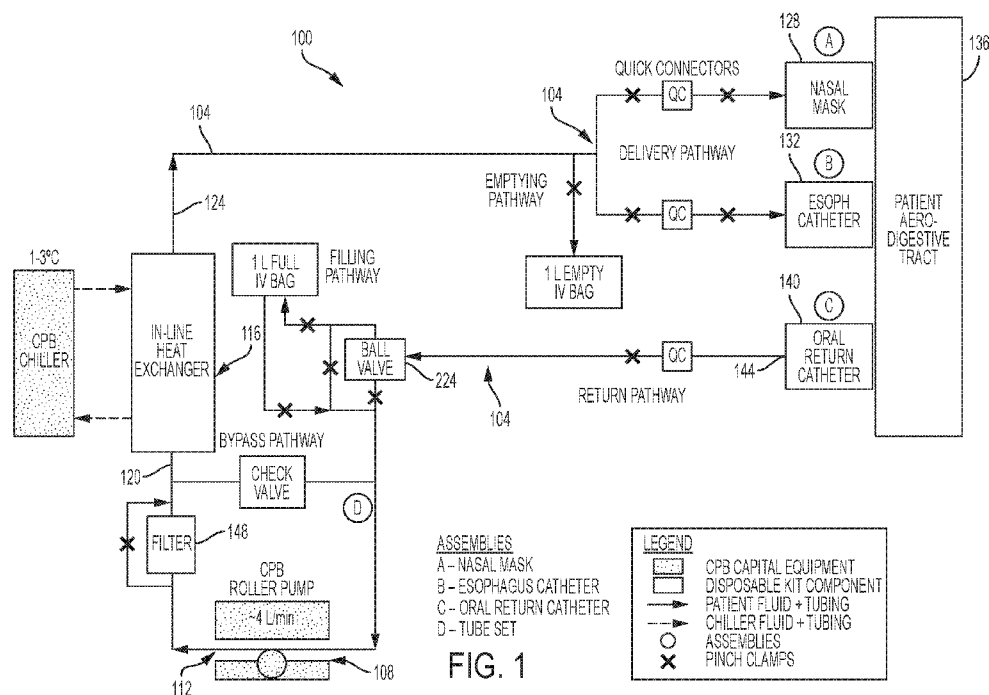


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(54) Title: NON-INVASIVE, SINGLE USE SYSTEM AND METHODS FOR SELECTIVE BRAIN COOLING



(57) Abstract: Cooling devices and methods, such as those, for example, configured to cool the brain of a subject.

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NON-INVASIVE, SINGLE USE SYSTEM AND METHODS FOR SELECTIVE BRAIN COOLING

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Provisional Patent
5 Application No. 62/343,929, filed June 1, 2016, which is hereby incorporated by reference in
its entirety.

BACKGROUND OF THE INVENTION

A. Field of the Invention

[0002] Brain injury is common, devastating, and often expensive to treat.
10 Management of a subject's brain temperature has been recommended by the American Heart
Association (AHA) as the standard of care for survivors of cardiac arrest. Brain temperature
management also has been used to treat birth-related cerebral damage. Brain temperature
management has been studied as a method that reverses and prevents fever after stroke and
traumatic brain injury. In addition to its use after brain injury, brain temperature management
15 has been used for more than 50 years to prevent brain injury during cardiac, vascular, and
neurological surgery. Brain temperature management is relevant to a variety of central
nervous system conditions, including stroke, mechanical brain trauma, and spinal cord injury.
A variety of devices have been proposed for therapeutic organ cooling and, in particular,
therapeutic cooling of the brain. Such devices generally fall into one of two broad categories:
20 systemic devices and selective devices.

[0003] Systemic devices are widely used today, but limitations, such as systemic
toxicity caused by cooling the body core and delays in reaching desired brain temperature,
diminish the benefit that subjects may receive. On the other hand, selective cooling enables,
for example, the creation of a temperature gradient between the brain and the body core.
25 Selective cooling also may reduce complications associated with body core cooling, improve
subject safety, and enable deep cooling of the brain tissue to achieve neuro-protection.

