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Woo

(54) **CONTROL OF BODY FLUID CONDITION USING DIURETICS, BASED ON BIOLOGICAL PARAMETERS**

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Publication Classification

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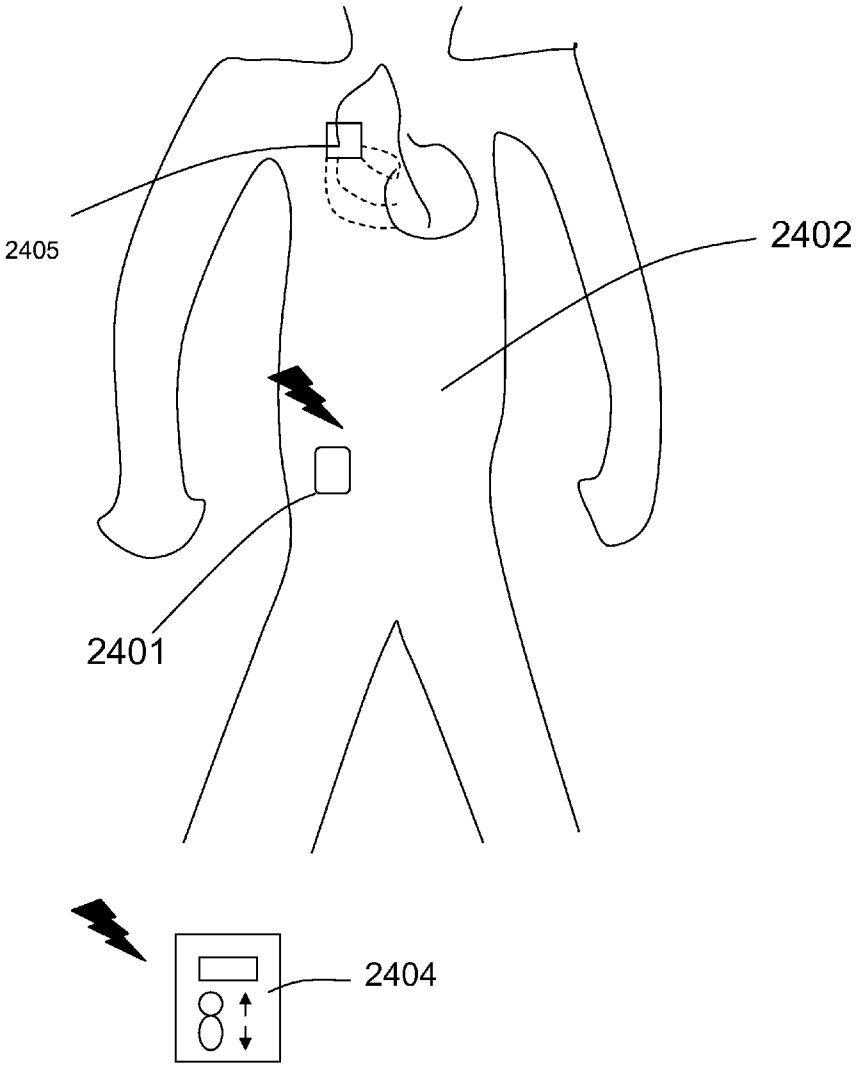
(52) **U.S. Cl.** **604/66**

(57) **ABSTRACT**

The system for controlling body fluids overcomes the limitations of the prior art by automatically infusing diuretic and/or other drugs into a human patient. In one approach, the rate of infusion of the diuretic is adjusted based on a measured biological parameter of the patient. For example, this biological parameter can be transmitted wirelessly to a portable diuretic infusion device attached to the patient.



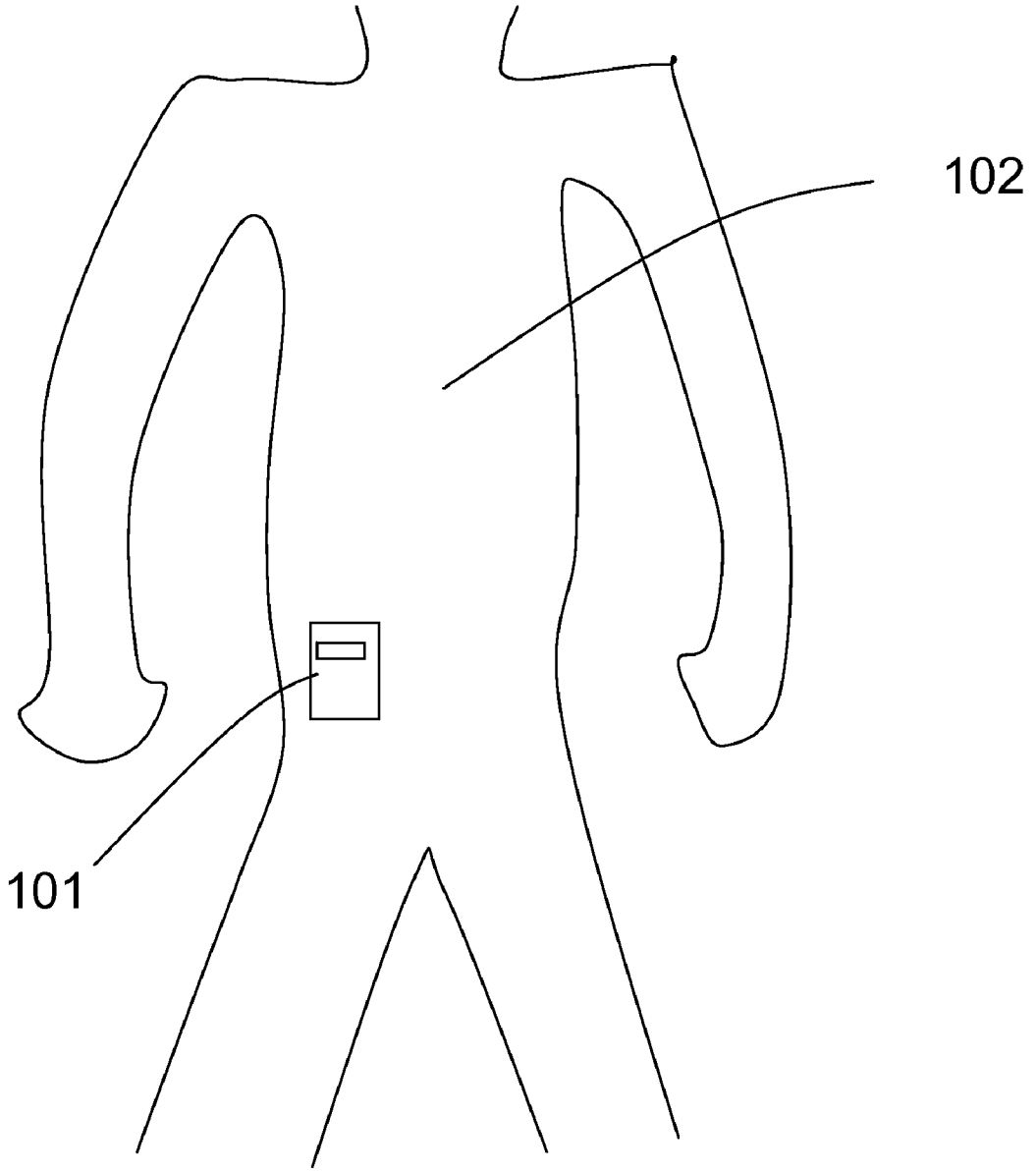


Figure 1

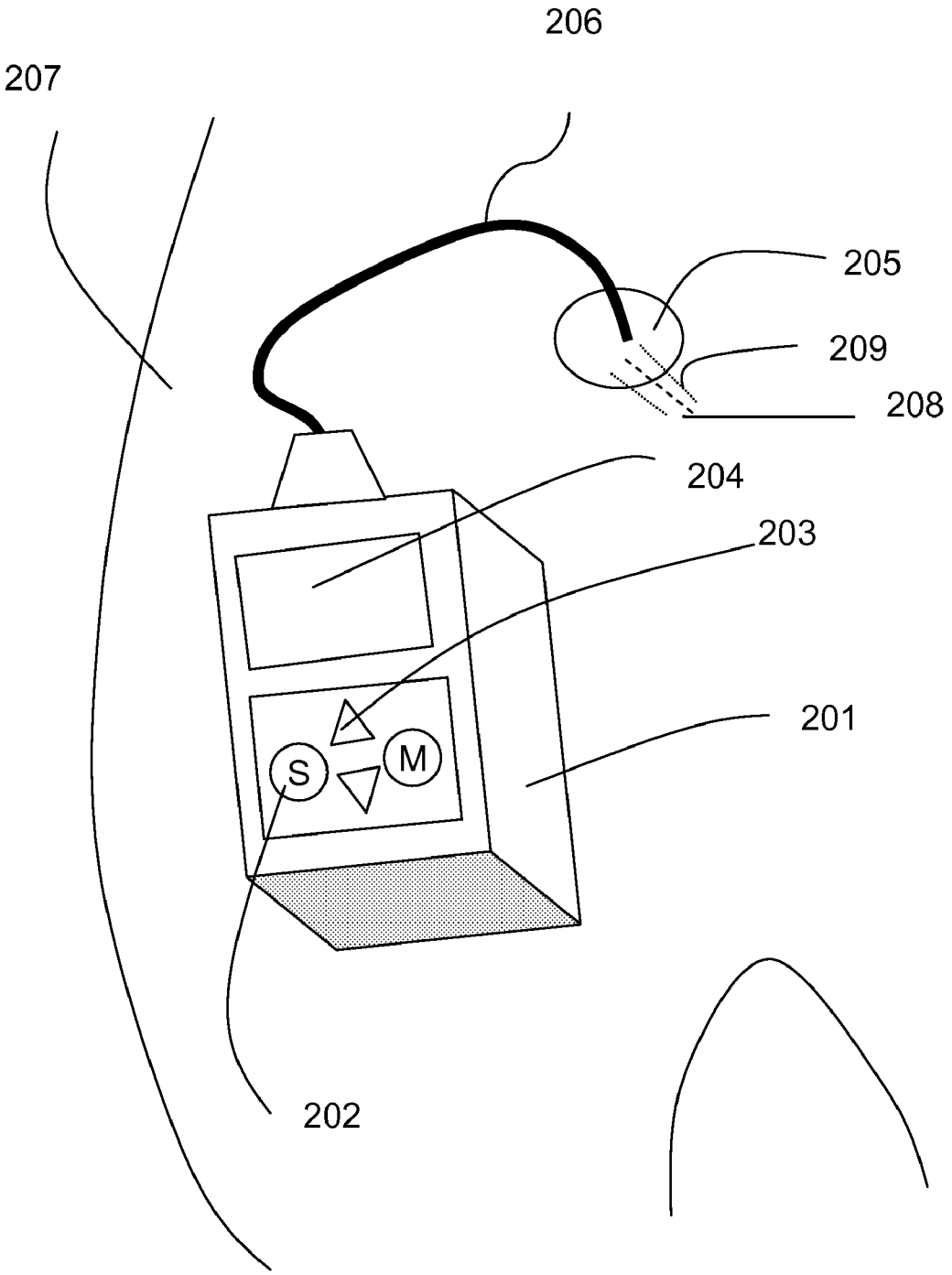


Figure 2

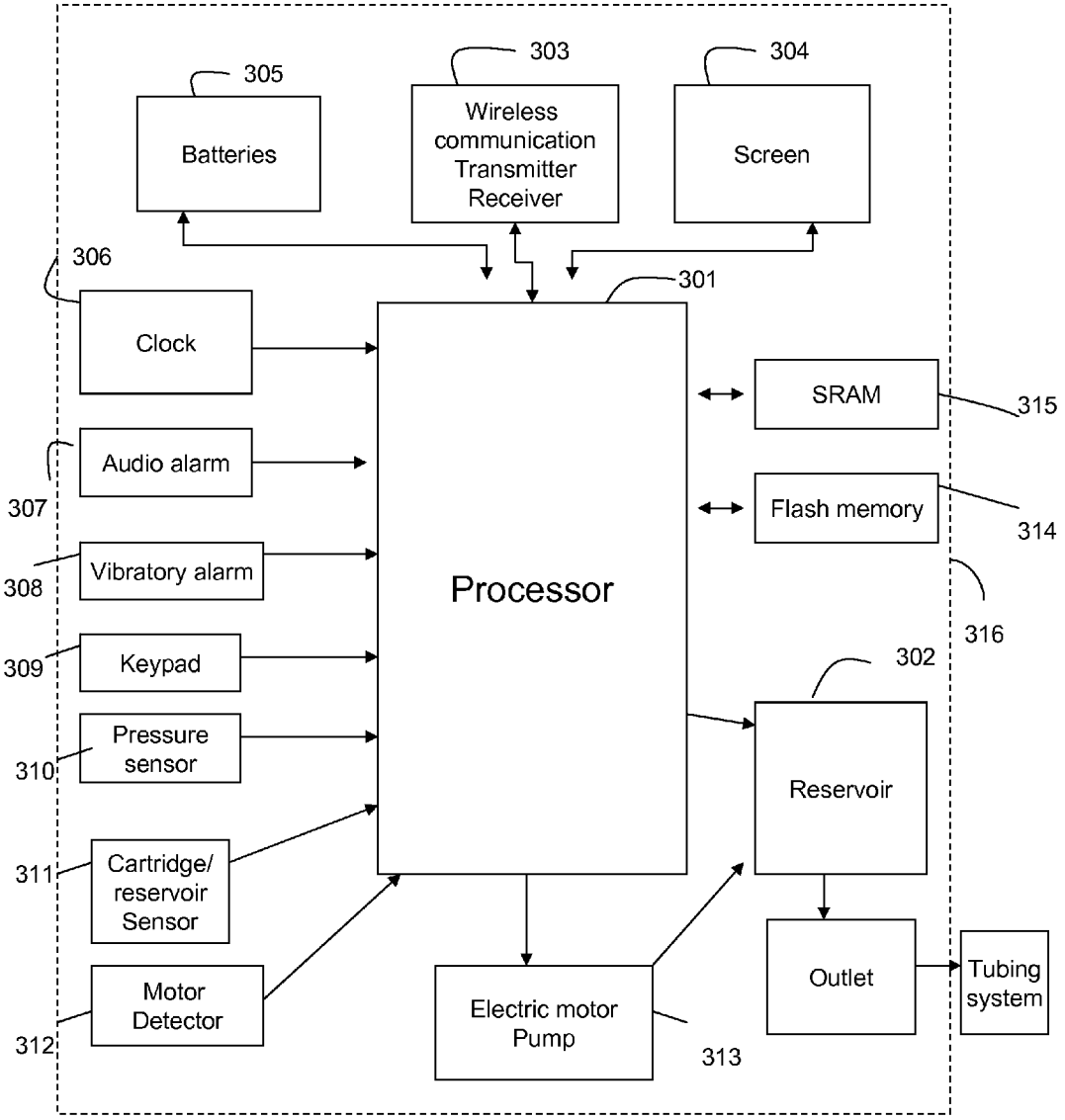

305
Batteries
303
Wireless communication Transmitter Receiver
304
Screen
306
Clock
301
Processor
SRAM
315
Audio alarm
307
Flash memory
314
Vibratory alarm
308
316
Keypad
309
302
Pressure sensor
310
Reservoir
Cartridge/ reservoir Sensor
311
Outlet
Tubing system
Motor Detector
312
Electric motor Pump
313

Figure 3

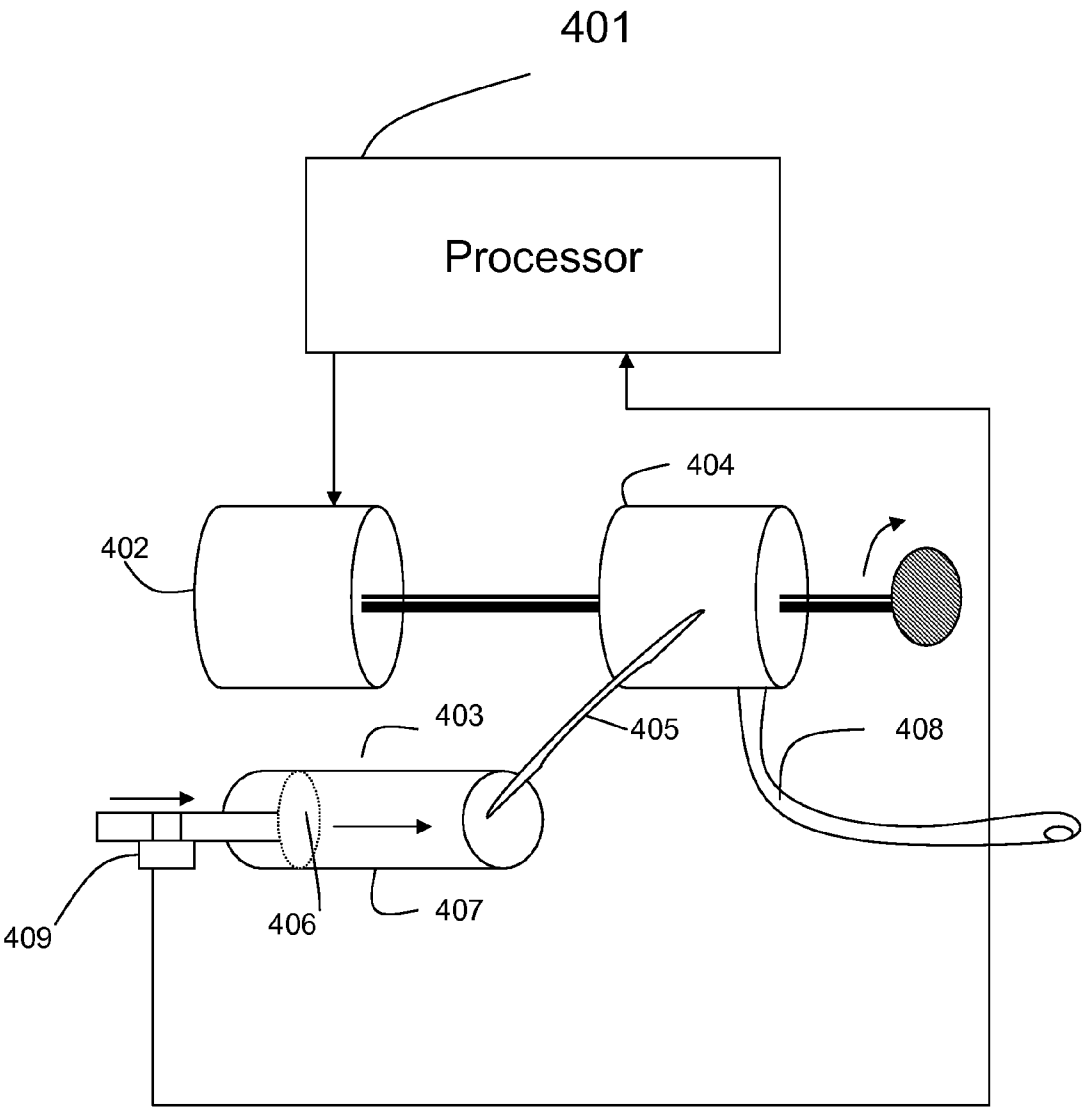


Figure 4

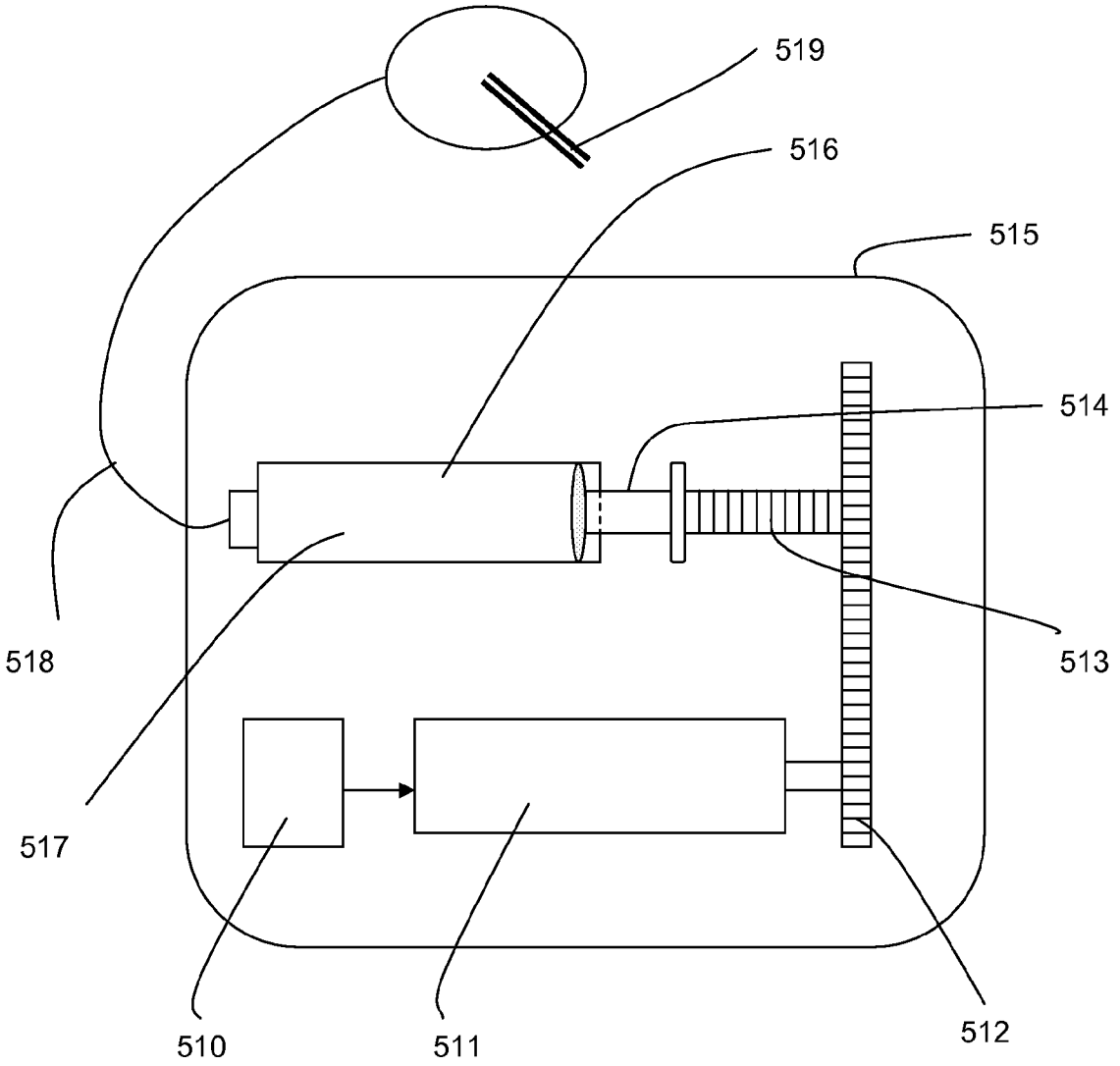


Figure 5

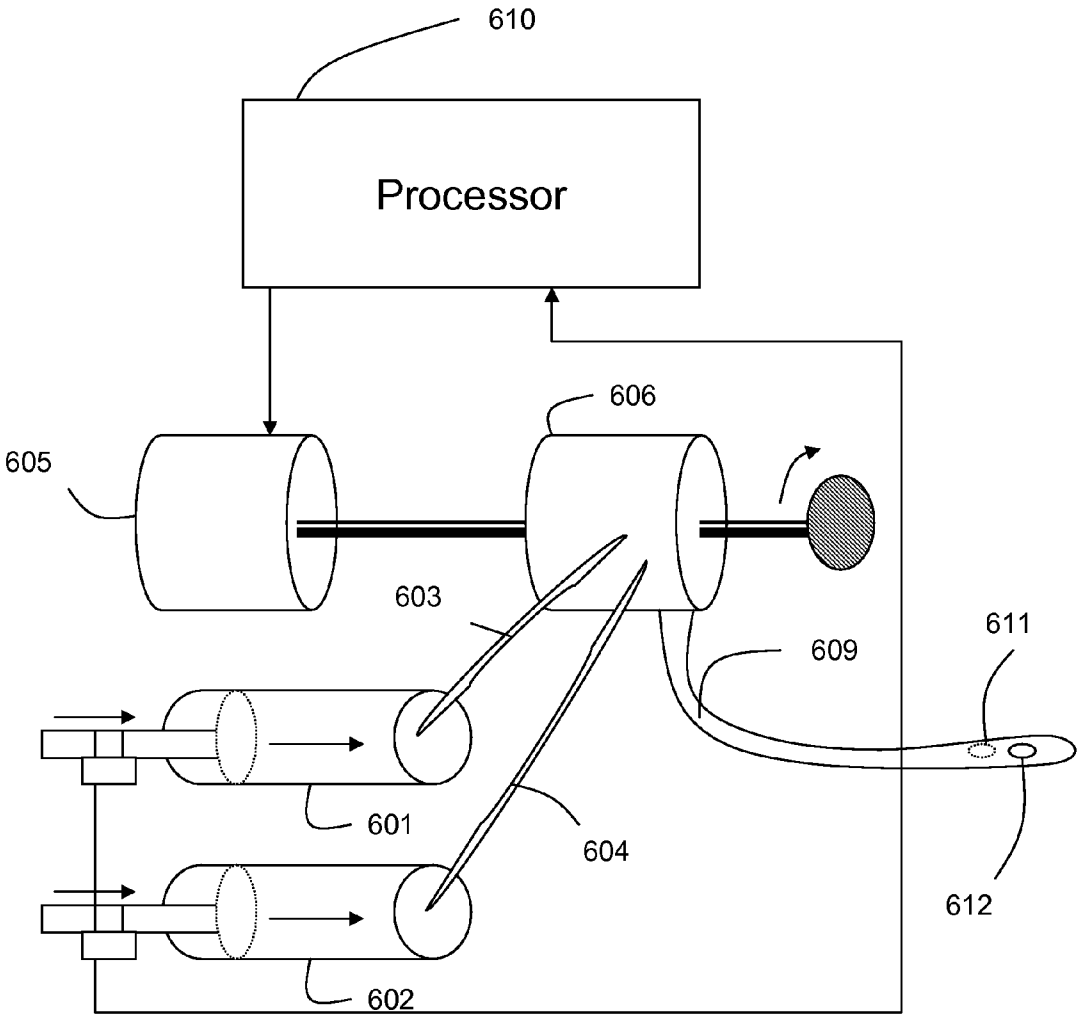


Figure 6

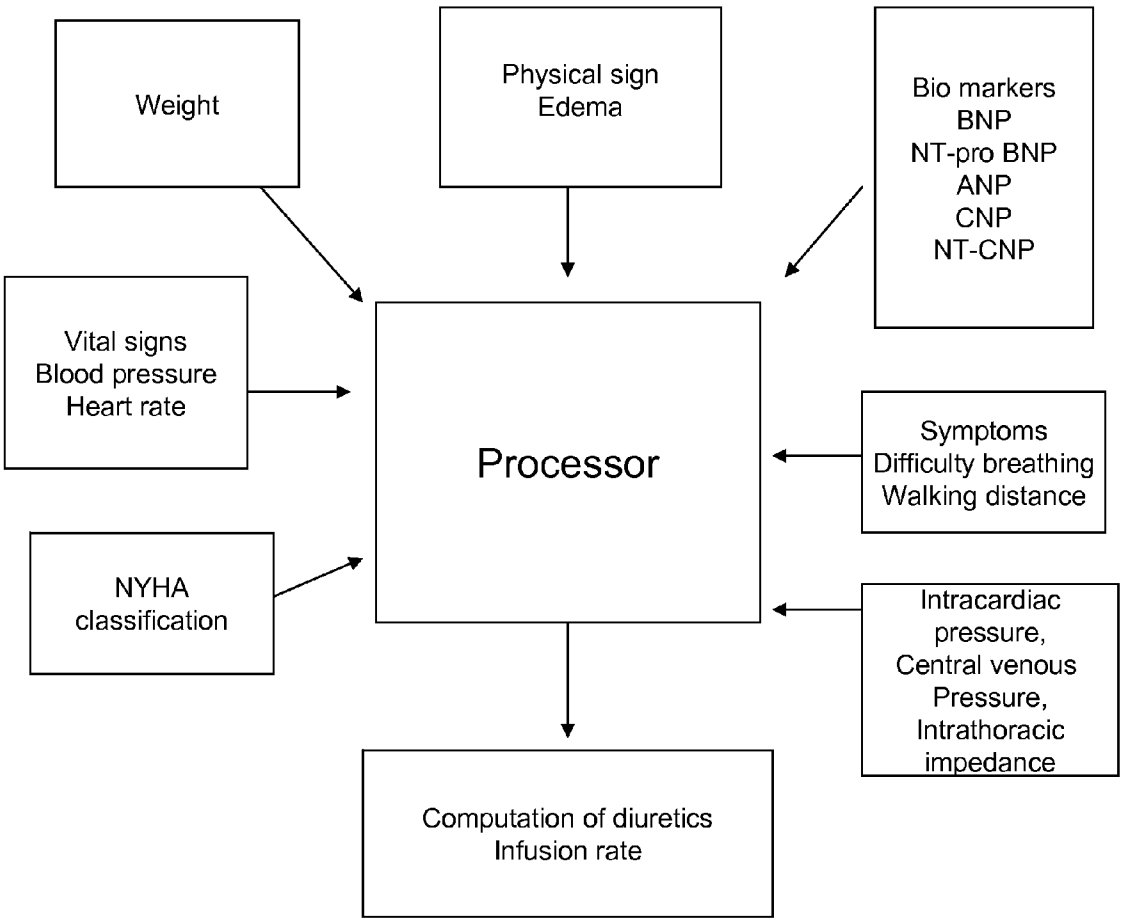

Weight
Physical sign
Edema
Bio markers
BNP
NT-pro BNP
ANP
CNP
NT-CNP
Vital signs
Blood pressure
Heart rate
Processor
Symptoms
Difficulty breathing
Walking distance
NYHA
classification
Intracardiac
pressure,
Central venous
Pressure,
Intrathoracic
impedance
Computation of diuretics
Infusion rate

