



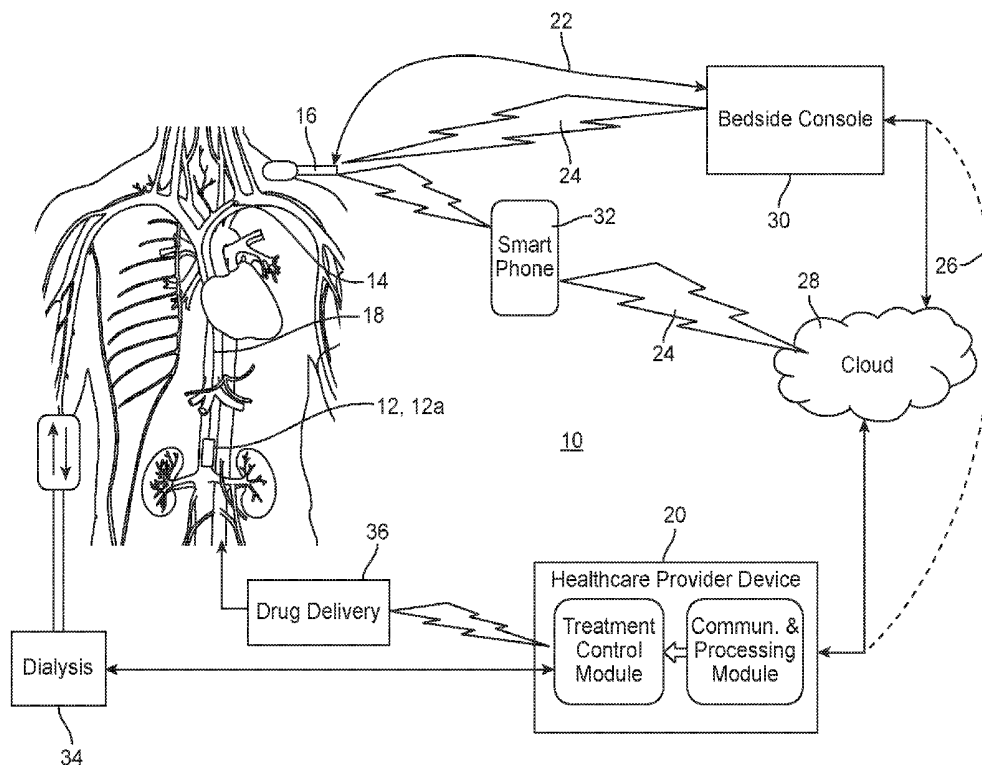
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Gifford, III et al.(10) **Pub. No.: US 2019/0167188 A1**(43) **Pub. Date: Jun. 6, 2019**(54) **SYSTEMS AND METHODS FOR PATIENT
FLUID MANAGEMENT***A61B 5/07* (2006.01)*A61B 8/08* (2006.01)*A61B 8/00* (2006.01)*A61B 5/107* (2006.01)(71) Applicant: **Foundry Innovation & Research 1,
Ltd., Dublin (IE)**(72) Inventors: **Hanson S. Gifford, III**, Woodside, CA
(US); **Mark E. Deem**, Portola Valley,
CA (US); **Conor M. Hanley**, Dublin
(IE); **Fiachra M. Sweeney**, Dublin (IE);
Jeffrey J. Grainger, Portola Valley, CA
(US); **John R. Britton**, Dublin (IE);
Annette Kent, Dublin (IE)(52) **U.S. Cl.**CPC *A61B 5/4839* (2013.01); *A61B 8/12*
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(2013.01); *A61B 5/6876* (2013.01); *A61B*
5/746 (2013.01); *A61B 8/5223* (2013.01);
A61B 8/0891 (2013.01)(21) Appl. No.: **16/271,798**(22) Filed: **Feb. 9, 2019****Related U.S. Application Data**(63) Continuation of application No. PCT/US2017/
046204, filed on Aug. 10, 2017.(60) Provisional application No. 62/534,329, filed on Jul.
19, 2017, provisional application No. 62/427,631,
filed on Nov. 29, 2016, provisional application No.
62/373,436, filed on Aug. 11, 2016.**Publication Classification**(51) **Int. Cl.***A61B 5/00* (2006.01)*A61B 8/12* (2006.01)*A61B 5/0205* (2006.01)

(57)

ABSTRACT

Systems and methods are disclosed that provide for regular, periodic or continuous monitoring of fluid volume based on direct measurement of an inferior vena cava (IVC) physical dimension using a wireless measurement sensor implanted in the IVC. By basing diagnostic decisions and treatments on changes in an IVC physical dimension, information on patient fluid state is available across the entire euvolemic range of fluid states, thus providing earlier warning of hypervolemia or hypovolemia and enabling the modulation of patient treatments to permit more stable long-term fluid management.



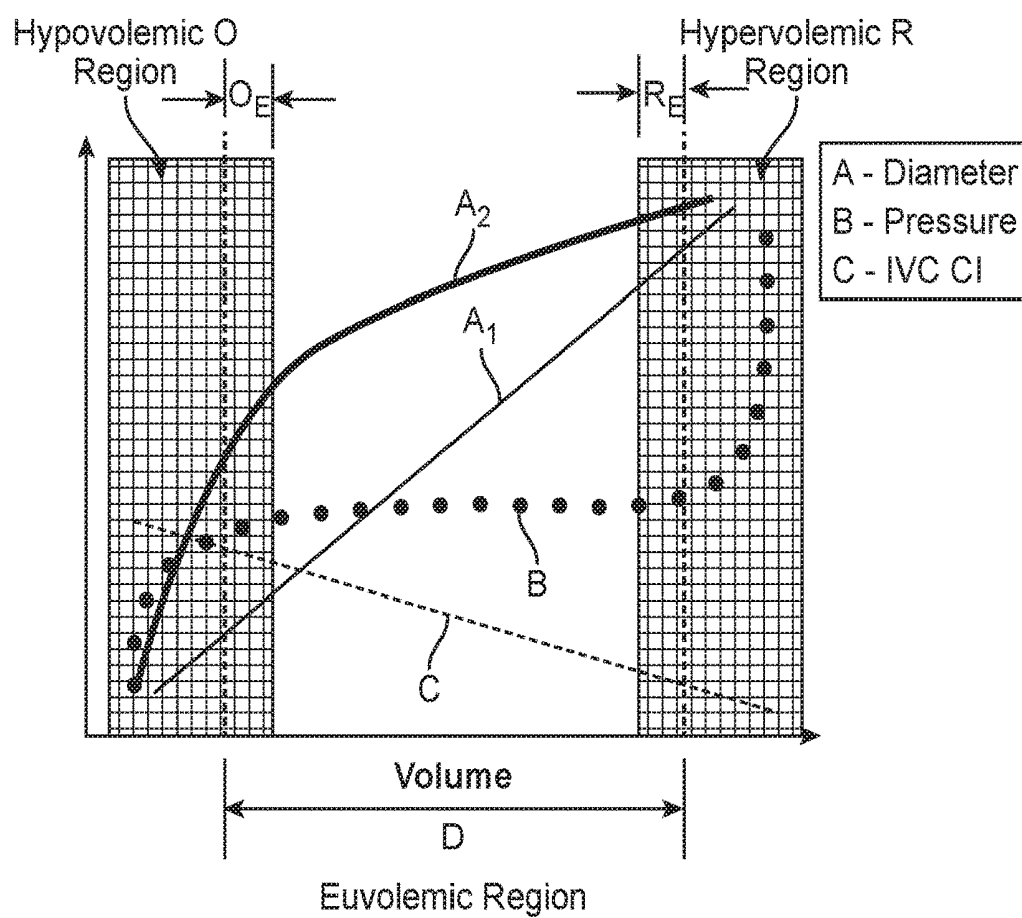


FIG. 1

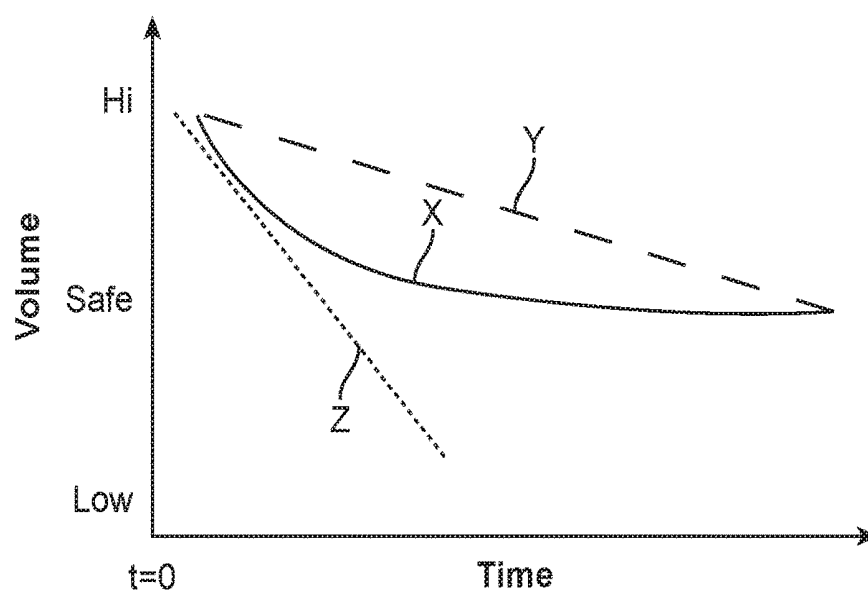


FIG. 2

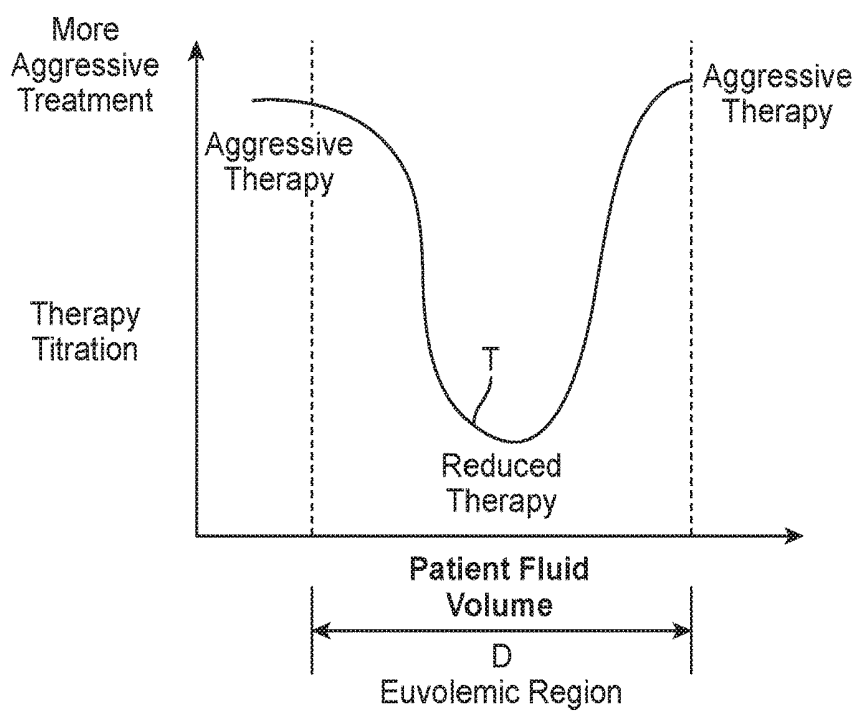


FIG. 3A

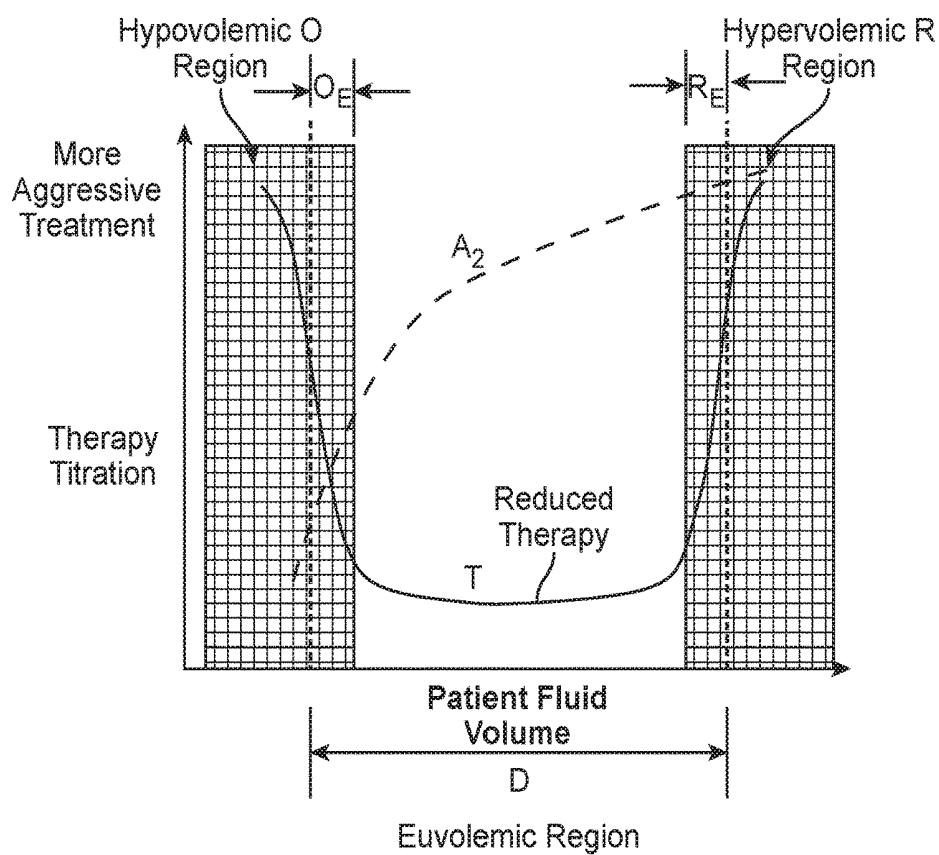
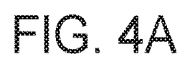