[0004] In general, a high degree of selectivity in temperature management has
required a high, and generally undesirable, degree of invasiveness. Surgically invasive
devices, such as intravascular devices, often focus on cooling the blood supply to a target
30 area and warming the returning blood supply to prevent cooling of the body core.
Intravascular systems and other similarly invasive devices, however, may not be suitable for

rapid deployment because, for example, they may require intervention by a surgeon. A further limitation of tube-/catheter-based devices is that they require surgical invasion of a major blood vessel, introducing risk of infection, bleeding, thrombosis, rupture of the blood vessel, dissection of the blood vessel wall, and introduction or dislodging debris in the vasculature. These risks are further increased when an intravascular warming catheter is introduced to re-warm blood flow returning from the cooled organ(s).

SUMMARY OF THE INVENTION

[0005] This disclosure includes embodiments of cooling devices and methods configured to cool the brain of a subject. Such devices are configurable to be stationary or substantially stationary in some embodiments (e.g., configured for use in hospitals, medical clinics, and any other health care facility), and in other embodiments, the devices of this disclosure may be mobile/transportable (e.g., configured for use at the scene of an accident, in an ambulance, helicopter, or other vehicle used to provide health care, and the like). Further, methods described in this disclosure may be continuous, intermittent, or a combination thereof, depending on the circumstances. For example, in some instances, a health care provider may implement an intermittent method described in this disclosure to begin cooling the aerodigestive tract of a subject, whether in a health care facility or elsewhere, and then implement a continuous method of cooling the aerodigestive tract of a subject described in this disclosure to continue cooling, whether in a health care facility or elsewhere. In other instances, a health care provider may implement continuous cooling described in this disclosure to begin cooling the aerodigestive tract of a subject, whether in a health care facility or elsewhere, and then implement an intermittent method of cooling the aerodigestive tract of a subject described in this disclosure to continue cooling, whether in a health care facility or elsewhere. Such continuous and intermittent methods may be alternated as necessary under the circumstances. Applications of the present devices and methods are relevant to numerous medical procedures and conditions, such as, for example, aneurism coiling/stenting, neurosurgery/neurotrauma surgery, traumatic brain injury, body trauma/exsanguination, surgical exsanguination, birth/maternal exsanguination, atrial ablation, ortho surgery, cardiac surgery, general surgery, cardiac arrest, respiratory arrest, stroke-ischemic, stroke-hemorrhagic, transcatheter aortic valve implantation, full arrest surgery, carcinoembryonic antigen, vascular surgery, birth anoxia, and the like.

[0006] NeuroSave, Inc. has previously disclosed systems and methods for non-invasive, selective brain cooling see U.S. Patent Nos. 8,308,787 and 9,320,644. Systems and methods like these and others, for inducing rapid hypothermia allow cooling a region of the aerodigestive tract for rapid selective brain cooling. Rapid cooling may be more effective in
5 urgent situations so that effective cooling may be induced prior to completion of irreversible tissue damage. These systems and methods may also effectively maintain cooling for sustained periods of time to provide maximal therapeutic benefit. Some embodiments may achieve targeted or selective cooling of the brain, or less selective cooling of both the brain and the body, as required by clinical conditions.

[0007] Prior art systems and methods to deliver fluid to the aerodigestive tract require multiple pumps to operate, which may add complexity and require more user training and attention. Multiple independently controlled pumps also introduce more potential failure modes – some of which may increase patient risk. Specifically, for a therapy that introduces free-flowing fluid into the patient's aerodigestive tract, fluid aspiration into the lungs is a
15 potential risk. The endotracheal tube cuff is the primary risk mitigation against fluid aspiration. Endotracheal tube cuffs are designed to prevent fluids from entering the lungs during mechanical ventilation. However, on rare occasions (typically less than 0.1%), the endotracheal tube cuff may fail resulting in a collapse of the cuff. In these instances, any fluid proximal to the cuff may enter the lungs. Depending on the delivery apparatus used to
20 supply cooling fluid, the amount of fluid entering the lungs may be significant without designing in additional safety features.