Figure 7

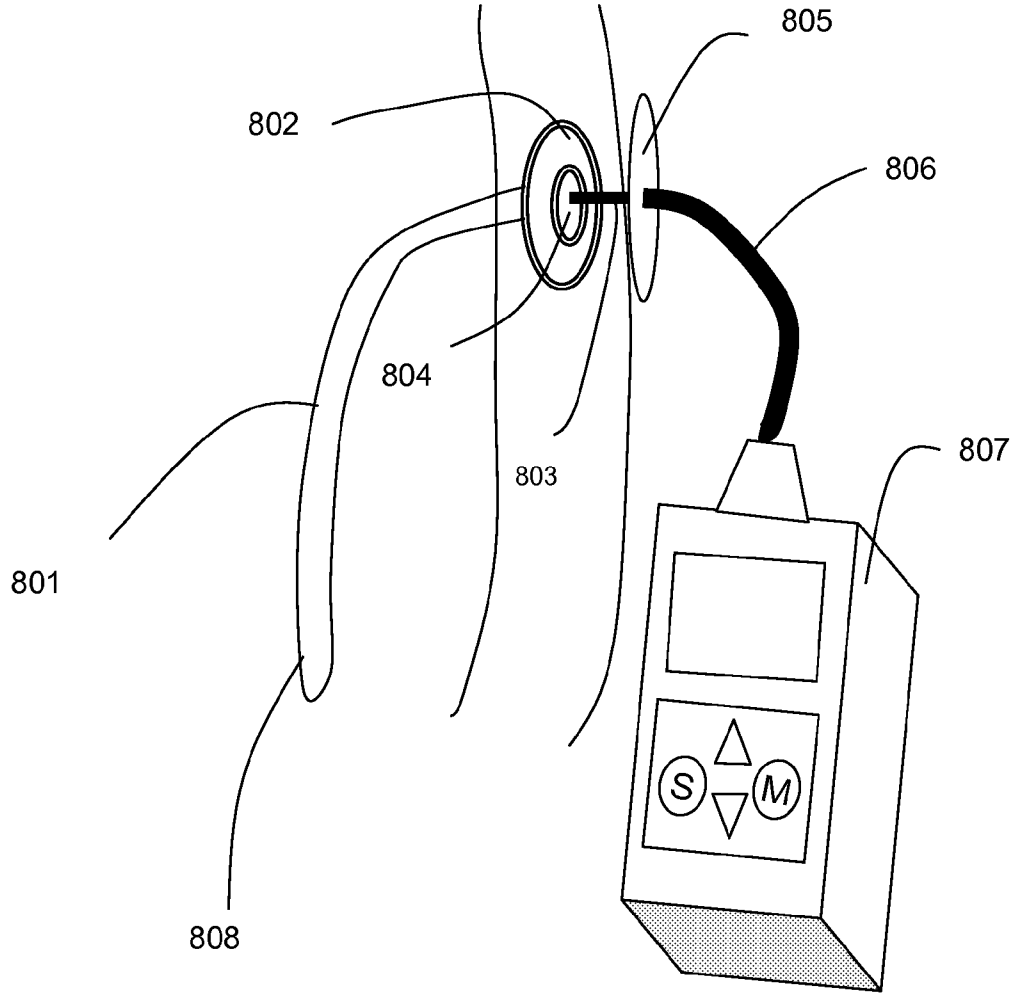


Figure 8

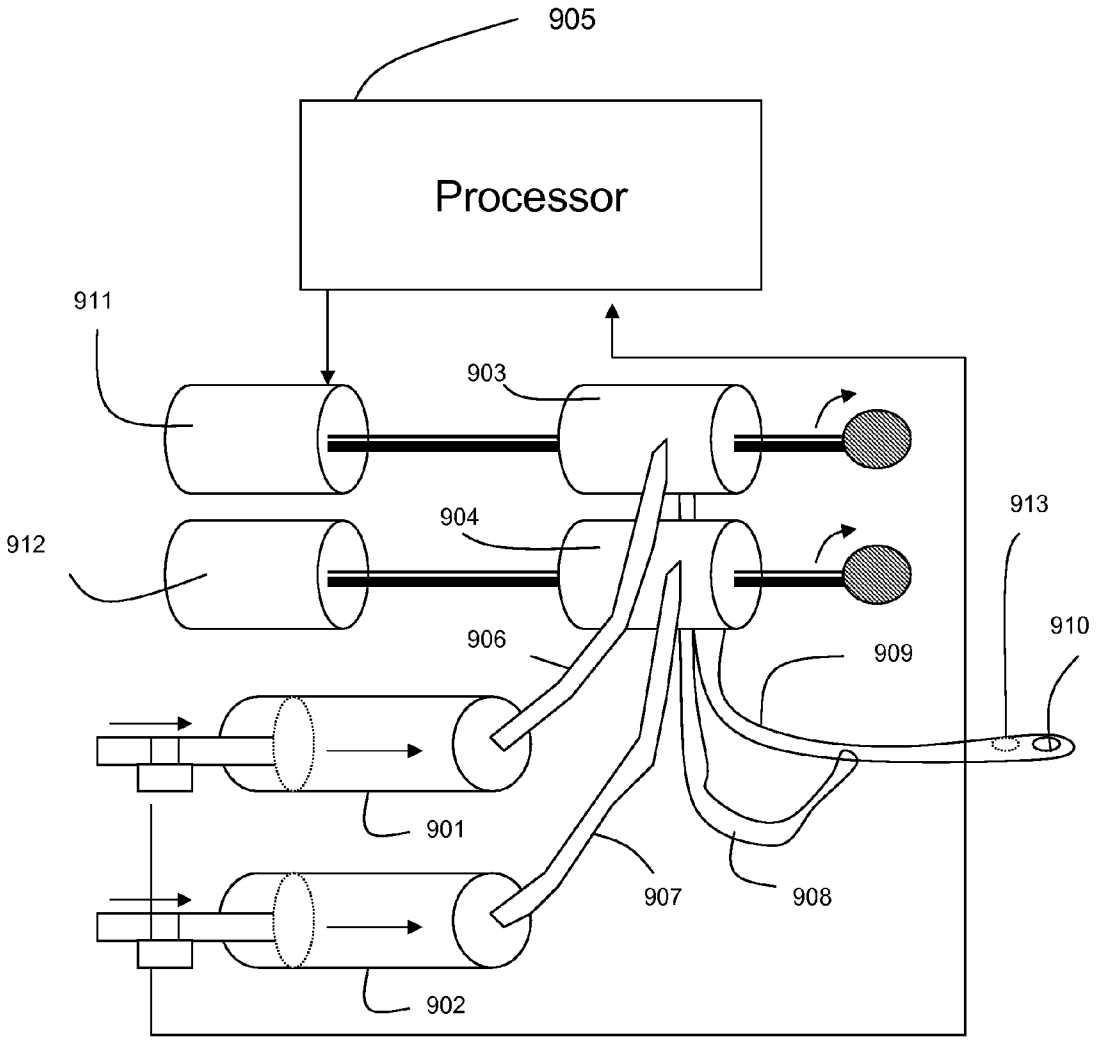


Figure 9

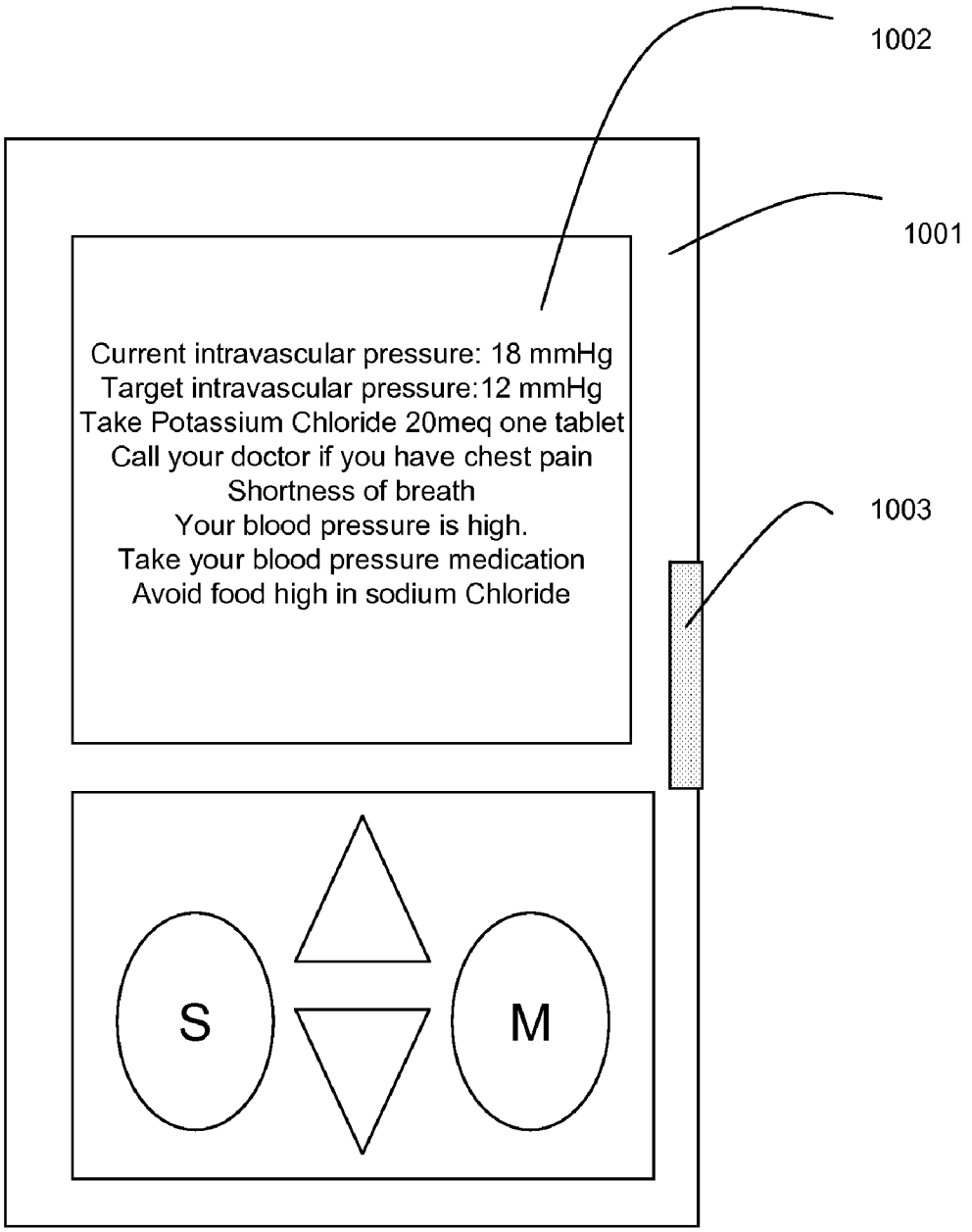

1002
1001
1003
Current intravascular pressure: 18 mmHg
Target intravascular pressure:12 mmHg
Take Potassium Chloride 20meq one tablet
Call your doctor if you have chest pain
Shortness of breath
Your blood pressure is high.
Take your blood pressure medication
Avoid food high in sodium Chloride
S
M

Figure 10

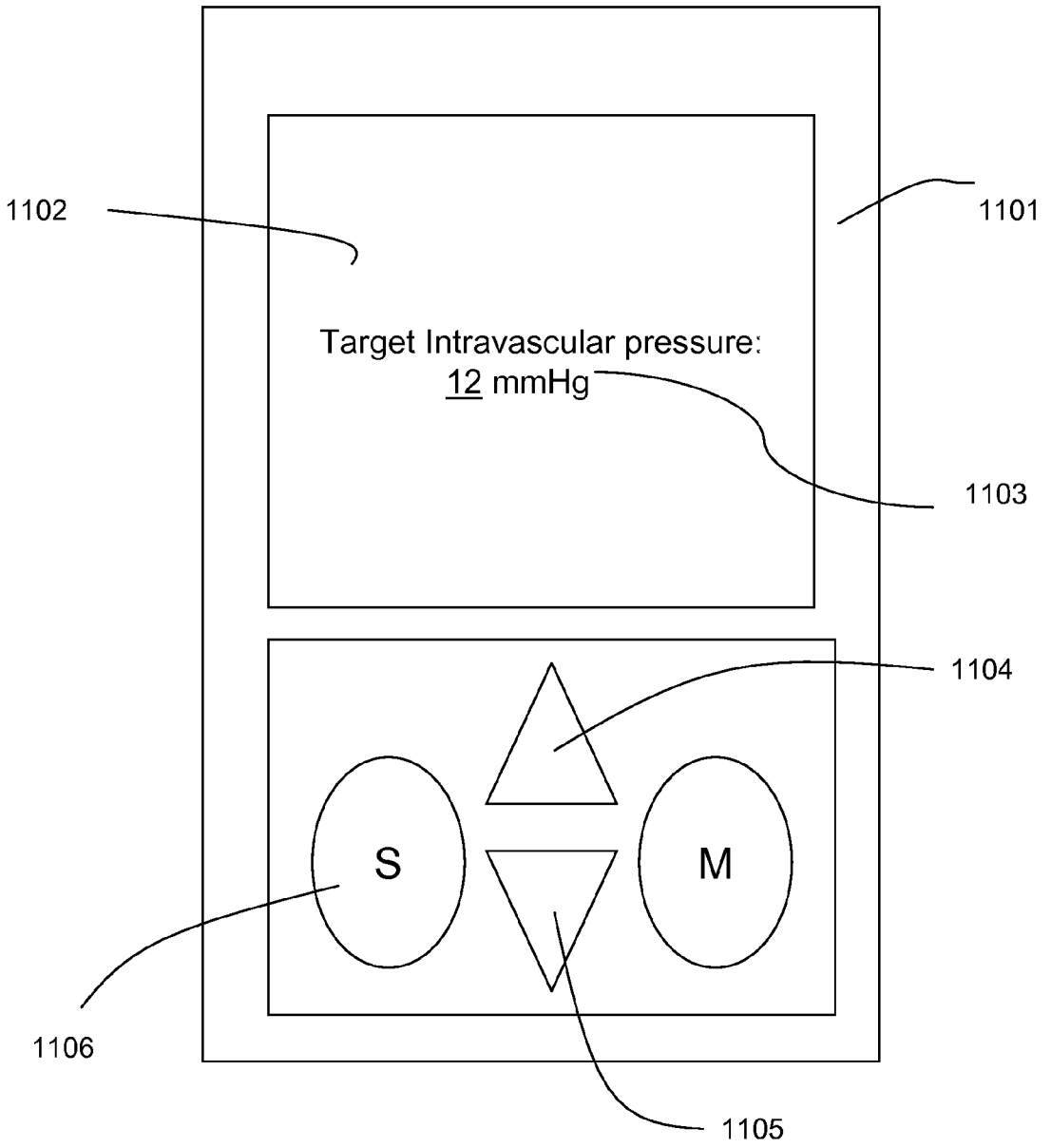

1102
1101
Target Intravascular pressure:
12 mmHg
1103
1104
S
M
1106
1105

Figure 11

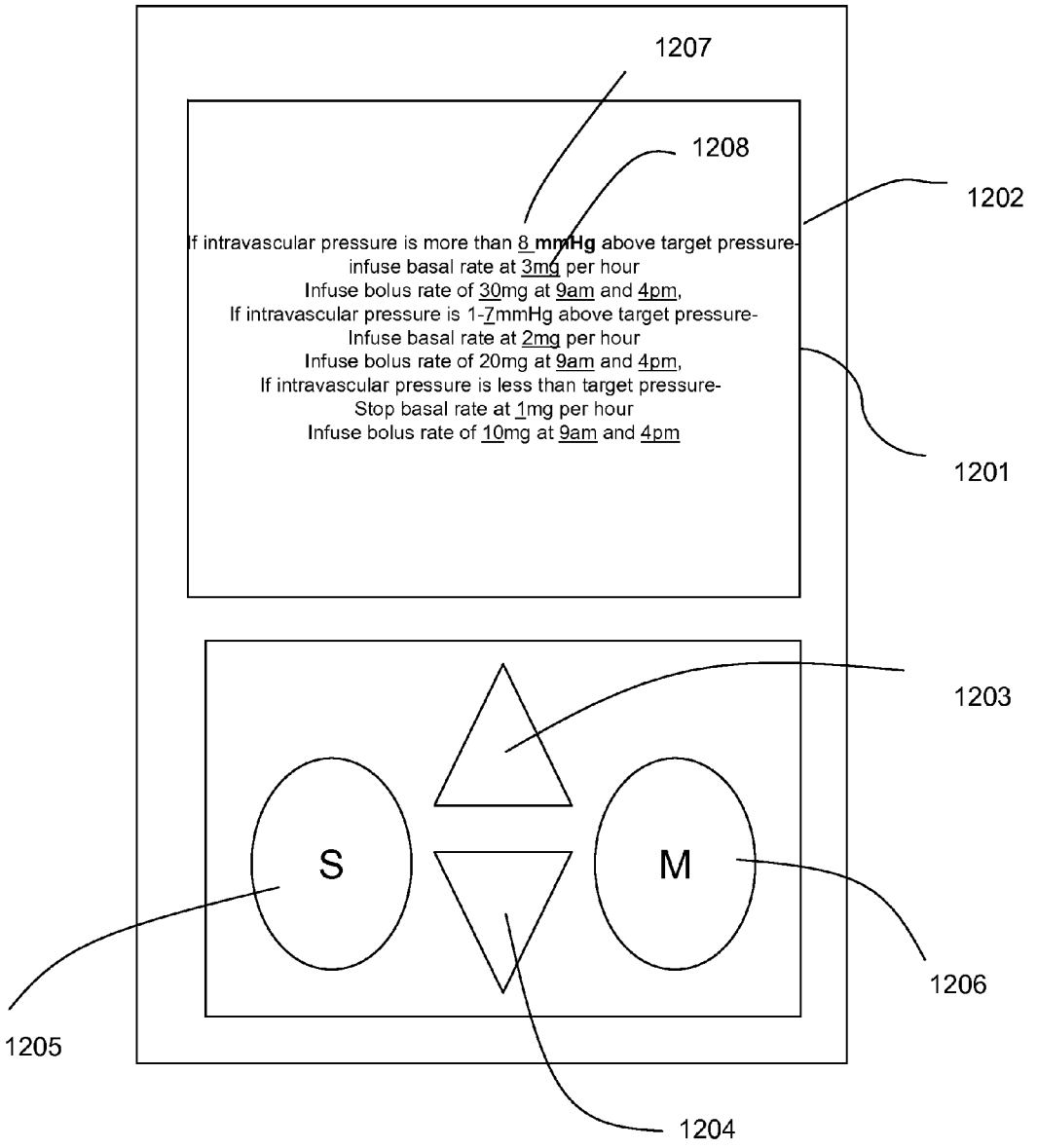

1207
1208
1202
If intravascular pressure is more than 8 mmHg above target pressure-
infuse basal rate at 3mg per hour
Infuse bolus rate of 30mg at 9am and 4pm,
If intravascular pressure is 1-7mmHg above target pressure-
Infuse basal rate at 2mg per hour
Infuse bolus rate of 20mg at 9am and 4pm,
If intravascular pressure is less than target pressure-
Stop basal rate at 1mg per hour
Infuse bolus rate of 10mg at 9am and 4pm
1201
1203
S
M
1206
1205
1204

Figure 12

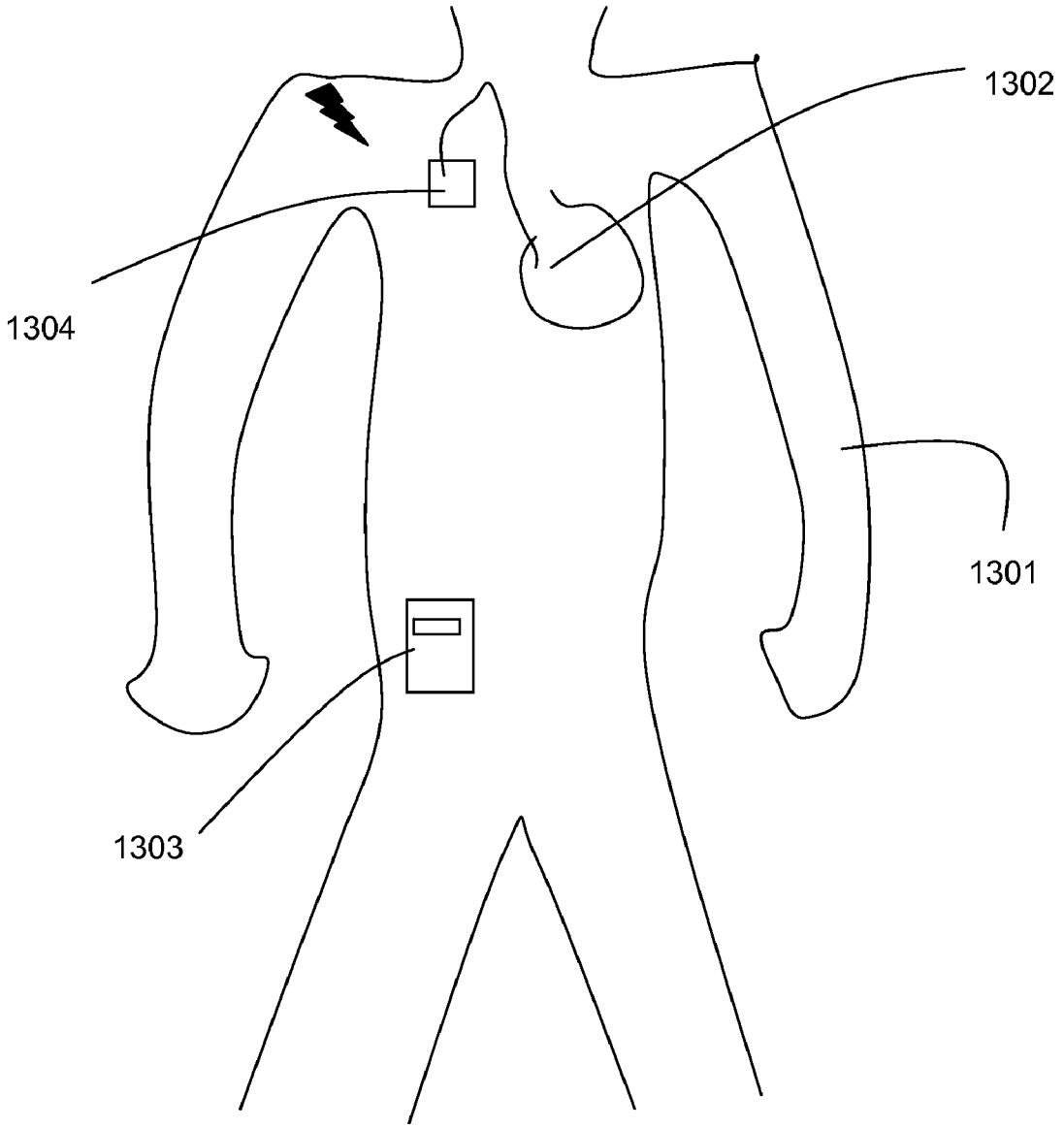


Figure 13

<furosemide infusion protocol following pressure>

If central venous pressure is more than 25 mmHg-
Infuse basal rate at 3mg per hour for 12 hours starting at 6am
Infuse bolus of 60mg at 6am and 4pm
If central venous pressure is 22-24mmHg -
Infuse basal rate at 2mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 50mg at 6am and 4pm.
If central venous pressure is 18-21mmHg -
Infuse basal rate at 0.7mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 40mg at 6am and 4pm.
If central venous pressure is 14-17mmHg-
Infuse bolus rate of 30mg at 6am and 4pm.
If central venous pressure is 10-13mmHgt -
Infuse bolus rate of 20mg at 6am and 4pm
If central venous pressure is 6-9mmHg,
Infuse bolus rate of 5mg at 6am.
If central venous pressure is less than 5mmHg,
Stop infusion

Figure 14

<Oral furosemide dose titration protocol following pressure>

Put in baseline dose

If central venous pressure is more than 25 mmHg-
Increase current dose by 200% from baseline dose.
Display instruction "call your doctor".