FIG. 3B



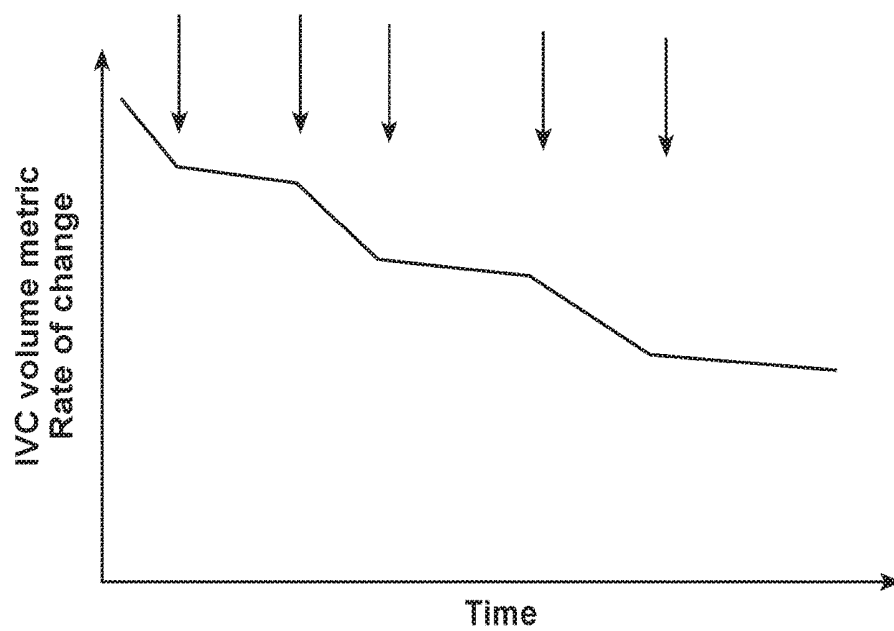


FIG. 4B

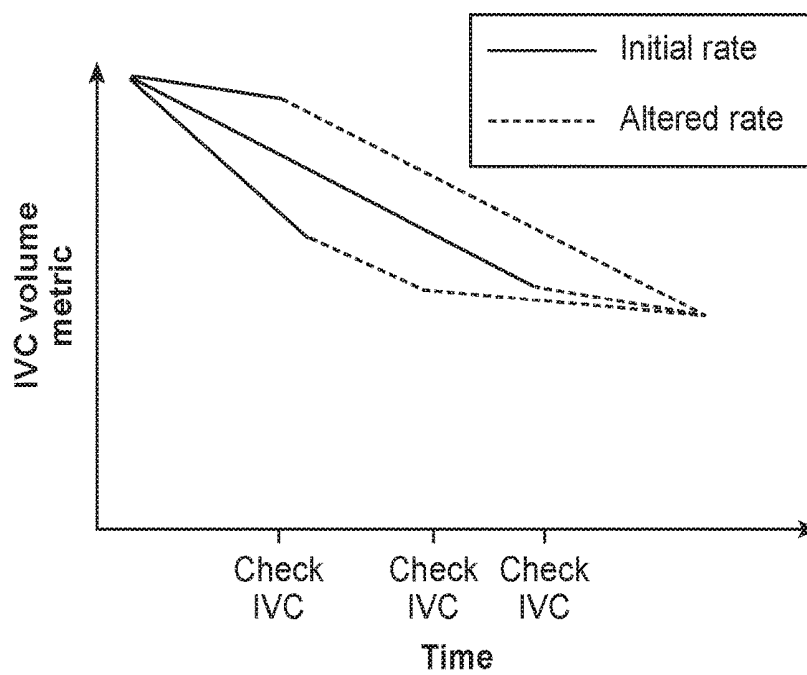


FIG. 4C

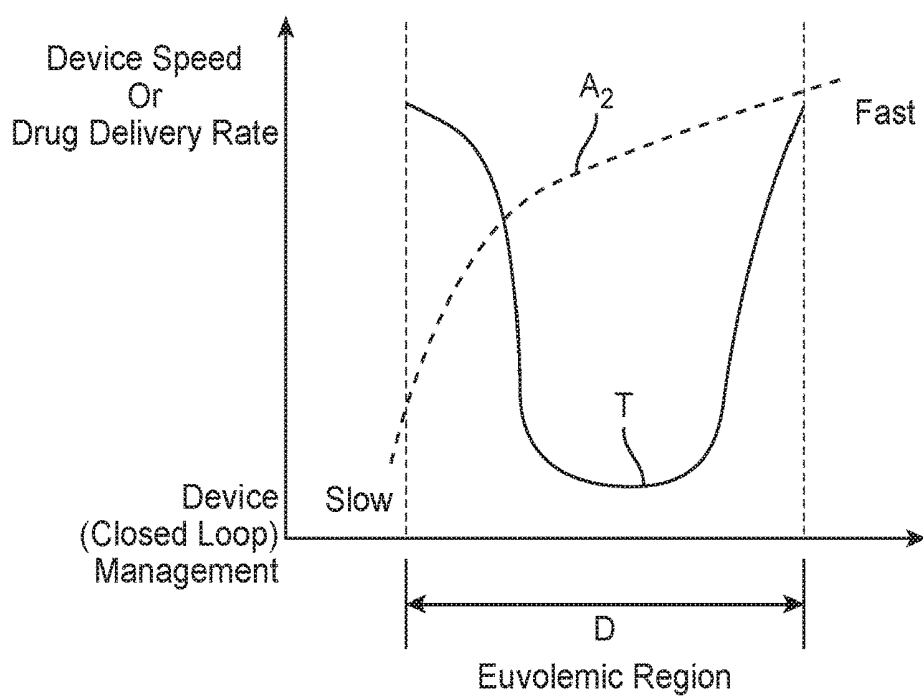


FIG. 5A

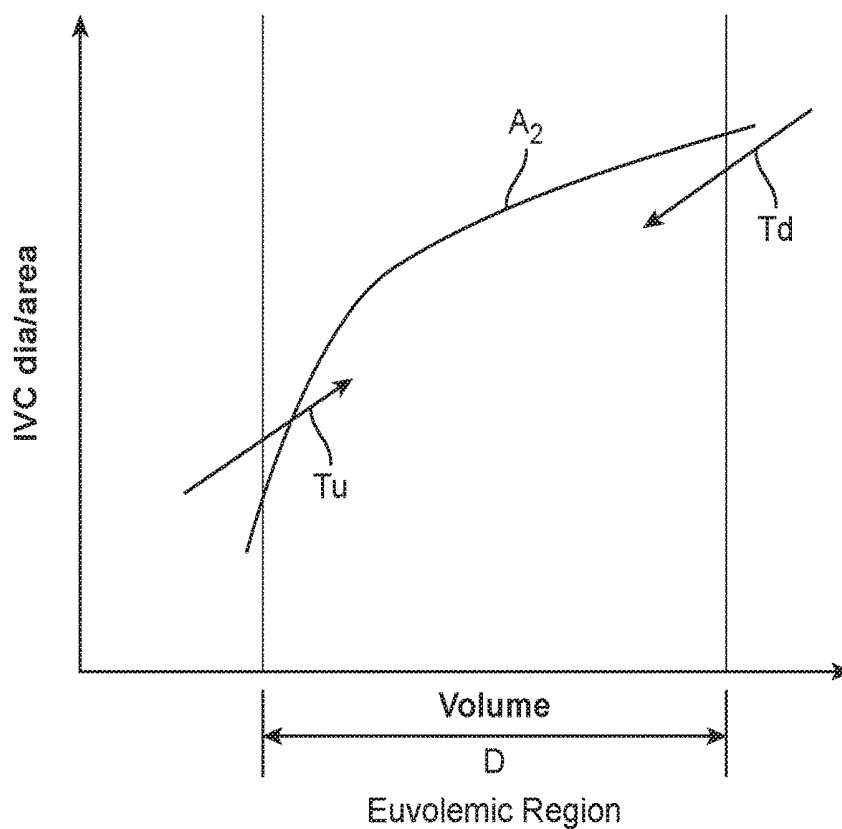


FIG. 5B

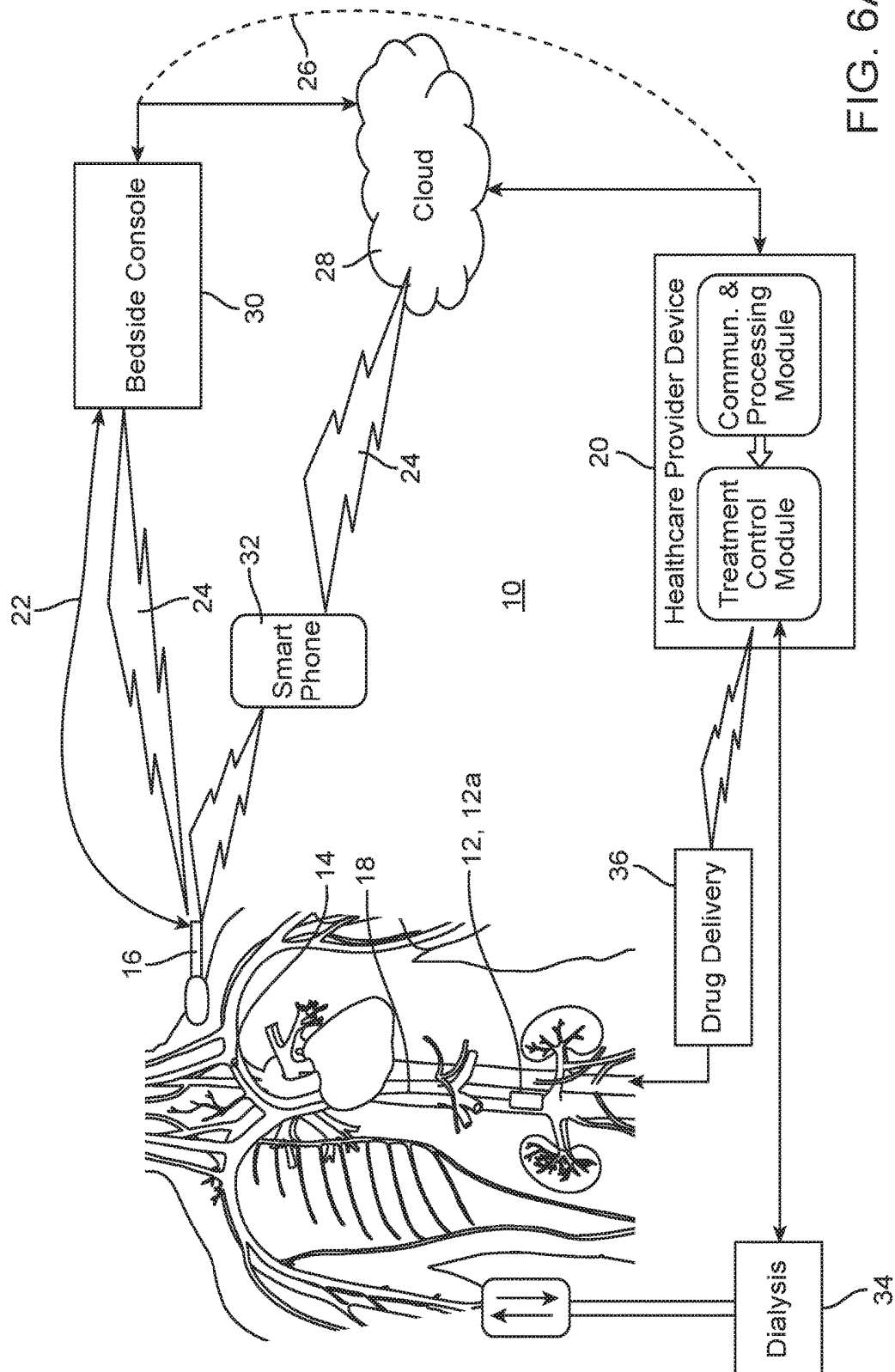


FIG. 6A

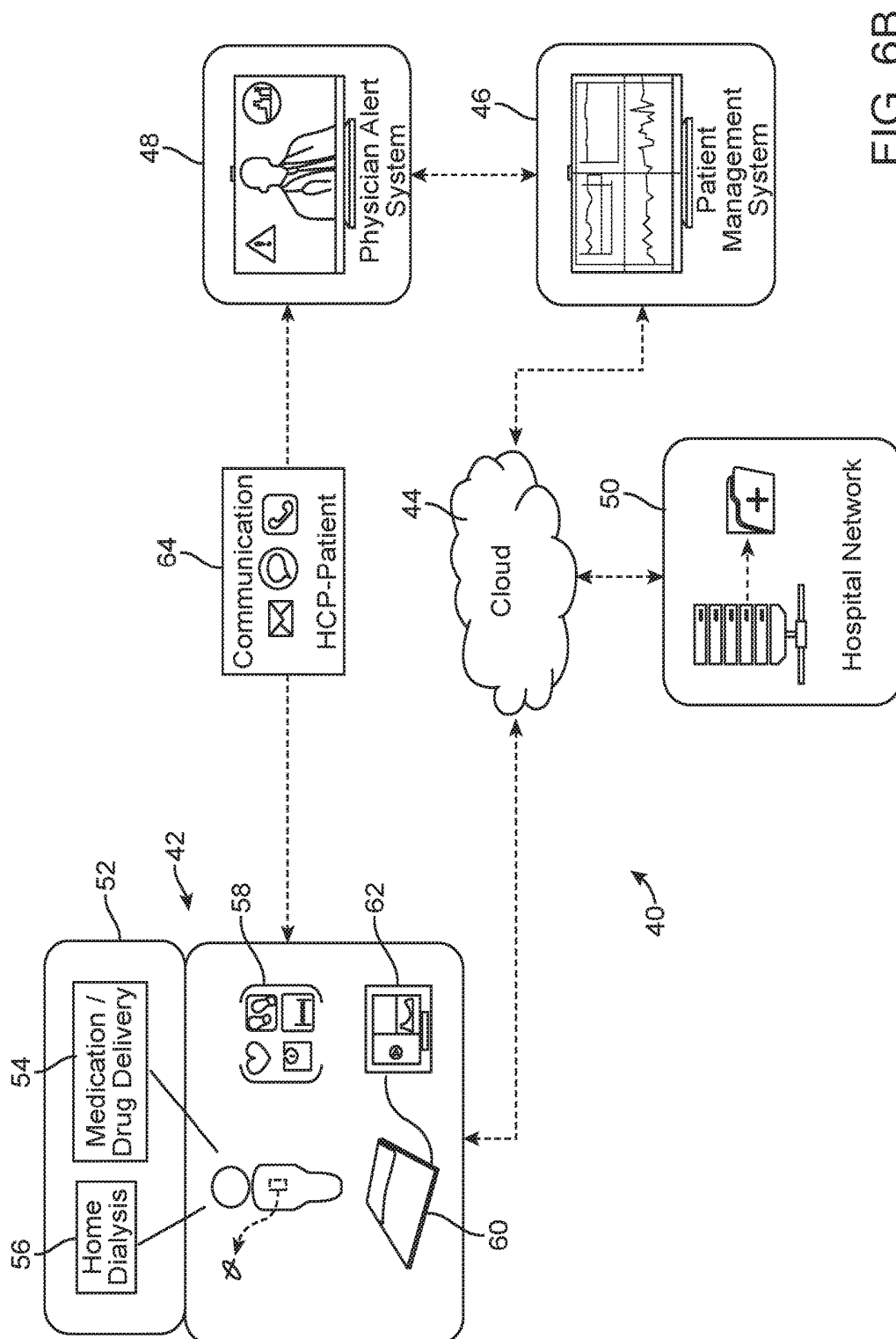
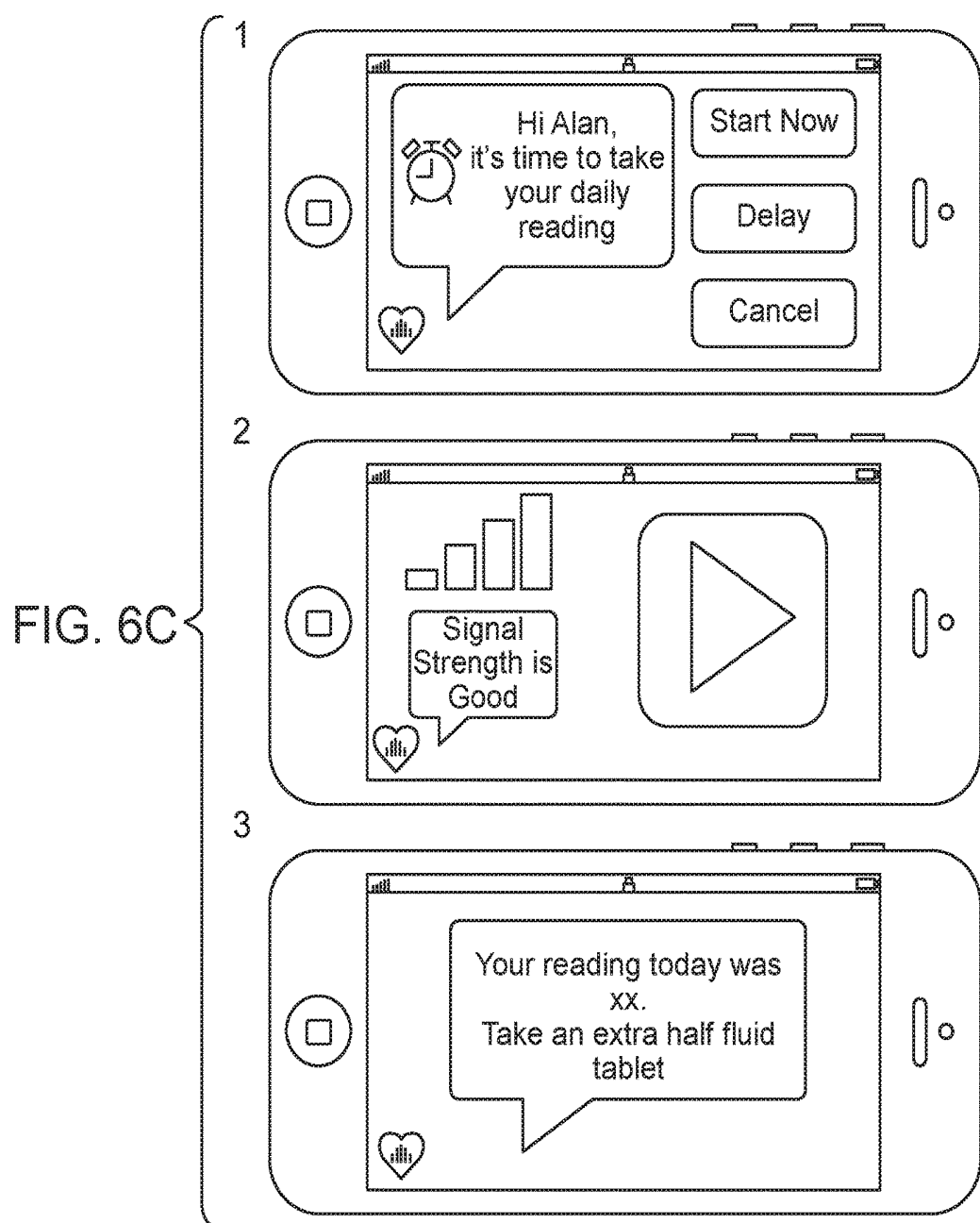