[0008] One embodiment of the present disclosure is a tube set to allow for the circulation of free-flowing fluid to and from the aerodigestive tract for selective brain cooling. The tube set may be used with a single pump that provides both the fluid delivery
25 and fluid recovery functionalities. In some embodiments, the tube set is coupled to a single pump to further provide a system to limit fluid aspiration when a specialized oral return catheter is utilized. In some embodiments, the tube set is coupled to a single pump to further provide a system to limit fluid aspiration when coupled to a specialized safety valve. In some embodiments, the tube set is coupled to an esophageal catheter to deliver free-flowing fluid
30 into the esophagus for selective brain cooling and to prevent fluid from entering the stomach, comprising: an esophagus lumen, a gastric lumen, a gastric balloon, and a connection manifold. In still other embodiments, the tube set is coupled to a nasal mask to deliver free-flowing fluid into the nasal cavity for selective brain cooling, comprising: nostril pads

through which fluid is delivered into the nostrils, a head strap, and tubing coupling the nostril pads to a fluid delivery pump. In some embodiments, the tube set is coupled to an oral return catheter to recover free-flowing fluid from the oral cavity for selective brain cooling, having at least one fluid inlet port and a rounded tip.

5 [0009] In some embodiments, a single pump is used to provide flows of cooling fluid to the nasal cavity and/or esophagus from the outlet side of the pump, while receiving fluid returning from the patient by active suction from the inlet side of the pump. In this embodiment, the patient's aerodigestive tract represents the only fluid reservoir that is open to atmosphere. Therefore, the outlet side of the pump establishes the positive pressure
10 gradient needed to push fluid from the pump to the patient while the inlet side of the same pump establishes the negative pressure gradient needed to pull fluid from the patient. With a single pump, at steady state and with negligible entrainment of air, the fluid entering the pump is the same volume as the fluid leaving the pump. Therefore, a single pump conveniently allows for the fluid flow rate entering a patient to be substantially equal to the
15 fluid flow rate leaving a patient. In some embodiments, equivalence of delivery and recovery fluid flow rates provides for additional safety features against fluid aspiration in the lungs.

[0010] In some embodiments, a tube set is coupled to the pump and provides the fluid delivery pathway from the pump to the patient and the fluid return pathway from the patient back to the pump. In some embodiments, the tube set is preferentially small in total volume.
20 For example, in some embodiments, the total amount of circulating fluid is less than 1.5 liters. In other embodiments it is less than 1 liter and in still others it is less than 750 mL. Minimizing the volume of circulating liquid is advantageous in the event of unplanned leak into the lungs or stomach or in the event of a spill. In some embodiments a 0.2 micron pore size filter and a heat exchanger are placed in the fluid pathway leading to the patient to
25 provide filtration and cooling of the fluid before reaching the patient. Some embodiments rely on a single pump for circulation of cooling fluid to the aerodigestive tract where the cooling fluid does not contact the pump directly (i.e., the pump-fluid interface may be disposable). Examples of pumps 'isolated' from the cooling fluid path are peristaltic pumps, centrifugal pumps with disposable fluid contacting parts or diaphragm pumps with disposable
30 fluid contacting parts as used on cardiopulmonary bypass or dialysis systems. Gear pumps with disposable fluid contacting parts may also be used.

[0011] In some embodiments, fluid is delivered to two locations in the aerodigestive tract (e.g., the nose and the esophagus) with a single pump using parallel fluid delivery

pathways. To maintain flows that are roughly balanced through two parallel pathways, the total resistance of each pathway needs to be similar. A person of ordinary skill will appreciate that in this case, the total resistance includes the resistance of the tubing, tube fittings, the patient-contacting portion (e.g., the esophageal catheter or nasal mask), and the resistance of the patient anatomy itself. In some embodiments, the tubing, tube fittings, and patient-contacting parts are designed to have fluid flow resistance that is significantly larger than the resistance to flow presented by the delivery location (e.g., the esophagus or nasal cavity). In these embodiments, natural variations in patient anatomy will have little negligible impact on the total flow resistance through each parallel pathway. Therefore, the flows through each parallel pathway may be maintained roughly equal. In some embodiments, flow indicators (e.g., paddlewheels, flow sensors/meters, variable area flow indicators, flow switches, and/or the like) are used to show the fluid flow through each parallel pathway. Some other embodiments comprise flow adjustment devices (e.g., pinch clamps, Roberts clamps, needle valves, and/or the like) are used to adjust flows in each parallel pathway to maintain roughly equal flows. Flow adjustment devices may be electronically or manually actuated based on signals or readings from electronic or manual flow indicators. Valves that do not contact the circulating cooling fluid during normal operation (e.g. pinch valves) may be preferred in some embodiments. Pinch valves and other external valves have the benefit of being readily re-positioned to minimize leaks when connections are made and/or broken.