If central venous pressure is 22-24mmHg –
Increase current dose by 150% from baseline dose.
If central venous pressure is 18-21mmHg -
Increase current dose by 100 % from baseline dose.
If central venous pressure is 14-17mmHg-
Increase current dose by 75% from baseline dose.
If central venous pressure is 10-13mmHgt -
Increase current dose by 50% from baseline dose
If central venous pressure is 6-9mmHg,
continue baseline dose
If central venous pressure is less than 5mmHg,
Stop taking oral furosemide dose

Figure 15

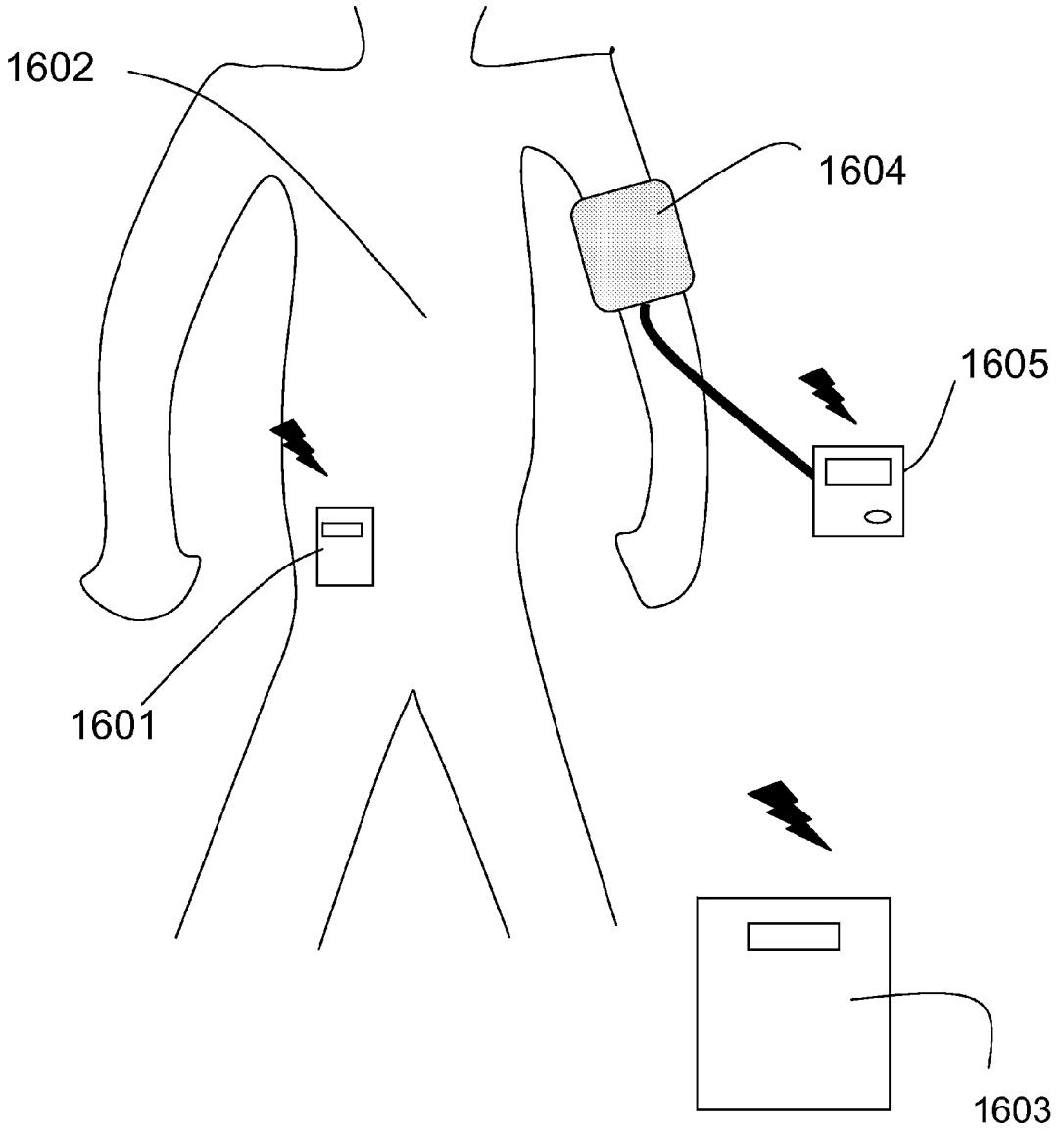


Figure 16

<furosemide infusion protocol>

If body weight is more than 2kg above target weight and blood pressure is above 100/70 -
Change the protocol to high dose furosemide infusion protocol
Infuse the dose according to the high dose furosemide protocol.
If body weight is 1.5-2kg above target weight and blood pressure is above 100/70 -
Infuse basal rate at 2mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 50mg at 6am and 4pm.
If body weight is 1-1.5kg above target weight and blood pressure above 100/70 -
Infuse basal rate at 0.7mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 40mg at 6am and 4pm.
If body weight is 0.5-1kg above target weight and blood pressure is above 100/70 -
Infuse bolus rate of 30mg at 6am and 4pm.
If body weight is 0-0.5kg above target weight and blood pressure is above 100/70-
Hold basal rate infusion,
Infuse bolus rate of 20mg at 6am and 4pm.
If systolic blood pressure is less than 100, or
diastolic blood pressure is less than 60,
hold furosemide infusion and notify a physician

Figure 17

<furosemide and enalaprilat infusion protocol>

If body weight is more than 2kg above target weight and blood pressure is above 100/70 -
Change the protocol to high dose furosemide infusion protocol
Infuse the dose according to the high dose furosemide protocol.
If body weight is 1.5-2kg above target weight and blood pressure is above 100/70 -
Infuse basal rate at 2mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 50mg at 6am and 4pm.
If body weight is 1-1.5kg above target weight and blood pressure above 100/70 -
Infuse basal rate at 0.7mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 40mg at 6am and 4pm.
If body weight is 0.5-1kg above target weight and blood pressure is above 100/70 -
Infuse bolus rate of 30mg at 6am and 4pm.
If body weight is 0-0.5kg above target weight and blood pressure is above 100/70-
Hold basal rate infusion,
Infuse bolus rate of 20mg at 6am and 4pm.
If blood pressure is less than 100/70, hold furosemide infusion and notify a physician

If blood pressure is above 160/110, infuse enalaprilat 0.625mg every six hours
If blood pressure remains above 160/110 after enalaprilat 0.625mg infusion,
Increase enalaprilat to 1.25mg every six hours
If blood pressure is less than 100/70, stop enalaprilat
If blood pressure is above 180/120, notify a physician
Send blood pressure and drug dose information to physician's office computer system

Figure 18

<furosemide and enalaprilat infusion protocol 2>

If body weight is more than 2kg above target weight and blood pressure is above 100/70 -
Change the protocol to high dose furosemide infusion protocol
Infuse the dose according to the high dose furosemide protocol.
If body weight is 1.5-2kg above target weight and blood pressure is above 100/70 -
Infuse basal rate at 2mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 50mg at 6am and 4pm.
If body weight is 1-1.5kg above target weight and blood pressure above 100/70 -
Infuse basal rate at 0.7mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 40mg at 6am and 4pm.
If body weight is 0.5-1kg above target weight and blood pressure is above 100/70 -
Infuse bolus rate of 30mg at 6am and 4pm.
If body weight is 0-0.5kg above target weight and blood pressure is above 100/70-
Hold basal rate infusion,
Infuse bolus rate of 20mg at 6am and 4pm.
If blood pressure is less than 100/70, hold furosemide infusion and notify a physician

If blood pressure is above 180/120, notify a physician
If systolic blood pressure is above 160 or diastolic blood pressure is above 110,
infuse enalaprilat 1.25mg every six hours
If systolic blood pressure is between 140-160 or
diastolic blood pressure is between 90-110,
infuse enalaprilat 0.625mg every six hours
If systolic blood pressure is less than 140 or
diastolic blood pressure is less than 99,
hold enalaprilat infusion
If systolic blood pressure is less than 90 or diastolic blood pressure is less than 60,
notify a user to hold all the antihypertensive drugs and notify a physician

Send blood pressure and drug dose information to physician's office computer system

Figure 19

<furosemide and metoprolol infusion protocol>

If body weight is more than 2kg above target weight and blood pressure is above 100/70 -
Change the protocol to high dose furosemide infusion protocol
Infuse the dose according to the high dose furosemide protocol.
If body weight is 1.5-2kg above target weight and blood pressure is above 100/70 -
Infuse basal rate at 2mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 50mg at 6am and 4pm.
If body weight is 1-1.5kg above target weight and blood pressure above 100/70 -
Infuse basal rate at 0.7mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 40mg at 6am and 4pm.
If body weight is 0.5-1kg above target weight and blood pressure is above 100/70 -
Infuse bolus rate of 30mg at 6am and 4pm.
If body weight is 0-0.5kg above target weight and blood pressure is above 100/70-
Hold basal rate infusion,
Infuse bolus rate of 20mg at 6am and 4pm.
If blood pressure is less than 100/60, hold furosemide infusion and notify a physician

If systolic blood pressure is above 160 or diastolic blood pressure is above 110 and heart rate is above 65,
infuse metoprolol 5mg over 5 minutes every six hours
If systolic blood pressure is less than 160 or diastolic blood pressure is less than 110, hold metoprolol
If heart rate is above 130 and systolic blood pressure is above 110,
infuse metoprolol 5mg over 5 minutes and notify a physician
If systolic blood pressure is less than 100, stop metoprolol
If heart rate is less than 60, stop metoprolol.
If blood pressure is above 180/120, notify a physician
Ask a user if he has chest pain, shortness of breath. If user says yes, instruct a user to call 911
Send blood pressure and drug dose information to physician's office computer system

Figure 20

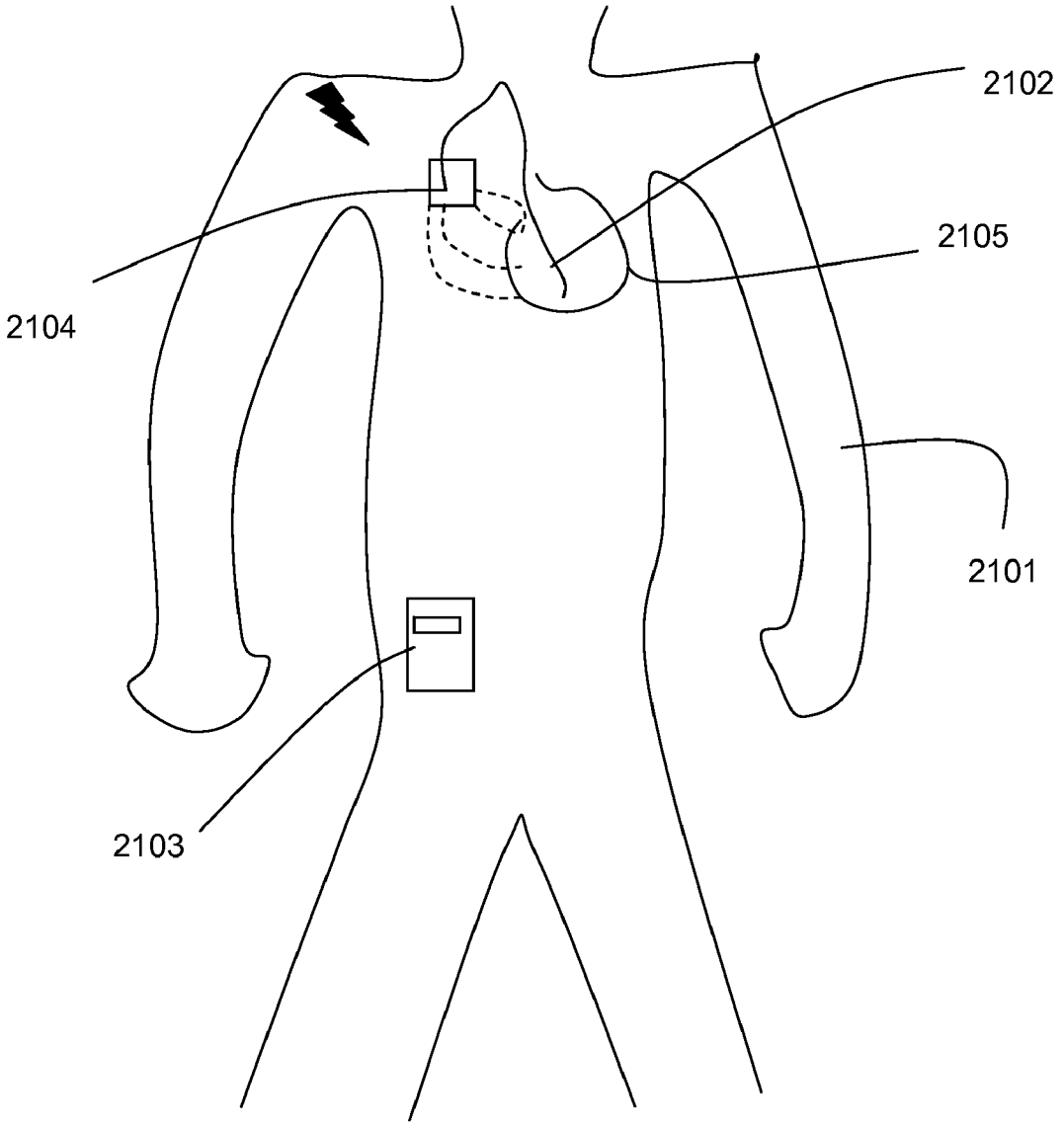


Figure 21

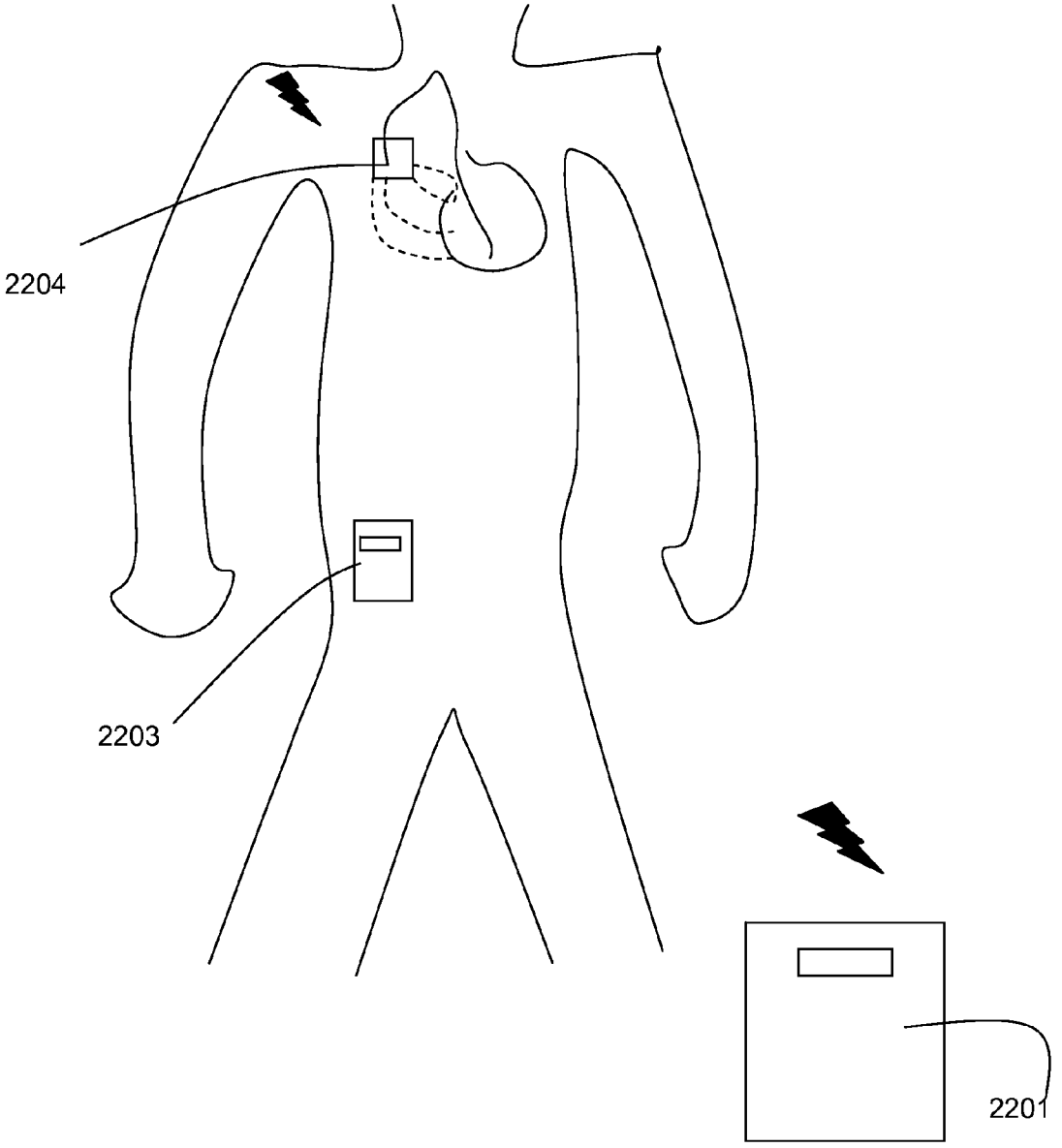


Figure 22

<furosemide infusion protocol according to intrathoracic impedance>

If intrathoracic impedance is less than 45 Ω -
Infuse basal rate at 3mg per hour for 12 hours starting at 6am
Infuse bolus of 60mg at 6am and 4pm
If intrathoracic impedance is between 45 and 50 Ω -
Infuse basal rate at 2mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 50mg at 6am and 4pm.
If intrathoracic impedance is between 51 and 55 Ω -
Infuse basal rate at 0.7mg per hour for 10 hours starting at 6am,
Infuse bolus rate of 40mg at 6am and 4pm.
If intrathoracic impedance is between 56 and 60 Ω -
Infuse bolus rate of 30mg at 6am and 4pm.
If intrathoracic impedance is between 61 and 65 Ω -
Infuse bolus rate of 20mg at 6am and 4pm
If intrathoracic impedance is between 66 and 70 Ω,
Infuse bolus rate of 5mg at 6am.
If intrathoracic impedance is above 70 Ω
Stop infusion

Figure 23

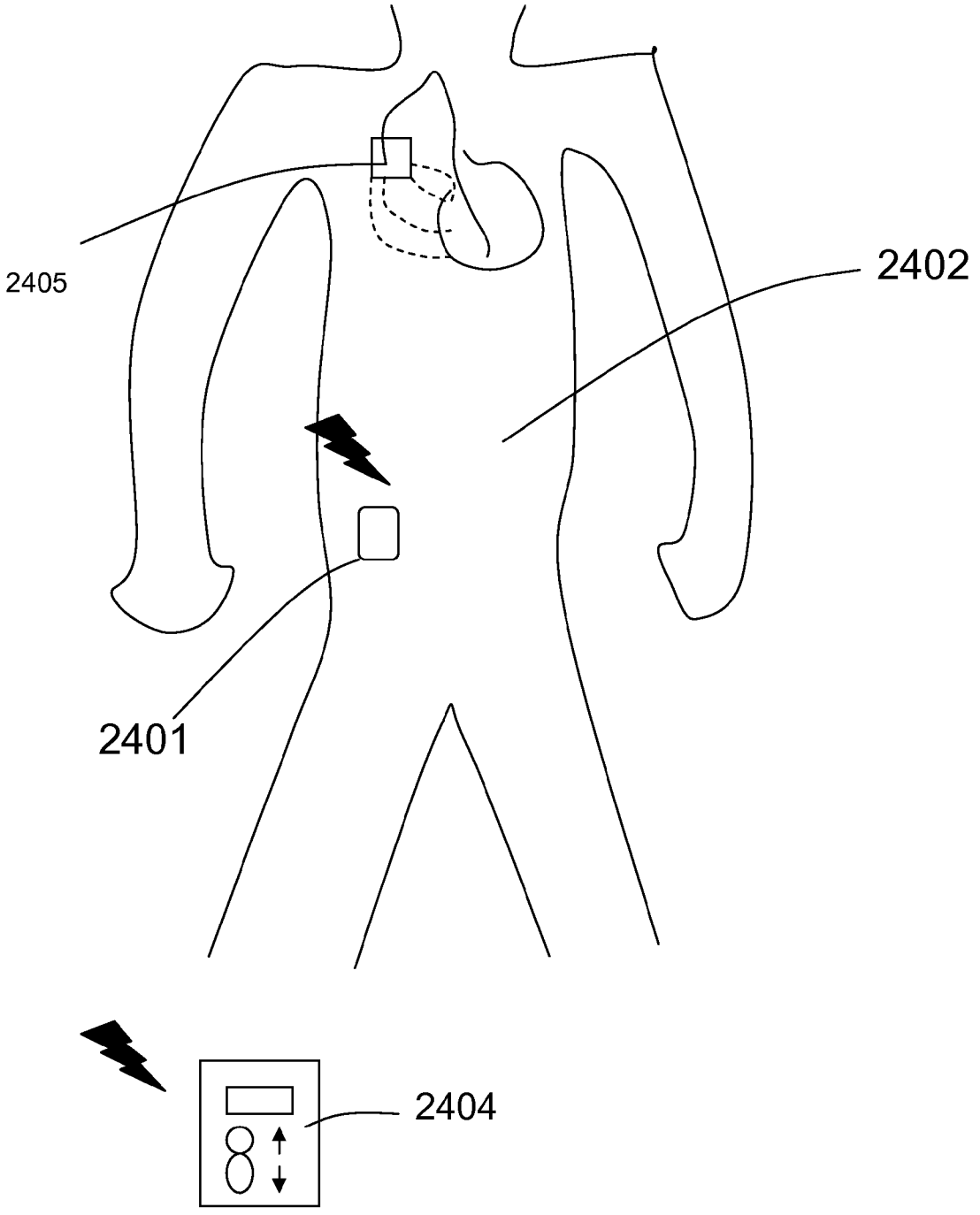


Figure 24

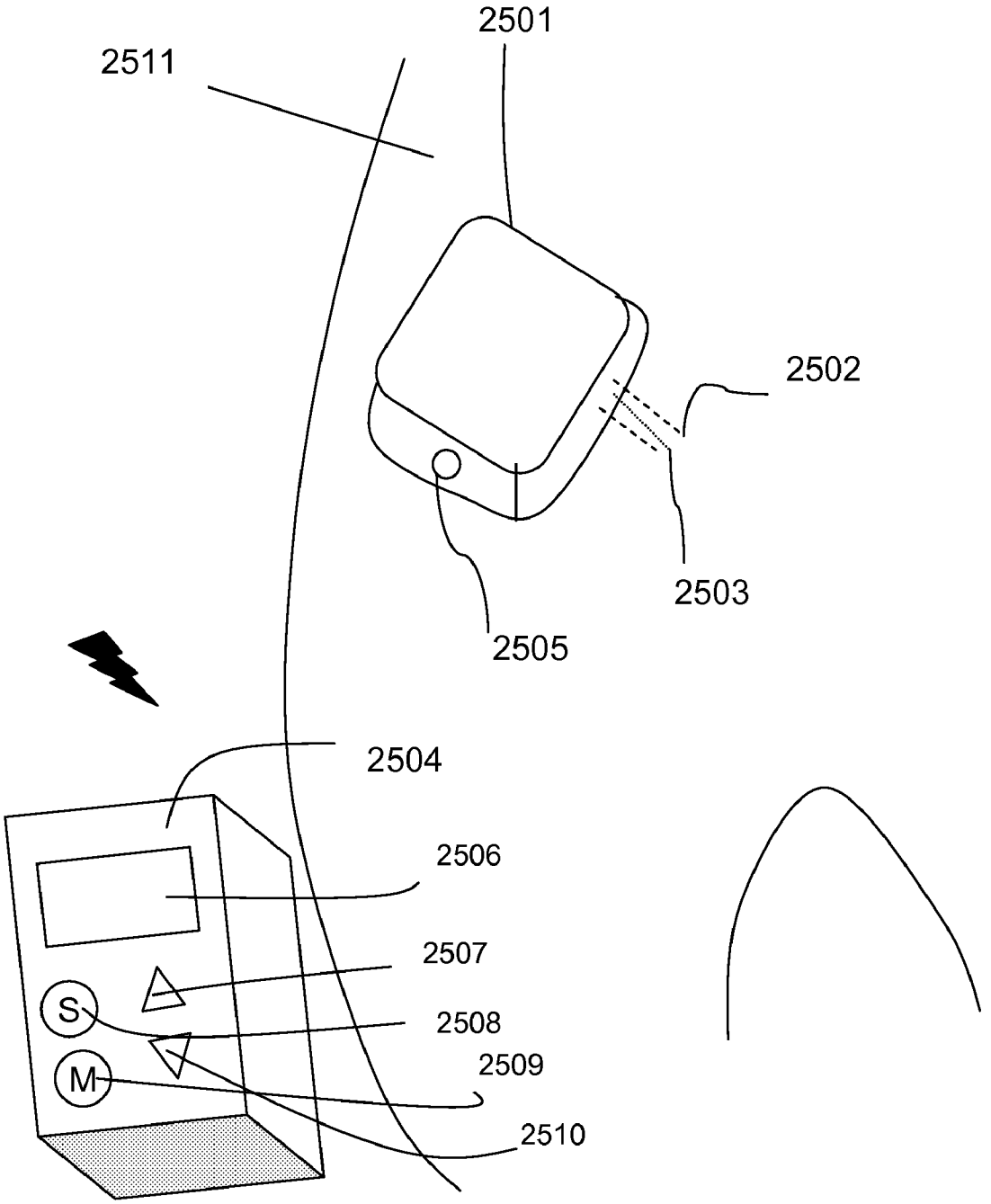


Figure 25

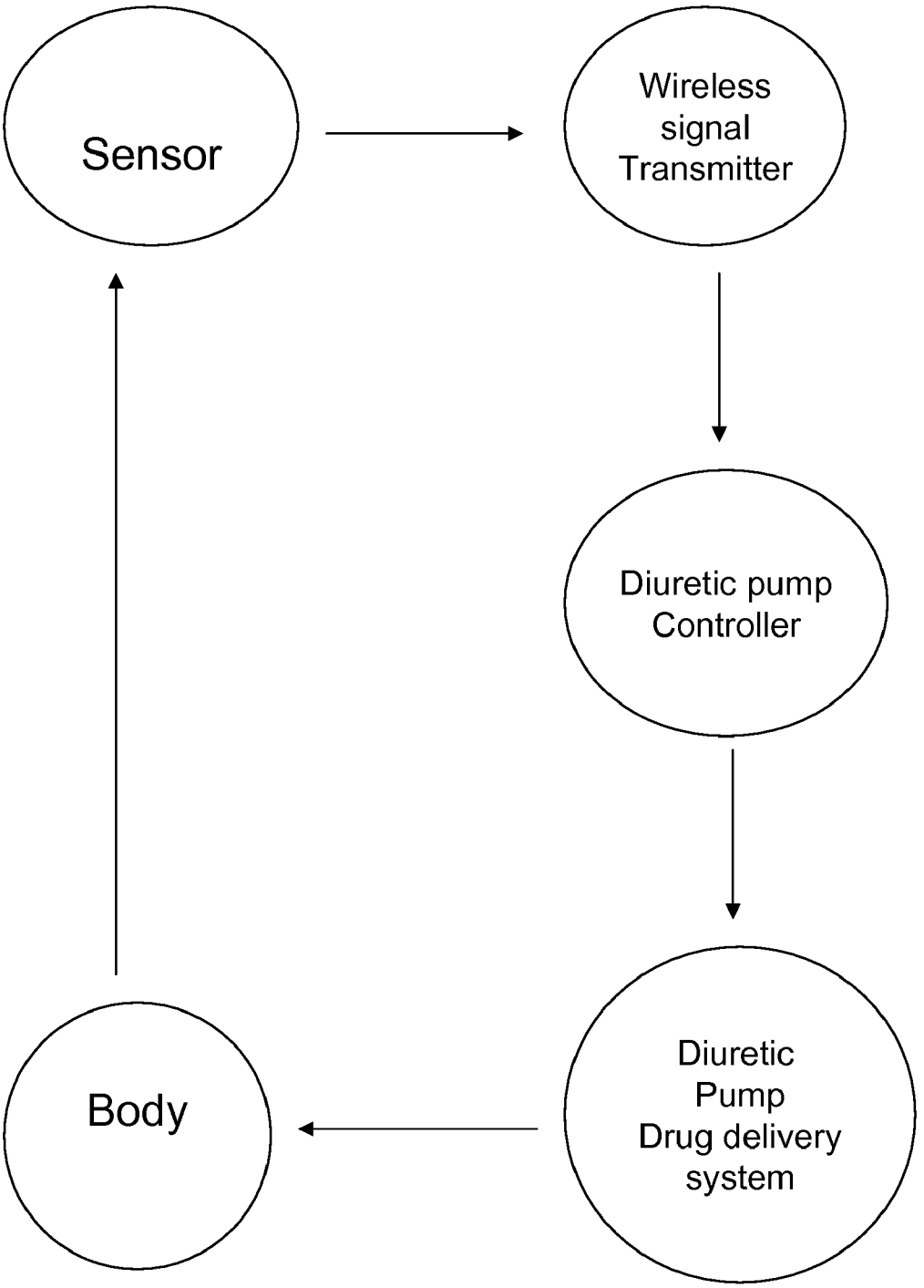

Sensor
Wireless signal Transmitter
Diuretic pump Controller
Diuretic Pump Drug delivery system
Body