FIG. 6B



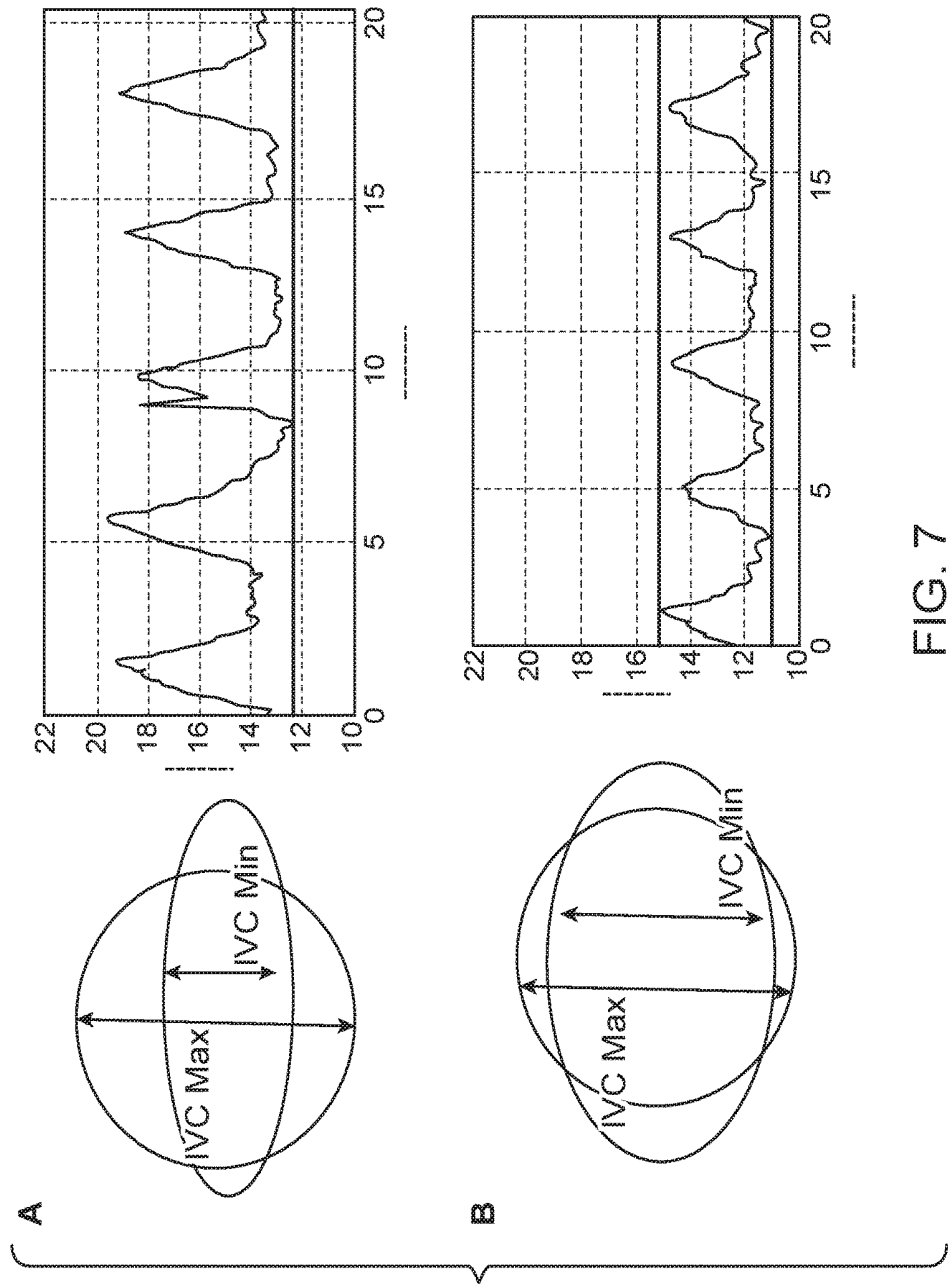


FIG. 7

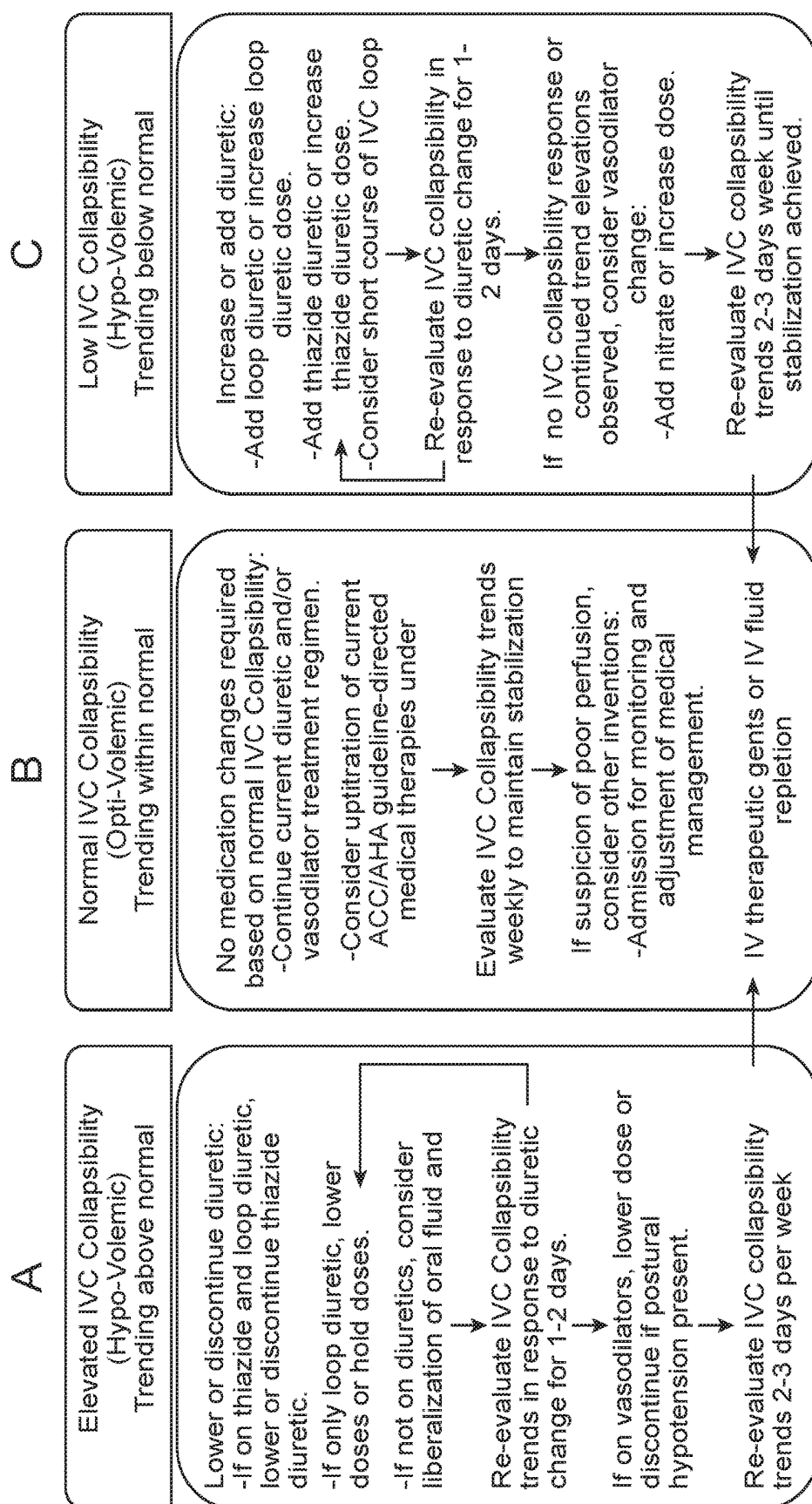


FIG. 8

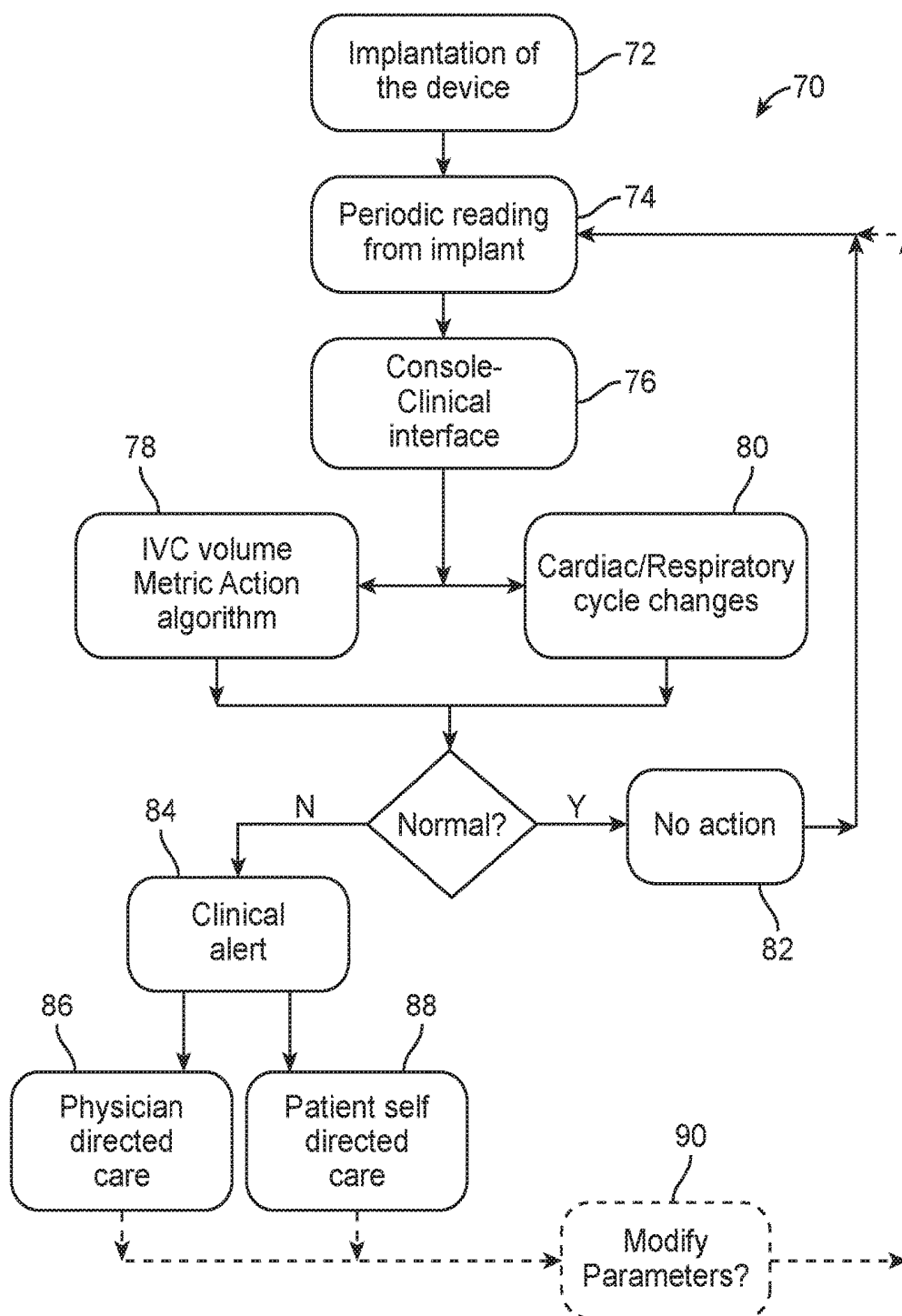


FIG. 9

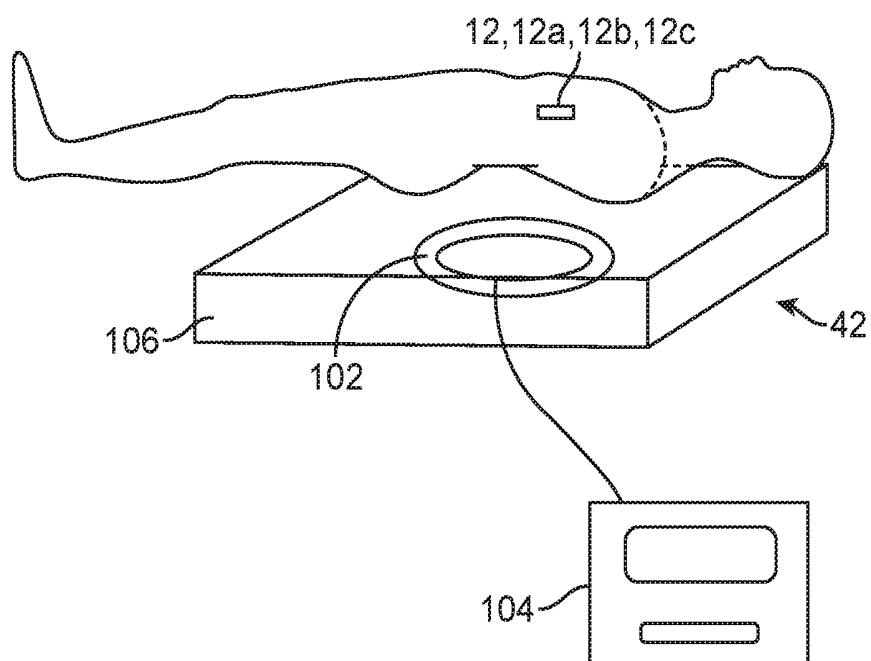


FIG. 10

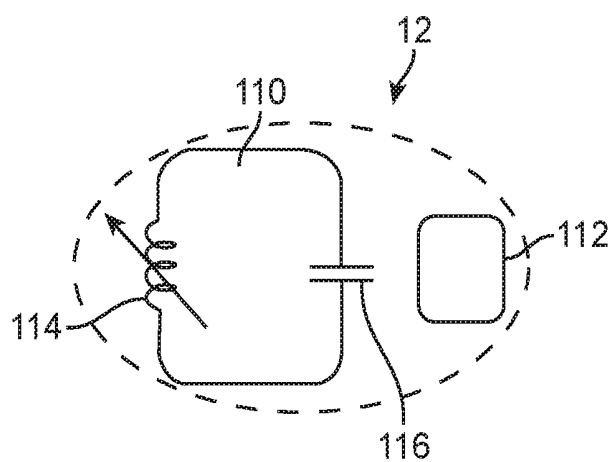


FIG. 11

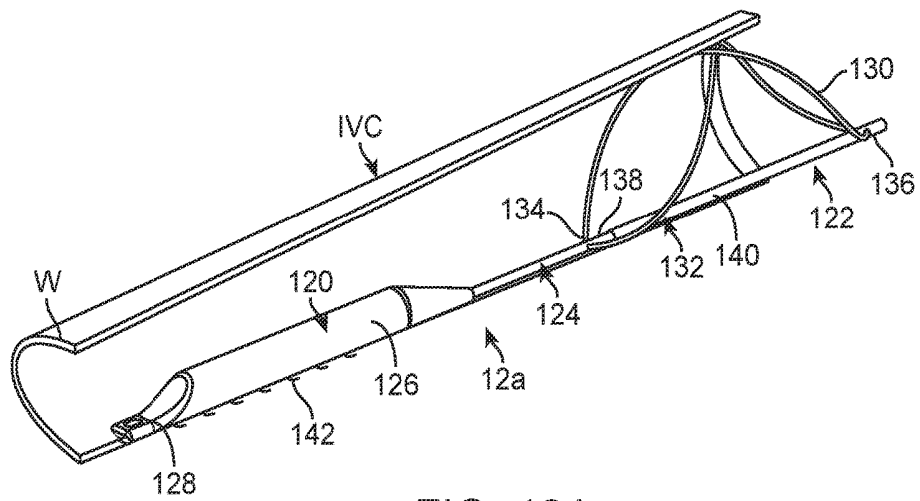


FIG. 12A

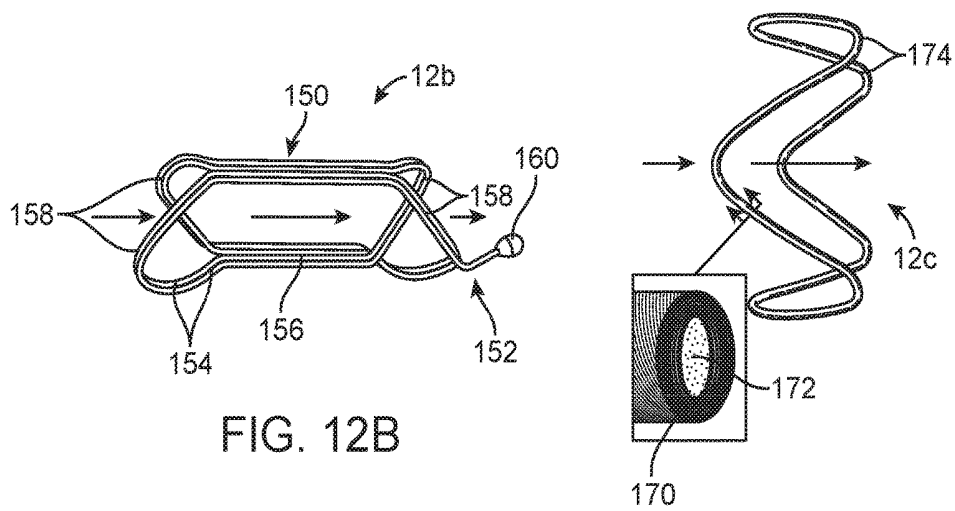


FIG. 12B

FIG. 12C

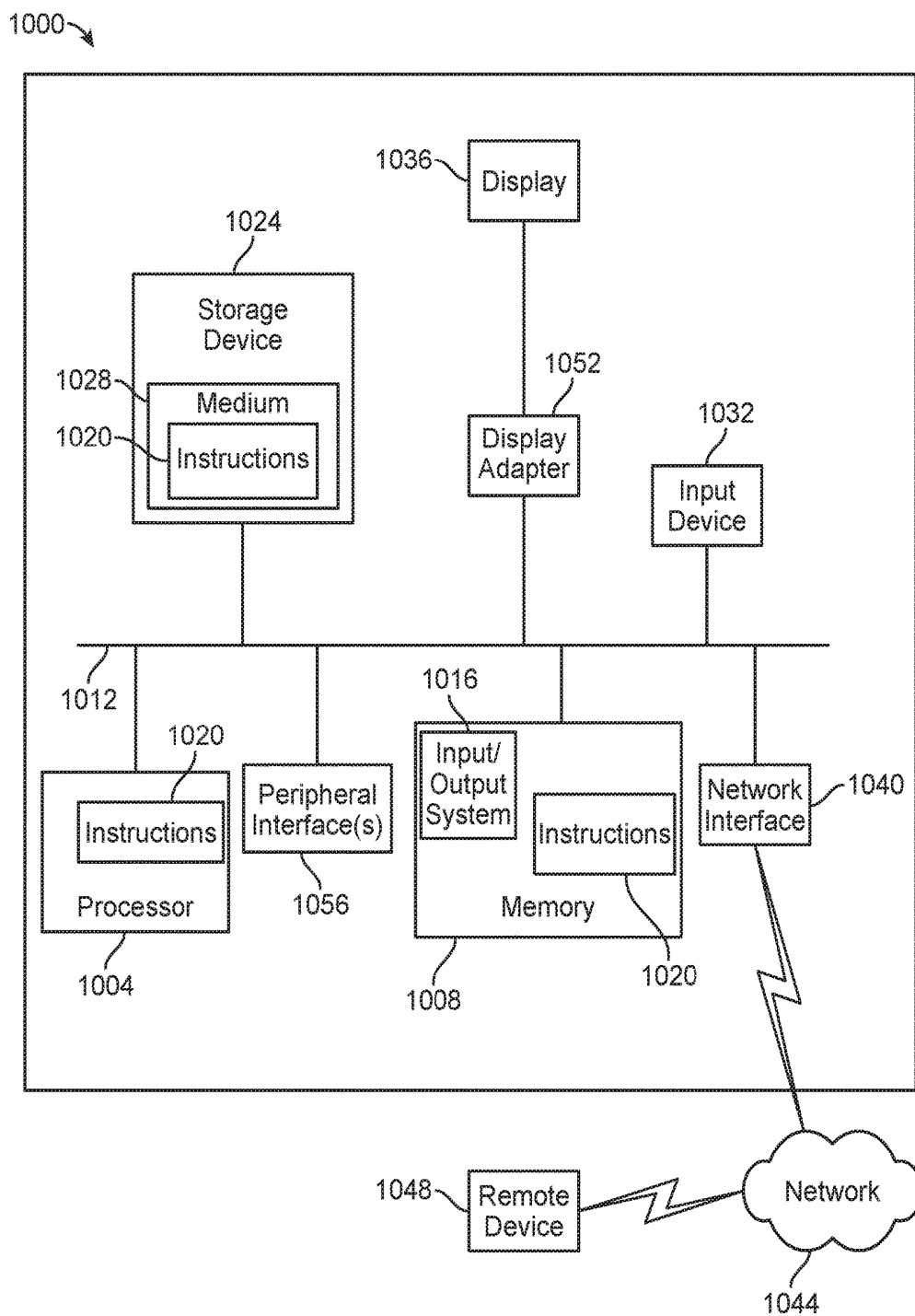


FIG. 13

SYSTEMS AND METHODS FOR PATIENT FLUID MANAGEMENT

RELATED APPLICATION DATA

[0001] This application is a continuation of PCT/US017/046204, filed Aug. 10, 2017, entitled Systems and Methods for Patient Fluid Management, which PCT application claims the benefit of priority of U.S. Provisional Patent Application Ser. No. 62/373,436, filed Aug. 11, 2016, and titled “Methods and Systems For Patient Fluid Management”, this application also claims the benefit of priority of U.S. Provisional Patent Application Ser. No. 62/427,631, filed Nov. 29, 2016, and titled “Wireless Vascular Monitoring Implants, Systems, Methods, and Software”, and also claims the benefit of priority of U.S. Provisional Patent Application No. 62/534,329, filed Jul. 19, 2017, and titled “Wireless Vascular Monitoring Implants, Systems and Methods”. Each of these applications is incorporated by reference herein in their entirety.

FIELD OF THE DISCLOSURE

[0002] Embodiments disclosed herein relate to systems and methods for patient fluid management, for example in connection with heart failure or renal failure conditions, as well as other disease states requiring careful management of patient fluid balance.

BACKGROUND

[0003] A significant challenge in the treatment of acute heart failure patients is the management of the patient fluid volume. Similar challenges are also presented in the treatment of renal failure patients, and, in fact, studies have shown a direct correlation, and potentially causal relationship, between heart and renal failure conditions with respect to patient fluid management [e.g., Silverberg, et al., *The association between congestive heart failure and chronic renal disease*, Curr. Opin. Nephrol. Hypertens. (2004) 13:163-170]. Acute heart or renal failure can lead to peripheral and pulmonary edema if not properly treated, but too aggressive of a treatment can lead to a hypovolemic state in which the patient lacks sufficient fluid volume. Treatments may include dialysis, ultrafiltration, diuretics and other drug administration. For longer term patients, fluid and dietary intake also may be monitored and modulated. Traditionally, diagnostic techniques used in monitoring fluid status were based on various externally observable symptoms (e.g., jugular vein distention, edema, patient weight change). Also, central venous catheterization (CVC) to monitor central venous pressure (CVP) has been used as a fluid status indicator. However, there are a number of serious risks associated with CVC, such as infection and thrombosis, and reliance on externally observable or measurable symptoms presents an obvious drawback in that the observable response to a therapy is often significantly delayed relative to acute changes in physiological status.

[0004] Monitoring fluid status can also be used as a predictor for onset of acute decompensated heart failure (ADHF), which is a significant factor driving rehospitalization of heart failure patients. There is potential to significantly reduce hospitalizations if there is a sufficiently early signal of increasing patient fluid volume. However, draw-

backs of traditional diagnostic tools as mentioned above make such tools relatively ineffective as early predictors of ADHF.

[0005] In an attempt to overcome risks and drawbacks associated with more traditional diagnostic techniques, different types of diagnostic devices or techniques have been developed to measure central venous pressure (CVP) [e.g., Shuros, et al., *Coronary Vein Hemodynamic Sensor*, US 2009/01497666, Jun. 11, 2009] or pulmonary artery pressure (PAP) [e.g., Abraham, et al., *Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomized controlled trial*, Lancet (2011) 377:658-66]. Also, research using external ultrasound observation of the Inferior Vena Cava (IVC) has led to a general understanding of a correlation between the IVC volume and patient health in terms of proper fluid balance [e.g., Feissel et al., *The respiratory variation in inferior vena cava diameter as a guide to fluid therapy*, Intensive Care Med (2004) 30:1834-1837]. Based on this understanding, external ultrasound systems are now sometimes used in emergency treatment situations to provide the attending physicians with information on patient fluid state. In addition, more recent techniques have been proposed in which devices indirectly measure vessel pressure or volume based on changes in impedance in response to an applied current within the vessel.

[0006] While devices and techniques now available may offer advantages over more traditional techniques based on observation of externally visible symptoms, each has its own disadvantages that limit effectiveness as a diagnostic tool to support more aggressive therapies. Many newer monitoring devices or techniques either do not provide sufficiently accurate data to allow early warning of changes in patient stability or do not provide guidance with respect to a particular type of intervention [see, e.g., Marik, et al., *Does Central Venous Pressure Predict Fluid Responsiveness?*: A Systematic Review of the Literature and the Tale of Seven Mares*, Chest (2008) 134(1):172-178]. Examples include that impedance-based devices have not shown sufficient sensitivity and PAP measurements do not provide a warning of hypovolemia. External measurement of IVC dimensions with external ultrasound systems is heavily reliant on proper and consistent positioning of the patient and the imaging device, both initially and over the period of monitoring, and may not always provide accurate prediction of fluid state [e.g., Blehar, et al., *Inferior vena cava displacement during respirophasic ultrasound imaging*, Critical Ultrasound Journal (2012) 4:18]. It is also impractical for use as a longer term diagnostic tool for regular (e.g. daily) monitoring of patients who are not hospitalized.

SUMMARY OF THE DISCLOSURE

[0007] Embodiments disclosed herein include a system for managing patient body fluid volume, comprising a wireless sensing device, a sensing control module and a patient management system. The wireless sensing device is configured to be positioned within a patient's IVC to measure a physical dimension of the IVC and generate a measurement signal indicative of the measured IVC physical dimension. The sensing device control module is configured to wirelessly communicate with the sensing device to at least receive the measurement signal from the sensing device. The patient management system may include a processor and memory, and is configured to receive or generate measure-

ment data representative of the measured IVC physical dimension based on the measurement signal, to receive patient specific information, and to execute instructions contained in the memory responsive to received patient specific information and the measurement data. The instructions contained in memory may include instructions to prompt for initiation of a sensor measurement of the IVC physical dimension and generate an alert signal when the measured IVC physical dimension is outside predetermined clinical limits for the patient. The instructions may further include instructions to wirelessly communicate with the implanted sensing device to monitor changes in the measured IVC dimension throughout an euvoletic region defined for said patient. In some embodiments, the physical dimension of the patient's IVC is at least one of IVC diameter or IVC area.

[0008] In another, alternative embodiment, a system for managing patient body fluid volume includes a processor and memory configured to communicate with the implanted wireless sensing device and the sensing device control module. The processor may be configured to receive measurement data representing the IVC physical dimension measurement by the sensing device and execute instructions contained in the memory responsive that measurement data. The processor also may be configured to receive patient specific information. The instructions stored in memory may comprise defining euvoletic, hypovolemic and hypervolemic regions for the patient wherein the euvoletic range, the hypovolemic range and the range are correlated to IVC diameter or volume measurements for the patient, identifying a hypovolemic warning zone for the patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent the hypovolemic region, identifying a hypervolemic warning zone for the patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent the hypervolemic region, generating an alert signal when measured IVC diameter or volume falls within either of the hypovolemic warning zone or hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

[0009] In some embodiments the wireless sensing device may comprise an ultrasound transducer and anchor element configured to anchor the ultrasound transducer in the IVC in a fixed position relative to the IVC wall. In other embodiments, the wireless sensing device may comprise a resilient coil forming a resonant circuit, wherein the resilient coil is configured to engage the wall of the IVC and deform therewith to provide a variable characteristic frequency correlated to an IVC physical dimension in response to activation of the resonant circuit. Such a system may further include an antenna configured to activate the resonant circuit and receive the signal representative of the measured IVC physical dimension in response to activation.

