with the sensor and programmed to control flow output from the infusion catheter into a patient based on the patient parameter without removing fluid from the patient. In some embodiments, the sensor may be incorporated into the catheter, and in other embodiments, the sensor may be separate from the catheter. The sensor may be, e.g., an ECG sensor; an EEG sensor; a pulse oximetry sensor; a blood pressure sensor; a cardiac output sensor; a thermodilution cardiac output sensor; a cardiac stroke volume

sensor; a heart rate sensor; a blood flow sensor; a pH sensor; a blood pO_2 sensor; an intracranial pressure sensor; and/or a solute sensor.

[0006] In embodiments of the invention, the catheter may be a peripheral venous catheter; a central venous catheter; an arterial catheter; or a peritoneal catheter (possibly incorporating an intraperitoneal pressure sensor).

[0007] Another aspect of the invention provides a method of controlling infusion of a fluid to a patient. The method includes the following steps: monitoring a patient parameter with a sensor to generate a sensor signal; providing the sensor signal to a controller; and adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient. In some embodiments, the method includes the step of monitoring cardiac output with the sensor and, possibly, adjusting fluid flow to the patient based on cardiac output monitored by the sensor. In embodiments of the invention, the patient parameter includes an electrocardiogram; an electroencephalogram; blood oxygen saturation; blood pressure; cardiac output; cardiac stroke volume; heart rate; blood flow; total circulating blood volume; whole body oxygen consumption; pH; blood pO_2; osmolarity; peritoneal cavity compliance; intrathoracic pressure; bladder pressure; and/or rectal pressure.

[0008] In some embodiments, the adjusting step includes the step of adjusting fluid flow to achieve or maintain patient euvolumia; adjusting flow of a therapeutic agent (such as a chilled medium) to the patient; adjusting fluid flow to the patient through a peripheral venous catheter; adjusting fluid flow to the patient through a central venous catheter; adjusting fluid flow to the patient through an arterial catheter; and/or adjusting fluid flow to the patient's peritoneal cavity.

[0009] Yet another aspect of the invention provides a method of treating hypotension in a patient. The method includes the following steps: monitoring a patient parameter (such as blood pressure or cardiac output) with a sensor to generate a sensor signal; providing the sensor signal to a controller; and adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient.

[00010] Still another aspect of the invention provides a method of treating sepsis in a patient. The method includes the following steps: monitoring a patient parameter (such as blood pressure, central venous pressure, or cardiac output) with a sensor to generate a sensor signal; providing the sensor signal to a controller; and adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient. Prevention of hypotension and/or hypovolemia is critical in the care of patients that have suffered severe

hemorrhage or are septic. These patients are very difficult to monitor and treat, taking significant nursing time and still resulting in suboptimal therapy due to the intermittent nature of the blood pressure, central venous pressure and/or cardiac output checks. The present invention, then, will optimize fluid flow to the patient while also freeing up the already over-taxed nursing staff for other duties.

[00011] Yet another aspect of the invention provides a method of inducing and reversing therapeutic hypothermia in a patient. The method includes the steps of: monitoring intracranial pressure to generate a sensor signal; providing the sensor signal to a controller; and adjusting rate of hypothermia induction or rewarming based on intracranial pressure (such as by adjusting fluid flow to the patient), or depth of hypothermia, based on the sensor signal.

[00012] In some embodiments of the invention, irrigation and/or lavage of bodily tissues, cavities or spaces (or other patient interventions) may be optimized using a sensor or sensors to report electrical, chemical, acoustic, mechanical properties, pressure, temperature, pH or other parameters surrounding the access device in order to automate and optimize the irrigation/lavage.

[00013] Embodiments of the invention include a peritoneal catheter containing one or more sensors which may detect changes in electrocardiograph monitoring, electroencephalograph monitoring, pulse oximetry (either internally or peripherally), peritoneal cavity compliance, intrathoracic pressure, intraperitoneal pressure, intraperitoneal pressure waveforms, bladder pressure, rectal pressure, cardiac output, cardiac stroke volume, cardiac rate, blood flow (e.g., in superior mesenteric, celiac, renal or other arteries), pressure in veins (particularly the inferior vena cava or those that empty into the inferior vena cava, e.g., femoral vein), pressure in arteries (particularly those distal to the aorta, e.g., the femoral artery), total circulating blood volume, blood oxygenation (e.g., in rectal mucosa, peripheral fingers and toes, etc.), whole body oxygen consumption, pH and/or arterial pO_2 (or any other parameter that shows a measurable change with increased peritoneal pressure) to ensure safety of automated or manual peritoneal lavage. The invention also includes methods of performing peritoneal lavage using such devices.