Figure 26

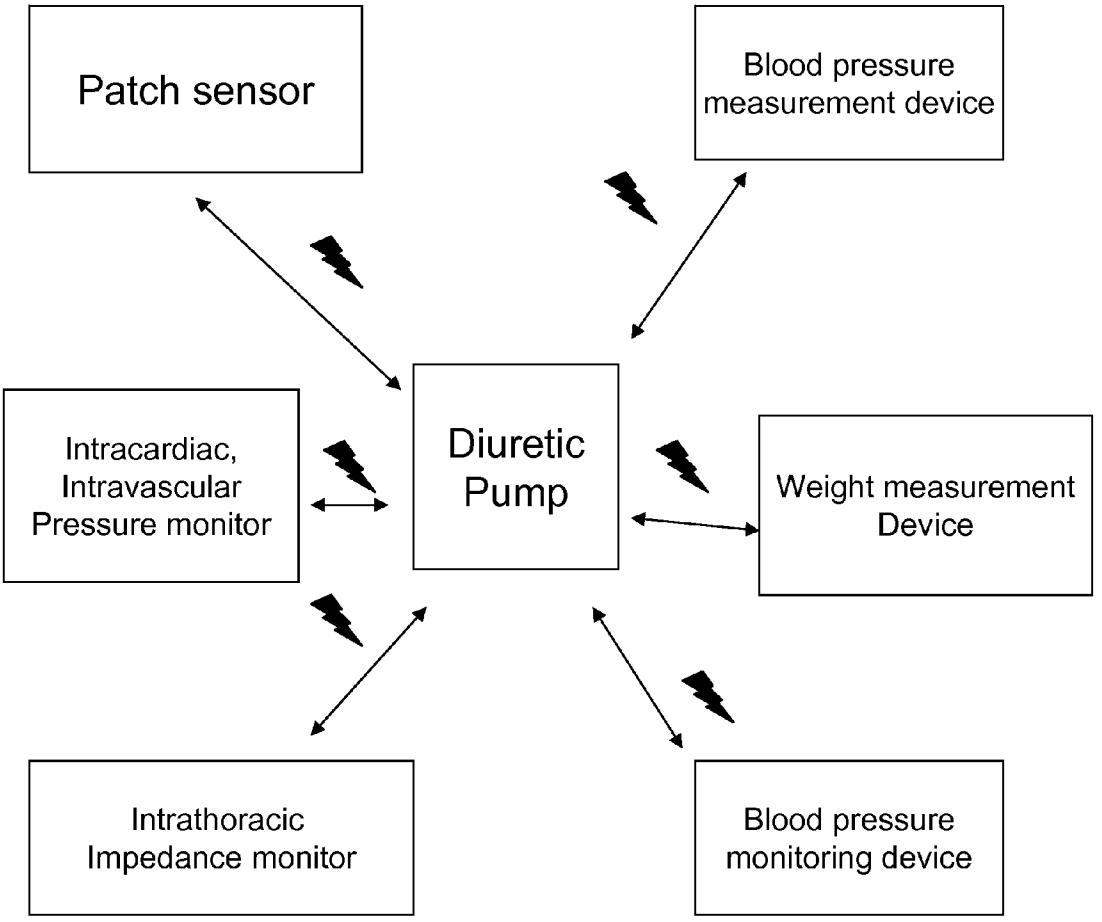

Patch sensor
Blood pressure measurement device
Intracardiac, Intravascular Pressure monitor
Diuretic Pump
Weight measurement Device
Intrathoracic Impedance monitor
Blood pressure monitoring device

Figure 27

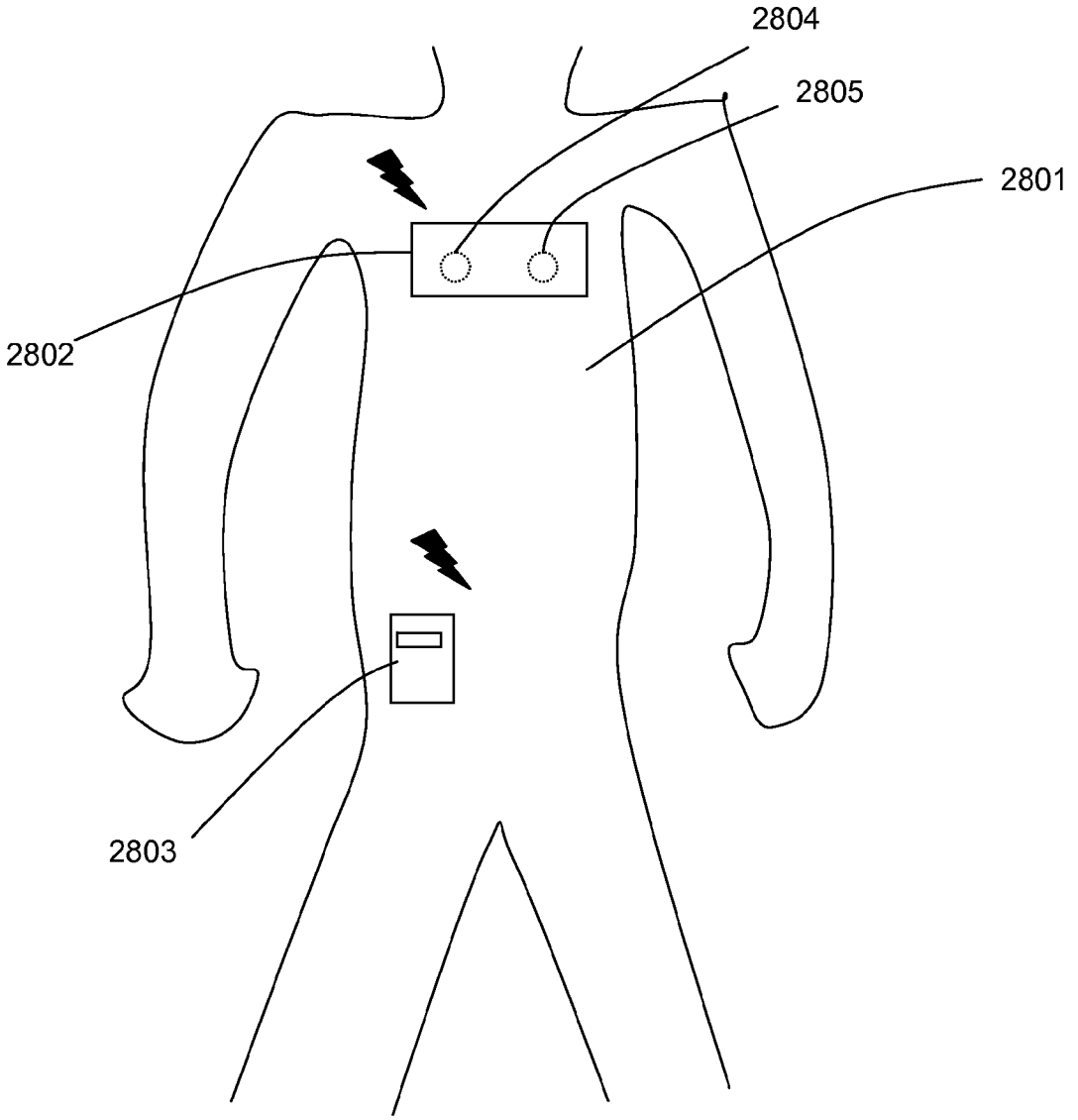


Figure 28

- <furosemide infusion protocol>

- If measured intracardiac pressure is above the target intracardiac pressure, increase basal rate by 0.3mg multiplied by multiples of 1 mmHg of the difference between target intracardiac pressure and measured intracardiac pressure per hour for 8 hours.
- If measured intracardiac pressure is below target intracardiac pressure, decrease basal rate by 0.3mg multiplied by multiples of 1 mmHg of the difference between target intracardiac pressure and measured intracardiac pressure per hour for 8 hours.
- If measured intracardiac pressure is more than 5 mmHg below target intracardiac pressure, hold furosemide infusion.

Figure 29

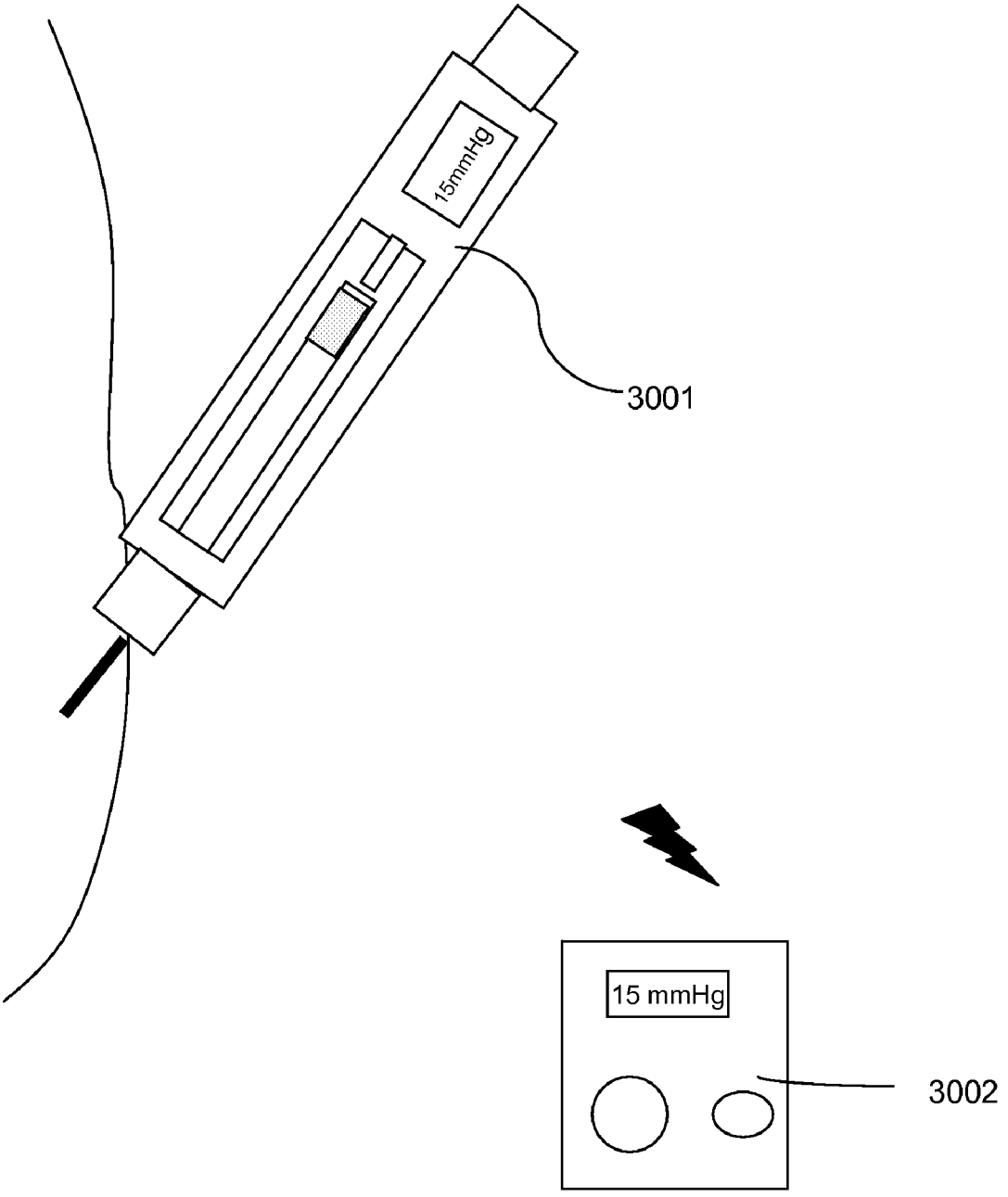


Figure 30

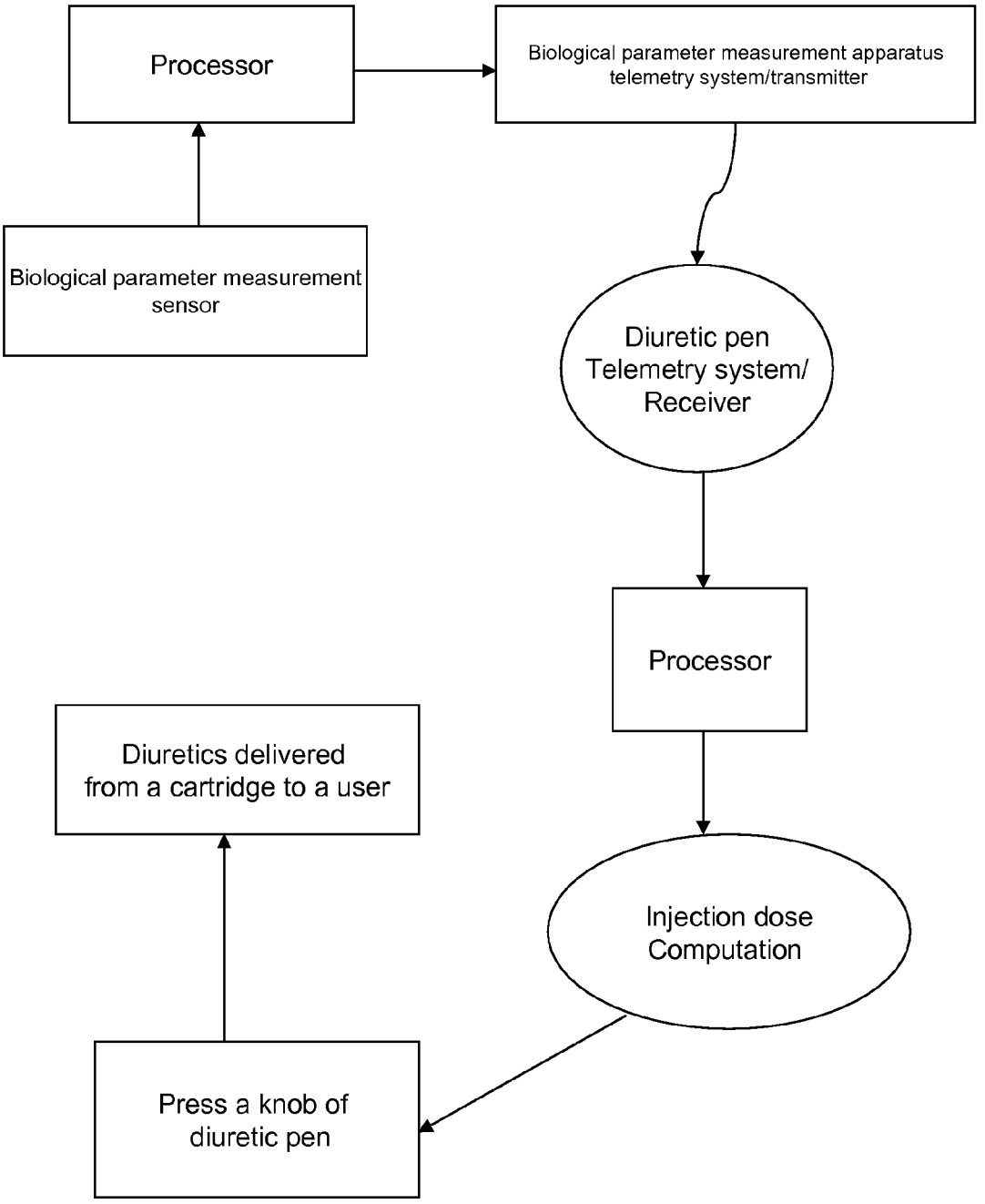

Processor
Biological parameter measurement apparatus telemetry system/transmitter
Biological parameter measurement sensor
Diuretic pen Telemetry system/ Receiver
Processor
Diuretics delivered from a cartridge to a user
Injection dose Computation
Press a knob of diuretic pen

Figure 31

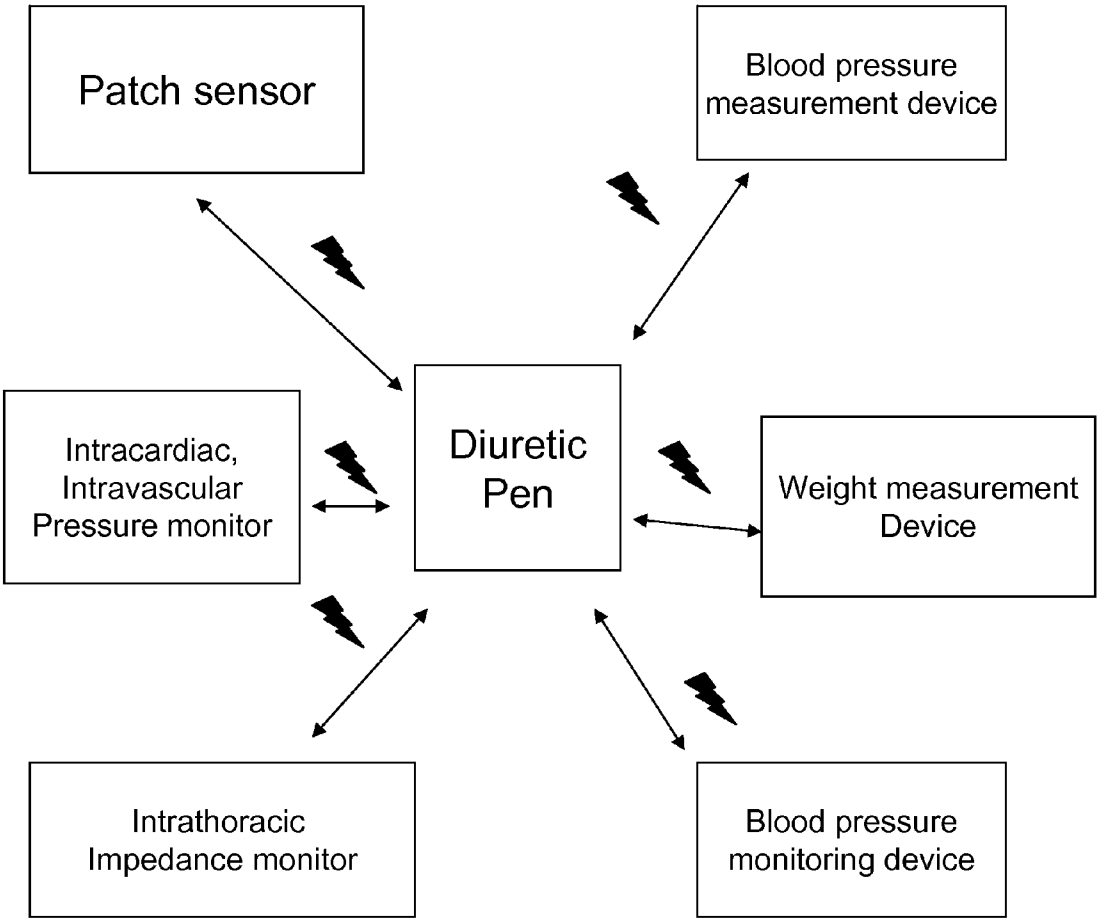

Patch sensor
Blood pressure measurement device
Intracardiac, Intravascular Pressure monitor
Diuretic Pen
Weight measurement Device
Intrathoracic Impedance monitor
Blood pressure monitoring device

Figure 32

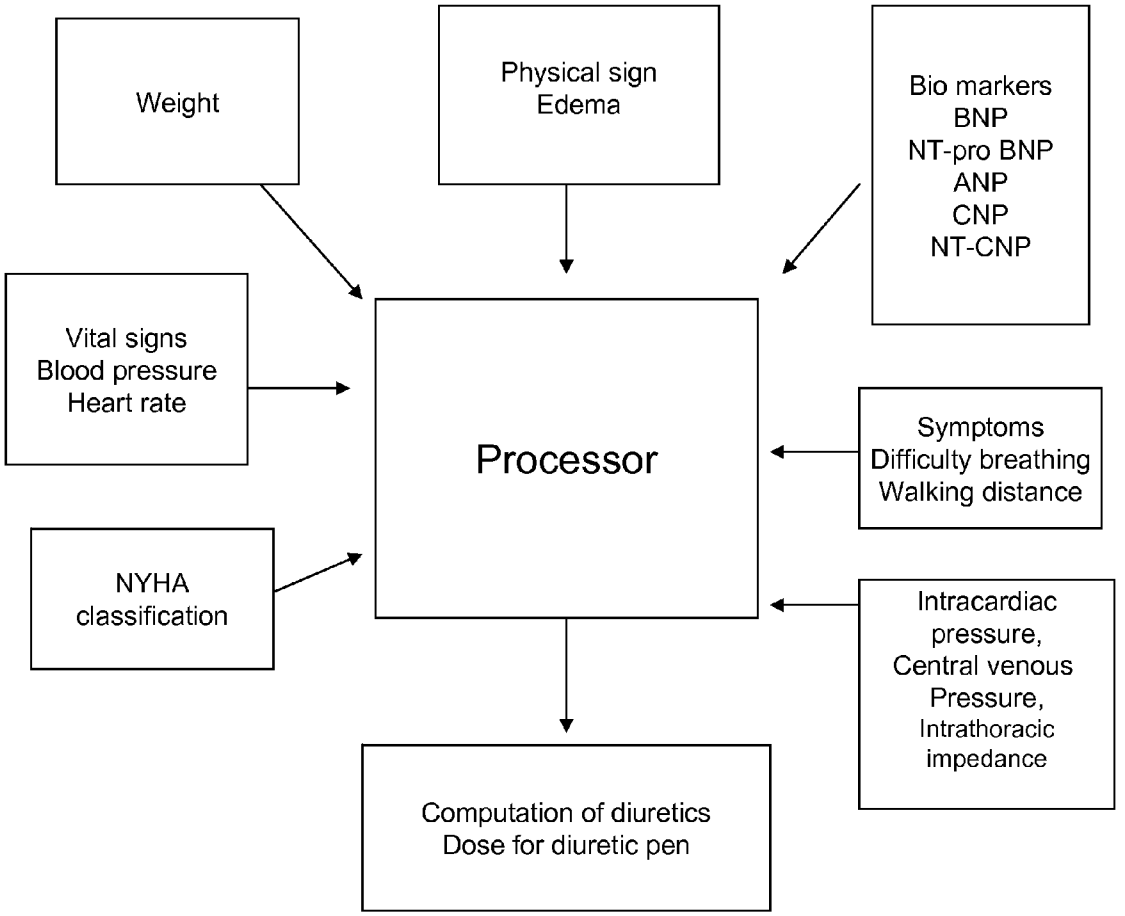

Weight
Physical sign
Edema
Bio markers
BNP
NT-pro BNP
ANP
CNP
NT-CNP
Vital signs
Blood pressure
Heart rate
Processor
Symptoms
Difficulty breathing
Walking distance
NYHA
classification
Intracardiac
pressure,
Central venous
Pressure,
Intrathoracic
impedance
Computation of diuretics
Dose for diuretic pen