[0010] Further alternative embodiments disclosed herein include methods of managing patient body fluid volume. One embodiment of the disclosed methods may include directly measuring a physical dimension of the patient's IVC with a sensing device implanted within the IVC, wirelessly communicating with the implanted sensing device to monitor changes in the measured IVC dimension throughout an euvoletic region defined for said patient, and generating an alert signal when measured IVC diameter or area approaches

or falls outside predetermined clinical limits for the patient. The alert signal may be direct to a healthcare provider or to the patient. When directed to the patient, the alert signal may include a prompt to initiate a patient self-directed treatment.

[0011] In some embodiments the predetermined clinical limits may include at least a first, lower limit indicative of the patient fluid state trending towards hypovolemia, and a second, higher limit indicative of the patient fluid state trending towards hypervolemia. Further, each of the predetermined limits falls within the euvoletic range defined for the patient. In such embodiments, further method steps may comprise setting (1) a hypovolemic warning zone for the patient encompassing a portion of the defined euvoletic region at the lower end of the euvoletic region adjacent a hypovolemic region and (2) a hypervolemic warning zone for the patient encompassing a portion of the defined euvoletic region at the upper end of the euvoletic region adjacent a hypervolemic region, wherein the euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC physical dimension measurements for the patient.

[0012] In another alternative embodiment disclosed herein, a diagnostic method for monitoring patient body fluid volume comprises positioning a sensing device within the patient's IVC, wherein the sensing device is configured to measure at least one physical dimension of the IVC. Wirelessly monitoring changes in measured IVC physical dimension over time throughout an euvoletic region defined for said patient. Identifying (1) a hypovolemic warning zone for the patient encompassing a portion of the defined euvoletic region at the lower end of the euvoletic region adjacent a hypovolemic region and (2) a hypervolemic warning zone for the patient encompassing a portion of the defined euvoletic region at the upper end of the euvoletic region adjacent a hypervolemic region, wherein the euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC physical dimension measurements for the patient. Another step in such a method as disclosed may include signaling a warning state when measured IVC physical dimension falls within either of the hypovolemic warning zone or hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] For the purpose of illustrating the disclosed embodiments, the drawings show aspects thereof. It is to be understood, however, that the teachings of the present disclosure are not limited to the precise arrangements and instrumentalities shown in the drawings, wherein:

[0014] FIG. 1 is a schematic plot of patient fluid volume versus response for disclosed embodiments employing on IVC diameter or area measurement (curves A₁ and A₂) in comparison to prior pressure-based systems (curve B) and in general relationship to IVC collapsibility index (IVC CI, curve C).

[0015] FIG. 2 illustrates a hypothetical comparison of patient fluid volume over time in treatment for hypervolemia as between an IVC diameter or area measurement-based approach according to the present disclosure (curve X) and a typical pressure-based approach (curves Y and Z).

[0016] FIGS. 3A and 3B schematically illustrate alternative treatment embodiments employing titration of therapy based on disclosed systems.

[0017] FIG. 3C illustrates a treatment scenario based on disclosed system embodiments.

[0018] FIGS. 4A, 4B, 4C, 5A and 5B schematically illustrate embodiments of closed loop control of dialysis and therapy/treatment devices based on systems disclosed herein.

[0019] FIGS. 6A and 6B schematically depict components and possible arrangement of alternative system embodiments as disclosed herein.

[0020] FIG. 6C shows examples of screen shots from a patient's mobile device presenting patient prompts as part of a patient self-directed therapy algorithm.

[0021] FIG. 7 illustrates an exemplary algorithm for determination of IVC collapsibility (IVC CI) on which a treatment algorithm may be based.

[0022] FIG. 8 illustrates a possible treatment algorithm according to the present disclosure.

[0023] FIG. 9 illustrates an exemplary workflow utilizing a system employing an implanted IVC Volume Metric monitoring device as disclosed herein.

[0024] FIG. 10 schematically illustrates one embodiment of a local system for receiving signals/communicating with an implant according to embodiments disclosed herein.

[0025] FIG. 11 presents a block diagram of one embodiment of an IVC measurement implant.

[0026] FIGS. 12A, 12B, and 12C illustrate more details of further embodiments of IVC measurement implants according to the present disclosure.

[0027] FIG. 13 a block diagram of a computing system that can be used to implement any one or more of the methodologies disclosed herein and any one or more portions thereof.

DESCRIPTION OF EMBODIMENTS

[0028] Embodiments disclosed herein include systems and methodologies allowing for regular, periodic or continuous monitoring of fluid volume more accurately than current techniques and with reduced lag time before changes in volume status are observed, thus providing earlier warning of hypervolemia or hypovolemia and enabling the modulation of patient treatments to permit more stable long term fluid management. Further, in acute situations, the methods and systems disclosed enable more rapid reduction of excessive intravascular volume and edema and restoration of more ideal fluid balance, with lessened risk of creating a hypovolemic state as can be created when patient "drying" treatments overshoot due to the response of patient monitoring devices or protocols.

[0029] A challenge presented by patients in decompensated heart failure is managing patient fluid balance, bringing down excess fluid volume as quickly as possible, but without overshooting and taking the patient into a potentially equally dangerous hypovolemic state. In the longer term management of heart failure, maintaining fluid balance is still a challenge, but in this case it involves maintaining the patient well within a safe fluid state without unintentionally migrating into a hypervolemic or hypovolemic state.

[0030] Existing clinical devices focused on pressure measurement present certain difficulties in meeting these challenges. Pressure measurements can be useful as an indicator of gross fluid volume change, and as a predictor of acute

decompensation when fluid levels are already at a relatively high level. However, detectable changes in PAP can lag changes in physiological state to an extent that a patient may be in an early stage of the risk zone before the change is identified. Also, as shown in FIG. 1, the relationship between pressure and volume in the IVC is highly nonlinear over the entire range from hypovolemic to euvoletic to hypervolemic, exhibiting significant volume change within the mid-range, generally euvoletic state, with minimal corresponding change in pressure that can be measured. (See FIG. 1, curve B). For these reasons, PAP and CVP can be limited predictors of volume status and likelihood of acute decompensation before a near acute stage is reached.

[0031] While there is a general knowledge of a correlation between IVC diameter and patient health and fluid state, existing devices and techniques for monitoring patient fluid state across the full volume range have not led to treatment systems or methodologies permitting more rapid stabilization of acute patients and longer term maintenance without that avoids the critical fluid states and may thus lead to otherwise unnecessary treatments or hospitalizations.

[0032] "Euvoletmia" refers to the normal fluid volume in a patient's body, and "euvoletic region" refers to a range of fluid volume within the patient that is clinically characterizable as normal or not requiring intervention. ("Euvoletmia" is also sometimes referred to in the medical literature as "normovolemia.") The euvoletic region, as explained in more detail below, also a fluid state or volume range across which measurement of central venous pressure (CVP) in the IVC is generally non-responsive to changes in fluid volume. "Hypervolemia" refers to a state in which a patient's body fluid volume exceeds a normal range, and "hypervolemic range" refers to a range of fluid volume within the patient that is clinically characterizable as excessive. Intervention may be indicated when a patient trends towards, enters into or persists within the hypervolemic range. "Hypovolemia" refers to a state in which a patient's body fluid volume is below a normal range, and "hypovolemic range" refers to a range of fluid volume within the patient that is clinically characterizable as insufficient. As with the hypervolemic range, intervention also may be indicated when a patient trends towards, enters into or persists within the hypovolemic range. As is well-understood by clinicians and other persons of skill in the art, these body fluid states are not static nor are they uniform or in terms of absolute volume. While it is possible for a person of ordinary skill to assign approximate ranges of parameters generally corresponding to the different fluid states, it can be difficult in practice for ordinary skilled persons, with existing diagnostic tools and methods, to identify where a particular patient's fluid state may reside with respect to the euvoletic, hypovolemic and hypervolemic ranges.