[0012] In some embodiments, the tube set includes a filter and an inline heat exchanger to filter and cool the fluid before it is divided into two parallel tubing pathways to be delivered to the patient. In some examples, the inline heat exchanger is positioned in countercurrent orientation to maximize heat transfer. In some embodiments, the priming volumes of the heat exchanger and filter are minimized to maintain a small total fluid volume in the tube set. Some embodiments comprise a single pump that couples to the tube set and drives the cooling fluid through the filter and the heat exchanger, after which the fluid is divided between two paths. In some of these embodiments, the first path leads to the nasal cavity via a nasal mask and a second path leading to the esophagus via an esophageal catheter. The fluid paths recombine in the patient's oropharynx, and fluid is withdrawn from the patient's mouth using a specific oral return catheter. In some embodiments, the tube set contains a safety valve on the return tubing pathway. In some embodiments, the tube set contains a bypass loop triggerable by a check valve to couple the fluid delivery side of the

tube set directly to the fluid return side of the tube set, effectively short circuiting fluid delivery to the patient when the check valve is open. One benefit of this configuration is reduced strain on the pump. Further benefits arise from the fact that the check valve will be opened in some embodiments when the pressure differential across it is increased past its threshold usually between two pounds per square inch and thirty pounds per square inch (i.e., safely below burst pressure of commonly used tubing). This may be accomplished either by increased pressure in the flow path to the patient or by decreased pressure in the flow path returning from the patient or by a combination of increased pressure in the flow path to the patient and decreased pressure in the flow path returning from the patient. Note that pinch clamps or other valves may be added to the circuit at any point beyond the check valve entrance on the delivery side of the circuit and any point before the entrance to the check valve on the return side of the circuit. The valves may be actuated by external measurements such as patient temperature, fluid temperature, fluid flow rate, physiological variables, or a timer. While any valve may be used, a valve that does not contact the cooling fluid, such as a pinch clamp is preferred. One or more such valves may be used to allow the system to respond to multiple inputs.

[0013] In some embodiments a multi-lumen esophageal catheter is used to deliver fluid to the esophagus. In some embodiments, the esophageal catheter has a first lumen coupled to a compliant balloon that may be inflated to form a seal at the gastro-esophageal junction. This minimizes the loss of cooling fluid from the esophagus to the stomach. In some embodiments, a second lumen for delivery of cooling fluid is present, in the multi-lumen esophageal catheter that comprises fluid ports that are situated to enable localized liquid delivery to the esophagus at about the level of the aortic arch. This configuration improves heat transfer from the tissues surrounding the carotid and vertebral arteries. In some embodiments a third lumen is present to allow access to the stomach for delivery of gasses or liquids.

[0014] Some embodiments comprise a soft silicone nasal mask that may be interfaced with the nostrils to form a relatively liquid tight seal. In some embodiments, fluid is delivered to the nasal cavity via the nasal mask. Pressure to enhance the seal may be applied by connecting the mask to a head strap. In other embodiments the nasal mask may use sealing pillows at the patient interface.

[0015] In some embodiments, the oral return catheter has a 'blind' distal end (i.e., a rounded tip) and one or more side ports configured at a specific level for withdrawing fluid.

In these embodiments, the distance between the inlet side ports and distal end is optimized such that the inlet side ports reside below the level of the glottis in a supine patient or in a patient in a head-down tilted position. In some embodiments, the inlet side ports are less than 3 cm from the distal tip. In other embodiments, the inlet side ports are less than 2 cm from the distal tip. In some embodiments, the oral return catheter contains a bite block positionable on the cheek, gums, or teeth of the patient and coupled to the shaft of the oral return catheter. The bite block provides friction against the oral return catheter and functions to maintain the location of the inlet side ports below the level of the glottis. In some embodiments, two or more side ports are used to prevent suction injury (e.g., hickeying or other injury related to suction pressure).