[00014] Embodiments of the invention include an intravascular catheter containing one or more sensors which may detect changes in electrocardiograph monitoring, electroencephalograph monitoring, pulse oximetry (either internally or peripherally), partial pressure of oxygen or CO_2, pH, temperature, blood pressure, central venous pressure, cardiac output, cardiac stroke volume, cardiac rate, blood flow (e.g., in superior

mesenteric, celiac, renal or other arteries), total circulating blood volume, pressure in veins (particularly those that empty into the inferior vena cava, e.g., femoral vein), pressure in arteries (particularly those distal to the aorta, e.g., the femoral artery), blood oxygenation (e.g., in rectal mucosa, peripheral fingers and toes, etc.), whole body oxygen consumption, pH and/or arterial pO_2 (or any other parameter that shows a measurable change with intravascular volume overload) to ensure safety of manual or automated intravascular infusion. The invention also includes methods of using such devices.

[00015] Other embodiments of the invention include control of the rate of infusion to minimize negative effects observed by the sensors. The invention may be used to induce and/or maintain hypothermia or hyperthermia; maximize hydration and/or intravascular volume in a patient receiving intravenous fluids (such as, e.g., post-operative patients, post-hemorrhage patients, septic patients or other intensive care patients).

BRIEF DESCRIPTION OF THE DRAWINGS

[00016] The novel features of the invention are set forth with particularity in the claims that follow. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[00017] Figure 1 shows an automated infusion system in which infusion is controlled based on patient parameters sensed by multiple sensors.

[00018] Figure 2 shows an automated infusion system in which a sensor controlling infusion is separate from the infusion catheter.

[00019] Figure 3 shows an automated infusion system in which sensing and infusion are performed with the same catheter.

DETAILED DESCRIPTION OF THE INVENTION

[00020] Figures 1-3 show embodiments of the invention wherein intravenous fluid delivery may be automated, or manually adjusted, based on feedback from one or more sensors. In these embodiments, the infusion catheter may have a sensor to aid in insertion, but this is not necessary for this invention.

[00021] In one embodiment, the infusion catheter also is used to detect the parameters used to optimize therapy. Figure 1 shows an infusion system with an infusion controller 10 operably connected to an intravenous infusion catheter 12 via an infusion line 14.

Infusion catheter 12 also has a sensor (not shown) attached to or associated with it to monitor a patient parameter. The sensor also communicates with controller 10 either through line 14 or via some other communication channel. Suitable patient parameters include electrocardiograph monitoring, electroencephalograph monitoring, pulse oximetry (either internally or peripherally), blood pressure, central venous pressure, cardiac output, cardiac stroke volume, cardiac rate, blood flow (e.g., in superior mesenteric, celiac, renal or other arteries), total circulating blood volume, pressure in veins (particularly those that empty into the inferior vena cava, e.g., femoral vein), pressure in arteries (particularly those distal to the aorta, e.g., the femoral artery), blood oxygenation (e.g., in rectal mucosa, peripheral fingers and toes, etc.), whole body oxygen consumption, pH, arterial pO_2, or any other parameter that shows a measurable change with intravascular volume overload.