[0033] In response to the need for more accurate devices with faster response times, the Assignee of the present disclosure has developed a number of new devices that provide fluid volume data based on direct measurement of physical dimensions of the IVC, such as the diameter or area. Examples of these new devices are described, for example, in PCT/US2016/017902, filed Feb. 12, 2016, U.S. Provisional Patent Application, Ser. No. 62/427,631, filed Nov. 29, 2016, and U.S. Provisional Application, Ser. No. 62/534,329, filed Jul. 19, 2017 by the present Applicant, each of which is incorporated by reference herein in its entirety. Devices of the types described in these prior

disclosures facilitate new management and treatment techniques as described herein based on regular intermittent (e.g., daily) or substantially continuous (near real-time), direct feedback on IVC diameter.

[0034] In further alternative embodiments disclosed herein, patient fluid state can be further modulated based on a combination of IVC data with other monitoring signals; symptoms and clinical input, by use of IVC data as it is influenced by some stimulus (e.g., exercise; leg raises) to indicate either system capacitance or redistribution of fluid, by use of IVC measurements from an implanted sensor to transmit regular information locally to help the clinical management of patients, e.g. patients managing their own dialysis and/or diuresis at home, or by use of IVC measurement from an implanted sensor to control drug delivery (e.g., like a closed loop implanted system for diabetes). Advantages achievable with disclosed systems and methods may include improved reduction of excessive intravascular blood volume in the clinical setting, through the controlled use of diuretics, more accurate management of blood volume in the home setting, through the monitoring of patients and use of a treatment algorithm, more rapid dialysis through the monitoring of volume and informed variation of dialysis rate.

[0035] As an illustration of the presently disclosed methodology, FIG. 1 presents a schematic plot of patient fluid volume versus a number of responses. IVC diameter or measurement versus Volume are shown by curves A₁ and A₂ in comparison to IVC Pressure versus Volume (curve B) and the IVC collapsibility index versus Volume (IVC CI, curve C). The IVC collapsibility index (CI) is equal to the measured IVC dimension at maximum extension minus the same dimension at minimum extension divided by the maximum extension dimension. (CI=Max-Min/Max). Any single dimension measurement may be used, i.e. major diameter, minor diameter or area (see FIG. 7). It should be noted that FIG. 1 is intended only to summarize and illustrate overall relationships of the parameters discussed, and does not represent specific data points or data plotted to scale. (Curves A₁ and A₂ represent data from preclinical and benchtop testing conducted by the present Applicant based

to IVC volume and IVC CI (hereinafter “IVC Volume Metrics”) provides relatively consistent information on patient fluid state across the full range of states.

[0037] Using IVC diameter or area measurement as an indicator of patient fluid volume as disclosed herein thus provides an opportunity for earlier response both as a hypovolemic warning and as an earlier hypervolemic warning. With respect to hypovolemia, when using pressure as a monitoring tool, a high pressure threshold can act as a potential sign of congestion, however when pressure is below a pressure threshold (i.e., along the flat part of curve B), it gives no information about the fluid status as the patient approaches hypovolemia. With respect to hypervolemia, IVC diameter or area measurements potentially provide an earlier signal than pressure-based signals due to the fact that IVC diameter or area measurements change a relatively large amount without significant change in pressure. Hence, a threshold set on IVC diameter or area measurements can give an earlier indication of hypervolemia, in advance of a pressure-based signal.

[0038] Based on systems and methods disclosed herein, a patient healthcare provider can devise defined early warning zones for the hypovolemic region (O_E) and hypervolemic region (R_E). Just as the euvoletic region boundaries vary from patient to patient based on many physical and health related factors, such as age, sex, obesity and disease state. The early warning zones reside within the euvoletic range immediately adjacent the hypovolemic and hypervolemic regions such that the patient may still be considered to be within acceptable fluid balance parameters when in the early warning zones. However, the ability to define early warning zones as such based on IVC diameter or area measurements means that appropriate interventions may be initiated earlier, before the patient reaches higher levels of criticality, and thus also may be controlled more precisely and smoothly to minimize risk of shock from sudden interventions and/or overshoot of therapy targets. Table II below illustrates an example of possible fluid state regions for a hypothetical patient in accordance with the teachings of the present disclosure.

TABLE I

Example of Fluid State Regions for Hypothetical Patient				
Hypovolemic Region (O)	Hypovolemic Early Warning Zone (O _E)	Euvoletic Region	Hypervolemic Early Warning Zone (R _E)	Hypervolemic Range (R)
IVC Ø <14 mm + IVCCI >75%	IVC Ø = 14-16 mm + IVCCI = 60-75%	IVC Ø ~ 14-21 mm + IVCCI ~ 50-75%	IVC Ø = 19-21 mm + IVCCI = 50-60%	IVC Ø >21 mm + IVCCI <50%

on prototype devices of a type described herein. Curve B is adapted from canine IVC results published by Moreno et al., Circ. Res. (1970) 27 (5): 1069-1080.

[0036] As can be seen in FIG. 1, the response of pressure-based diagnostic tools (B) over the euvoletic region (D) is relatively flat and thus provides minimal information as to exactly where patient fluid volume resides within that region. Pressure-based diagnostic tools thus tend to only indicate measureable response after the patient's fluid state has entered into the hypovolemic region (O) or the hypervolemic region (R). In contrast, a diagnostic approach based on IVC diameter or area measurement across the respiratory and/or cardiac cycles (A₁ and A₂), which correlates directly

[0039] FIG. 2 illustrates a hypothetical comparison of patient fluid volume over time in treatment for hypervolemia as between an IVC Volume Metrics-based approach according to the present disclosure (curve X) and a typical pressure-based approach (curve Y). Because of the greater information available in the euvoletic region, the IVC Volume Metrics-based approach permits more aggressive initial treatment with lower risk of overshoot into the hypovolemic region (low), resulting in bringing the patient into the euvoletic region (safe) more quickly as compared to a pressure-based system, which must modulate therapy more gradually. Curve Z illustrates the potential risk for a pressure-based system if treatment were initially applied in

a manner similar to the IVC Volume Metrics-based system. Without the greater information and feedback available (as illustrated by FIG. 1, curves A_1 and A_2), by the time the treatment provider sees a response from the diagnostic tools, the aggressive treatment may have already pushed the patient into the hypovolemic region (low).

[0040] Use of IVC diameter or area measurements as described herein thus offers advantages in titrating patient therapies. FIGS. 3A and 3B illustrate embodiments of possible therapy titration schedules over the patient fluid state ranges based on the teachings of the present disclosure. Because IVC diameter/area changes more accurately reflect changes in patient fluid volume consistent with actual fluid state, IVC diameter or area measurements can be used to help titrate treatments more precisely and adjust the therapeutic intervention more subtly and incrementally, rather than just using a hard threshold as is now the clinical norm. Use of IVC diameter or area measurements also allows the flexibility of potentially titrating patients to a personalised volume, for example, keeping a patient with reduced cardiac ejection fraction (HFrEF) at a wetter point, while maintaining a patient with preserved cardiac ejection fraction (HFpEF) at a drier point.

[0041] FIG. 3A describes one possible treatment algorithm in this regard in which patient therapy is reduced when the patient's fluid volume comfortably falls in the mid-range of the euvoletic region. In this treatment algorithm example, in which curve (T) represents a relative therapy level plotted against patient fluid volume, therapy is increased relatively rapidly once the patient's fluid volume moves from the mid-range of the euvoletic region as indicated by monitored changes in the IVC diameter or area. Such a treatment algorithm may be appropriate, for example, for a patient that is known to have a slow response to therapy in order to avoid having the patient move too far into the hypovolemic or hypervolemic regions before responding to the treatment. FIG. 3B describes another possible treatment algorithm based on the teachings of the present disclosure. In this example, relative therapy curve (T) is flatter across the majority of the euvoletic region (D) and only significantly increases once fluid volume, as determined based on sensed changes in IVC diameter or area, moves into one of the predefined early warning regions O_E or R_E that have been determined to be clinically appropriate for the specific patient being monitored. For illustration purposes, curve A_2 from FIG. 1 (representing change in IVC diameter/area vs. fluid volume) is superimposed over treatment curve (T) in FIG. 3B so that the relative relationship between IVC diameter/area change and treatment algorithm in this example may be better appreciated.

[0042] FIG. 3C schematically illustrates practical application of the relationships illustrated in FIG. 1 and potential advantages of treatment algorithms such as described in FIGS. 3A and 3B, based on sensed changes in IVC diameter or area as disclosed herein. In FIG. 3C, relative patient fluid volumes for hypothetical patients (whose therapy is titrated according to a treatment algorithm as described above) are plotted against relative time. Curves FVR1 and FVR2 thus represent two hypothetical examples of patient fluid volume response to therapy over time. In each case, applying a treatment algorithm such as described in the examples of FIG. 3A or 3B, patient therapy can be titrated more accurately with respect to actual fluid state within the euvoletic region such that therapy may be applied at appropriate times

earlier and more gradually to ensure that overall patient fluid volume stays within or as close as possible to the euvoletic region.

[0043] IVC diameter or area measurements also may be used in combination with other diagnostic signals to provide guidance on therapeutic intervention, e.g., diuretics versus vasodilators. When used with intervention, the IVC diameter or area measurement time dynamics response may be used to give information on the fluid status/distribution of the patient to guide therapy intervention. Response of IVC diameter or area measurements to a perturbation, e.g., physical activity, can cause sympathetic nerve response and fluid redistribution. Looking at changes in IVC diameter or area will thus provide information on fluid volume status. In other words, an act as simple as a leg raise may cause a fluid change/redistribution that could also provide information on fluid volume status that would not be visible with pressure-based systems. Thus, in certain embodiments, at-risk patients may have continuous or near-continuous monitoring of IVC diameter or area changes during physical activity.

[0044] Sensed changes in IVC diameter or area also may be combined with other parameters such as with BNP or pressure/edema signals to help guide therapy intervention or differentiate patient phenotype (HFrEF v HFpEF). Examples include detection of low collapsibility plus peripheral edema as an indication for diuretic therapy or detection of low collapsibility without peripheral edema as an indication for indicate vasodilator therapy. Combination of monitoring IVC diameter or area changes with implanted pressure-based monitors (in the IVC, right atrium, right ventricle, pulmonary artery, left atrium, or other vessel) also may permit determination of abdominal pressure and flow in the IVC. In addition, the IVC monitoring device of the invention may include additional sensors to measure non-dimensional parameters within the IVC such as blood flow rate and venous pressure. Further, measurement of the dimensions or non-dimensional parameters of other vessels, such as the superior vena cava, pulmonary artery, or heart chambers, may in some cases be advantageous to supplement IVC measurement. In such cases, dimensional measurement devices similar to the IVC monitoring device of the present invention may be configured for implantation in such other vessels. In such embodiments, the methods and systems of the invention may be adapted to receive such supplementary data from these sources and incorporate such data in the determination of fluid status, heart failure status, appropriate thresholds for communicating alerts or messages, or therapeutic treatment plans or recommendations.

[0045] Use of IVC diameter or area measurements also leads to the development of new systems such as closed-loop systems for therapy intervention as described herein. Examples include modification of a standard dialysis system filtration rate from a constant rate to a faster or variable rate using information that was previously unavailable to the clinician or patient. In one example, as illustrated in FIG. 4A, IVC diameter or area measurements may provide faster dialysis treatment in a closed-loop system, such as described below, by guiding higher filtration rates while the fluid load is high and inform reducing filtration rate as the fluid is reduced, ultimately resulting in a faster and safer treatment. Hypotensive events may occur in patients undergoing dialysis due to fluid removal occurring too rapidly. FIG. 4A plots patient fluid volume against rate of dialysis for a closed-loop system based on embodiments described herein, which may

allow for more efficient dialysis, e.g., fast enough to remove fluid without the side effects of fast fluid removal. When ultrafiltration (UF) is constant, the degree of vascular refilling will differ from patient to patient, therefore using additional information provided by IVC diameter or area measurements may allow the UF rate to be more accurately individualized in a time dependent fashion over the course of the dialysis session for specific patients. IVC diameter or area measurement information may be combined with other diagnostic tools such as blood pressure monitoring to more accurately estimate fluid volume status as a basis for altering the rate of filtration.

[0046] FIG. 4B illustrates another embodiment in which alteration of dialysis filtration rate may be based on periodic assessments of IVC diameter or area change, e.g., a percent change in IVC volume metric per hour coinciding with a total desired volume that needs to be removed. (Each downward arrow in FIG. 4B indicates relative time of each assessment.) This is another alternative approach to control of UF rate, which allows increased accuracy and individualization of treatment for specific patients in a time dependent fashion over the course of a dialysis session. Another alternative dialysis control methodology is described in FIG. 4C in which the IVC volume metric rate of change, based on measured changes in IVC diameter or area, is plotted against time through a hypothetical dialysis session. Employing systems as described herein, time-based check points may be provided, at which time the measured IVC volume metric is checked against predefined patient specific targets. At each check point, UF rate may be altered as needed to direct the patient more efficiently and smoothly to the final fluid volume target. Compared to existing systems, which rely primarily on dry weight estimation based on inter-dialytic weight gain, employing methodologies as described in any of FIGS. 4A, 4B and 4C with systems disclosed herein provides for increased individualization of UF rate for specific patients over the course of the dialysis session.

[0047] In another example, illustrated in FIG. 5A, an implanted drug pump or device may be provided, for example as a closed-loop dialysis management system. In such a system, at a hypervolemic end of the scale the device runs at high speed/delivers large load. As volume is reduced the device slows. This allows time for the interstitial fluid to return to the intravascular space. As the fluid load approaches hypovolemia the device speed/drug load rate could increase proportionally to avoid a hypovolemic state. Such control requires knowledge of incremental changes in fluid state across the euvoletic ranges, which is provided by methodologies and systems described herein. As a point of reference, curve A2 indicating relative IVC diameter or area measurement (from FIG. 1) is superimposed on the treatment curve (T) in FIG. 5A. In yet a further example, illustrated in FIG. 5B, a closed loop system according to embodiments described herein allows for volume control-based therapy delivery modulated based on measured changes in IVC diameter or area. In this example, at either end of the euvoletic region (D), therapy delivery, e.g., drug delivery such as a diuretic or dialysis filtration, may be altered up (T_u) or alerted down (T_d) in accordance with IVC diameter or area measurements.

[0048] FIG. 6A schematically illustrates one exemplary system 10 including an IVC diameter/area measurement monitoring device 12 positioned at a monitoring location in the IVC. In the example illustrated, monitoring device 12 is

an ultrasound-based device 12a anchored within the IVC and uses an ultrasound signal reflected off the opposite wall of the IVC to detect the distance by measuring the time-of-travel of this signal and thus provide a diameter measurement. Other examples of monitoring devices include resonant circuit-based devices in which characteristic inductance varies as the devices expand or contract with the IVC wall. Non-limiting examples of monitoring devices that may be used in systems according to the present disclosure are described below and shown in FIGS. 10, 11, and 12A-C. Further examples and details of suitable IVC diameter/area monitoring devices are disclosed in the aforementioned and incorporated PCT and provisional applications by the present Applicant.

[0049] Measurements of IVC diameter or area by monitoring device 12 may be made continuously over one or more respiratory cycles to determine the variation in IVC dimensions over this cycle. Further, these measurement periods may be taken continuously, at preselected periods and/or in response to a remotely provided prompt from a health care provider/patient. In this example, monitoring device 12 may communicate via an implanted antenna 14 positioned in the left brachiocephalic vein or other location close to an insertion point or location facilitating signal detection by an external antenna or detector 16. External antenna/detector 16 may be configured to be handheld by the patient or healthcare provider, or worn by or affixed to the patient in an anatomical location selected for optimal communication with the implanted antenna 14. Communication between the implanted antenna 14 and monitoring device 12 occurs via an intravascular lead 18, which extends through the venous vasculature to the monitoring device 12. This is just one example of a communications arrangement with a monitoring device such as device 12. In another example, wireless communication to receiver(s) outside the body may be effected directly by the monitoring device itself, without a separate, implanted antenna and connecting intravascular lead.

[0050] External antenna/detector 16 may be configured to communicate via wireless or wired connection with bedside console 30, smart phone 32, or other external communication/control device. Data collected by the monitoring device may be communicated ultimately to a healthcare provider device 20 via wired 22 and/or wireless 24 communications and/or directly through hard wired links such as telephone or local area networks 26 or through Internet or cloud based systems 28. Communications may be facilitated by a bedside console 30 in a home or clinical treatment location or, particularly in the case of implanted monitoring devices, through a mobile device 32, such as a smart phone. Healthcare provider device 20 may be configured with appropriate user interface, processing and communications modules for data input and handling, communications and processing, as well as treatment and control modules, which may include treatment algorithms as described herein for determining treatment protocols based on collected IVC diameter or area measurements, and systems for automated remote control of treatment devices based on determined treatment protocols as elsewhere described herein. Examples of such treatment devices include, but are not limited to, dialysis machine 34 and drug delivery devices 36. Examples of treatments include, when measured dimensions fall within the hypovolemic warning zone, administration of fluids or vasoconstricting drugs, and when measured dimensions fall

within the hypervolemic warning zone, dialysis or administration of diuretics or vasodilating drugs.