Figure 33

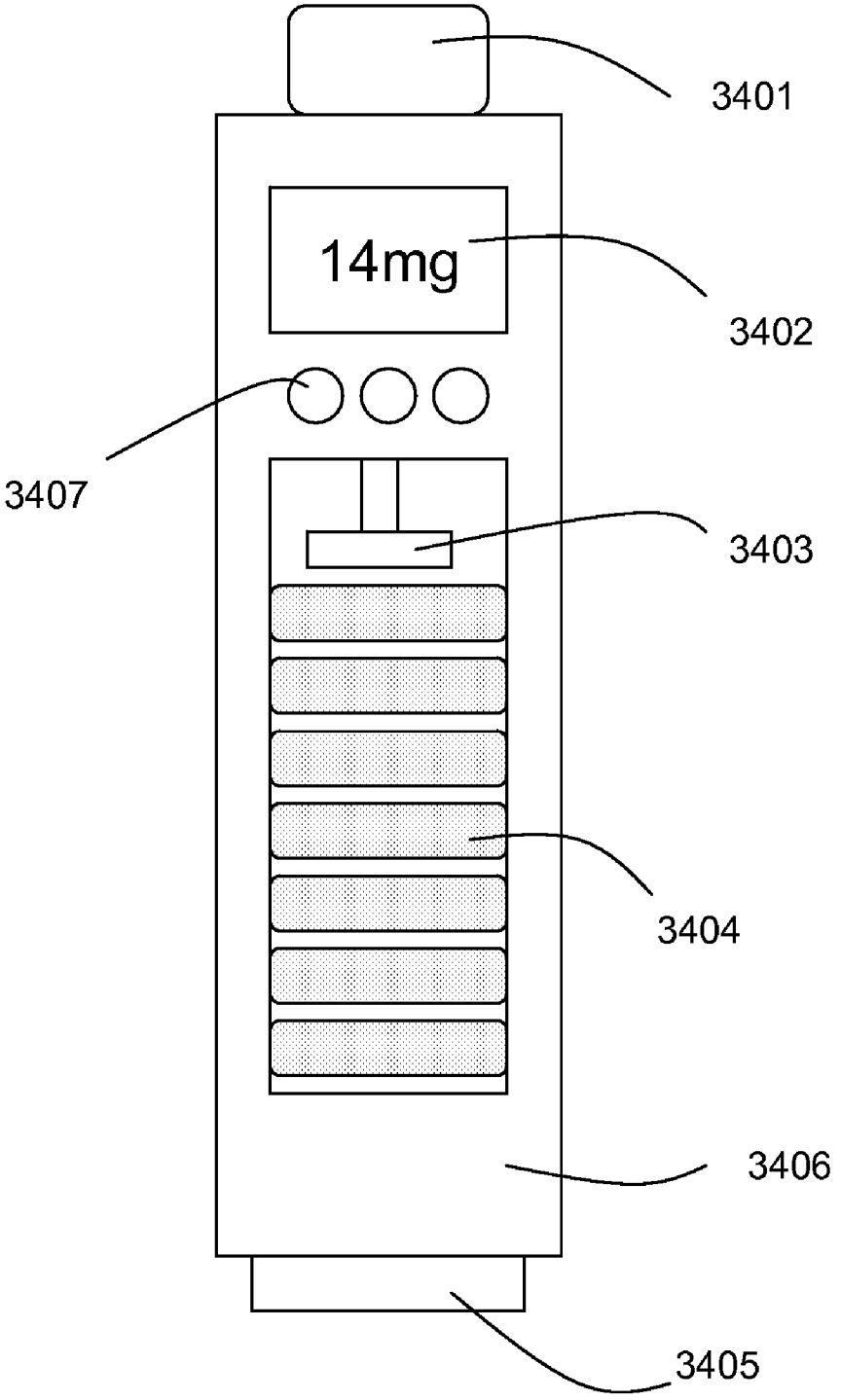


Figure 34

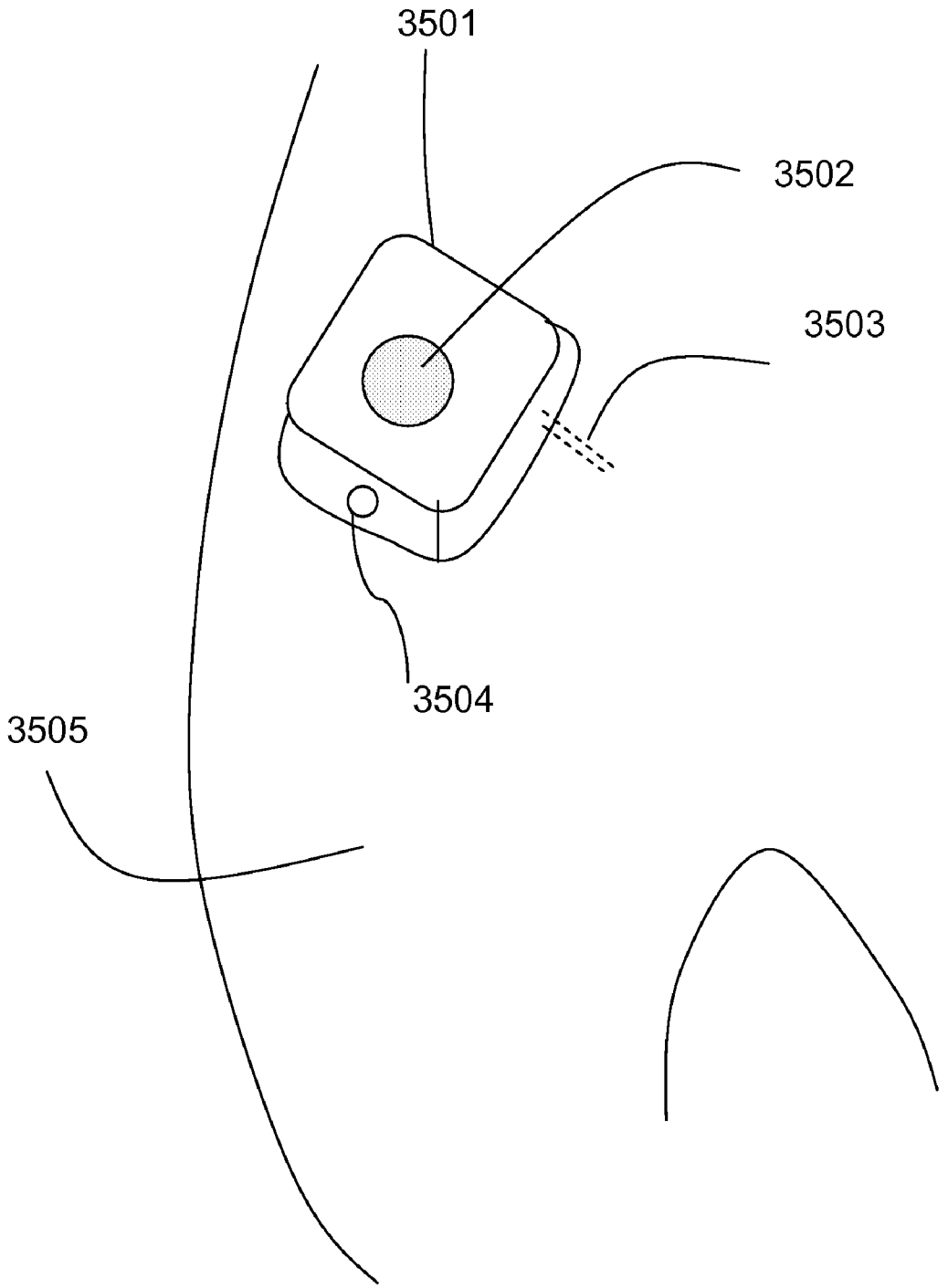


Figure 35

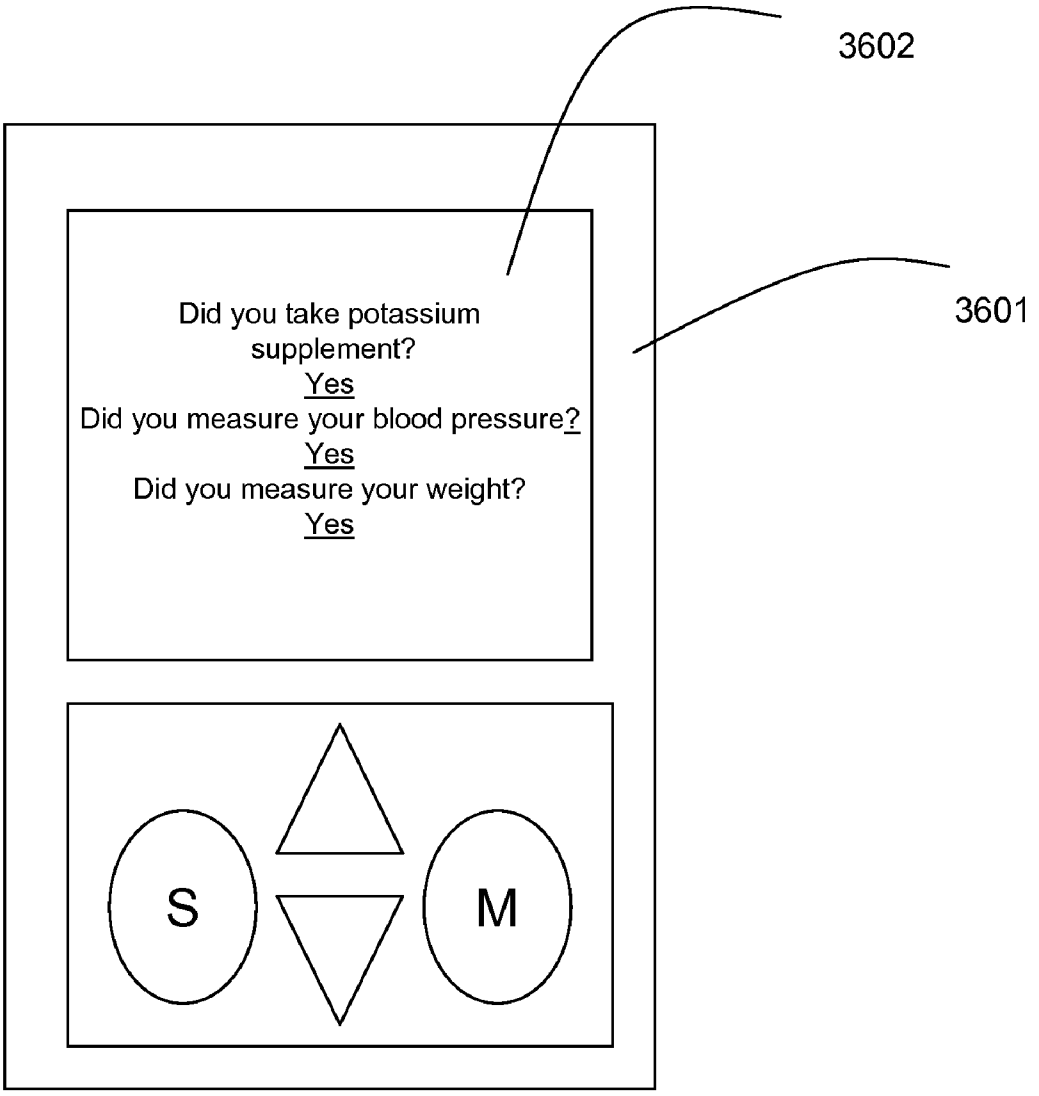

3602
3601
Did you take potassium supplement?
Yes
Did you measure your blood pressure?
Yes
Did you measure your weight?
Yes
S
M

Figure 36

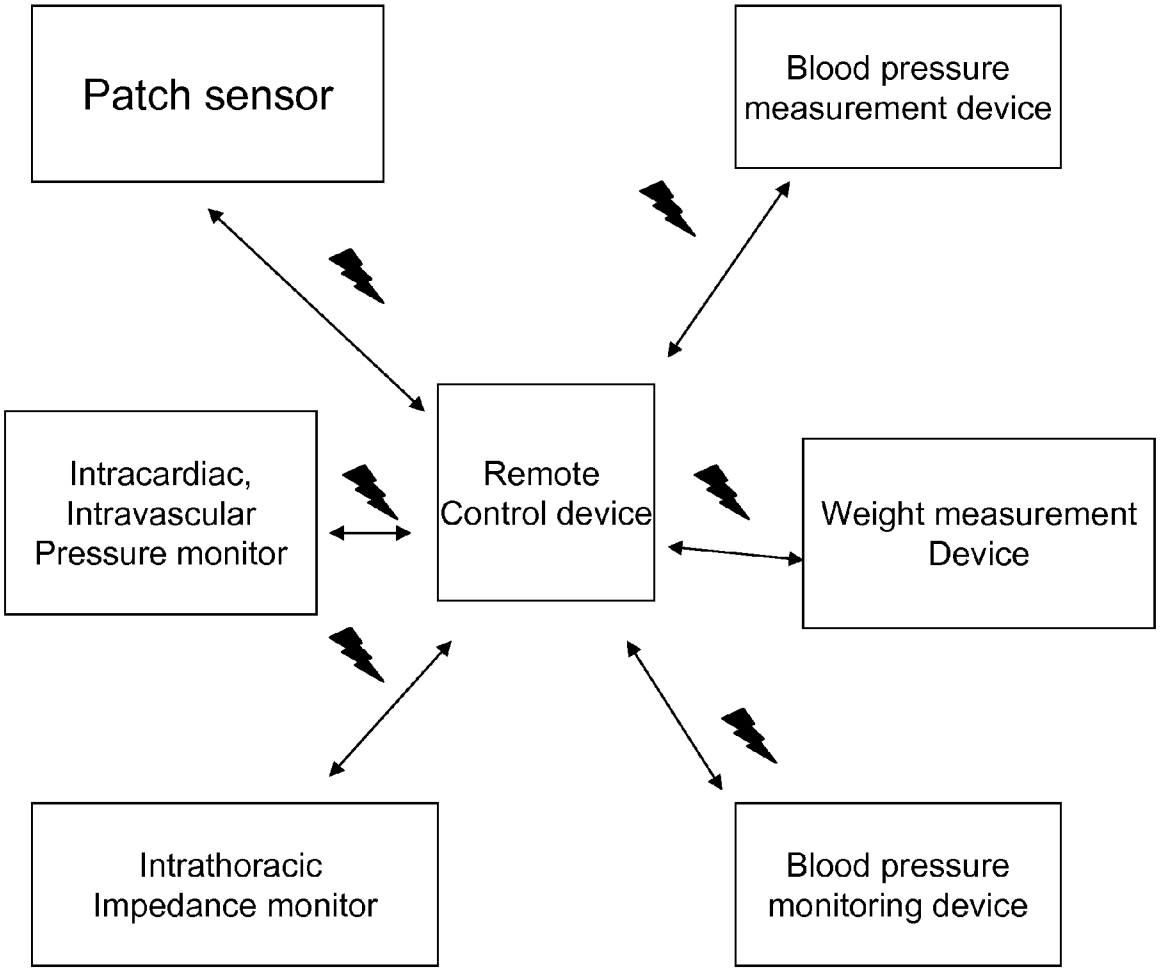

Patch sensor
Blood pressure measurement device
Intracardiac, Intravascular Pressure monitor
Remote Control device
Weight measurement Device
Intrathoracic Impedance monitor
Blood pressure monitoring device

Figure 37

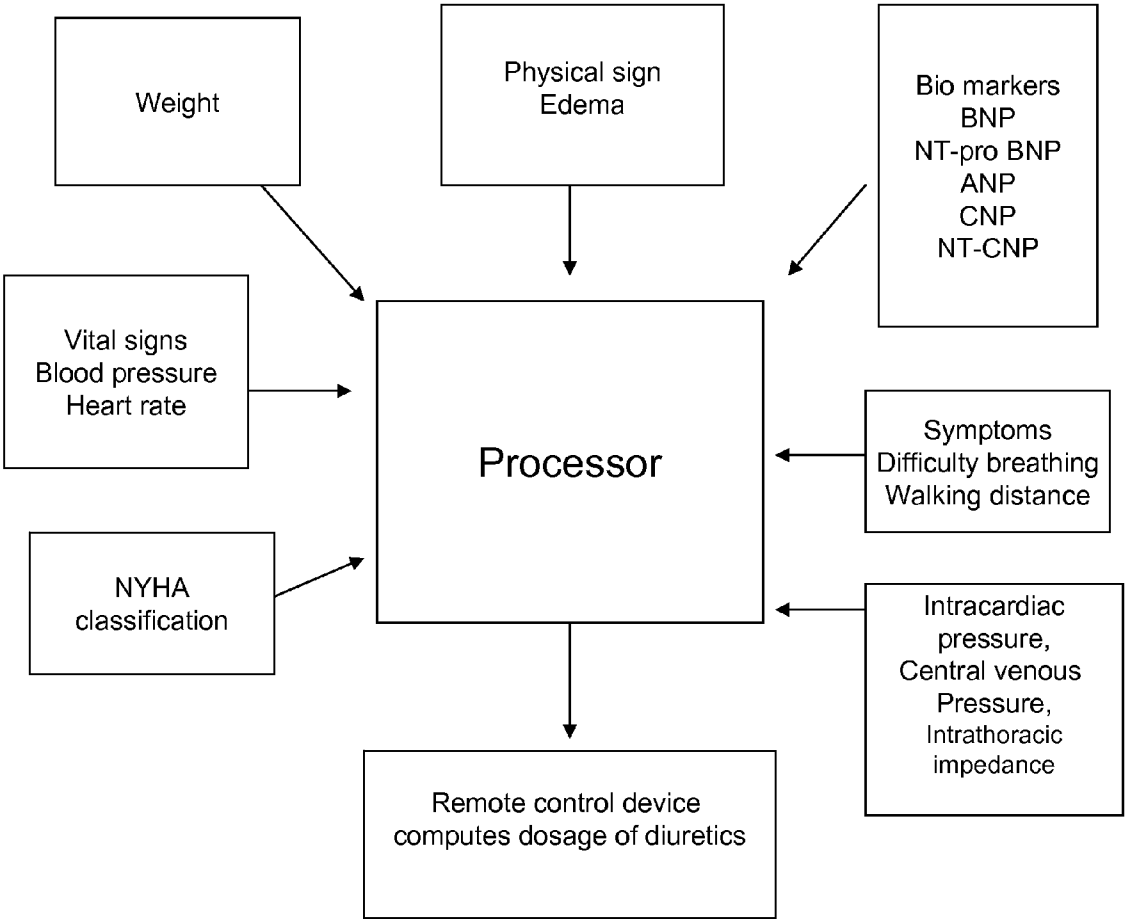

Weight
Physical sign
Edema
Bio markers
BNP
NT-pro BNP
ANP
CNP
NT-CNP
Vital signs
Blood pressure
Heart rate
Processor
Symptoms
Difficulty breathing
Walking distance
NYHA
classification
Intracardiac
pressure,
Central venous
Pressure,
Intrathoracic
impedance
Remote control device
computes dosage of diuretics

Figure 38

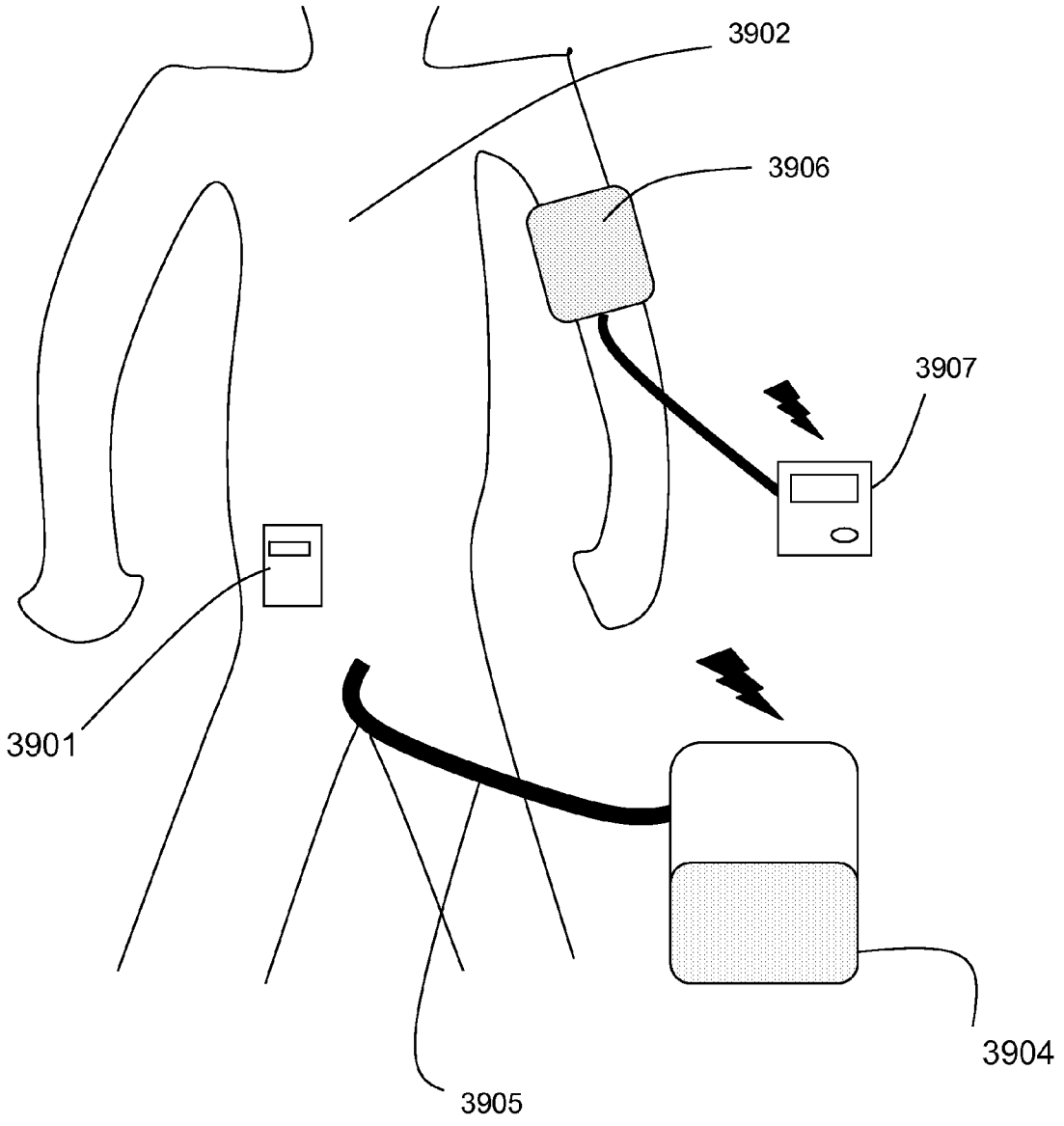


Figure 39

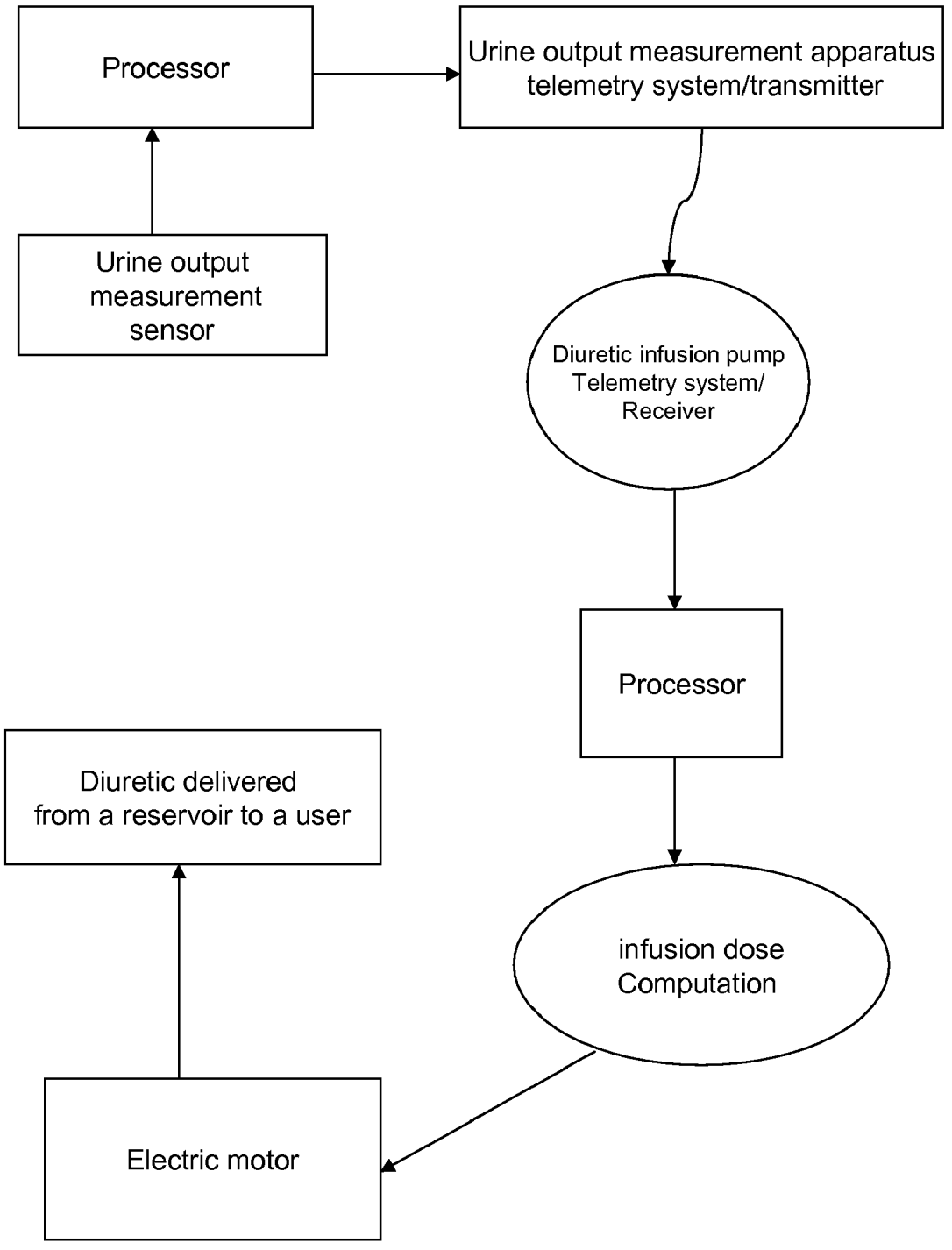

Processor
Urine output measurement apparatus telemetry system/transmitter
Urine output measurement sensor
Diuretic infusion pump Telemetry system/ Receiver
Processor
Diuretic delivered from a reservoir to a user
infusion dose Computation
Electric motor

Figure 40

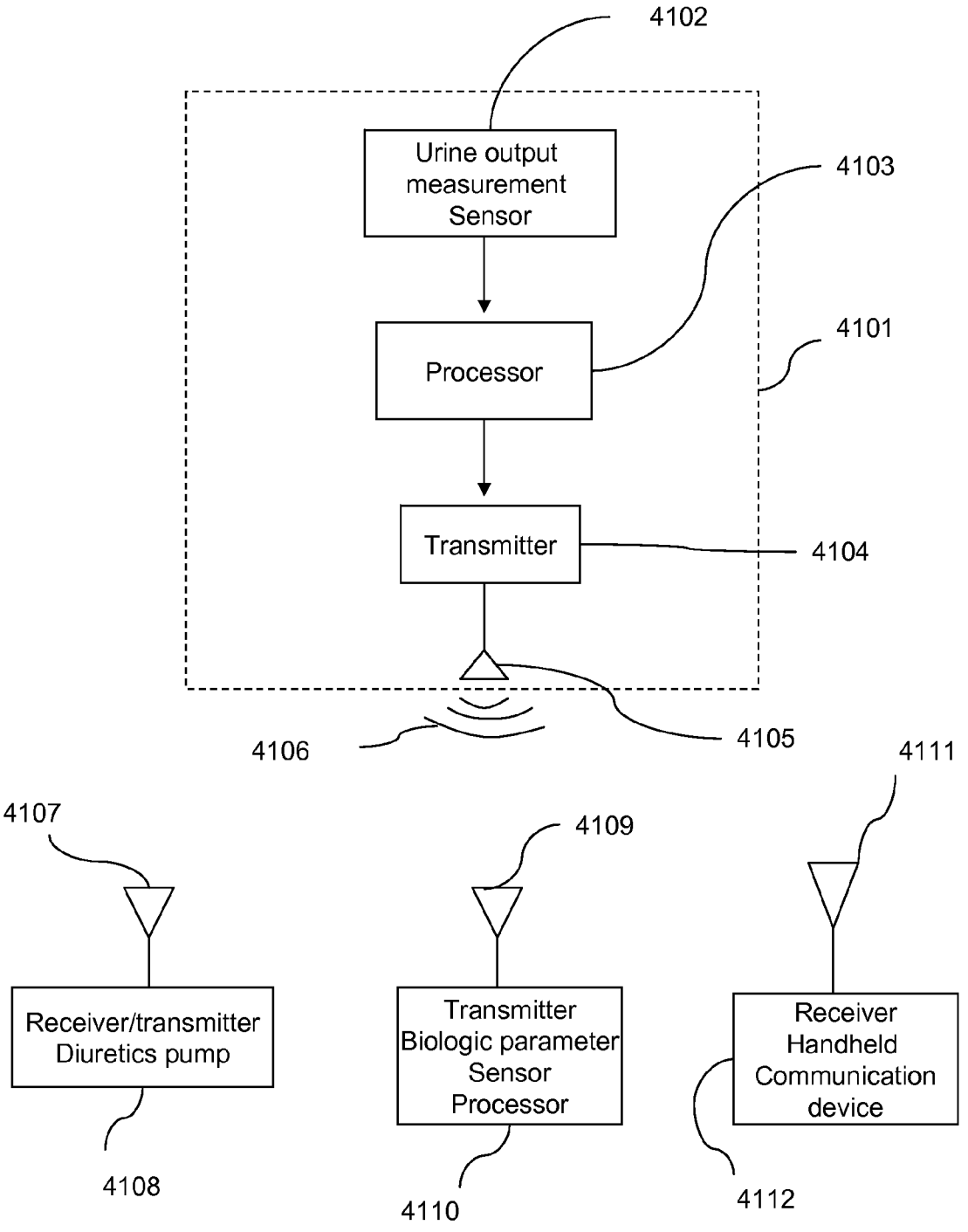

4102
Urine output measurement Sensor
4103
Processor
4101
Transmitter
4104
4106
4105
4111
4107
4109
Receiver/transmitter Diuretics pump
Transmitter Biologic parameter Sensor Processor
Receiver Handheld Communication device
4108
4110
4112