[00022] As shown in Figure 1, additional catheters, here envisioned as a peripherally inserted central catheter (PICC) 16 and/or a peritoneal catheter 18, or additional sensors on infusion catheter 12 may be used to monitor these or other parameters, and to optimize the infusion rate and achieve euvolemia without fluid overload or dehydration. Flow of fluid and/or a fluid/solid mixture (e.g. an ice slurry) to catheters 16 and/or 18 is controlled by controller 10 through lines 14, 15 and/or 17, respectively. The information from the sensors may then be transmitted to central controller 10, which integrates all of this information to determine the flow of intravenous fluid through catheter 12 and/or catheter 16 and flow of peritoneal fluid through catheter 18. This information may be used to achieve or maintain euvolemia (e.g., in sepsis, hemorrhagic shock, etc.) or to maximize infusion for delivery of a therapeutic agent, e.g., chilled fluid and/or solids to achieve hypothermia. Alternatively, catheters 16 and 18 may be used with sensors to obtain patent information, and fluid may be infused into the patient solely through catheter 16 or catheter 18. In yet further embodiments, the depth of hypothermia and/or rate of hypothermia induction or rewarming may be tailored based on intracranial pressure sensor(s) (not shown) communicating with controller 10 via communication line 35. This system and method may be used with any method of inducing hypothermia (e.g. cooling blankets, intravascular catheters, intravenous fluid infusion, peritoneal lavage, etc.) so long as the change in temperature, particularly rewarming, is controlled at least in part by an intracranial pressure sensor.

[00023] The sensor or sensors, whether cables/catheters or percutaneous monitoring technologies, and whether wired or wireless, may also be separate from the infusion line

so long as the information from this sensor or sensors is transferred to the control unit in order to optimize fluid flow. Thus, as shown in Figure 2, the patient parameter sensor may be associated with PICC 24 and communicate with controller via line 26, and infusion to the patient may be via line 22 and infusion catheter 20, as controlled by controller 10. In some embodiments, of course, sensing and infusion may be performed through a single catheter, such as PICC 30, and controlled by controller 10 through lines 32 and 34, as shown in Figure 3. In some embodiments, the infusion and monitoring device of the current invention may incorporate an access sensor, such as that described in a concurrently filed and commonly owned patent application titled "Device and Method for Safe Access to a Body Cavity" (Attorney docket number 10729-700.200).

[00024] One example of such a device is a peripheral venous, central venous or arterial catheter that is capable of maintaining hydration without causing fluid overload. The catheter may incorporate a sensor that may detect central venous pressure, total circulating blood volume, peripheral venous pressure, cardiac output or osmolarity, and/or solute concentrations (e.g., chloride, sodium, etc.) in order to prevent fluid overload. The sensor may also be external to the catheter, so long as the output of said sensor is capable of controlling fluid flow through the catheter. In this embodiment, fluid flow is controlled by the output of the sensor, which is integrated by a fluid flow control unit which alters the rate of fluid flow based on this output. This embodiment may allow the user to bolus large volumes of fluids or solids into the vascular space in order to rehydrate, induce hypothermia or reverse hypothermia, or deliver a therapeutic agent or maintain blood pressure in sepsis.

[00025] In addition, this technology may provide a fully automated mechanism to optimize fluid flow into the vessel without fluid overloading the patient. Without this automated fluid delivery coupled to hemodynamic parameter monitoring, the patient is in danger of dehydration or fluid overload from infusion of fluid into any body cavity. This technology may also be applied to liquid or solid infusion into any body cavity or space in so long as the fluid flow is automated based on feedback from sensors within the body (possibly incorporated into the catheter itself) in order to optimize the volume of infusion.

[00026] This device and method of automating fluid flow based on hemodynamic sensor-based feedback may also be used to generate intravenous hypothermia. In its current state, IV hypothermia induction is limited due to concerns of fluid overload. If the hemodynamic parameters of the patient can be measured and fluid flow directly or indirectly controlled based on the output of these measurements, the volume of fluid can

be maximized while ensuring hemodynamic instability. In this embodiment, the sensor may be incorporated within the catheter, and fluid flow into the vasculature may be tailored based on central venous pressure, total circulating blood volume, peripheral venous pressure, cardiac output or osmolarity, and/or solute concentrations (e.g., chloride, sodium, etc.) in order to prevent fluid overload.

[00027] In one embodiment, the fluid infusion catheter also may function as a thermodilution cardiac output sensor such that the same fluid that is used to generate hypothermia may also be used to detect cardiac output. This information may then be relayed, either directly or indirectly, back to the fluid infusion controller to increase, decrease or even halt fluid flow based on these parameters. For example, if cardiac output is low and venous pressure or total circulating volume is low, the patient has a low circulating volume and large volumes of fluid may be safely delivered. If the cardiac output is normal, fluid may also be safely delivered, but the cardiac output must be monitored to ensure that it does not begin to decrease (an indication of fluid overload). Blood flow, as detected by, for instance, thermodilution may determined in a peripheral vessel as well. These data, while relatively useless on their own in a clinical setting due to variability in peripheral blood flow, may provide a baseline flow profile which may be rechecked over time in order to compare flow within that individual vessel to the baseline flow. Relatively improved flow may be correlated to improved cardiac output, while a relative reduction in flow may be correlated to fluid overload.