[0051] IVC physical dimension data and/or fluid volume state information derived therefrom may also be communicated directly to the patient themselves, along with therapy advice based on this data and using pre-determined algorithms/implanted medical devices. Communications protocols throughout the system may include bidirectional communications to permit a healthcare provider (or other appropriately trained operator at another point in the system) to alter overall monitoring protocols executed at the monitoring device or, for example, to request additional queries by the monitoring device outside the current operational protocol.

[0052] Other embodiments include systems for patient self-directed therapy, for example with IVC volume metrics data utilized directly by the patient with or without clinician overview, e.g., for self-administration of drugs or other therapies. Such systems may also be implemented for home dialysis and/or peritoneal dialysis. Wireless communication between the IVC monitor and the patient's cell phone or computer would allow continuous or periodic transmission of IVC data and the use of software applications to provide alarms or reminders, graphically present trends, suggest patient actions, drug dosage options, or treatment system settings, and allow communication with physicians.

[0053] FIG. 6B schematically illustrates another exemplary system, which may, in one alternative, incorporate patient self-directed therapy. As shown in FIG. 6B, system 40 provides for communication between the patient home system 42, cloud storage 44, a patient management system 46, a physician alert system 48, and optionally a hospital network 50. Data transmission from the patient home system 42 to the cloud 44 for storage and access facilitates remote access for clinical and nursing teams. In patient self-directed therapy embodiments, patient's home may include home therapy devices 52, which may independently access cloud storage 44, and based on predetermined limits/treatment algorithms, indicate patient self-administration of medications or drug delivery 54 or home dialysis machines 56. In such a system a patient with wireless implant 12 may receive prompts from a cell phone or other device in the home at specific time intervals or in response to data 58 generated by other patient monitoring devices such as blood pressure, heart rate or respiration monitors that also communicate with the home device and may transmit data to cloud 44 for storage. System 40 may also include communication links (direct, networked or cloud-based) with such other monitoring devices to receive data 58 inputs used in setting warning zones and alert limits and assessing patient fluid state. Further inputs may be made by a user through a user interface, which may be, for example, configured as part of patient management system 46. User inputs may include additional patient-specific information such as patient age, sex, height, weight, activity level, or health history indicators.

[0054] In response to a prompt from system 40 to take a reading, the patient would position him/herself with respect to antenna/detector 60 as appropriate to communicate with selected implant 12. Antenna/detector 60 may communicate locally with a control console 62 to receive and interpret signals from implant 12. FIG. 6C shows screen shots of a patient mobile device with examples of sequential prompts as may be provided on a home/mobile/cellular device.

[0055] Varying levels of response may be generated by the home system 42 depending on IVC measurements received from implant 12 and as may be interpreted in light of other patient data 58. Minimal responses may indicate to the patient that fluid status is within acceptable ranges and no action is required. Mid-level responses may include prompts for medication administration or changes in home drug delivery, or home dialysis. Examples of treatment protocols are explained further below. When home dialysis or drug delivery is prompted, it may be controlled directly in a closed-loop system as described above or may be controlled by the patient with prompts from the system. Patient data 58 and IVC measurements from implant 12 also may be communicated continuously or periodically by system 40 to cloud storage 44 and further communicated to a remote patient management system 46. Functionality for system 40 may be largely contained in home system 42 or in patient management system 46 or appropriately distributed across the network. Optionally, patient related data including sensor results and patient health and fluid states also may be communicated to or accessible by a hospital network 60. System 40 also may receive patient related data, including for example, medical records related to past therapies and medical history.

[0056] When a patient condition is recognized by system 40 as outside acceptable limits, an alert may be generated by physician alert system 48. Information supporting the alert condition may be communicated, for example, through patient management system 46 to physician alert system 48. Physician alert system 48 may reside at a healthcare provider office or may include a mobile link accessible by the health care provider remotely, and which permits communication 64 between the healthcare provider and the patient. Communication 64 between healthcare provider and patient may be network, Internet or telephone based and may include email, SMS (text) messaging or telephone/voice communication. Physician alert system 48 allows the healthcare provider to review logs of IVC measurements over time and make decisions regarding therapy titration, and in critical cases, hospital admissions, remote from the patient.

[0057] Exemplary system embodiments 10 and 40 are each illustrated, respectively, in FIGS. 6A and 6B with various system functions assigned to particular functional elements of the systems. For the sake of clarity of the disclosure, not all possible distributions of functions in functional elements across the system are described. As will be appreciated by persons of ordinary skill, other than the function of the sensor implant itself and, in some instances, an antenna communicating wirelessly with the sensor implant, all functions may be distributed among functional elements in any number of arrangements as best suited to a home or clinical application and the intended location of sensor reading function, e.g., in a home or hospital setting. For example, all system functions (except sensor specific functions as mentioned) may be contained in a single functional unit in the form of a stand-alone patient management system. Alternatively, functions may be highly distributed among mobile devices networked with secure cloud computing solutions. For example, the sensor implant or, in cases where specific external antenna configuration is required, an antenna control module may communicate directly with a patient-owned smart phone to receive signals indicating IVC physical dimension measurements and, in turn, transmit those signals via WiFi or cell network to the

cloud for distribution to further mobile devices in the possession of healthcare providers. Hand-held devices such as tablets or smart phones may communicate directly with controlled treatment delivery devices, or such devices may be controlled by a self-contained patient management system. Further, processing necessary for operation of the system also may be distributed or centralized as appropriate, or may be duplicated in multiple devices to provide safety and redundancy. As just one example, as shown in FIG. 6A, both bedside console 30 and smart phone 32 may be capable of performing identical functions and communicating with healthcare provider device 20 to report results of execution of the assigned functions. Thus, the specific arrangement of the functional elements (blocks) in the schematic presentations of the illustrative examples in FIGS. 6A and 6B are not to be considered as limiting with respect to possible arrangements for distribution of disclosed functions across a network.

[0058] Various care algorithms may be developed based on systems 10 and 40. In one scenario, a first, home-care algorithm governs interactions in the home system including periodic IVC diameter/area measurements using implant 12 and dictates whether to maintain current therapies or to change therapies within the scope of home-care team capabilities. As long as IVC volume metrics stay within predefined limits, the first, home-care algorithm continues to govern monitoring and treatment. However, if monitored parameters, for example IVC volume metrics, exceed the predefined limits, then an alert is generated that engages a second, healthcare provider algorithm. Such an alert may be generated internally by home system 42, or may be generated in patient management system 46 (or physician alert system 48) based on monitored data communicated by home system 42 and received by the other systems either periodically or on a continuous basis. In one embodiment, an alert initially is received by a physician's assistant or heart failure nurse who can triage the situation through patient management system 46. At that level the assistant or nurse may elect to generate a message for communication 64 to the patient through the network related to modulation of therapy or other parameters such as level of physical activity. However, if triage indicates the alert to represent a more critical event, the physician may be alerted through physician alert system 48. Multiple layers of care and review based on measured IVC volume metrics are thus provided to efficiently manage patient fluid status and where possible avoid hospitalizations.

[0059] As mentioned above, IVC collapsibility or IVC CI are parameters that may be generated to facilitate diagnostic decisions based on IVC metrics. FIG. 7 illustrates one exemplary algorithm for determination of IVC collapsibility on which a treatment algorithm may be based. One example of such a treatment algorithm is illustrated in FIG. 8. Another example is described below in Table I. Plots A and B in FIG. 7 show two different IVC collapsibility conditions plotted as diameter versus time over several respiratory cycles (in this case based on ultrasound detection, but diameter/area detection of the IVC may be based on any other modalities described herein to achieve similar results).

[0060] Based on a calculated IVC collapsibility, a treatment algorithm such as shown in FIG. 8 may be employed. Based on several published research studies, an IVC Collapsibility Index (IVC CI) of 15% or less indicates significant fluid overload, which may imply an imminent risk of acute decompensation. An IVC CI of 20-30% might be considered normal, and an IVC CI of greater than 40% might indicate a hypovolemic state. These percentages may be adjusted for patients with certain conditions. For example, a patient with heart failure with reduced ejection fraction might preferably be maintained at a lower IVC CI (i.e., with more circulating blood volume) to maximize cardiac output.

[0061] In developing any treatment algorithm a starting point is existing clinical guidelines, which a physician may then customize to an individual patient. Consistent with medically accepted best practices changes to treatment algorithms are made in conjunction with normal clinical exam and other data that treating physician has available. Embodiments described herein offer a new and powerful tool in this regard by making available regular IVC diameter or volume measurements without requiring a patient to be in a clinical setting and, potentially, providing continuous information on IVC volume metrics in near-real time.

[0062] With more and more accurate data on IVC volume metrics available to the healthcare provider based on systems described herein, more refined treatment algorithms may be devised. Such algorithms also may include a significant home-care component that was not previously possible. Table II below sets forth an alternative treatment algorithm in the form of IVC metrics to guide to patient volume status over the course of 4-5 respiratory cycles (IVC metrics employed in this algorithm include maximum and minimum diameters & IVCCI calculation (max-min)/max×100).

TABLE II

Example of Treatment Algorithm				
Measurement	IVC Ø <14 mm and IVCCI >75%	IVC Ø <21 mm and IVCCI >50%	IVC Ø <21 mm and IVCCI <50%, IVC Ø >21 mm and IVCCI >50%	IVC Ø >21 mm and IVCCI <50%, sniff or <20% quiet inspiration
Characterize	Low IVC Ø and high IVCCI (hypovolemic)	Normal IVC Ø and IVCCI (euvolemic)	Intermediate IVC Ø and IVCCI (intermediate)	Dilated IVC Ø, low IVCCI (hypervolemic)
Trend	Trending below normal	Trending within normal	Trending towards thresholds	Trending above normal
Assessment	Review diuretic dosing in line with the trend in IVC metric	No medication changes required based on normal metrics	Increase monitoring frequency	Consider increasing or adding diuretic

TABLE II-continued

Example of Treatment Algorithm				
Intervention or no intervention	If on diuretic and other signs of hypovolemia are present omit half a diuretic dose until signal changes e.g. stop diuretic for 24-48 hrs If not on diuretics, consider liberalization of oral fluid/salt If on vasodilators, lower dose or discontinue if postural hypotension present	Continue current treatment regimen in line with current guideline driven standard of care, ensuring optimal dosing of one medicine	Consider up-titration of current medications in line with current guideline standard of care	Add or increase loop diuretic (e.g. 40 mg furosemide or 1 mg bumetanide) Add or increase thiazide or thiazide-like diuretic dose Consider switching from furosemide to IV loop diuretic: initiate with 20-80 mg
Follow up	Re-evaluate IVC trends in response to diuretic change for 2-3 days; adjust thresholds if necessary	Evaluate weekly to maintain stability	Evaluate 2x weekly to maintain stability; adjust thresholds if necessary	Re-evaluate IVC trends in response to diuretic change for 2-3 days Measure renal function within 5-10 days of diuretic change: if creatinine increase by 20% or greater, consider reducing or discontinuing diuretic or reducing the vasoactive medication If no IVC response or continued trend elevations observed, consider vasodilator change
Additional actions	n/a	n/a	n/a	

[0063] Treatment algorithms as described above may allow more precise titration and management of a patient's circulating blood volume than pulmonary artery pressure. As mentioned above, a patient might have a significant increase in circulating blood volume with only minor changes in pressure. Despite the normal pressure, this added volume may have deleterious short- and long-term effects on the patient's cardiac or renal function. By directly using IVC diameter or area measurements, the patient's fluid volume could be managed more closely, without a risk of inducing hypovolemia, which could also have deleterious effects.

[0064] Utilizing embodiments described herein, it is possible to determine not only IVC metrics indicating blood volume status, but also respiration and heart rates. New clinical work flows also may be employed based on these multiple metrics to increase opportunities for improved patient outcomes. For example, as shown in FIG. 9, utilizing a system employing an implanted IVC diameter/area monitoring device, workflow 70 may include, for example, after device implantation 72, an initial detection algorithm that calls for periodic readings 74 of IVC diameter/area when the patient is at home. Such periodic readings may, for example, be taken weekly, daily or on other appropriate periods as determined by the healthcare provider based on patient parameters. In some embodiments the reading may be taken with the patient lying supine in bed and in proximity to a bedside console. Alternatively, the IVC diameter/area monitoring implant may include on-board memory, in which case it may also monitor IVC diameter or area measurements continuously or every few minutes and record the readings over the course of a day, and transmit once a day. Trend data for the selected period could be developed in this manner. Readings may be transmitted through the communications network as established to the clinical interface 76. Based on

IVC metrics, i.e., blood volume as determined in the clinical interface, the treatment algorithm determines necessary interventions if any. When conditions or trends are indicated within predetermined "normal" parameters for the specific patient, no action 82 is indicated and the system resets for the next periodic reading 74. However, if a condition or trend is indicated outside of the predetermined "normal" parameters, a clinical alert 84 may be generated and suggested interventions established by the applicable treatment algorithm employed. For example, in response to clinical alert 84, the healthcare provider directed care 86 or patient self-directed care 88 may be considered as suggested interventions and one or more effected consistent with the patient treatment plan. For patients already in a clinical setting, this may include instructions to other treatment devices connected to or working with the patient (for example, as shown in FIG. 6A with system 10). Other interventions or hospitalizations may be dictated for ambulatory patients or those otherwise outside a clinical setting when the alert is generated. Particularly for patients outside a clinical setting when an initial alert is generated, through bidirectional communication, the system allows the healthcare provider to instruct the monitoring device to generate one or more confirmatory monitoring signals before treatments are added or changed, or hospitalization required. After an intervention, the system may optionally reset for the next periodic reading 74. Depending on the nature or type of the initial clinical alert 84 and interventions 86, 88, patient parameters may be modified 90 by healthcare provider input or, optionally, in some cases, automatically by the system. Modifications may include, for example, changes in frequency of prompts for periodic readings 74 or changes in treatment algorithms that may be directed by the healthcare provider 86 or patient self-directed 88.

[0065] Further exemplary embodiments may include patient fluid management methods comprising steps such as measuring the diameter of the IVC in a patient, calculation of IVC collapsibility index and/or estimating patient blood volume based on IVC collapsibility, applying a treatment to the patient to effect a change in patient fluid level when determined fluid level is outside predetermined limits, continuously or substantially continuously monitoring IVC diameter or area measurements, such as change in IVC diameter, during said treatment and modulating said treatment in response to monitored change in the IVC diameter. With such methods, treatment modulation may be accomplished in near real-time as desired. The measurement and treatment may be directly linked and operate directly in a closed loop.

[0066] In one alternative, measurement of IVC diameter or area measurements may be performed by applying an electromagnetic signal from an external transmitter to a passive implant, and sensing the electromagnetic behavior of the passive implant in response to that signal using an external receiver. In another alternative, the measuring and monitoring may comprise positioning a monitoring device at a monitoring location within the IVC configured to detect a distance between opposed walls in the IVC or the diameter/area of the IVC at the monitoring location. Examples of suitable passive implants of this type are also disclosed in the aforementioned and incorporated PCT applications by the present Applicant.

[0067] Further alternative embodiments may involve monitoring IVC dimension variation over the respiratory and cardiac cycle, which may additionally include measurement/derivation of both breathing rate and heart rate on their own and/or in conjunction with different breathing maneuvers, or exercise. Longitudinal variation over days or weeks also may be a factor monitored. In another aspect, embodiments disclosed may include algorithms that incorporate other physiologic data, such as vascular pressures, heart rate, weight, posture, exercise status, etc. and also may use data from other implanted sensors, or other external devices.

[0068] In yet another alternative, the modulating may comprise use of multiple treatment algorithms including trend analysis and reference baselines with daily or near-daily titration of medications, diet, and other therapeutic actions. Diuretic delivery also may be added with algorithms generally applicable to patient populations, or custom algorithms based on specific patient status or physiology, for example, HFpEF vs HFrEF, renal functional status.

[0069] Other exemplary embodiments include fluid management systems comprising at least one monitoring device positioned in a patient IVC and configured to monitor IVC diameter or area measurements, such as changes in the IVC diameter, and output a signal representative of those changes. A healthcare provider device may be configured to communicate with the monitoring device in the patient IVC and determine patient treatment protocols based on the output signal and an executable treatment algorithm. Interventional devices are included providing patient treatment or therapies controlled by the healthcare provider device based on the determined treatment protocols.

[0070] A further alternative embodiment is a dialysis or ultrafiltration management method comprising continuously measuring the diameter of the IVC in a patient during dialysis or ultrafiltration, estimating patient blood volume based on measured IVC diameter, and adjusting the rate of

fluid removal to continuously optimize the patient's circulating blood volume. The measurement of the diameter may track diameter variations over the respiratory and/or cardiac cycle. With such a method, a patient's circulating blood volume may be rapidly reduced to an optimal level at the beginning of the dialysis session, and then maintained at that level throughout the session as interstitial fluid migrates into the circulatory system. Further alternatives in such a method may be used to optimize the dialysis procedure so as to maximize safety, by preventing episodes of hypovolemia, effectiveness, by maximizing safe fluid removal from the interstitial space over a given time period and/or long-term patient health, by safely maintaining the patient at a lower total body fluid volume than could otherwise be maintained.