Figure 41

<Furosemide infusion rate protocol>

If urine output is less than 10ml per hour -
infuse basal rate at 10mg per hour
provide bolus infusion of 40mg
If urine output is between 11ml per hour and 20ml per hour -
infuse basal rate at 8ml per hour
provide bolus infusion of 20mg
If urine output is between 21ml per hour and 30ml per hour -
infuse basal rate at 6 ml per hour
If urine output is between 31ml per hour and 60 ml per hour -
infuse basal rate at 4 ml per hour
If urine output is between 61 ml per hour and 80 ml per hour-
infuse basal rate at 2 ml per hour
If urine output is between 81 ml per hour and 100 ml per hour-
discontinue basal rate
provide bolus infusion at 20mg at 8AM
If urine output is over 100ml per hour--
discontinue both basal rate and bolus infusion

Figure 42

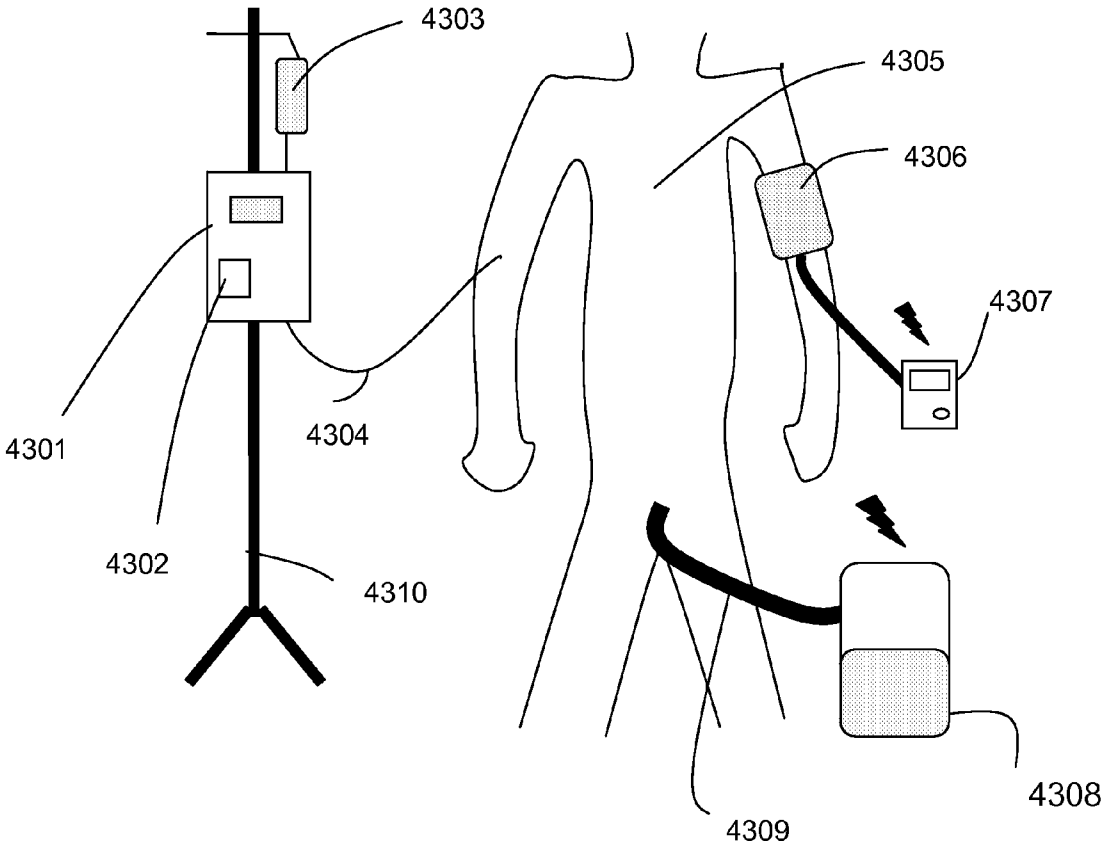


Figure 43

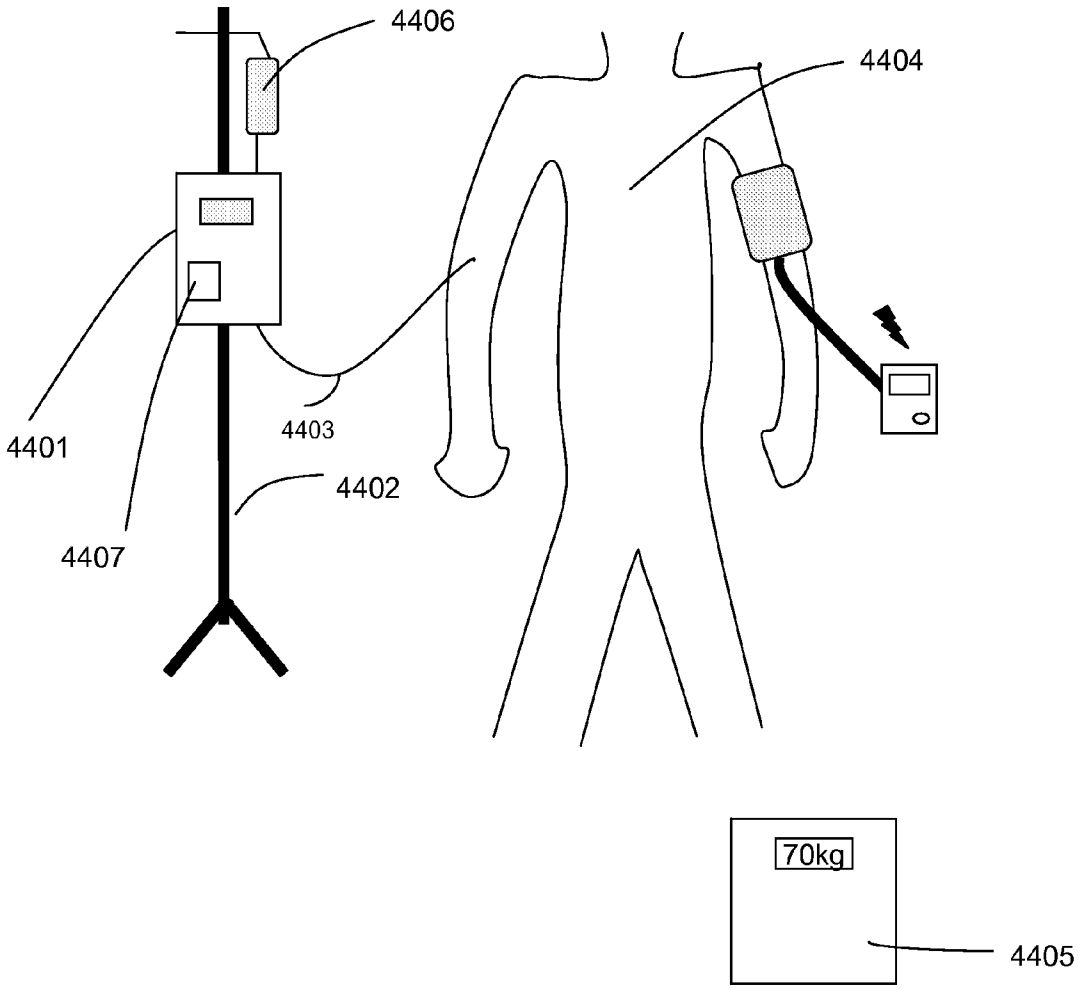


Figure 44

CONTROL OF BODY FLUID CONDITION USING DIURETICS, BASED ON BIOLOGICAL PARAMETERS

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority under 35 U.S.C. §119(e) to (a) U.S. Provisional Patent Application Ser. No. 60/967,025, "Apparatus and method to control body fluid balance," filed Sep. 1, 2007, (b) U.S. Provisional Patent Application Ser. No. 60/979,634, "Controlling body fluid condition using diuretics," filed Oct. 12, 2007, (c) U.S. Provisional Patent Application Ser. No. 60/986,974, "Controlling body fluid condition using diuretics," filed Nov. 9, 2007, and (d) U.S. Provisional Patent Application Ser. No. 60/988,375, "Controlling body fluid condition using diuretics," filed Nov. 15, 2007, and (e) U.S. Provisional Patent Application Ser. No. 61/048,113, "Controlling body fluid condition using diuretics," filed Apr. 25, 2008. The subject matter of all of the foregoing is incorporated herein by reference in its entirety, including any appendices or attachments, for all purposes.

BACKGROUND OF THE INVENTION

[0002] 1. Field of the Invention

[0003] This invention relates to controlling body fluid condition using diuretics.

[0004] 2. Description of the Related Art

[0005] Body fluid imbalance is associated with many diseases such as congestive heart failure, liver cirrhosis and kidney disease. Congestive heart failure in particular is a major cause of death and hospitalization. Despite currently available treatment, mortality and hospitalization from congestive heart failure remains high. Causes of heart failure include coronary artery disease, hypertension, valvular heart disease, myocardial infarction, etc. As pump function of the heart deteriorates, body fluid often increases and may lead to complications such as pulmonary edema.

[0006] When pumping capacity of the heart deteriorates, blood perfusion to the kidneys decreases. This results in retention and accumulation of body fluid because excessive body fluid is not delivered to the kidneys to be excreted. This excessive body fluid often manifests as swelling of the legs. If body fluid continues to expand, a weak heart may be no longer able to handle increased blood volume and finally fails to pump blood forward adequately. Symptoms of congestive heart failure include shortness of breath, fatigue, swelling of legs, orthopnea, paroxysmal nocturnal dyspnea (not being able to breathe suddenly at night). Many people come to the emergency room due to congestive heart failure exacerbation. People do not breathe well when fluid builds up in the lungs.

[0007] Diuretics such as hydrochlorothiazide, furosemide and bumetanide are often used to treat this fluid accumulation by increasing the excretion of body fluid and sodium through the kidneys. However, use of oral diuretics often fails to prevent heart failure exacerbation. This failure of diuretics to prevent heart failure can be explained by several mechanisms. First, the dosage of oral diuretics prescribed by the doctor is often fixed, but the ideal dosage often changes depending on changing body conditions. For example, when people with heart disease eat salty food high in sodium content, their body fluid may increase significantly. We often see people come to the emergency room after they eat excessive amount of salt at a party. In this situation, people will require a higher dose of diuretics in order to excrete excessive body fluid and salt. The required dose of diuretics is affected by the dietary intake of sodium, water and tendency to retain sodium. When body fluid builds up in the digestive system, it may cause intestinal edema (swelling). Bioavailability of diuretics may decrease with intestinal swelling. The body may not be able to absorb diuretics effectively. Patients may need to take higher dose of diuretics when poor bioavailability occurs.

[0008] Second, poor compliance plays a role. People sometimes forget to take medications. This poor compliance could result in heart failure. Third, treatment delay plays a role. When there is a sign of body fluid accumulation such as swelling of legs, many people ignore this early sign of heart failure and wait until their condition gets severe enough to require hospitalization. These explanations are associated with many cases of heart failure.

[0009] Sliding scale diuretic titration of oral diuretics has been attempted for the treatment of congestive heart failure by some heart failure management programs. In sliding scale diuretic titration, patients are instructed to measure body weights and adjust diuretics pill dose according to the instruction given by their physician or nurse. However, conventional diuretic sliding scale titration has several significant drawbacks. First, patients may not understand the sliding scale instruction or may not comply with it. Poor understanding of the instruction may also lead to inappropriate use of medication. Second, conventional instructions may be limited to instructions and sliding scale titration that are simpler than would be desired. In real clinical situations, a more complex diuretic titration may be required to maintain ideal body fluid condition. However, some patients may not be able to follow such complex instructions so instructions may be simplified at the cost of a less effective titration.

[0010] In addition, if the sliding scale diuretic titration changes frequently, some patients may not understand the change of sliding scale diuretic titration and may end up taking the wrong dose of medication. This may lead to serious complications. Taking too much medication may lead to complications such as dehydration, electrolyte imbalance, hypotension, and kidney failure. Conventional sliding scale diuretic titration is also limited to oral diuretics, which may not be as effective as, for example, continuous infusion of diuretics.

[0011] As a result of these possible complications, sliding scale diuretic titration, when attempted, is typically based on a straightforward and simple protocol. More complex protocols generally have not been attempted because there is not a reliable way to carefully monitor and control the dispensing of diuretic or to adjust the dose according to varying conditions. In addition, there are not reliable safety measures to safeguard against the possible inappropriate use of diuretics. Without such controls and safety measures, more complex protocols can have a higher risk of inappropriate use of diuretics and possible adverse effects such as dehydration, electrolytes abnormalities, hypotension, and kidney failure.

[0012] Thus, there is a need for better, and preferably automatic, approaches to control body fluid condition using diuretics.

SUMMARY OF THE INVENTION

[0013] One aspect of the present invention overcomes the limitations of the prior art by automatically infusing diuretic into a human patient. In one approach, the rate of infusion of the diuretic is adjusted based on various biological parameter

(s) other than body weight, although possibly in combination with body weight. The biological parameter(s) can be transmitted wirelessly to a portable diuretic infusion device attached to the patient, for example.

[0014] In one aspect of the invention, a portable diuretic infusion device includes a reservoir, a pump and a controller. The reservoir can hold a diuretic or an antihypertensive drug to be infused into the patient. The pump is connected to the reservoir and is also connectable to the patient, for example using an infusion set. The pump is operated to infuse diuretic or other drug from the reservoir into the patient. The controller controls the pump based on some biological parameter(s), thereby controlling the rate of infusion of the diuretic or other drug.

[0015] In one embodiment, the controller adjusts the rate of infusion based on a measured intrathoracic electrical impedance of the patient. For example, the protocol may be designed to maintain a target intrathoracic electrical impedance for the patient, so that more diuretic is infused when the patient is over the target and less diuretic is infused when the patient is under the target. In another aspect, the patient's intrathoracic electrical impedance can be measured by an implantable device and then wirelessly transmitted to the diuretic infusion device. The controller on the diuretic infusion device receives the intrathoracic electrical impedance information and automatically adjusts the infusion rate.

[0016] In another aspect of the invention, the diuretic infusion device adjusts the diuretic infusion rate based on various biological parameter(s). These biological parameters can include, for example, vital signs, blood pressure, intracardiac pressure, intravascular pressure, biomarker(s), physical sign (s), weight, NYHA classification, and/or symptoms,

[0017] In still a further aspect of the invention, the diuretic infusion system includes a biological parameter measurement apparatus with a biological parameter measurement sensor for measuring a biological parameter of a human patient and a wireless transmitter for wirelessly transmitting measured biological parameter information. The diuretic infusion system also includes a portable diuretic infusion device with a reservoir for holding diuretic, a pump connected to the reservoir and connectable to the human patient, for infusing diuretic from the reservoir into the human patient, a wireless receiver for wirelessly receiving the biological parameter information transmitted by the biological parameter measurement apparatus, and a controller coupled to the wireless receiver, for controlling the pump and rate of infusion of the diuretic based on the received biological parameter information.

[0018] In further embodiments, the diuretic infusion system is remote control operated. The system can include a biological parameter measurement apparatus having a sensor for measuring a biological parameter of a human patient and a wireless transmitter for wirelessly transmitting biological parameter information based on the measured biological parameter. The system can further include a portable diuretic infusion device with a reservoir for holding diuretic, a pump connected to the reservoir and connectable to the patient, a controller for controlling the pump, and a wireless receiver for wirelessly receiving commands. The system can also include a remote control device with a wireless receiver for wirelessly receiving the biological parameter information transmitted, a wireless transmitter for wirelessly transmitting one or more commands to the portable diuretic infusion device, and a controller coupled to the receiver/transmitter for wirelessly controlling the pump and rate of infusion based on weight information. Other embodiments of the diuretic infusion system can include fewer or more components within the biological parameter measurement apparatus, the portable diuretic infusion device, and the remote control device.

[0019] In yet another embodiment, the diuretic infusion system includes a urine output measurement apparatus with a urinary catheter, a urinary drainage apparatus, and a urine output sensor for measuring urine output of a human patient. In some embodiments, the urine output measurement apparatus also includes a wireless transmitter for wirelessly transmitting urine output information based on the measured urine output. The system can also include a portable diuretic infusion device with a reservoir for holding diuretic, a pump connected to the reservoir and connectable to the patient for infusing diuretic from the reservoir into the patient, and a controller that controls the pump, thereby controlling a rate of infusion of the diuretic based on received urine output information. Where the urine output measurement apparatus is configured for wireless communication, the portable diuretic infusion device can include a wireless receiver for wirelessly receiving the urine output information transmitted from the urine output measurement apparatus. In some embodiments, the infusion system further includes a remote control device with a wireless receiver for wirelessly receiving the urine output information transmitted from the urine output measurement apparatus, and a wireless transmitter for wirelessly transmitting one or more command to the portable diuretic infusion device. The remote control device can also include a controller coupled to the wireless receiver and transmitter for wirelessly controlling the pump and rate of infusion of the diuretic based on the received urine output information

[0020] Different protocols can be implemented using these devices and systems. For example, the infusion rate can include both basal and bolus components. Diuretic infusion can be supplemented and/or replaced by other delivery mechanisms, such as oral diuretics. Fairly complex protocols can be implemented, since the protocol is more automated and depends much less on the patient implementing the protocol. For example, infusion rate can vary by time of day, thus reducing urination at nighttime. Prospective infusion can also be implemented, for example if heavy salt intake is expected. The infusion rate can also be adjusted based on feedback other than just weight.

[0021] These approaches allow the dose of diuretics to be controlled much more carefully than by patient instructions alone, resulting in many possible advantages. For example, early detection and early treatment of various body fluid related diseases may be possible. This can reduce hospitalizations and death from congestive heart failure, pulmonary edema and fluid overload. In addition, patients can now have continuous infusion of diuretics by using a portable, ambulatory infusion pump. Continuous infusion of diuretics may be more effective than bolus use of diuretics. These approaches may also be more effective in maintaining target weight and/or dry weight, compared with using oral diuretics. The automated approach is also easier for patients and allows the implementation of more complex protocols, while also reducing the risk of over- or under-treatment. The automated devices can also record diuretic use (and also body weight), thus providing a reliable medical history. This information can be sent over the internet to the healthcare providers or others, for analysis or remote monitoring of patients.

[0022] Other aspects of the invention include methods corresponding to the devices and systems described above, and protocols for use with same.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] The invention has other advantages and features which will be more readily apparent from the following detailed description of the invention and the appended claims, when taken in conjunction with the accompanying drawings, in which:

[0024] FIGS. **1** depicts a diuretic infusion system.

[0025] FIG. **2** depicts a more detailed view of a diuretic infusion device.

[0026] FIG. **3** is a block diagram of a diuretic pump.

[0027] FIGS. **4** and **5** are a mechanical depiction of a diuretic pump.

[0028] FIG. **6** is a mechanical depiction of a diuretic pump with two reservoirs.

[0029] FIG. **7** shows data flow for computation of diuretic infusion rate.

[0030] FIG. **8** illustrates infusion of diuretic into the body.

[0031] FIG. **9** is a mechanical depiction of another diuretic pump.

[0032] FIGS. **10-11** further illustrate operation of further embodiments for diuretic dispensing.

[0033] FIG. **12** illustrates further embodiments for a diuretic infusion system.

[0034] FIG. **13** illustrates another diuretic infusion system.

[0035] FIGS. **14** and **15** show protocols for use with the diuretic infusion system of FIG. **13**.

[0036] FIG. **16** illustrates another diuretic infusion system including an electric scale.

[0037] FIGS. **17-20** show protocols for use with the diuretic infusion system of FIG. **16**.

[0038] FIG. **21-22** illustrates another diuretic infusion system including an implantable device.

[0039] FIG. **23** shows a protocol for use with the diuretic infusion system of FIG. **21**.

[0040] FIG. **24** illustrates another diuretic infusion system including a remote control device.

[0041] FIG. **25** illustrates a more detailed view of the diuretic infusion device and the remote control device.

[0042] FIG. **26** illustrates the operation of a closed loop drug infusion system for a diuretic infusion pump system.

[0043] FIG. **27** illustrates wireless communication of a diuretic infusion pump system with biological parameter measurement apparatuses.

[0044] FIG. **28** a diuretic infusion device with a patch sensor system.

[0045] FIG. **29** illustrate additional drug-infusion protocols

[0046] FIG. **30** illustrates a wirelessly-operated diuretic injecting pen-type device.

[0047] FIG. **31** illustrates the components of the diuretic injecting pen-type device.

[0048] FIG. **32** illustrates examples of the biological parameters measured by devices or sensor communicatively coupled to the diuretic injecting pen-type device.

[0049] FIG. **33** illustrates a data flow for computation of the diuretics dose for the diuretic injecting pen-type device.

[0050] FIG. **34** illustrates another type of drug-dispensing pen-type apparatus for dispensing pills.

[0051] FIG. **35** illustrates a disposable external diuretic infusion pump.

[0052] FIG. **36** shows another embodiment of a diuretic infusion pump with a feedback mechanism.

[0053] FIGS. **37** and **38** show various biological parameters and factors that may be used with various embodiments, such as that of FIG. **25**.

[0054] FIG. **39** illustrates a diuretic infusion system including a urine output measurement apparatus.

[0055] FIG. **40** illustrates the operation of the system of FIG. **39**.

[0056] FIG. **41** illustrates a wirelessly operated diuretic infusion system with urine output measurement apparatus.

[0057] FIG. **42** illustrates an example of a furosemide infusion protocol based on urine output.

[0058] FIG. **43** illustrates an ambulatory diuretic infusion pump with urine output measurement apparatus.

[0059] FIG. **44** illustrates another ambulatory diuretic infusion pump.

[0060] The figures depict embodiments of the present invention for purposes of illustration only. One skilled in the art will readily recognize from the following discussion that alternative embodiments of the structures and methods illustrated herein may be employed without departing from the principles of the invention described herein.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0061] FIG. **1** depicts a diuretic infusion system according to the invention. Diuretic infusion device **101** is located on the patient's body **102**. Weight sensor **103** measures the patient's body weight. In one embodiment, the weight sensor **103** is an electric scale. A user inputs measured body weight into the diuretic infusion device **101**. The diuretic infusion device **101** delivers diuretic to the human body **102**. The dose of the diuretic is determined based on the measured body weight.

[0062] Various diuretics may be used with the diuretics infusion device. Examples include hydrochlorothiazide, chlorothiazide, chlorthalidone, metolazone, furosemide, bumetanide, ethacrynic acid, torsemide, spironolactone, indapamide and eplerenone. Vasopressin receptor antagonist may also be used. Examples include conivaptan, tolvaptan. Brain natriuretic peptide may also be used. One example is nesiritide.

[0063] FIG. **2** is a close-up of the diuretic infusion device **101** of FIG. **1**. In this example, the diuretic infusion device **101** is a diuretic pump **201** that is attached to the body **207**. A preferred location is around the body waist and abdomen. The size of the diuretic infusion pump can vary. In one implementation, the diuretic pump is 2.2×3.7×1 inches. This diuretic infusion pump **201** includes a wireless communications chip, processing module, batteries and processor (see FIG. **3** for further detail). The diuretic infusion pump **201** may not include the wireless communications chip in alternative embodiments.

[0064] An external keypad to allow the user to program an onboard processor. The onboard processor controls the rate of diuretic infusion. Various buttons **202**, **203** are used for various functions, such as programming the diuretics pump and adjusting the diuretic infusion rate. Information such as rate of diuretic infusion, name of diuretics in use, weight information, and optimal or target weight, can be displayed on the screen **204**. This screen also shows signals that indicate malfunction of the device and other signals such as time to change a diuretics cartridge or time to change a battery.

[0065] This diuretic infusion pump **201** includes a disposable reservoir or a disposable cartridge for the diuretic. The prefilled cartridge containing diuretics is replaced when empty. In alternative embodiments, the reservoir and/or cartridge may not be disposable. Instead, the reservoir may be refilled when empty.

[0066] A disposable infusion set for the diuretic infusion pump may include a cannula **209**, an adhesive pad **205**, a needle **208** and tubing system **206** (that delivers the diuretic reservoir to a user). The user inserts the needle **208** together with the cannula **209** under the skin. The needle **208** may be removed, leaving the cannula **209** under the skin. Preferably, the tip of the cannula **209** is located at the subcutaneous tissue. Alternatively, the tip of cannula **209** may be located in the abdominal cavity, intramuscular space, intravascular space or peritoneal cavity. The cannula **209** may be made with biocompatible materials such as polyethylene.

[0067] FIG. **3** is a block diagram of a diuretic pump. Processor **301** (the controller) is contained in the interior of the housing **316** of the diuretic infusion pump. The housing **316** may be made of plastic or steel, for example. Processor **301** runs software programs and controls components of the diuretics infusion pump. The Freescale Dragonball microprocessor is one example of a processor that may be used. The Motorola 6805 is another example. The Freescale MC9S08RX32A is another example. The MC9S08RX32A includes an RF integrated circuit and microcontrollers (MCU). Other processors that are used in insulin pumps may also be used.