[0016] Some embodiments comprise a safety valve enabled to detect the presence of a fluid leak and automatically cease fluid delivery to the patient. For example, the safety valve may be located just distal to the oral return catheter along the fluid path returning from the patient and in close proximity of the patient to decrease response time. The safety valve may also be a safety check valve (e.g., a floating ball check valve) and comprise an air-trap chamber designed to separate air from fluid. In some embodiments, the cross-sectional area of the air-trap chamber is large compared to the input port cross-sectional area in order to substantially slow the fluid velocity entering the air-trap chamber. In other embodiments, a change of direction, such as 90 degree turn in the normal fluid pathway in the chamber is used to further separate the air from the fluid. Within the air trap chamber, a floating ball or float functions as the moving part of the valve. The density of the ball or float is chosen such that it does not sink to the bottom of the air-trap chamber as long as sufficient fluid is present. Density ranges between 0.6g/cc and 0.95g/cc work best. When sufficient fluid is not present in the chamber, the air-trap chamber fills with air and the float falls to the bottom of the chamber, seating the float over the valve outlet or inlet (depending on the location of the valve in the system). In some instances, a silicone seat is secured at the bottom of the air-trap chamber to improve sealing between the float and the air-trap chamber. The volume of the air-trap chamber is chosen such that the safety valve responds before excessive fluid aspiration occurs. In some instances, the volume of the air-trap chamber is below 150 mL, in other instances, the volume of the air-trap chamber is below 100 mL; in other instances, the volume of the air-trap chamber is below 50 mL.

[0017] In some embodiments, electronic bubble or level sensors are used to detect liquid loss in the circuit or the presence of air in the oral return or pump inlet fluid path. The

pump may be automatically stopped based on input from these sensors. In some embodiments, electronic temperature sensors are used to stop the pump if the temperature of the subject or the cooling fluid is too far from that desired for therapy. In some embodiments, valves may be controlled electronically and/or with valve actuation sequences for certain common operations such as filling, emptying and resetting a safety check valve may be automated.

[0018] In some embodiments, a bypass loop triggerable by a check valve allows the coupling of the fluid delivery side of the tube set directly to the fluid return side of the tube set, largely preventing fluid from being delivered to the patient. In some embodiments, the check valve is triggered automatically by an increase in differential pressure across the check valve. For example, the check valve may remain closed below a differential pressure of 2 psi but may then open when a differential pressure of 2 psi is exceeded. In other examples, the check valve may open at 5 psi, 7 psi, 10 psi, or 25 psi. In some embodiments, the check valve crack pressure is optimized such that the check valve remains closed during normal operation but opens if the tube set becomes occluded. For instance, a pinched tube on the delivery side of the tube set would result in large positive pressures when the roller pump is on. Large pressures may result in tube burst or rupture. In this instance, the check valve opens and relieves the pressure in the tube set by providing a bypass fluid pathway connecting the delivery tubing directly to the return tubing. In other embodiments, the check valve crack pressure is optimized such that the check valve remains closed during normal operation but then opens optimally to minimize the response time of the fluid aspiration safety feature. In some embodiments, the optimal pressure to prevent over pressure in the case of occlusion may be substantially equivalent to the optimal pressure to prevent fluid delivery in the case of fluid aspiration. In other embodiments, the valve on the bypass circuit may be triggerable electronically and may function as an electromechanical switch, the inputs to which may be, for example, a flow switch, a pressure switch, or a bubble sensor switch.

[0019] In the event fluid flow returning from the patient is interrupted in these embodiments, such as due to leaks or fluid aspiration into the lungs, the safety valve and check valve will operate in concert to limit the total amount of fluid lost from the system. For example, when air is drawn into the air-trap chamber of the safety valve from the oral return catheter, there will no longer be sufficient liquid to suspend the floating ball, which will then fall, thereby sealing the safety valve. Once the valve is closed, action of the pump creates a large suction pressure in the line supplying the pump inlet. In some instances, this