Sensor Implant Examples

[0071] Examples of sensors **12** for use with systems and methods described herein are shown in FIGS. **10**, **11**, **12A**, **12B** and **12C**. As mentioned previously, systems according to the present disclosure may generally comprise an implant **12** configured for placement in a patient's IVC. Such implants **12** may in some embodiments include control and communications modules, and one or more remote systems such as processing systems, user interface/displays, data storage, etc., communicating with the control and communications modules through one or more data links, preferably remote/wireless data links. FIG. **10** shows aspects of such systems, which in some embodiments may comprise all or part of home system **42** as shown in FIG. **6B**. Such a system may include an antenna/detector module **102** to communicate with and, in some embodiments, power or actuate the implant. Antenna/detector module **102** is controlled by controller **104**, which may comprise a bedside console as previously described. For patient comfort, as well as repeatability in positioning, antenna/detector module **102** may be placed in a pad or bed **106**.

[0072] One form of implant **12** may employ a variable inductance L-C circuit **110** for performing measuring or monitoring functions described herein, as shown in FIG. **11**. Implant **12** may also include means **112** for securely anchoring the implant within the IVC. Using a variable inductor **114** and known capacitance **116**, L-C circuit **110** produces a resonant frequency that varies as the inductance is varied. With the implant securely fixed at a known monitoring position in the IVC, changes in shape or dimension of the IVC cause a change in configuration of the variable inductor, which in turn cause changes in the resonant frequency of the circuit. These changes in the resonant frequency can be correlated to changes in the vessel shape or dimension by the implant control and communication system. Thus, not only should the implant be securely positioned at a monitoring position, but also, at least a variable coil/inductor portion **114** of the implant may have a predetermined compliance (resilience) selected and specifically configured to permit the inductor to move with changes in the vessel wall shape or dimension while maintaining its position with minimal distortion of the natural movement of the vessel wall. Thus, in some embodiments, the variable inductor is specifically configured to change shape and inductance in proportion to a change in the vessel shape or dimension.

[0073] Variable inductor **112** is configured to be remotely energized by an electric field delivered by one or more transmit coils within antenna/detector module **102** positioned external to the patient. When energized, L-C circuit

110 produces a resonant frequency which is then detected by one or more receive coils of the antenna module. Because the resonant frequency is dependent upon the inductance of the variable inductor, changes in shape or dimension of the inductor caused by changes in shape or dimension of the vessel wall cause changes in the resonant frequency. The detected resonant frequency is then analyzed by the control and communication components of the system to determine the IVC diameter or area, or changes therein.

[0074] Turning to specific embodiments of implant **12**, implant **12a**, shown in FIG. **12**, is an ultrasound-based device. As shown therein, **12a** comprises three major components or assemblies, electronics capsule **120**, anchor element **122** and anchor isolation structure **124** connecting the electronics capsule and anchor element. Electronics capsule **120** comprises a sealed housing **126** for containing control, power and other alternative functional modules as elsewhere described herein to provide a self-contained, sealed device. Capsule **120** also provides support for marker element **128**, which in the case of implant **12a** is a single ultrasound marker element positioned at the inferior end of the device. Such a marker element may utilize one or more ultrasound crystals to measure IVC diameter by emitting an ultrasound pulse, and then detecting the reflection of that pulse from the opposing wall of the IVC.

[0075] Electronics capsule **120** is connected to anchor element **122** at the superior end of the capsule. Anchor element **122** as depicted in this embodiment includes a single anchor wire **130** configured in a generally figure-eight or double helix shape. Alternatively, the same configuration can be provided with two or more wires. Anchor wire **130** is pinned to telescoping deployment member **132** at both its inferior end **134** and superior end **136**. Telescoping deployment member **132** includes inner member **138**, which is secured to electronics capsule **120**, through anchor isolation structure **124** and outer member **140**. Relative motion between inner member **138** and outer member **140** moves anchor wire **130** from a collapsed position to a deployed or anchoring position. Barbs **142** may be included to ensure fixation.

[0076] Various actuation mechanisms may be utilized for deploying and securing anchor element **122**. In one alternative, anchor wire **130** is resilient, with shape-memory properties configured to provide a rest state in the deployed configuration. In this alternative, implant **12a** may be delivered to the desired location in the IVC via a conventional guide catheter or other suitable sheath type delivery device. When position is confirmed as described below, implant **12a** is ejected from the delivery catheter or sheath with anchor element **122** self-deploying upon ejection.

[0077] A further feature of implant **12a** is spacing between the marker element position relative to the anchor element, provided by anchor isolation structure **124**. In general, anchor element **122** is positioned sufficiently distant from the marker elements so as to not have an effect upon the IVC size or shape at or close to the location of measurement due to the anchoring force imparted to the IVC wall. Anchor isolation structure **124** facilitates the desired positioning, which may be distance approximately 1 to 4 times the IVC diameter from the measurement location.

[0078] FIGS. **12B** and **12C** illustrate further details of resonant circuit-based implants **12b** and **12c**, respectively. Implant **12b** may comprise a “dog-bone”-like shape with a coil portion **150** and a capacitor portion **152**. Implant **12b**

may comprise an electrically conductive wire or bundle of wires that is wound or otherwise formed into a single continuous coil comprising multiple turns or loops having an oval or rounded rectangular shape. It may be advantageous to use “Litz” wire, which has multiple independently insulated strands of wire, for the coil, since that may enhance the inductance of the implant. The coil is configured to be oriented such that the longer dimension of the rectangular loops extends longitudinally in a cranial-caudal direction within the IVC. The wire or group of wires may be wound multiple times in a continuous overlapping manner such that the rectangles each are defined by two or more parallel strands or bundles of wire about their periphery. The rectangles have central regions bounded by two or more longitudinal wires **154** forming spines **156** approximately defining a central plane running longitudinally in a cranial-caudal direction. This central region is configured to be disposed in a plane generally perpendicular to the anterior-posterior axis of the vessel, and remains relatively undeformed as the vessel collapses and expands in the anterior-posterior direction. The longitudinal elements may engage opposing walls of the vessel. At the caudal and cranial ends of the central regions of the rounded rectangles, the wire or wires form two lobes or a pair of coil ears **158** that flare outwardly away from each other and from the central plane of the implant in the anterior and posterior directions, as shown in FIG. **12B**. Coil ears **158** are configured to engage opposing anterior and posterior walls of the vessel and to leave the central lumen of the vessel completely unobstructed for flow of blood as indicated by the arrows.

[0079] As the IVC changes shape, the longitudinal wires may move closer together or farther apart, and the coil ears may also move closer together or farther apart, thereby changing the inductance of the coil. The ears may be separated by about 1 cm to about 5 cm at the apex of the curved ends of the ears. An implant as adapted for an average IVC size may be about 2.5 cm to 10 cm long. It may be appreciated that as the IVC collapses in the anterior-posterior direction, the ears deform inwardly thereby changing the inductance of the coil. However, the central region of the coil remains relatively undeformed and maintains sufficient size that the inductance of the coil is high enough to produce a field sufficiently strong for external detection, as described more fully below. Capacitor portion **152** of implant **12b** includes a capacitor element **160** to complete the RC circuit. Capacitor portion **152** can be located in a number of locations, such as distal to the ears, or along the spine.

[0080] FIG. **12C** illustrates another alternative implant embodiment. The enlarged detail in the box of FIG. **12C** represents a cross-sectional view taken as indicated. In this embodiment, implant **12c** includes multiple parallel strands of wire **170** formed around a frame **172**. With multiple strands of wires, the resonant circuit may be created with either the inclusion of a discrete capacitor, element or by the inherent inductance of the coils without the need for a separate capacitor as capacitance is provided between the wires **170** of the implant. Note that in the cross-sectional view of FIG. **12C**, individual ends of the very fine wires are not distinctly visible due to their small size. The wires are wrapped around frame **172** in such a way to give the appearance of layers in the drawing. Exact capacitance required for the RC circuit can be achieved by tuning of the capacitance through either or a combination of discrete

capacitor selection and material selection and configuration of the wires. In one alternative implant **12c**, there may be relatively few wire strands, e.g. in the range of about 15 strands, with a number of loops in the range of about 20. In another alternative implant **12c**, there may be relatively more wire strands, e.g., in the range of 300 forming a single loop.

[0081] Frame **172** may be formed from Nitinol, either as a shape set wire or laser cut shape. One advantage to a laser cut shape is that extra anchor features may cut along with the frame shape and collapse into the frame for delivery. When using a frame structure as shown in FIG. **12C**, the frame should be non-continuous so as to not complete an electrical loop within the implant. As with the previous embodiment, coil wires may comprise fine, individually insulated wires wrapped to form a Litz wire. Factors determining inherent inductance include the number of strands and number of turns and balance of capacitance, Frequency, Q, and profile. One illustrative example of implant **12c** may be configured as follows:

[0082] 0.010" NiTi frame with 8 crowns (174 in FIG. **12C**)—insulated with 0.013"×0.00025" wall PET heat-shrink/parylene

[0083] overall approximately 25-30 mm diameter

[0084] overall approximately 24 mm long

[0085] 25 turns, 25 strand, 46AWG gold Litz wire

[0086] No discrete capacitor element—capacitance inherent in configuration of implant

[0087] PET heat-shrink insulation (0.065"×0.00025" wall)/parylene coated

[0088] Insertion of devices into the circulatory system of a human or other animal is well known in the art and so is not described in significant detail herein. Those of ordinary skill in the art will understand after reading this disclosure in its entirety that implants **12** can be delivered to a desired location in the IVC using, e.g., a loading tool to load a sterile implant **12** into a sterile delivery system, which may be used to deliver the implant to the IVC via a femoral vein or other peripheral vascular access point, although other methods may be used.

Computer—Software Implementation

[0089] It is to be noted that any one or more of the aspects and embodiments described herein, such as, for example, related to communications, monitoring, control or signal processing, may be conveniently implemented using one or more machines (e.g., one or more computing devices that are utilized as a user computing device for an electronic document, one or more server devices, such as a document server, etc.) programmed according to the teachings of the present specification. Appropriate software coding can readily be prepared by skilled programmers based on the teachings of the present disclosure, as will be apparent to those of ordinary skill in the software art. Aspects and implementations discussed above employing software and/or software modules may also include appropriate hardware for assisting in the implementation of the machine executable instructions of the software and/or software module.

[0090] Such software may be a computer program product that employs a machine-readable storage medium. A machine-readable storage medium may be any non-transitory medium that is capable of storing and/or encoding a sequence of instructions for execution by a machine (e.g., a computing device) and that causes the machine to perform

any one of the methodologies and/or embodiments described herein. Examples of a machine-readable storage medium include, but are not limited to, a magnetic disk, an optical disc (e.g., CD, CD-R, DVD, DVD-R, etc.), a magneto-optical disk, a read-only memory "ROM" device, a random access memory "RAM" device, a magnetic card, an optical card, a solid-state memory device, an EPROM, an EEPROM, and any combinations thereof. A machine-readable medium, as used herein, is intended to include a single medium as well as a collection of physically separate media, such as, for example, a collection of compact discs or one or more hard disk drives in combination with a computer memory. As used herein, a machine-readable storage medium does not include transitory forms of signal transmission.

[0091] Such software may also include information (e.g., data) carried as a data signal on a data carrier, such as a carrier wave. For example, machine-executable information may be included as a data-carrying signal embodied in a data carrier in which the signal encodes a sequence of instruction, or portion thereof, for execution by a machine (e.g., a computing device) and any related information (e.g., data structures and data) that causes the machine to perform any one of the methodologies and/or embodiments described herein.

[0092] Examples of a computing device include, but are not limited to, an electronic book reading device, a computer workstation, a terminal computer, a server computer, a handheld device (e.g., a tablet computer, a smartphone, smart watch, etc.), a web appliance, a network router, a network switch, a network bridge, any machine capable of executing a sequence of instructions that specify an action to be taken by that machine, and any combinations thereof. In one example, a computing device may include and/or be included in a kiosk.

[0093] FIG. **13** shows a diagrammatic representation of one embodiment of a computing device in the exemplary form of an IVC diameter/area measuring implant control and communication system **1000** within which a set of instructions for causing an implant control and communication system, such as a waveform generator, an oscilloscope, an EFM circuit, or an implant, among other systems and devices disclosed herein, to perform any one or more of the aspects and/or methodologies of the present disclosure may be executed. It is also contemplated that multiple computing devices may be utilized to implement a specially configured set of instructions for causing one or more of the devices to perform any one or more of the aspects and/or methodologies of the present disclosure. Computer system **1000** includes a processor **1004** and a memory **1008** that communicate with each other, and with other components, via a bus **1012**. Bus **1012** may include any of several types of bus structures including, but not limited to, a memory bus, a memory controller, a peripheral bus, a local bus, and any combinations thereof, using any of a variety of bus architectures.

[0094] Memory **1008** may include various components (e.g., machine-readable media) including, but not limited to, a random access memory component, a read only component, and any combinations thereof. In one example, a basic input/output system **1016** (BIOS), including basic routines that help to transfer information between elements within control and communication system **1000**, such as during start-up, may be stored in memory **1008**. Memory **1008** may

also include (e.g., stored on one or more machine-readable media) instructions (e.g., software) **1020** embodying any one or more of the aspects and/or methodologies of the present disclosure. In another example, memory **1008** may further include any number of program modules including, but not limited to, an operating system, one or more application programs, other program modules, program data, and any combinations thereof.

[0095] Control and communication system **1000** may also include a storage device **1024**. Examples of a storage device (e.g., storage device **1024**) include, but are not limited to, a hard disk drive, a magnetic disk drive, an optical disc drive in combination with an optical medium, a solid-state memory device, and any combinations thereof. Storage device **1024** may be connected to bus **1012** by an appropriate interface (not shown). Example interfaces include, but are not limited to, SCSI, advanced technology attachment (ATA), serial ATA, universal serial bus (USB), IEEE 1394 (FIREWIRE), and any combinations thereof. In one example, storage device **1024** (or one or more components thereof) may be removably interfaced with control and communication system **1000** (e.g., via an external port connector (not shown)). Particularly, storage device **1024** and an associated machine-readable medium **1028** may provide nonvolatile and/or volatile storage of machine-readable instructions, data structures, program modules, and/or other data for control and communication system **1000**. In one example, software **1020** may reside, completely or partially, within machine-readable medium **1028**. In another example, software **1020** may reside, completely or partially, within processor **1004**.

[0096] Control and communication system **1000** may also include an input device **1032**. In one example, a user of control and communication system **1000** may enter commands and/or other information into control and communication system **1000** via input device **1032**. Examples of an input device **1032** include, but are not limited to, an alphanumeric input device (e.g., a keyboard), a pointing device, a joystick, a gamepad, an audio input device (e.g., a microphone, a voice response system, etc.), a cursor control device (e.g., a mouse), a touchpad, an optical scanner, a video capture device (e.g., a still camera, a video camera), a touchscreen, and any combinations thereof. Input device **1032** may be interfaced to bus **1012** via any of a variety of interfaces (not shown) including, but not limited to, a serial interface, a parallel interface, a game port, a USB interface, a FIREWIRE interface, a direct interface to bus **1012**, and any combinations thereof. Input device **1032** may include a touch screen interface that may be a part of or separate from display **1036**, discussed further below. Input device **1032** may be utilized as a user selection device for selecting one or more graphical representations in a graphical interface as described above.

[0097] A user may also input commands and/or other information to control and communication system **1000** via storage device **1024** (e.g., a removable disk drive, a flash drive, etc.) and/or network interface device **1040**. A network interface device, such as network interface device **1040**, may be utilized for connecting control and communication system **1000** to one or more of a variety of networks, such as network **1044**, and one or more remote devices **1048** connected thereto. Examples of a network interface device include, but are not limited to, a network interface card (e.g., a mobile network interface card, a LAN card), a modem, and

any combination thereof. Examples of a network include, but are not limited to, a wide area network (e.g., the Internet, an enterprise network), a local area network (e.g., a network associated with an office, a building, a campus or other relatively small geographic space), a telephone network, a data network associated with a telephone/voice provider (e.g., a mobile communications provider data and/or voice network), a direct connection between two computing devices, and any combinations thereof. A network, such as network **1044**, may employ a wired and/or a wireless mode of communication. In general, any network topology may be used. Information (e.g., data, software **1020**, etc.) may be communicated to and/or from control and communication system **1000** via network interface device **1040**.

[0098] control and communication system **1000** may further include a video display adapter **1052** for communicating a displayable image to a display device, such as display device **1036**. Examples of a display device include, but are not limited to, a liquid crystal display (LCD), a cathode ray tube (CRT), a plasma display, a light emitting diode (LED) display, and any combinations thereof. Display adapter **1052** and display device **1036** may be utilized in combination with processor **1004** to provide graphical representations of aspects of the present disclosure. In addition to a display device, control and communication system **1000** may include one or more other peripheral output devices including, but not limited to, an audio speaker, a printer, and any combinations thereof. Such peripheral output devices may be connected to bus **1012** via a peripheral interface **1056**. Examples of a peripheral interface include, but are not limited to, a serial port, a USB connection, a FIREWIRE connection, a parallel connection, and any combinations thereof.