[0068] The processor **301** is in electrical communication with an electric motor and pump **313**. The processor controls the electric motor **313** according to its program. The processor also controls a screen **304**, an audible alarm **307**, vibratory alarm **308** and telemetry system. Weight information that is transmitted from the weight measurement apparatus is received by the telemetry system of the diuretic infusion pump. It then enters the processor **301**. Alternately, weight information may be input into the diuretic infusion pump manually by a user, for example from a keypad or a remote controller.

[0069] In this example, flash memory **314** and SRAM **315** are used for memory storage. This memory may store information such as pump settings, a historical log of weight, malfunctions of the pump, infusion rate, a historical log of infusion rate, medication, etc. In one design, the RAM has 100 kilobytes, ROM has 4 megabytes and flash memory has 4 megabytes memory. Alternate memory media include RAM, ROM, EPROM, DRAM, hard-drives and other types of flash memory.

[0070] The user may program the processor **301** using a keypad (or other user interface) on the diuretic infusion pump. In alternative embodiments, a user may use a remote controller or a computer station to program the processor **301**.

[0071] Information and commands from other computers, portables devices such as PDAs (personal digital assistant), handheld computers, portable phones, remote controllers and the internet may be received through receiver **303**. Examples of wireless technologies include radio frequency (RF), infrared (IR) and optical. Specific technologies include Bluetooth, DECT, ZigBee, NFC, GSM, UWB, UMTS, DAB, CDMA, WiFi and WIMAX. Wired communications ports can include Universal Serial Bus (USB) ports and/or RS-232 ports, as well as other technologies.

[0072] The diuretic infusion pump displays on its screen whether new weight information, command, or alerts are received. The diuretic infusion pump, weight measurement apparatus, corresponding computer systems and/or remote controller may be assigned a unique identifier and/or password to provide privacy for its users.

[0073] In FIG. **3**, a keypad **309** is located on the housing **316**. A touch screen input device may also be used. The keypad **309** shown in FIG. **2** includes buttons **203**, **202** to provide input to the processor **301**.

[0074] Various other inputs, such as various types of sensors, may also be included in the diuretic infusion pump (or communicate to the diuretic pump from other parts of the system). For example, motion detection sensor **312** may be used to detect the motion of a gear in the drive mechanism for the pump. Cartridge sensor or reservoir sensor **311** may be used to detect the amount of diuretic left within a cartridge or reservoir, and to notify a user when a new cartridge is required or a reservoir requires refilling.

[0075] In one embodiment, LCD is used as a screen. Feedback from the weight measurement apparatus, a computer, a remote control device as well as diuretic infusion pump status and programming changes may be displayed on a LCD screen. Time, name of drug, dose of drug used during a particular period of time, reservoir or cartridge usage and history may also be displayed.

[0076] A speaker can be used to send audio feedback. A user may choose to use a vibratory alarm instead of audible alarm. For example, if measured body weight is too low or too high, an audible or vibratory alarm may warn a user. If measured body weight is lower than a set value, a certain instruction such as "Drink more water and eat more because you may be dehydrated" may be shown on the screen or played through the speaker. When measured body weight is higher than a set value, certain instructions may be expressed, such as "Calibrate your weight measurement scale" or "Call your doctor if you feel shortness of breath." Alarms may also be activated for pump malfunction, low battery, dead battery, occlusion of infusion set, near-empty cartridge (or reservoir), pump delivery error, if bolus is changed, if mode is changed, if pump is not primed, if infusion exceeds maximum limits, etc.

[0077] The diuretic infusion pump preferably uses a AAA alkaline battery. More than one AAA alkaline batteries may be used. Alternatively, different types of batteries may be used such as nickel cadmium battery, nickel metal hydride battery, lithium ion battery, carbon battery, lithium battery and 3.6V lithium battery. The battery may be included inside the housing **316** of the diuretic infusion pump.

[0078] Not all embodiments require all of the components described above.

[0079] FIG. **4-5** are mechanical depictions of a diuretic pump. The diuretic infusion pump contains a processor **401**. The processor is electrically connected or otherwise communicatively coupled to an electric motor **402**, for example a DC motor with gear-reducer. The processor **401** controls the electric motor **402** according to its programming. The electric motor **402** is connected to a peristaltic pump **404**. The peristaltic pump **404** has a rotor inside. A flexible tube inside the peristaltic pump **404** is connected with a tube **405** and **408**. The flexible tube is in contact with the rollers. When the rotor turns, one or more rollers squeeze and release the flexible tube to deliver drug from a reservoir **403** to a user via the infusion tube **408**. In order to detect if the diuretics solution is depleted and needs to be replaced or refilled, a sensor **409** can be used.

FIG. **5** is a simplified mechanical depiction of a syringe pump system. The pump housing **515** contains a syringe **516**. The syringe **516** contains diuretics. The processor **510** is electrically connected or otherwise communicatively coupled to an electric motor **511**. The processor **510** controls the electric motor **511** according to its programming. The motor **511** rotates a motor gear which moves a screw **513** axially. A screw **513** is configured to move axially to push a plunger **514** inside a syringe and push diuretics out of a syringe **516** or a reservoir through an infusion tube **518** and a cannula **519**. The plunger mechanism transfers the diuretics solution from a diuretics cartridge or reservoir through an outlet of the housing to the patient via tubing system **405**, **408** and the infusion set. Technologies used in insulin pumps may be used also for diuretic pumps.

[0080] In alternative embodiments, more than one type of drug may be used in the diuretic infusion pump. A processor may be coupled with more than one program, software, protocols and/or parameters that are tailored according to the specific drug that is used. The diuretic infusion pump may automatically recognize the inserted drug. Drug reservoir or cartridge may have a unique identification code. One example of a drug name recognition method is to decode the bar code of the drug name, which is attached on the reservoir or cartridge. Alternatively, the name of the inserted drug may be manually put into the diuretic infusion pump using the keypad which can select alphabets on the screen.

[0081] Examples of medications that may be contained in the reservoir **807** or cartridge include hydrochlorothiazide, chlorothiazide, chlorthalidone, metolazone, furosemide, bumetanide, ethacrynic acid, torsemide, spironolactone, eplerenone, vasopressin receptor antagonists, conivaptan, tolvaptan, brain natriuretic peptide, and nesiritide.

[0082] FIG. **6** is a mechanical depiction of a diuretic pump with two reservoirs: in this case a diuretics reservoir **601** and an insulin reservoir **602**. Patients with diabetes may also have congestive heart failure. This device delivers both diuretics and insulin using one ambulatory infusion pump. In embodiments that use two reservoirs, each medication is delivered via tubes **603**, **604** inside an ambulatory infusion pump and leaves the housing of the pump via a tube **609** outside the ambulatory infusion pump. There may be two separate channels within the tube **609** through which each medication is delivered separately. Each medication is delivered to a user through different holes **611**, **612**. In alternative embodiments, a syringe pump system can be used instead of a peristaltic pump **606**. Two syringes can have separate electric motors that control the movement of the plunger of the respective syringes and release of each medication.

[0083] Some medications may not be compatible each other so these medications may need to be delivered through separate channels. More than two medications, channels and holes may be used in alternative embodiments. A processor **610** controls an electric motor **605** and a pump **606** according to its program. More than two electric motors and pumps may be used in alternative embodiments. A separate electric motor and pump may be used to deliver different medications in alternative embodiments.

[0084] FIG. **7** shows possible data flow for computation of the diuretic infusion rate. In preferred embodiments, the processor of the diuretic infusion pump uses weight to compute the diuretics infusion rate. In alternative embodiments, the processor may use various other factors to compute diuretic infusion rate. Examples include physical signs, vital signs, bio markers, symptoms, intracardiac pressure, intravascular pressure, intrathoracic electrical impedance and New York Heart Association (NYHA) classification, as shown in FIG. **7**. For example, if BNP (B-type natriuretic peptide) is elevated, this may indicate increased body fluid volume and congestive heart failure. If BNP is above 100 pg/ml, the diuretic infusion pump may increase (or adjust) the infusion rate until the levels returns to normal.

[0085] ANP (Atrial natriuretic peptide), CNP (C-type natriuretic peptides), NT-pro BNP, ventricular natriuretic peptides and other bio markers that indicate volume overload and heart failure may also be used to compute the diuretic infusion rate.

[0086] Physical signs of volume overload, such as ankle swelling, leg swelling, arm swelling, and abdominal distension can also be used. For example, a user may use a scale of one to four in body swelling as one being no swelling, four being severe swelling, three being moderate swelling, two being mild swelling. The diuretic infusion pump might adjust the infusion rate to return body swelling to the zero score condition of no swelling. The diuretic infusion pump may also adjust the infusion rate based on blood pressure.

[0087] The diuretic infusion pump may also adjust the infusion rate by using symptom scores such as a shortness of breath scale (one to four, one-no difficulty breathing, two-mild difficulty, three-moderate difficulty, four-severe difficulty) or a walking scale (one- can walk without limitations, two-can walk less than one block, three-can barely walk even inside home).

[0088] The diuretic infusion pump may use the NYHA (New York Heart Association) classification to compute the diuretics infusion rate. The NYHA classification is widely used to assess the stage of heart failure. The diuretic infusion pump may adjust diuretics infusion rate to improve patient condition from class II, III or IV to class I.

[0089] Combinations of variables may be used for the computation of diuretic infusion rate and/or dose. These variable (s) may be used for the computation of the dose and/or infusion of other drugs. Some examples of these drugs include, but not limited to, anti-hypertensive drug, inotropic agents, and anti-arrhythmic drugs.

[0090] Adjusting the diuretic dose according to intracardiac pressure or central vein pressure is another possibility.

[0091] FIG. **8** illustrates infusion of diuretic into the body. In FIG. **2**, diuretic medication is infused into subcutaneous tissue. In alternative embodiments shown in FIG. **8**, diuretic medication may be infused into a peritoneal cavity, an intravascular space (e.g., into a vein) or intramuscularly. The diuretic infusion pump **807** attaches to a tubing system **806**, an adhesive **805** and a needle **803**.

[0092] A plastic tube **801** (a catheter) is attached to a silicone bubble **804** (septum). Tip **808** of the plastic tube may be located into a peritoneal space or a vein (or an artery). A needle **803** is inserted into the silicone bubble. Medication is delivered from the infusion pump **807** through a tubing system **808**, a needle **803** and a plastic tube **801** into a target space of a user. Examples of a target space include a peritoneal space, a vein, an artery and a muscle. A port **802** and silicone bubble **804** may be located in subcutaneous tissue or may be located outside the skin.

[0093] FIG. **9** is a mechanical depiction of yet another diuretic pump. More than two drugs may be infused in alternative embodiments. Two drugs are contained in the separate drug reservoir or cartridge. One example of two drugs that

may be used includes diuretics and insulin. Another example of two drugs that may be infused includes loop diuretics and thiazide diuretics. Other examples of two drugs that may be used includes "loop diuretics and vasopressin receptor antagonist", "thiazide diuretics and vasopressin receptor antagonist", "loop diuretics and potassium sparing diuretics", "thiazide diuretics and potassium sparing diuretics" and "loop diuretics and carbonic anhydrase inhibitor." Using the combination of diuretics with a different site of action may be more effective than using only one type of diuretic. Loop diuretics act on the ascending loop of Henle in the kidney. Thiazide diuretics act on distal convoluted tubule in the kidney. Examples of vasopressin receptor antagonists include conivaptan and tolvaptan.

[0094] FIG. **6** shows an infusion pump with two drug reservoirs **601**, **602** that share one pump **606**. FIG. **9** shows two peristaltic pumps **903**, **904** connecting with two different reservoirs **901**, **902**. A processor **905** is electrically connected with electric motors **911**, **912**. The processor **905** controls these electric motors **911**, **912** and pumps **903**, **904** to deliver medication from each medication reservoir **901**, **902**. The pump **903** is connected with a reservoir **901** and delivers a medication from a reservoir **901** through a tubing system **906**, **908** to a user. The pump **904** is connected with the reservoir **902** and delivers medication from the reservoir **902** through a tubing system **907**, **909** to a user.

[0095] In this example, the tube **908** merges with tube **909**. However, there are different channels within the tube to deliver each medication through different channels to prevent mixture of non-compatible medications. These two medications are delivered through separate openings **910**, **913**. Two medications may be delivered according to two separate programs, protocols, parameters.

[0096] In alternative embodiments, a diuretic inhaler may be used. Examples include a furosemide inhaler, a bumetanide inhaler, and so forth. If measured body weight is above a previously set target weight, the display on the weight measurement apparatus, the diuretic inhaler or a separate device may show instructions on the dose of drug to be inhaled. For example, if measured body weight is one kilogram above the target weight, a user may be instructed to have one extra-inhalation of furosemide. Other diuretic inhalers, including (but not limited to) furosemide, bumetanide, and torsemide, may be used in alternative embodiments.

[0097] FIGS. **10** further illustrate operation of other embodiments. In FIG. **10**, the diuretic infusion device has various other functions that may improve the health of patients. For example, if intravascular pressure increases due to increased body fluid, it helps to remind patients to control the amount of salt (sodium) that they take daily. The display **1002** shows instructions to avoid food high in sodium chloride. This device may also provide a list of foods high in sodium content, low in sodium content, high in potassium, magnesium, calcium, and/or low in potassium, magnesium, calcium. Diet information may be provided for educational purposes. In alternative embodiments, the device may have a scanner to scan food to notify users whether scanned foods are appropriate for users to take or not. The data (e.g. images) obtained from food scanning may be compared with data saved in the database within the diuretic infusion device to retrieve information on the scanned food. If the scanned food is high in sodium content, instruction to avoid this food may be shown on the display of the diuretic infusion pump. The food scanning can be performed by a separate device such as PDA, a handheld computer, a remote control device, a portable phone, an iPHONE™, an iPOD™, and so forth.

[0098] The diuretic infusion device may also be connected with a blood pressure cuff, either wirelessly or in a wired manner. Blood pressure information measured by the blood pressure cuff is transmitted to the diuretic infusion pump. Certain instructions may be provided on the display **1002**. See FIG. **16**. A database of references on health topics, drug information, emergency instruction, BLS (basic life support) may be saved in the memory within diuretic infusion device or diuretic dose instruction device and can be viewed on the display of the device. Examples of instructions include reminding a user to take antihypertensive medications as scheduled, instructing a user to adjust the dose of antihypertensive medications if blood pressure is low or high. If a user develops chest pain, shortness of breath or other urgent medical conditions, the user may be instructed to call his doctor or go to the nearby emergency room or call 911. A user may press an emergency button **1003** to notify family, help agent, 911 or hospital for help during emergent situations. These various functions may be programmed by a healthcare provider.

[0099] Instructions to take potassium supplement, magnesium supplement and other electrolyte supplement may be displayed on the screen. These electrolytes may be lost by the kidneys as diuretics dose increases. In FIG. **10**, a user is instructed to take potassium chloride (KCL) 20 meq. See also FIG. **35**.

[0100] FIGS. **12** and **14** show additional protocols for diuretic dispensing.

[0101] FIG. **11** illustrates another example. Diuretic infusion pump **1101** has a screen **1 102**. A user uses a keypad to edit target intravascular pressure information. The target intravascular pressure is displayed on the screen. A cursor is located on the number of the intravascular pressure. In this FIG. **11**, it is located on the digit **12 1103**. A user can choose different number using scrolls **1104**, **1105**. S button **1106** is pressed to select a number. The current intravascular pressure can be manually put into the diuretic infusion pump in a similar manner.

[0102] In FIG. **12**, a furosemide infusion protocol is shown on the screen **1201** of the diuretic infusion pump **1202**. The underlined numbers can be changed using scroll buttons **1203**, **1204**. If scroll button **1203** is pressed, the number increases. If scroll button **1204** is pressed, the number decreases. The cursor is located on underlined thick number **1207**, which is a 8. If scroll button **1203** is pressed once, the 8 changes to 9. If scroll button **1204** is pressed once, the 8 changes to 7. If button S **1205** is pressed, the number is selected. If button S is pressed when number **1207** is 8, the 8 is selected and cursor moves on to next underlined number **1208**. If all numbers are selected, button M is pressed to move on to another menu.

[0103] FIG. **13** illustrates another diuretic infusion system. An implant **1304** is located under the skin of human body **1301**. The tip of the wire of the implant is located inside a cardiac chamber **1302** to monitor intracardiac pressure. The tip of the wire of the implant may be located in a central vein, pulmonary artery or other vessel in alternative embodiments. A pressure measuring sensor is attached to the tip or other portion of the wire of the implant. The implant may be coupled with a processor, wireless communication module, a controller and a software program. The diuretic infusion pump **1303** communicates wirelessly with the implant **1304**

that monitors intracardiac pressure and/or central vein pressure. If the pressure is elevated inside the cardiac chamber or central vein, this may indicate a sign of volume overload. The diuretic infusion pump may adjust its infusion rate according to the pressure measured by this implant.

[0104] In one approach, a user inputs a target pressure into the diuretic infusion pump. The diuretic infusion pump adjusts its infusion rate to maintain the target pressure. One example of a suitable implant is the Chronicle heart monitor made by MEDTRONIC™. In alternative embodiments, a pacemaker, an automatic implantable cardioverter defibrillator (AICD), or a cardiac resynchronization therapy (CRT) device may be coupled with the pressure measuring sensor, wireless communication module, processor and software program to transmit pressure signals to the diuretic infusion pump.

[0105] FIG. **14** illustrates a diuretics protocol that may be used with the diuretic infusion device of FIG. **13**. A pressure monitoring sensor is located in the central vein, for example the superior vena cava. The implant shown in FIG. **13** transmits a pressure signal wirelessly to the diuretic infusion pump. The diuretic infusion pump adjusts the diuretic infusion rate according to the pressure measured by the pressure monitoring sensor, as shown in FIG. **14**. The diuretic infusion pump adjusts the infusion rate to maintain a target pressure within the cardiac chamber, central vein or other vessel. Various other protocols may be used to adjust diuretic infusion according to the pressure. The pressure signal can also be used to trigger safety measures. For example, the diuretic infusion device can be programmed to automatically stop infusion and notify a user if the blood pressure falls below a previously set value. This is to avoid hypotension that may occur with use of high dose diuretics. For example, a diuretic infusion pump may be programmed to automatically stop infusion and notify the user (and/or doctor), if the systolic blood pressure is below 90 mmHg. Various non-invasive biological parameter measurement device such as a patch sensor system, a non-invasive central aortic pressure measurement device, a non-invasive intravascular blood pressure measurement device may be coupled with a diuretic infusion pump wirelessly or via other means such as manual data input and wired communication.

[0106] FIG. **15** shows another example of furosemide protocol. A blood pressure monitoring sensor located in a central vein can transmit a measured blood pressure signal to the diuretic infusion pump. The diuretic infusion pump displays the instructions regarding the dosage of oral furosemide.

[0107] FIG. **16** depicts another embodiment of the present invention. A blood pressure cuff **1604** is attached to an arm of a human body **1602**. The blood pressure cuff **1604** can be connected to a blood pressure measuring device **1605**. The blood pressure measuring device **1605** can be coupled to a processor, wireless communication module, a controller and a software program, though it may not be coupled to all of these in some embodiments. The diuretic infusion pump **1601** can communicate wirelessly or via other means with the blood pressure measuring device **1605**. In alternative embodiments, the blood pressure measuring device **1605** can communicate wirelessly or via other means with an electric scale **1603**. In alternative embodiments, a user manually inputs measured blood pressure into a diuretic infusion device or a remote control device.

[0108] FIG. **17** illustrates another example of a furosemide infusion protocol. As shown in FIG. **16**, the diuretic infusion pump receives the measured blood pressure wirelessly from the blood pressure measurement device. If the measured blood pressure is below a set blood pressure, the diuretic infusion pump can be programmed to stop furosemide infusion automatically to prevent hypotension, dehydration.

[0109] FIG. **18** illustrates an example of a furosemide and enalaprilat infusion protocol. As shown in other figures, the diuretic infusion pump can contain more than one drug reservoir. In this example, the diuretic infusion pump has one reservoir containing furosemide and another reservoir containing enalaprilat. Enalaprilat is an angiotensin converting enzyme (ACE) inhibitor which is an antihypertensive drug. The protocol in FIG. **45** shows the diuretic infusion pump infusing enalaprilat as well as furosemide according to measured blood pressure to maintain target blood pressure.

[0110] FIG. **19** illustrates another example of a furosemide and enalaprilat infusion protocol. The diuretic infusion pump adjusts the infusion rate and a dose of enalaprilat and furosemide according to the measured blood pressure to maintain target blood pressure.

[0111] FIG. **20** illustrates an example of furosemide and metoprolol infusion protocol. Metoprolol is a beta blocker which lowers blood pressure and heart rate. The diuretic infusion pump may contain one reservoir containing furosemide and one reservoir containing metoprolol. The diuretic infusion pump adjusts the infusion rate and dose of metoprolol and furosemide according to the measured blood pressure to maintain target blood pressure. The diuretic infusion pump may adjust the infusion rate and dose of metoprolol to maintain target heart rate. A patient with heart disease may develop arrhythmia, such as supraventricular tachycardia (rapid heart rate), atrial fibrillation, or ventricular tachycardia. The diuretic infusion pump can infuse metoprolol to lower heart rate. In alternative embodiments, the diuretic infusion pump can communicate wirelessly with an implantable cardioverter defibrillator (ICD), a pacemaker. If an ICD or a pacemaker detects arrhythmia, the ICD or pacemaker can send this arrhythmia information wirelessly or via other means to the diuretic infusion pump. The diuretic infusion pump may infuse an anti-arrhythmic drug to treat the arrhythmia. Examples of anti-arrhythmic drugs include, but are not limited to, amiodarone, metoprolol, sotalol, esmolol, lidocaine, disopyramide, propafenone, dofetilide, flecainide, procainamide and atropine. The diuretic infusion pump may contain and infuse only anti-arrhythmic drug communicating with an ICD or a pacemaker in alternative embodiments.

[0112] In another embodiment, a user can use one reservoir that contains diuretics and a second reservoir that contains an inotropic drug that increases blood pressure. Examples of inotropic drugs include (but are not limited to) dopamine, dobutamine, phosphodiesterase inhibitor, amrinone, milrinone, enoximone, pimobendan, levosimendan, calcium sensitizing agent, venarinone, and ibopamine. In alternative embodiments, the diuretic infusion pump contains a combination of antihypertensive drugs, inotropic agents, diuretics, and it adjusts the infusion rate according to blood pressure measured by non-invasive blood pressure measurement device and/or measured body weight.

[0113] FIG. **21** depicts another embodiment. An implantable device **2104** has a pair of electrodes on the surface. The implantable device **2104** is connected to a cardiac ring electrode or coil electrode positioned in the heart **2105** in the human body **2101** via a wire **2102**. Intrathoracic impedance between the implantable device case and the right ventricular

lead can be measured multiple times a day. If the intrathoracic impedance decreases, this may suggest fluid is accumulating in the lungs due to worsening heart failure. The implantable device **2104** can be a pacemaker, an implantable cardioverter defibrillator, or a cardiac resynchronization therapy device. One example of a suitable implant is OptiVol fluid status monitoring device from Medtronic. The diuretic infusion pump **2103** can communicate wirelessly with the implantable device **2104**. The diuretic infusion pump **2103** can adjust the infusion rate of diuretics according to the measured impedance to maintain the target impedance. FIG. **49** illustrates an example of a furosemide infusion protocol according to measured intrathoracic impedance. The diuretic infusion pump may adjust the infusion rate of diuretics according to the average of impedance measurements taken over a predetermined period of time to maintain target measured average impedance.

[0114] FIG. **22** depicts another embodiment. The diuretic infusion pump **2203** receives weight information wirelessly or manually from a weight measurement device **2201** and communicates wirelessly with the implantable device **2204** which was shown in FIG. **21**.

[0115] FIG. **23** illustrates an example of a furosemide infusion protocol according to measured intrathoracic impedance. The diuretic infusion pump may adjust the infusion rate of diuretics according to the average of impedance measurements taken over a predetermined period of time to maintain target measured average impedance.

[0116] FIG. **24** illustrates another embodiment. A diuretic infusion device **2401** is attached to a human body **2402**. This portable diuretic infusion device **2401** delivers diuretics from a reservoir to the human body **2402**. The diuretic infusion device **2401** may be smaller in size compared to other embodiments shown in other figures. This diuretic infusion device **2401** can be disposable. The diuretic infusion device **2401** contains a reservoir, a programmable processor, an exit port, a cannula and a motor, though some embodiments may contain fewer components or additional components. The diuretic infusion device **2401** can communicate wirelessly or via other means with a remote control device **2404**. The remote control device **2404** can communicate wirelessly with an intrathoracic impedance measurement device **2405** and a diuretic infusion device **2401** in one embodiment. The remote control device **2404** may communicate wirelessly with only the diuretic infusion device **2401**, and not with the intrathoracic impedance measurement device **2405** in alternative embodiments.

[0117] FIG. **25** further illustrates the diuretic infusion device **5101**. The diuretic infusion device **2501** has a needle **2503** and cannula **2502**. The diuretic infusion device **2501** is connected to a human body **2511** subcutaneously via a cannula **2502**. The diuretic infusion device **2501** is disposable in some embodiments, but the reservoir of the diuretic infusion device can alternatively be refilled via a hole **2505**. The remote control device **2504** programs and controls the diuretic infusion device **2501**. The remote control device **2504** contains a programmable processor, a controller, a wireless transmitter/receiver, a keypad with order entry buttons **2507**, **2508**, **2509**, **2510** and a display screen **2506**, though some embodiments may contain fewer components or additional components. Measured biological parameters shown in other figures can be transmitted wirelessly from a biological parameter measurement device to the remote control device **2404**, **2504** in this embodiment. In alternative embodiments, a user manually inputs measured biological parameters into the remote control device **2504**. A controller of the remote control device **2504** may be coupled to a processor and a wireless receiver/transmitter. When biological parameter information enters the processor of the remote control device **5104**, the processor can compute the dosage of diuretic based on the biological parameter(s). The remote control device **2504** wirelessly transmits commands to the diuretic infusion device **2501**. The remote control device **2504** can control the infusion rate of the diuretic infusion device **2501** wirelessly or by other means (e.g., wired). A user can choose and program particular diuretic infusion protocol(s) using button(s) **2507**, **2508**, **2509**, **2510** on the keypad of the remote control device **2504**. Various drug infusion protocols and methods shown in other figures (see FIGS. **14-15**, **17-20**, **23**, **55** and other figures) may be embedded in the processor of the remote control device **2504**. The processor within the remote control device **2504** may be able to compute the dosage of a diuretic based on the amount of salt, sodium and/or water of food. A user may infuse a diuretic before or when the user eats food that contains salt and/or water to excrete extra salt and water to maintain optimal body fluid condition. In other embodiments, the processor within the remote control device **2504** computes the dosage of diuretic based on various biological parameters using protocols shown in other figures. For example, FIGS. **36** and **37** show various biological parameters and factors that may be used in these embodiments. The biological parameter measurement sensors can be coupled with an implantable device(s) like a pacemaker, an implantable cardioverter defibrillator, a cardiac resynchronization therapy, etc. The remote control device **2504** can communicate wirelessly with the biological parameter measurement sensor(s). An intracardiac/intravascular pressure monitoring sensor, an intrathoracic impedance monitor sensor, or a patch sensor can communicate wirelessly with the remote control device **2504** in alternative embodiments.