[00028] This same system may be used to infuse normal fluids or hypothermic fluids to sepsis patients or patients requiring intensive maintenance of their hemodynamic status. Sepsis patients that are aggressively monitored do much better than those that are not. Aggressive monitoring is very nurse-intensive, however. A system that provides automated optimal fluid infusion based on sensed parameters to ensure that fluid overload does not occur and that fluid infusion is not insufficient would be an improvement over current methods of treating sepsis patients. The devices and methods for automated sensor-based input to control fluid flow to a patient may be applicable to a wide range of conditions and should not be limited to the narrow scope of the conditions requiring fluid infusion described here.

[00029] The logic controller of the present invention may provide improved safety by monitoring for any of the deleterious changes expected with excess fluid flow, e.g. into the peritoneal cavity or vascular space. Examples of monitored parameters that may signal a warning or automatically result in an adjustment to rate of fluid infusion/extraction and/or

fluid temperature include: electrocardiograph monitoring, electroencephalograph monitoring, pulse oximetry (either internally or peripherally), peritoneal cavity compliance, intrathoracic pressure, intraperitoneal pressure, intraperitoneal pressure waveforms, bladder pressure, rectal pressure, cardiac output, cardiac stroke volume, cardiac rate, total circulating blood volume, blood flow (e.g., in superior mesenteric, celiac, renal or other arteries), pressure in veins (particularly those that empty into the IVC, e.g., femoral vein), pressure in arteries (particularly those distal to the aorta, e.g., the femoral artery), blood oxygenation (e.g., in rectal mucosa, peripheral fingers and toes, etc.), whole body oxygen consumption, pH and arterial pO_2 and any other parameter that shows a measurable change once the peritoneal or vascular spaces have been overloaded.

[00030] These parameters in particular have been found to change with increases in peritoneal pressure, with significantly negative impact on each parameter found at 40 mmHg. Thus, monitoring for these changes in conjunction with a peritoneal infusion catheter of the present invention will allow for even greater safety with peritoneal infusion. These parameters may be measured a variety of ways and the data transmitted either wirelessly or via wires to the logic controller in order to alert the healthcare provider or to automatically adjust the fluid flow/temperature in order to optimize both the flow of the peritoneal fluid and patient safety.

WHAT IS CLAIMED IS:

1. An automated therapy system comprising:

an infusion catheter;

a sensor adapted to sense a patient parameter; and

a controller communicating with the sensor and programmed to control flow output from the infusion catheter into a patient based on the patient parameter without removing fluid from the patient.

2. The system of claim 1 wherein the sensor is incorporated into the catheter.

3. The system of claim 1 wherein the sensor is separate from the catheter.

4. The system of claim 1 wherein the sensor comprises an ECG sensor.

5. The system of claim 1 wherein the sensor comprises an EEG sensor.

6. The system of claim 1 wherein the sensor comprises a pulse oximetry sensor.

7. The system of claim 1 wherein the sensor comprises a blood pressure sensor.

8. The system of claim 1 wherein the sensor comprises a cardiac output sensor.

9. The system of claim 8 wherein the sensor comprises a thermodilution cardiac output sensor.

10. The system of claim 1 wherein the sensor comprises a cardiac stroke volume sensor.

11. The system of claim 1 wherein the sensor comprises a heart rate sensor.

12. The system of claim 1 wherein the sensor comprises a blood flow sensor.

13. The system of claim 1 wherein the sensor comprises a pH sensor.

14. The system of claim 1 wherein the sensor comprises a blood pO_2 sensor.

15. The system of claim 1 wherein the sensor comprises a solute sensor.

16. The system of claim 1 wherein the catheter comprises a peripheral venous catheter.

17. The system of claim 1 wherein the catheter comprises a central venous catheter.

18. The system of claim 1 wherein the catheter comprises an arterial catheter.

19. The system of claim 1 wherein the catheter comprises a peritoneal catheter.

20. The system of claim 19 wherein the sensor comprises an intraperitoneal pressure sensor.

21. A method of controlling infusion of a fluid to a patient comprising:
monitoring a patient parameter with a sensor to generate a sensor signal;
providing the sensor signal to a controller; and
adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient.