[0099] As will be appreciated by persons of ordinary skill embodiments described herein may provide a number of beneficial effects and advantages as follows:

[0100] As a fluid status indicator: Patients can be managed with greater confidence in euvolemia—i.e. with a greater margin of safety. The physician can take enough fluid off to restore some venous capacitance to act as a buffer against sudden fluid overload causing an acute decompensation—without taking so much fluid off as to cause kidney issues (IVC Volume Metric and collapsibility (IVC CI) are both key measures of patient's fluid status, and are more sensitive/responsive than pressure).

[0101] As a decompensation risk indicator: As IVC diameter or area measurements (e.g. diameter) increase/IVC collapsibility decreases (relative to an individual patient's baseline) it provides an earlier indicator of worsening fluid status, which in turn drives hemodynamic congestion, which drives clinical congestion (which may result in ADHF).

[0102] As an aid to therapeutic decision making: Healthcare providers can use IVC Volume Metrics to indicate optimal diuresis point with an ability to provide longitudinal measures over a period of hours/days/weeks, helping the physician to factor in the impact of fluid redistribution (e.g., from the interstitial tissue into the intravascular space).

[0103] As another aid to therapeutic decision making: IVC Volume Metrics assist healthcare providers in decision making as to whether to alter relative dosages of diuretics vis-à-vis vasodilators. For example, when a

patient's cardiac pressure is increased, disclosed systems and methods facilitate important clinical decisions such as whether the cause is increased volume or increased vasoconstriction, whether to increase diuretics or vasodilators, whether to use IVC Volume Metrics to rule in/out increased volume as a primary cause of increased pressures, i.e., if increased volume is confirmed then diuretics may be indicated, if not then vasodilators may be indicated

[0104] Algorithm based on inputs and output as disclosed also:

[0105] Assesses IVC metric

[0106] Compares daily result and trend to guideline based limits (and over time patient specific limits)

[0107] Determines if medication modification is required

[0108] Sends signal/message to patient and requests confirmation of medication alteration

[0109] By exception (based on multiple times exceeding limits/trends/other trigger)

[0110] Sends notification to managing physician

[0111] Physician can then use system to send message to patient to modify medication and confirm change

[0112] System may provide alarm to remind patient to take medication/take reading

[0113] All this info is stored in the cloud server

[0114] The foregoing has been a detailed description of illustrative embodiments of the disclosure. It is noted that conjunctive language such as is used herein in phrases like "at least one of X, Y and Z" and "one or more of X, Y, and Z," unless specifically stated or indicated otherwise, shall be taken to mean that each item in the conjunctive list can be present in any number exclusive of every other item in the list or in any number in combination with any or all other item(s) in the conjunctive list, each of which may also be present in any number. Applying this general rule, the conjunctive phrases in the foregoing examples in which the conjunctive list consists of X, Y, and Z shall each encompass: one or more of X; one or more of Y; one or more of Z; one or more of X and one or more of Y; one or more of Y and one or more of Z; one or more of X and one or more of Z; and one or more of X, one or more of Y and one or more of Z.

[0115] Various modifications and additions can be made without departing from the spirit and scope of this disclosure. Features of each of the various embodiments described above may be combined with features of other described embodiments as appropriate in order to provide a multiplicity of feature combinations in associated new embodiments. Furthermore, while the foregoing describes a number of separate embodiments, what has been described herein is merely illustrative of the application of the principles of the present disclosure. Additionally, although particular methods herein may be illustrated and/or described as being performed in a specific order, the ordering is highly variable within ordinary skill to achieve aspects of the present disclosure. Accordingly, this description is meant to be taken only by way of example, and not to otherwise limit the scope of this disclosure.

[0116] Exemplary embodiments have been disclosed above and illustrated in the accompanying drawings. It will be understood by those skilled in the art that various changes, omissions and additions may be made to that which

is specifically disclosed herein without departing from the spirit and scope of the present disclosure.

What is claimed is:

1. A method of managing patient body fluid volume, comprising:

directly measuring a physical dimension of the patient's IVC with a sensing device implanted within the IVC; wirelessly communicating with the implanted sensing device to monitor changes in the measured IVC dimension within an euvoletic region defined for said patient; and

generating an alert signal when IVC metrics based at least in part on the measured IVC physical dimension indicate the patient's fluid volume state meets predetermined clinical limits for the defined euvoletic region.

2. The method of claim 1, wherein said physical dimension of the patient's IVC is at least one of IVC diameter or IVC area.

3. The method of claim 1, further comprising positioning and anchoring the sensing device within the patient's IVC, the sensing device configured to measure at least one of IVC diameter or IVC area.

4. The method of claim 1, further comprising receiving said alert signal at a patient therapy device and automatically initiating a patient therapy via said therapy device in response to receiving said alert signal.

5. The method of claim 1, further comprising setting said predetermined clinical limits for the patient, wherein:

said predetermined clinical limits comprise at least an indication of the patient fluid state trending towards hypovolemia, and an indication of the patient fluid state trending towards hypervolemia; and

each of said predetermined limits falls within the euvoletic range defined for the patient.

6. The method of claim 5, wherein said setting said predetermined clinical limits comprises setting (1) a hypovolemic warning zone for said patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent a hypovolemic region and (2) a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent a hypervolemic region, wherein said euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC physical dimension measurements for said patient.

7. The method of claim 6, wherein the euvoletic range corresponds to a range of measured IVC diameters between about 14 mm and about 21 mm.

8. The method of claim 6, wherein the alert signal is generated when said IVC metrics indicate the patient fluid state falls within either of the hypovolemic warning zone or the hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

9. The method of claim 8, further comprising initiating fluid intervention to correct body fluid volume in response to said alert signal while patient fluid volume is within one of said hypovolemic warning zone of the euvoletic region or said hypervolemic warning zone of the euvoletic region.

10. The method of claim 9, wherein said alert signal comprises a hypovolemia alert generated in response to the IVC metrics indicating the patient fluid state falls within the hypovolemic warning zone and, in response to said hypov-

olemia alert, said intervention comprises at least one of administration of fluids or vasoconstricting drugs.

11. The method of claim 9, wherein said alert signal comprises a hypervolemia alert generated in response to the IVC metrics indicating the patient fluid state falls within the hypervolemic warning zone and, in response to said hypervolemia alert, said intervention comprises at least one of dialysis or administration of diuretics or vasodilating drugs.

12. The method of claim 1, wherein said steps of measuring and wirelessly communicating with the sensor implant are performed with the patient located outside of a healthcare facility.

13. The method of claim 1, wherein said IVC metrics are determined based on a combination of measured and calculated data including at least a measured IVC physical dimension and calculated collapsibility index.

14. The method of claim 13, further comprising:

determining patient fluid volume state based on said combination of measured and calculated data; and
said generating an alert signal comprises generating a patient level alert when patient fluid volume status is determined to fall within a first range, and generating a clinical level alert when patient fluid volume status is determined to fall within a second range.

15. The method of claim 14, wherein:

said patient level alert is transmitted to a patient device and prompts the patient to begin a self-directed treatment; and

said clinical level alert is transmitted to a healthcare provider device and prompts a healthcare provider to review patient fluid volume state information transmitted to the healthcare provider device.

16. The method of claim 1, wherein said communicating and generating are controlled by a processor executing instructions stored in a memory, and further comprising executing instructions stored in memory comprising instructions for:

defining euvoletic, hypovolemic and hypervolemic regions for said patient wherein said euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC diameter or volume measurements for the patient;

identifying a hypovolemic warning zone for said patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent the hypovolemic region;

identifying a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent the hypervolemic region; and

generating said alert signal when measured IVC diameter or volume falls within either of the hypovolemic warning zone or hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

17. A method of managing patient body fluid volume, comprising:

wirelessly receiving, from a sensor implanted in the patient's IVC, signals representing changes in a physical dimension of the patient's IVC;

processing the received signals to provide IVC metrics representative of patient fluid volume state throughout an euvoletic region defined for the patient, said IVC

metrics including at least one of IVC collapsibility index (CI), IVC diameter, IVC area, and a magnitude of IVC collapse over a selected period;

comparing said IVC metrics to predetermined values associated with a plurality of patient fluid volume states to determine a current patient fluid state; and
generating an alert signal when the determined patient fluid state meets predetermined clinical limits for the patient.

18. The method of claim 17, further comprising setting said determined clinical limits for the patient, wherein:

said predetermined clinical limits comprise at least an indication of the patient fluid state trending towards hypovolemia, and an indication of the patient fluid state trending towards hypervolemia; and

each of said predetermined limits falls within a euvoletic range defined for the patient.

19. The method of claim 18, wherein said setting said predetermined clinical limits comprises setting (1) a hypovolemic warning zone for said patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent a hypovolemic region and (2) a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent a hypervolemic region, wherein said euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC physical dimension measurements for said patient.

20. The method of claim 19, further comprising generating a prompt to initiate a fluid intervention to correct body fluid volume in response to said alert signal while patient fluid volume falls within one of said hypovolemic warning zone of the euvoletic region or said hypervolemic warning zone of the euvoletic region.

21. The method of claim 17, wherein said receiving, processing, comparing and generating are controlled by a processor executing instructions stored in a memory, and further comprising executing instructions stored in memory comprising instructions for:

defining euvoletic, hypovolemic and hypervolemic regions for said patient wherein said euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC diameter or volume measurements for the patient;

determining said clinical limits by

identifying a hypovolemic warning zone for said patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent the hypovolemic region, and

identifying a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent the hypervolemic region; and

generating said alert signal when measured IVC diameter or volume falls within either of the hypovolemic warning zone or hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

22. A diagnostic method for monitoring patient body fluid volume, comprising:

positioning a sensing device within the patient's IVC, the sensing device configured to measure at least one physical dimension of the IVC;

wirelessly monitoring changes in measured IVC physical dimension over time within an euvoletic region defined for said patient;

identifying (1) a hypovolemic warning zone for said patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent a hypovolemic region and (2) a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent a hypervolemic region, wherein said euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC physical dimension measurements for said patient; and
signaling a warning state when measured IVC physical dimension falls within either of the hypovolemic warning zone or hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

23. A system for managing patient body fluid volume, comprising:

a wireless sensing device implantable within the patient's IVC for directly measuring a physical dimension of the patient's IVC; and

a control system configured to wirelessly receive a measurement signal from the sensing device indicative of the measured physical dimension and derive data from the measurement signal indicative of a fluid volume state of the patient, the control system being further configured to generate an alert signal when IVC metrics based at least in part on the measured IVC physical dimension indicate the patient's fluid volume state meets predetermined clinical limits for a euvoletic region defined for said patient.

24. The system of claim **23**, wherein the control system comprises:

a sensing device control module configured to wirelessly communicate with said wireless sensing device when implanted in the IVC to at least receive said measurement signal; and

a patient management system comprising a processor and memory, the patient management system configured to receive or generate measurement data representative of said measured IVC physical dimension based on said measurement signal, to receive patient specific information, and to execute instructions contained in the memory responsive to received patient specific information and said measurement data, said instructions comprising instructions to—

prompt for initiation of a measurement of the IVC physical dimension;

determine IVC metrics based at least in part on data representative of said measured IVC physical dimension; and

generate an alert signal when the IVC metrics meet predetermined clinical limits for the patient.

25. The system of claim **24**, wherein said physical dimension of the patient's IVC is at least one of IVC diameter or IVC area.

26. The system of claim **24**, wherein said instructions further comprise instructions to wirelessly communicate with the implanted sensing device to monitor changes in the measured IVC dimension throughout an euvoletic region defined for said patient.

27. The system of claim **24**, wherein said instructions for generating an alert signal include instructions to generate the alert signal while the patient fluid state is within a euvoletic region defined for the patient if the IVC metrics meet said predetermined clinical limits.

28. The system of claim **24**, further comprising a user interface configured for user input of patient specific information and a communication link with diagnostic devices monitoring patient condition.

29. The system of claim **28**, wherein said user input patient specific information comprises information including at least one of patient age, sex, height, weight, activity level, or health history indicators.

30. The system of claim **28**, further comprising at least one of a heart rate monitor, blood pressure monitor or central venous pressure (CVP) monitor, configured to communicate with the patient management system through said communication link to provide patient specific information including at least one of heart rate, blood pressure or CVP.

31. The system of claim **24**, wherein:

said predetermined clinical limits comprise an indication of the patient fluid state trending towards hypovolemia, and an indication of the patient fluid state trending towards hypervolemia; and

each of said predetermined limits falls within the euvoletic range defined for the patient.

32. The system of claim **24**, wherein said instructions comprise instructions to set said predetermined clinical limits for the patient based at least in part on input patient specific information.

33. The system of claim **32**, wherein said instructions to set the predetermined clinical limits comprise instructions to define (1) a hypovolemic warning zone for said patient encompassing a portion of a defined euvoletic region at the lower end of a euvoletic region adjacent a hypovolemic region and (2) a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent a hypervolemic region, wherein said euvoletic range, hypovolemic range and hypervolemic range are correlated to IVC physical dimension measurements for said patient.

34. The system of claim **33**, wherein said instructions to generate the alert signal comprise instructions to generate the alert signal when said IVC metrics indicate the patient fluid state falls within either of the hypovolemic warning zone or the hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

35. The system of claim **34**, further comprising at least one treatment device configured to communicate with the patient management system, wherein said instructions further comprise instructions to initiate a treatment through said at least one treatment device to correct body fluid volume in response to said alert signal while patient fluid volume falls within one of said hypovolemic warning zone of the euvoletic region or said hypervolemic warning zone of the euvoletic region.

36. The system of claim **35**, wherein:

said instructions to generate an alert signal comprise instructions to generate a hypovolemia alert in response to the IVC metrics indicating a patient fluid state falling within the hypovolemic warning zone; and

said instructions to initiate a treatment comprise instructions to initiate at least one of administration of fluids or vasoconstricting drugs in response to said hypovolemia alert.

37. The system of claim **35**, wherein:

said instructions to generate an alert signal comprise instructions to generate a hypervolemia alert in response to the IVC metrics indicating a patient fluid state falling within the hypervolemic warning zone; and said instructions to initiate a treatment comprise instructions to initiate at least one of dialysis or administration of diuretics or vasodilating drugs in response to said hypervolemia alert.

38. The system of claim **24**, wherein said sensing device control module is configured as a function of the patient management system.

39. The system of claim **23**, wherein said wireless sensing device comprises an ultrasound transducer and anchor element configured to anchor said ultrasound transducer in the IVC in a fixed position relative to the IVC wall.

40. The system of claim **23**, wherein:

said wireless sensing device comprises a resilient coil forming a resonant circuit, said resilient coil configured to engage the wall of the IVC and deform therewith to provide a variable characteristic frequency correlated to an IVC physical dimension in response to activation of the resonant circuit; and

said system further comprises an antenna configured to activate the resonant circuit and receive the signal representative of the measured IVC physical dimension in response to said activation.

41. A system for managing patient body fluid volume, comprising:

a wireless sensing device configured to be positioned within the patient IVC to measure at least one of IVC diameter or volume and generate a measurement signal representative of the sensed measurement;

a sensing device control module configured to wirelessly receive said measurement signal and output measurement data based on said measurement signal;

a processor and memory, the processor configured to receive said measurement data and execute instructions contained in the memory responsive said measurement data and to receive patient specific information, said instructions comprising

defining a euvoletic range and at least one of a hypovolemic region and a hypervolemic region for said patient wherein said euvoletic range, hypovolemic region and hypervolemic region are correlated to IVC diameter or volume measurements for the patient,

identifying at least one of

(i) a hypovolemic warning zone for said patient encompassing a portion of the defined euvoletic region at a lower end of the euvoletic region adjacent the hypovolemic region, and

(ii) a hypervolemic warning zone for said patient encompassing a portion of the defined euvoletic region at an upper end of the euvoletic region adjacent the hypervolemic region, and

generating an alert signal when measured IVC diameter or volume indicates a patient fluid state falling within either of the hypovolemic warning zone or hypervolemic warning zone of the defined euvoletic region before the patient fluid state reaches one of the hypovolemic region or hypervolemic region, respectively.

42. The system of claim **41**, further comprising an interventional device configured to execute a predefined treatment algorithm for delivering a patient fluid therapy automatically in response to said alert signal.

43. The system of claim **41**, wherein said alert signal includes a prompt to initiate a patient self-directed treatment or treatment change.

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[标]发明人	GIFFORD III HANSON S DEEM MARK E SWEENEY FIACHRA M GRAINGER JEFFRY J BRITTON JOHN R KENT ANNETTE		
发明人	GIFFORD, III, HANSON S. DEEM, MARK E. HANLEY, CONOR M. SWEENEY, FIACHRA M. GRAINGER, JEFFRY J. BRITTON, JOHN R. KENT, ANNETTE		
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摘要(译)

公开了系统和方法，其基于使用植入IVC中的无线测量传感器直接测量下腔静脉 (IVC) 物理尺寸，提供对流体体积的定期，周期性或连续监测。通过基于IVC物理维度变化的诊断决策和治疗，可以在整个血容量范围的流体状态中获得患者液体状态的信息，从而提供血容量过多或血容量不足的早期警告，并使患者治疗的调节能够更长时间稳定 - 流体管理。