[0118] FIG. **26** illustrates another embodiment of the present invention. In this embodiment, the diuretic infusion pump system can be a closed loop drug infusion system. The closed loop drug infusion system includes a biological parameter measurement sensor and/or a biological parameter measurement device, a controller, drug infusion pump, a drug delivery system, wireless communication module, though not all of these may be included in alternative embodiments or additional modules or devices may be included. In the closed loop drug infusion system, measured biological parameter signal enters the controller of the diuretic infusion system wirelessly or via other means. The controller of the diuretic infusion pump automatically adjusts and controls the drug infusion according to the algorithms programmed in the diuretic infusion pump in the closed loop drug infusion system. The controller of the diuretic infusion pump adjusts the drug infusion to achieve or maintain a target biological parameter which is programmed into the diuretic infusion pump.

[0119] As shown in FIG. **27**, many different biological parameter measurement sensors and/or biological parameter measurement devices can be used for the present invention. Examples of these biological parameter measurement sensors/devices include, but are not limited to, a patch sensor system, an intracardiac pressure sensor system, an intravascular pressure sensor system, an intrathoracic impedance monitor sensor system, a non-invasive blood pressure measurement sensor system, a weight measurement sensor and/or

device, a blood pressure measurement cuff and device, a heart rate measurement sensor system, an electrocardiogram monitoring sensor and/or device, an arrhythmia monitoring sensor system and other vital sign measurement devices. These biologic sensors can be coupled with other implantable medical devices, such as a pacemaker, an ICD, or a cardiac resynchronization therapy. The biological parameter measurement sensor/device and the diuretic infusion pump can preferably communicate wirelessly. The sensor/device and the diuretic infusion pump may communicate via other means in alternative embodiments. Other means may include, but are not limited to, wired communication, manual data input and other methods described in the present invention. More than one biological parameter sensor and/or device may be used in combination with a diuretic infusion pump. For example, a weight measurement device and intravascular blood pressure measurement sensor system may be used in combination with a diuretic infusion pump. A weight measurement device and a patch sensor may be used in combination with a diuretic infusion pump. These different sensors and devices may communicate wirelessly or via other means. Different types of patch sensors may be included in the closed and/or open loop drug infusion system. The patch sensor is further described in FIG. **28**. The drug infusion system may adjust the infusion of drug(s) according to an average (e.g., a mean or median) value of biological parameters in alternative embodiments. For example, the drug infusion system can adjust the infusion of diuretics according to the average of the measured weight over three days. If the daily measured body weight is 70 kg, 72 kg, 71 kg over the past three days, the diuretic infusion pump can be programmed to adjust the rate of diuretic infusion according to 71 kg which is median value of three measured weights. The drug infusion system can adjust the infusion of diuretics according to the average value of measured intrathoracic electrical impedance over a period of time. In some embodiments, the diuretic infusion pump is programmed to adjust the rate of diuretic infusion according to an average value of biomarkers, blood pressure, intracardiac pressure or other biological parameters mentioned previously over a certain period of time.

[0120] In alternative embodiments, the diuretic infusion pump system is an open loop drug infusion system. The diuretic infusion pump can receive measured weight or other biological parameters from sensor(s) wirelessly or manually, however the diuretic infusion pump may or may not automatically adjust the rate of infusion in an open loop system. A user, a doctor, a nurse and/or other people that are involved in the use of the diuretic infusion pump system may need to approve or choose particular protocol(s) and methods. These people can also control the controller of the diuretic infusion pump. Healthcare provider(s) can transmit a new order or new drug infusion protocols to the diuretic infusion pump system via the Internet, a phone, or other methods. In an open loop drug infusion system, wireless communication among the devices may or may not be used.

[0121] In some embodiments, a user chooses an open loop system, a closed loop system, or mixed loop system (e.g., a closed loop system when a certain conditions are met and open loop system when a certain conditions are not met). The diuretic infusion pump system can be programmed to be a closed loop system when measured blood pressure is within a certain parameter, when a user does not have symptoms, such as chest pain, and/or when the dosage of an infused drug is within a certain range. The diuretic infusion pump can be programmed to be an open loop system when these conditions are not met in a mixed loop system.

[0122] FIG. **28** illustrates a patch sensor system **2802** and a drug infusion pump **2803**. The patch sensor system **2802** is attached to a human body **2801**. The patch sensor system can contain more than one sensor **2804**, **2805** and/or electrodes **2804**, **2805**. The patch sensor system can be coupled to a processor, wireless communication module, a controller and software program, though it may not be coupled to all of these in alternative embodiments or may be coupled to additional devices. In some embodiments, the patch sensor system **2802** measures blood pressure, heart rate, intrathoracic electrical impedance, body fluid status, heart rhythm, biomarkers, and detects heart arrhythmia. This patch sensor **2802** is preferably attached to the chest, but may be attached to back, head or other parts of the body in alternative embodiments. The patch sensor **2802** can include an electrode generating an electrical waveform and/or an optical system generating an optical waveform to measure various biological parameters, such as blood pressure, pulse, oxygen saturation, heart rhythm. Intrathoracic electrical impedance can be measured by the patch sensor system **2802** using multiple electrodes and/or multiple sensors. Intrathoracic impedance between multiple sensors and electrodes can be measured multiple times a day in one embodiment. The patch sensor system **2802** communicates wirelessly with the diuretic infusion pump **2803** in a closed loop drug infusion system or an open loop drug infusion system. The diuretic infusion pump **2803** adjusts the infusion of diuretics and/or other drugs according to biological parameter(s) measured by the patch sensor system **2802** to maintain the target biological parameter. The diuretic infusion pump can adjust the infusion of diuretics and/or other drug(s) to maintain, for example, target blood pressure, intrathoracic impedance, heart rate, body fluid condition surrogate marker, etc., using drug infusion protocols shown in other figures. More than one patch sensor system **2802** can be used and attached to different parts of the body. One example of a suitable external patch sensor monitoring system is MUSE™ clinical system from CORVENTIS™, INC.

[0123] FIG. **29** illustrates another example of a drug infusion protocol. In one example, the measured intracardiac pressure of a user is 17 mmHg and the target intracardiac pressure is set at 12 mmHg. There is 5 mmHg difference between the target cardiac pressure and measured cardiac pressure, and the measured cardiac pressure is above the target cardiac pressure. Following the protocol seen in FIG. **29**, the basal rate of furosemide infusion increases by 0.3 mg multiplied by 5 and 0.3 mg multiplied by 5 is equal to 1.5 mg. The basal rate of furosemide infusion increases by 1.5 mg per hour for 8 hours following the protocol. If the previously set basal rate of furosemide was 1 mg per hour for 8 hours daily, the new basal rate of the furosemide is 2.5 mg per hour for 8 hours daily. A user or a healthcare provider can change the underlined numbers according to a person's sensitivity to diuretics. The change of the protocol could occur automatically or occur upon the approval of a user and/or healthcare provider(s).

[0124] FIG. **30** illustrates wireless communication between a diuretic pen **3001** and a remote control device **3002** which receives biological parameter information from biological parameter measurement device. Measured biological parameter may be input into the diuretic pen wirelessly or manually. A user may input biological parameter manually by using button(s), a knob, etc. As shown in FIG. **31**, the diuretic pen

3001 can contain a processor, software, and telemetry system, though the diuretic pen may not have all of these components or may have additional components. The processor within the diuretic pen can compute the dose of diuretic drug based on the biological parameter.

[0125] FIG. **32** illustrates examples of sensors/devices measuring various biological parameters. These devices and/or sensors are connected to a diuretic pen wirelessly in some embodiments. The diuretic pen can compute the dose of diuretic injection based on these biological parameters.

[0126] FIG. **33** shows possible data flow for computation of the diuretics dose. In alternative embodiments, the processor uses various other factors to compute diuretics dose. Examples include physical signs, vital signs, bio markers, symptoms, intracardiac pressure, intravascular pressure, intrathoracic electrical impedance and NYHA classification, etc., as shown in FIG. **33**. For example, if B-type natriuretic peptide (BNP) is elevated, this may indicate increased body fluid volume and congestive heart failure. If BNP is above 100 pg/ml, the diuretic pen can increase (or adjust) the dose of the diuretics.

[0127] FIG. **34** illustrates another embodiment of the present invention. This figure shows another type of a drug dispensing apparatus. One embodiment of this drug dispensing apparatus is a pen-type apparatus **3406** which contains medication pills **3404**. Some embodiments of this pen-type apparatus contain drug suspension. For example, a user may use this pen-type drug dispensing apparatus **3406** based on "sodium counting." "Sodium counting" is utilized when a user or a processor of a device calculates the dosage of diuretic based on the amount of sodium intake. For example, a user may be instructed by a physician to use 2 mg of furosemide per 50 mg of sodium intake. The pen-type apparatus might contain multiple 2 mg or 1 mg furosemide pills, though various doses of furosemide can be contained in the apparatus. If a user plans to eat 350 mg of sodium, the user can take 14 mg of furosemide according to the "sodium counting." Thus, 14 mg can be input into the pen-type apparatus using a button **3407** and a knob **3401**. When knob **3401** is pushed, screw **3403** is moved to push the pills out of the drug container. Screw **3403** movement is controlled by a processor in some embodiments, though screw **3403** movement is controlled manually in other embodiments. The dosage of 14 mg furosemide is not readily available at a pharmacy because 14 mg is not a commonly used dose of furosemide pill. If the pen-type apparatus contains 2 mg furosemide pills, 7 furosemide tablets are taken out of the dispenser. This pen-type drug dispensing apparatus makes it easy to dispense various doses of diuretics and other medications. In one embodiment, this pen-type diuretic dispensing apparatus contains a processor which can compute the dose of diuretics when a user inputs the amount of sodium or salt into the pen-type diuretic dispensing apparatus. A user can input the amount of sodium or salt using knob **3401** and/or buttons on the apparatus. In alternative embodiments, when knob **3401** is pressed, a predetermined number of pills are released out of the container **3406**. For example, two tablets of 1 mg furosemide pill can be released out of the container when knob **3401** is pressed. The user may be instructed to press the knob **3401** one time when the user plans to eat food with low salt and/or water content, to press the knob **3401** twice when a user plans to eat food with moderate salt and/or water content, or press the knob **3401** three times when he plans to eat food with high salt and/water content.

[0128] FIG. **35** illustrates another embodiment of the invention. In this embodiment, a disposable external diuretic infusion pump **3501** is attached to the body **3505** of a user. This disposable external diuretic infusion pump includes a reservoir that contains the diuretic. This external diuretic infusion pump **3501** can be a metered dose infusion pump. The external diuretic infusion pump **3501** is set to deliver a predetermined volume of a drug to the user. When the user pushes a button **3502**, a predetermined volume of the drug is delivered via a cannula **3503** to the user. The tip of the cannula **3503** is located subcutaneously in a preferred embodiment. In some embodiments, a reservoir may be refilled through a hole **3504**. One example of a metered dose diuretic infusion is as follows. If a user is expected to eat food that contains salt, the user may be instructed to use this metered dose diuretic infusion pump before or at the time of eating this food. For example, a pump may deliver 1 mg of furosemide to the user each time button **3502** is pressed. The user can be instructed to press the button **3502** one time when the user plans to eat food with low salt content, twice when the user plans to eat food with moderate salt content, three times when the user plans to eat food with high salt content. The user may be able to urinate and excrete salt shortly after eating using this device system. People with heart failure are instructed to avoid food with high salt content because of body salt and fluid overload. This apparatus and method can allow people to take an extra amount of salt/water and still prevent them from developing salt/body fluid overload. The metered dose diuretic infusion pump can deliver a diuretic based on measured body weight. The user may be instructed to press the button **3502** once when the measured body weight is 1 kg above target weight, twice when the measured body weight is 1-2 kg above target weight, and three times when the measured body weight is more than 2 kg above target weight. The metered dose drug infusion pump can be implanted under skin in some embodiments.

[0129] FIG. **36** illustrates another embodiment. It can be important to measure body weight and/or biological parameters regularly, to take electrolyte supplements, such as potassium supplement or magnesium supplement, and to measure blood pressure while a user uses a diuretic infusion pump for safety reasons. As shown in FIG. **36**, the user is asked if he took potassium supplement, measured his body weight, and measured his blood pressure. If the user inputs "yes," the diuretic infusion pump is programmed to continue diuretic infusion. If the user inputs "no," the diuretic infusion pump can be programmed to discontinue diuretic infusion until the user inputs "yes." This feedback mechanism is a safety feature of the diuretic infusion system.

[0130] FIG. **37** illustrates examples of sensors/devices measuring various biological parameters. These devices and/or sensors are connected to a remote control device wirelessly in some embodiments. The remote control device can compute the dose of diuretic injection based on these biological parameters.

[0131] FIG. **38** shows possible data flow for computation of the diuretics dose. In alternative embodiments, the processor uses various other factors to compute diuretics dose. Examples include physical signs, vital signs, bio markers, symptoms, intracardiac pressure, intravascular pressure, intrathoracic electrical impedance and NYHA classification, etc. For example, if B-type natriuretic peptide (BNP) is elevated, this may indicate increased body fluid volume and congestive heart failure. If BNP is above 100 pg/ml, the

remote control device can compute the dosage and increase (or adjust) the dose of the diuretics.

[0132] A photograph of the user's legs or other parts of the body can be taken by the diuretic infusion pump system by a camera or a cell phone. The photograph can be transmitted to a healthcare provider. The healthcare provider reviews the photograph of legs, and may be able to verify the body fluid condition by comparing the measured weight with the photograph. The diuretic infusion pump can also have a built-in camera. The healthcare provider can detect malfunction of the weight scale when the measured body weight is far greater than the target weight but the photograph of the legs does not show any swelling.

[0133] FIG. **39** illustrates another embodiment of the invention. Urinary catheter **3905** is placed into a bladder of a human body **3902**. Urinary catheter **3905** is connected with a drainage bag **3904**. The amount of urine output over a period of time can be measured using this urinary catheter and drainage bag. In one embodiment, the urine output measurement system can include a urinary catheter, a drainage bag, a sensor to measure urine output, a transmitter, a receiver, a processor, software, etc., though it can have fewer or more components. The measured urine output over a predetermined period of time is transmitted wirelessly or by other means (e.g., wired, manual data input, etc.) to a diuretic infusion pump **3901**. The diuretic infusion pump **3901** automatically adjusts the infusion rate of diuretic based on the urine output in order to achieve a target urine output. In alternative embodiments, the diuretic infusion pump has a separate a remote control device, a portable computer system, a PDA, etc., which can communicate wirelessly or via other means (e.g., wired, manual data input, etc.) with the urine output measurement system.

[0134] As one example, a physician programs the diuretic infusion pump system to achieve 2400 ml of urine output over a 24-hour period. In order to achieve this, a urine output of 100 ml per hour is required on average over 24 hours. Various diuretic infusion protocols shown in other figures may be programmed into the diuretic infusion pump. The sensor of the urine output measurement system measures the amount of the urine output. The transmitter of the urine output measurement system transmits the urine output information wirelessly or by other means (e.g., wired, manual data input, etc.) to the diuretic infusion pump system and/or a separate computer, a remote control device, etc. If the urine output over a predetermined period of time is less than the target urine output, the diuretic infusion pump can increase diuretic infusion to increase urine output. If the urine output over a predetermined period of time is greater than the target urine output, the diuretic infusion pump can decrease diuretic infusion to decrease urine output. If the urine output were 80 ml over one hour, the diuretic infusion pump would increase the diuretic infusion to achieve 120 ml over the next hour to achieve 100 ml per hour of urine output. The diuretic infusion pump **3901** can deliver the diuretic intravascularly, subcutaneously, intramuscularly, etc. In one embodiment, the diuretic infusion pump **3901** can communicate wirelessly or by other means (e.g., wired, manual data input, etc.) with a non-invasive blood pressure monitoring system **3907**. The non-invasive blood pressure monitoring system **3907** can have a processor, a controller, software, a wireless transmitter/receiver, though it may have fewer or more components in alternative embodiments.

[0135] When blood pressure is measured using a blood pressure cuff **3906**, the measured blood pressure is transmitted wirelessly or by other means (e.g., wired, manual data input, etc.) to the diuretic infusion pump **3901**. If blood pressure is below a predetermined level, the diuretic infusion pump **3901** can stop the diuretic infusion or adjust the diuretic infusion based on the program. This system may reduce the risk of hypotension. If blood pressure is above a predetermined level, the diuretic infusion pump **3901** can increase diuretic infusion or adjust the diuretic infusion based on the program.

[0136] In alternative embodiments, the urine output measurement system comprises a urinary catheter, a urine drainage bag, and a sensor to measure urine output, but does not include a wireless transmitter and receiver. The user may input the urine output over a certain period of time manually into a diuretic infusion pump system and/or a separate computer or a remote control device. In alternative embodiments, the diuretic infusion pump system can communicate wirelessly or by other means (e.g., wired, manual data input, etc.) with the urine output measurement system and other biological parameter sensors (see other figures). The diuretic infusion pump system can adjust the diuretic infusion to maintain the target urine output, as well as to maintain the target biological parameter (e.g., the target intravascular pressure, the target intracardiac pressure, and/or the target intrathoracic impedance).

[0137] FIG. **40** illustrates the operation of a diuretic infusion system according to one embodiment. In FIG. **40**, the urine output measurement sensor and processor are onboard, within a housing of the urine output measurement apparatus. The urine output measurement sensor is electrically connected to the processor, and sends the measured urine output to the processor. The processor is connected to a telemetry system and a signal transmitter. The urine output information is sent from the telemetry system of the urine output measurement apparatus via the transmitter.

[0138] The urine output information signal is received by a receiver of the diuretic infusion pump. The receiver of the diuretic infusion pump is electrically connected to a processor which is housed in the diuretic infusion pump. The processor receives the urine output information and performs computations to determine the diuretic infusion rate, such as basal rate and bolus rate, according to programmed parameters, protocols and algorithms. The processor controls an electric motor to deliver diuretic from a reservoir to a user through an outlet, a tube, and an infusion set of the diuretic infusion pump. In alternative embodiments, the user manually inputs measured urine output into the diuretic infusion device. This urine output information enters a processor which is housed in the diuretic infusion pump. The processor performs computations to determine the diuretic infusion rate as described with regard to other figures.

[0139] FIG. **41** illustrates the wireless operation of the diuretic infusion pump system. The urine output measurement system **4101** includes a urine output measurement sensor **4102**, a processor **4103**, and a wireless transmitter **4104** (or a wireless receiver), a urinary catheter, a urine drainage apparatus, and an antenna **4105**. The transmitter **4104** sends signals **4106** that contain urine output information.

[0140] The urine output signal(s) can be sent to different receivers. The diuretic infusion pump receives the signal(s) **4106** through an onboard receiver **4108** via an antenna **4107**. A handheld communication device, such as a remote control device, an iPOD™, an MP3 player, a handheld computer, or a portable phone may receive the signal **4106** through an

onboard receiver **4112** via an antenna **4111**. The user may choose to send information to a computer or handheld communication device for the purpose of saving urine output information on the computer or connecting with the Internet to send urine output information to healthcare providers. The diuretic infusion pump system and/or handheld communication device can receive biological parameter signal(s) wirelessly or by other means (e.g., wired, manual data input, etc.) from the biological parameter sensor, transmitter, or processor **4110**. FIG. **38** provides examples of biological parameters.

[0141] FIG. **42** illustrates an example of furosemide infusion protocol based on urine output.

[0142] FIG. **43** illustrates an ambulatory diuretic infusion pump **4301** mounted at a pole **4310**. A diuretic contained in a bag **4303** is infused into a vein of a patient **4305** through an intravenous tube system **4304**. The diuretic infusion pump **4301** contains a controller which adjusts the rate of diuretic infusion based on urine output and/or other biological parameter(s). A user can input the urine output measured by urine output measurement system **4308**, **4309** using a keypad **4302** or using a remote controller. The urine output measured by the urine output measurement system can be transmitted wirelessly to the diuretic infusion pump **4301** in another embodiment. The blood pressure measured by blood pressure measurement system **4306**, **4307** can be manually input into the diuretic infusion pump **4301** or transmitted wirelessly into the diuretic infusion pump **4301**.

[0143] FIG. **44** illustrates an ambulatory diuretic infusion pump **4401** mounted at a pole **4402**. A diuretic contained in a bag **4406** is infused into a vein of a patient **4404** through intravenous tube system **4403**. The diuretic infusion pump **4401** contains a controller which adjusts the rate of diuretic infusion based on weight and/or other biological parameters. A user can input the weight measured by weight measurement scale **4405** into the diuretic infusion pump **4401** using a keypad. **4407** or using a remote control device. The weight measured by the scale **4405** can be transmitted wirelessly to the diuretic infusion pump in another embodiment.

[0144] Even though the term "diuretic infusion pump" (or "diuretic infusion system" or similar variants) is used in this application, one of ordinary skill in the art would know that this term is not limited to the use of diuretics, but can also use other types of drugs, as well. Thus, this term is not limited to diuretics. Many different drugs can be used for the diuretic infusion pump. Examples of such drugs are described in other parts of the application.

[0145] Diuretic infusion pumps can contain two reservoirs in some embodiments. One reservoir can contain furosemide. The other reservoir can contain buffering solution. Buffering solution includes (but is not limited to) sodium chloride solution, Lactated Ringer's solution, or Dextrose 5% solution. Some furosemide solution may have a high pH of about 9. Mixing a furosemide solution with a sodium chloride solution, Lactated Ringer's solution or Dextrose 5% solution may lower the pH of the furosemide solution.

[0146] Furosemide discolors when it is exposed to light. Discolored furosemide is not recommended to be used. A reservoir and cartridge within a diuretic infusion pump may be light resistant to protect furosemide or other drugs from being exposed to the light.

[0147] In all of the above embodiments, the diuretic infusion pump was located external to the body. However, alternatively, internal and implantable diuretic infusion pumps may also be made. The diuretic infusion pumps are also shown as portable in the above description. In alternative embodiments, the diuretic infusion pump may not be portable.

[0148] In another aspect of the invention, a user of the diuretic infusion pump may choose to use the device for long term or may choose to use it for short term when his body weight changes. The diuretic infusion pump can also be used in various locations: home, outpatient facilities and hospitals, as well as the intensive care unit.

[0149] Programs and protocols coupled with the diuretic infusion pump preferably have various safety measures to minimize side effects of diuretics. One example of a safety measure is that the diuretic infusion pump stops infusing diuretics when a user does not measure body weight in a certain period after previous weight measurements. For example, the diuretic infusion pump may be programmed to stop diuretic infusion in two days if the diuretic infusion pump does not receive a new body weight measurement. This safety measure helps to avoid using inappropriately high dose of diuretics when previously measured body weight is higher than actual body weight. Alarms and display on the screen may be programmed to request a user to enter a new body weight measurement into the diuretic infusion pump.

[0150] The above description and illustration of preferred embodiments of the invention has been presented to provide illustration and description. It is not intended to limit the invention to the precise forms that are disclosed. Many variations and modifications will be apparent to people skilled in this art.

[0151] Depending on the form of the components, "coupling" or "connection" between components may take different forms. Dedicated circuitry can be coupled to each other by hardwiring or by accessing a common register or memory location, for example. Software "coupling" can occur by any number of ways to pass information between software components (or between software and hardware, if that is the case). The term "coupling" is meant to include all of these and is not meant to be limited to a hardwired permanent connection between two components. In addition, there may be intervening elements. For example, when two elements are described as being coupled to each other, this does not imply that the elements are directly coupled to each other nor does it preclude the use of other elements between the two.

What is claimed is:

1. A diuretic infusion system comprising:

a biological parameter measurement apparatus including:

a biological parameter measurement sensor for measuring a biological parameter of a human patient; and

a diuretic infusion device including:

a reservoir for holding a diuretic;

a pump connected to the reservoir and connectable to the human patient, for infusing diuretic from the reservoir into the human patient; and

a controller for controlling the pump and rate of infusion of the diuretic based on the measured biological parameter.

2. The system of claim **1**, wherein:

the biological parameter measurement apparatus further includes a wireless transmitter for wirelessly transmitting measured biological information; and

the diuretic infusion device further includes a wireless receiver for wirelessly receiving the biological parameter information transmitted by the biological parameter

measurement apparatus, the controller controlling the pump and rate of infusion of the diuretic based on the received biological parameter information.

3. The system of claim **1**, wherein the biological parameter measurement sensor is a patch sensor.

4. The system of claim **1**, wherein the biological parameter measurement sensor is an intracardiac pressure measurement sensor and the controller adjusts the rate of infusion based on a measured pressure within a cardiac chamber of the patient.

5. The system of claim **4**, wherein the controller adjusts the rate of infusion based on the measured pressure within the cardiac chamber to maintain a target pressure in the cardiac chamber.

6. The system of claim **1**, wherein the biological parameter measurement sensor is an intravascular pressure measurement sensor and the controller adjusts the rate of infusion based on a measured pressure within a blood vessel of the patient.

7. The system of claim **6**, wherein the controller adjusts the rate of infusion based on the measured pressure within the blood vessel to maintain a target pressure in the blood vessel.

8. The system of claim **1**, wherein the biological parameter measurement sensor is an intrathoracic electrical impedance measurement sensor and the controller adjusts the rate of infusion based on a measured intrathoracic electrical impedance.

9. The system of claim **1**, wherein the biological parameter measurement apparatus is a non-invasive blood pressure measurement device. and the controller adjusts the rate of infusion based on a measured blood pressure of the patient

10. The system of claim **1** wherein the biological parameter measurement apparatus is coupled to a pacemaker.

11. The system of claim **1** wherein the biological parameter measurement apparatus is coupled to an implantable cardioverter defibrillator.

12. The system of claim **1** wherein the biological parameter measurement apparatus is coupled to a cardiac resynchronization therapy.

13. The system of claim **1**, wherein the biological parameter is a biomarket and the controller adjusts the rate of infusion based on the measured biomarker.

14. The system of claim **13**, wherein the biomarker is selected from the group consisting of an atrial natriuretic peptide, a brain natriuretic peptide, and a NT-pro brain natriuretic peptide.

15. The system of claim **1**, wherein the system is further configured for administering a drug selected from a group consisting of: ACE inhibitor, calcium channel blocker, beta blocker, inotropic agent, hydralazine, loop diuretics, thiazide diuretics, and vasopressin receptor antagonist

16. The system of claim **1**, wherein the pump is a portable pump.

17. The system of claim **1**, wherein the pump is a non-portable pump.

18. The system of claim **1**, wherein the pump is an ambulatory drug infusion pump.

19. The system of claim **1**, wherein the pump is an implantable drug infusion pump.

20. A method for infusing diuretic to a human patient comprising:

receiving non-weight biological parameter information based on measurements of a non-weight biological parameter for a patient; and

adjusting an infusion rate of diuretic into the patient based on the measured non-weight biological parameter according to a predetermined protocol.

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