22. The method of claim 21 further comprising monitoring cardiac output with the sensor.

23. The method of claim 22 further comprising adjusting fluid flow to the patient based on cardiac output monitored by the sensor.

24. The method of claim 21 wherein the patient parameter comprises an electrocardiogram.

25. The method of claim 21 wherein the patient parameter comprises an electroencephalogram.

26. The method of claim 21 wherein the patient parameter comprises blood oxygen saturation.

27. The method of claim 21 wherein the patient parameter comprises blood pressure.

28. The method of claim 21 wherein the patient parameter comprises cardiac output.

29. The method of claim 21 wherein the patient parameter comprises cardiac stroke volume.

30. The method of claim 21 wherein the patient parameter comprises heart rate.

31. The method of claim 21 wherein the patient parameter comprises blood flow.

32. The method of claim 21 wherein the patient parameter comprises total circulating blood volume.

33. The method of claim 21 wherein the patient parameter comprises whole body oxygen consumption.

34. The method of claim 21 wherein the patient parameter comprises pH.

35. The method of claim 21 wherein the patient parameter comprises blood pO_2.

36. The method of claim 21 wherein the patient parameter comprises osmolarity.

37. The method of claim 21 wherein the patient parameter comprises peritoneal cavity compliance.

38. The method of claim 21 wherein the patient parameter comprises intrathoracic pressure.

39. The method of claim 21 wherein the patient parameter comprises bladder pressure.

40. The method of claim 21 wherein the patient parameter comprises rectal pressure.

41. The method of claim 21 wherein the adjusting step comprises adjusting fluid flow to achieve or maintain patient euvolumia.

42. The method of claim 21 wherein the adjusting step comprises adjusting flow of a therapeutic agent to the patient.

43. The method of claim 42 wherein the therapeutic agent comprises a chilled medium.

44. The method of claim 21 wherein the adjusting step comprises adjusting fluid flow to the patient through a peripheral venous catheter.

45. The method of claim 21 wherein the adjusting step comprises adjusting fluid flow to the patient through a central venous catheter.

46. The method of claim 21 wherein the adjusting step comprises adjusting fluid flow to the patient through an arterial catheter.

47. The method of claim 21 wherein the adjusting step comprises adjusting fluid flow to the patient's peritoneal cavity.

48. A method of treating hypotension in a patient, the method comprising:
monitoring a patient parameter with a sensor to generate a sensor signal;
providing the sensor signal to a controller; and

adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient.

49. The method of claim 48 wherein the patient parameter is blood pressure.

50. The method of claim 48 wherein the patient parameter is cardiac output.

51. A method of treating sepsis in a patient, the method comprising:

monitoring a patient parameter with a sensor to generate a sensor signal;

providing the sensor signal to a controller; and

adjusting fluid flow to the patient based on the sensor signal without removing fluid from the patient.

52. The method of claim 51 wherein the patient parameter is blood pressure.

53. The method of claim 51 wherein the patient parameter is cardiac output.

54. A method of inducing and reversing therapeutic hypothermia in a patient, the method comprising:

monitoring intracranial pressure to generate a sensor signal;

providing the sensor signal to a controller; and

adjusting rate of hypothermia induction or rewarming based on intracranial pressure.

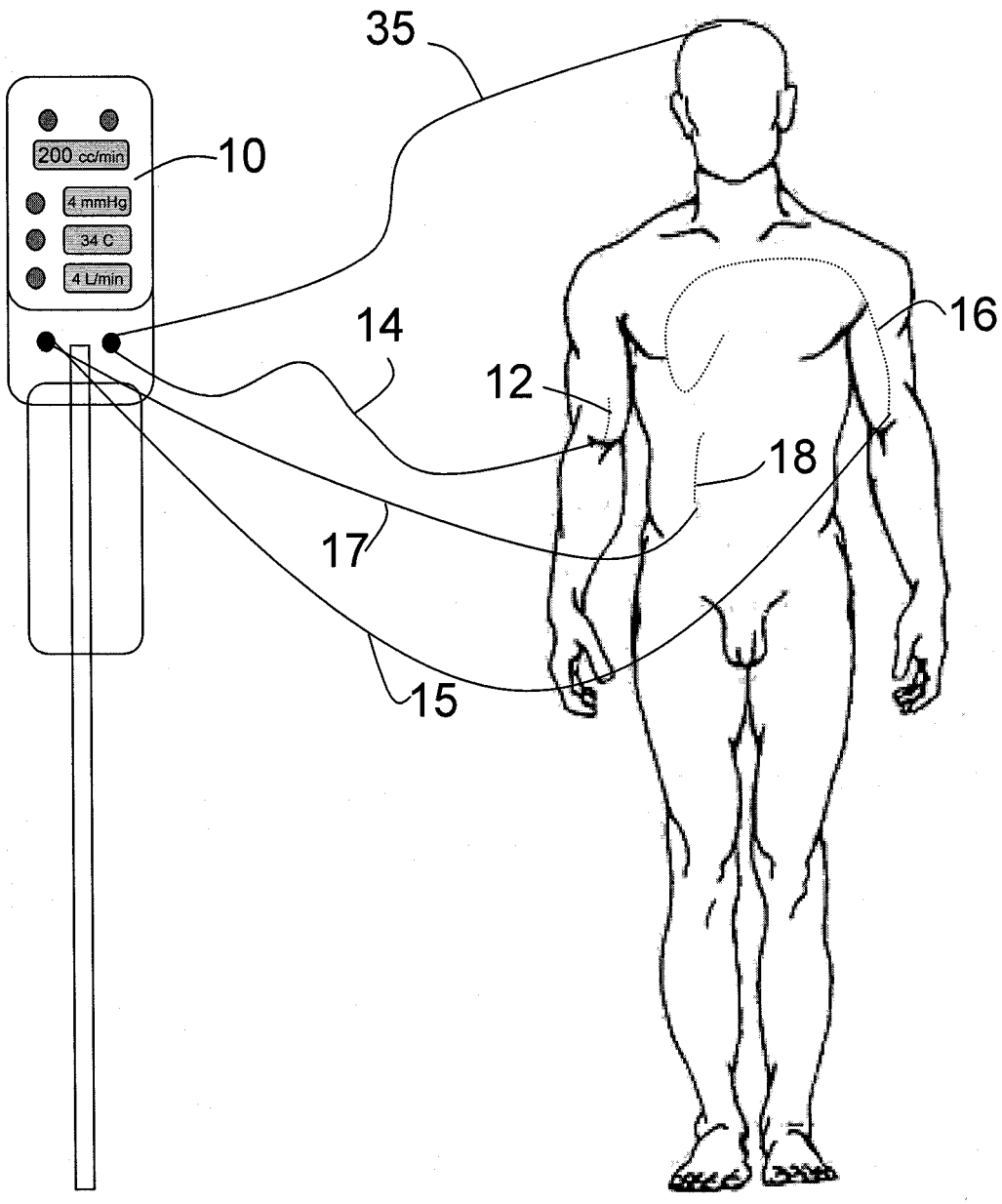

Figure 1

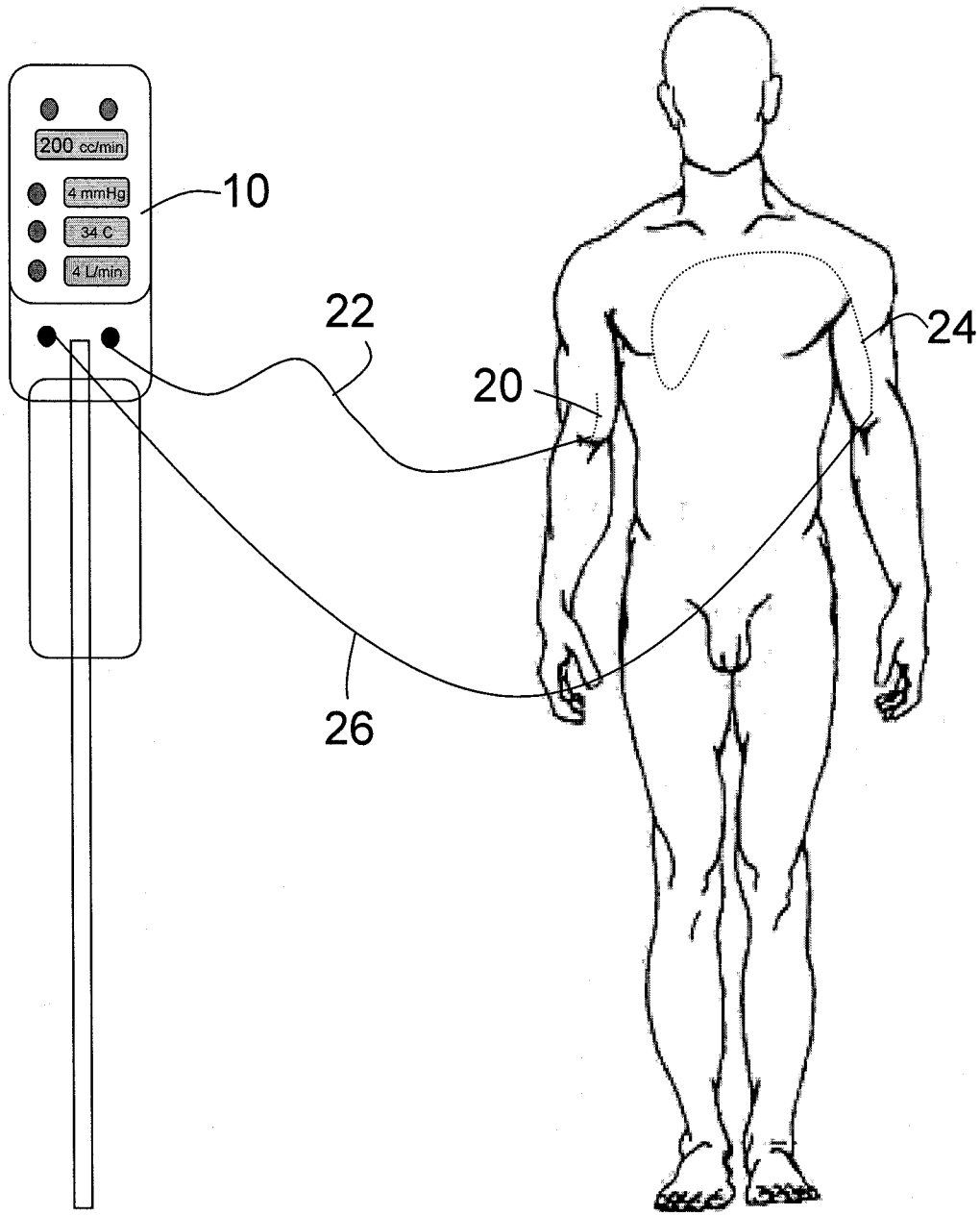

Figure 2

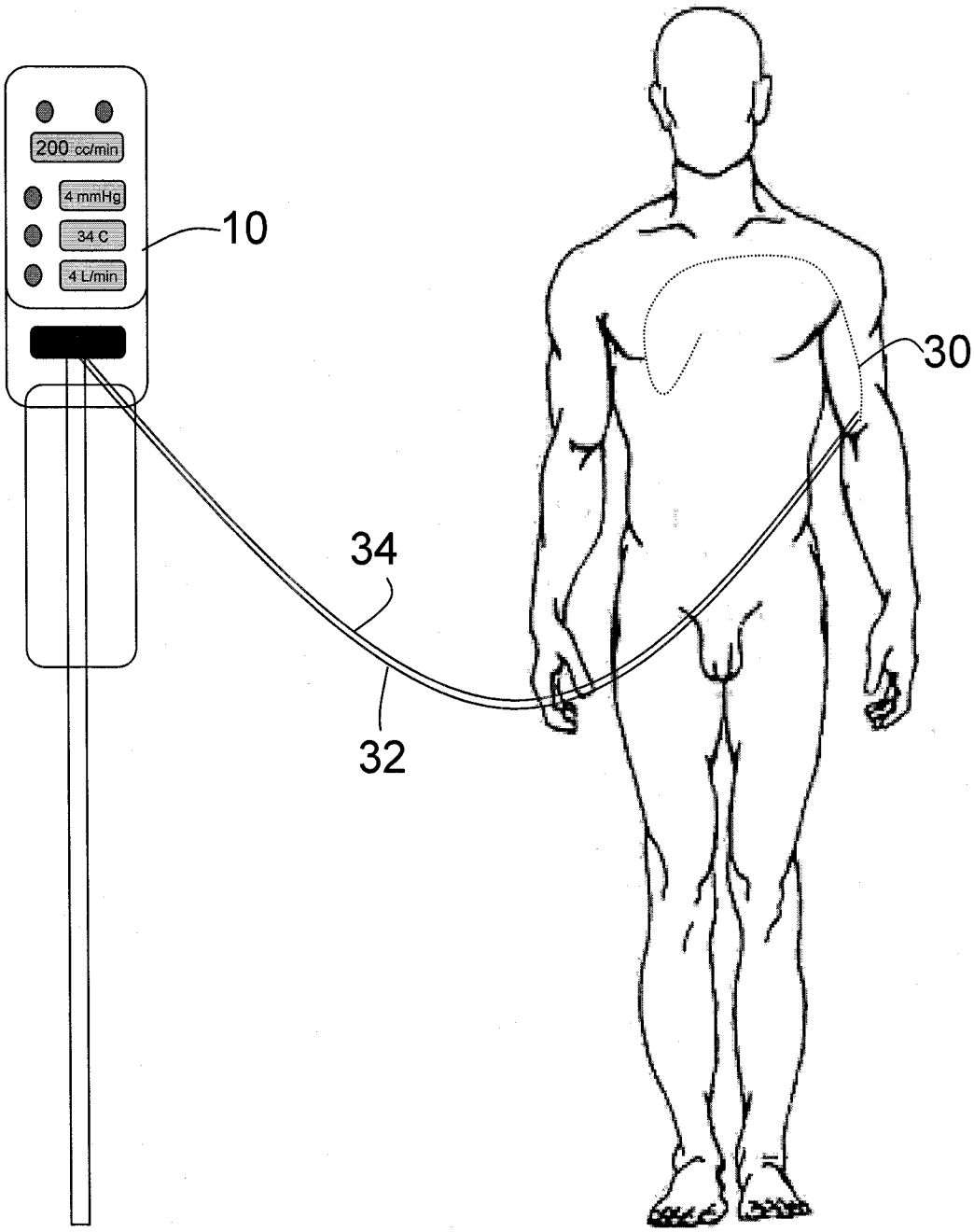

Figure 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/059496

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/172

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, *where appropriate, of the relevant passages*	Relevant to claim No.
X	US 2004/122353 A1 (SHAHMIRIAN VARAZ [US] ET AL) 24 June 2004 (2004-06-24) paragraph [0052] - paragraph [0067]	1-20
X	US 6 066 163 A (JOHN MICHAEL SASHA [US]) 23 May 2000 (2000-05-23) column 4, line 26 - line 59 column 10, line 17 - line 26	1-20
X	WO 2006/060514 A (MEDTRONIC INC [US]; SIGG DANIEL C [US]; UJHELYI MICHAEL R [US]; MORRIS) 8 June 2006 (2006-06-08) page 9, lines 14-16 - lines 24-28	1-20
A	WO 98/04191 A (VIA MEDICAL CORP [US]) 5 February 1998 (1998-02-05) page 4, line 4 - line 22	2

☐ 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 document 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
21 July 2008	31/07/2008
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Alvazzi Delfrate, S

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/059496

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

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

1. [X] Claims Nos.: 21-54
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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

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

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

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

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

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

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

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

Remark on Protest

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

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

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 21-54

Claims 21-47 relate to subject-matter mentioned in Rule 67.1 (iv) PCT, in particular to a method for treatment of the human body by therapy (the "method of controlling infusion of a fluid comprises the step of adjusting fluid flow to the patient based on sensor signal; it is clear from the whole application that this step is performed in order to optimize the therapy, i.e. it is a therapeutical step). Under terms of Art.17(2)(a)(I) an International Search Authority is not required to carry out an examination of such claims.
Furthermore, claims 48-54 relate also to subject-matter mentioned in Rule 67.1 (iv) PCT, since the method of treating hypotension, the method of treating sepsis and the method of inducing and reversing therapeutic hypothermia in a patient are all clearly method for treatment of the human body by therapy, therefore an International Search Authority is not required to carry out an examination of such claims (Art.17(2)(a)(i)).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/059496

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