large suction pressure collapses the roller pump tubing, which is optimally designed to retain normal shape during normal use but to collapse under suction resulting from engagement of the safety valve. The suction pressure also creates a large differential pressure across the check valve, causing it to open. When open, the check valve establishes fluidic communication between the tubes delivering fluid to the patient from the pump outlet and the tubes returning fluid to the pump inlet. In other words, opening the check valve creates a bypass loop that diverts fluid delivery away the patient even as the pump continues to operate. While the floating ball check valve is closed, the system operator has time to identify the cause of the cooling fluid loss and decide to continue or stop therapy. The closed state is readily detected by inspection of visual flow indicators, such as paddle wheels, in some embodiments. If the decision to continue therapy is made, the ball check valve is reset by closing the normally open valve or clamp on the fluid line leading from the lower or liquid port of ball check valve and opening the clamp or valve leading from the upper or gas port of the valve. In some embodiments, a three-way valve could also be used instead of these two valves. Placing the upper or gas side of the floating ball check valve in fluid communication with the pump inlet line purges it and allows the floating ball to recover its normal operating position as liquid enters the lower portion of the floating ball check valve.

[0020] In some embodiments, an ‘initial filling’ feature of the tube set is included. In these embodiments, a “T” or “Y” fitting with tubing terminating in quick connections may be used, for example, to join the two tubes that would deliver fluid to the patient during normal operation with the tube that would recover fluid from the patient in normal operation. Once this closed circuit is created, a fluid reservoir, such as an IV bag, is used to introduce fluid into the tube set while purging air from the tube set. The pump may be activated at slow speed in some embodiments to draw fluid into the system. In other embodiments, the tube set is gravity-fed. Valves may then be closed to allow removal of the reservoir or IV bag from the system if desired. This initial filling feature also permits circulating the fluid in a closed loop indefinitely, allowing chilling and filtration of the fluid before fluid connection is made with the patient. Other fittings besides “T” or “Y” fittings or multiple fittings may be used in some embodiments to the same effect. This may be particularly helpful in embodiments with a different number of delivery and recovery tubes and/or paths.

[0021] In some embodiments, an ‘emptying feature’ of the tube set is included. The emptying feature is included in some embodiments by adding, for example, a “T” or “Y” fitting and empty IV bag to the fluid delivery pathway. At the end of therapy, the pinch

clamp on the emptying pathway is opened and the clamp on the patient delivery pathway is closed, thus diverting flow away from the patient and toward an IV bag or other receptacle for the used cooling fluid. In some embodiments, the emptying feature may be implemented with a 3-way valve or the like to switch between the ‘normal’ fluid path and the ‘emptying’ path.

[0022] In some embodiments, the pumping may be provided with existing pumps used for cardiopulmonary bypass surgeries, while cooling may be provided by placing the heat exchanger in fluidic communication with a heater cooler that is also commonly used for bypass surgeries.

[0023] The feature or features of one embodiment may be applied to other embodiments, even though not described or illustrated, unless expressly prohibited by this disclosure or the nature of the embodiments.

[0024] Details associated with the embodiments described above and others are presented below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] The following drawings illustrate by way of example and not limitation. For the sake of brevity and clarity, every feature of a given structure is not always labeled in every FIG. in which that structure appears. Identical reference numbers do not necessarily indicate an identical structure. Rather, the same reference number may be used to indicate a similar feature or a feature with similar functionality, as may non-identical reference numbers. Some of the FIGS. illustrate some of the described elements using graphical symbols that will be understood by those of ordinary skill in the art.

[0026] **FIG. 1** is a block diagram of one embodiment of these present systems.

[0027] **FIG. 2** illustrates one configuration for the system shown in FIG. 1 according to the present methods and systems for initially filling and/or pre-chilling of various system parts.

[0028] **FIG. 3** illustrates one configuration of the embodiment depicted in FIG. 1 for “normal operations” (i.e., cooling/warming/maintaining temperature in a patient’s aerodigestive tract) when fluid is delivered to the patient.

[0029] **FIG. 4** illustrates one configuration for the embodiment shown in FIG. 1 for a flow path that may be created according to some embodiments of the present disclosure after a safety valve is engaged, such as when fluid is lost from the system.

[0030] **FIG. 5** illustrates one configuration for the embodiment shown in FIG. 1 for emptying fluid from the system.

[0031] **FIG. 6A** depicts one embodiment of the present disclosure, arranged on an IV pole.

[0032] **FIGS. 6B-6D** illustrate various components of the embodiment depicted in FIG. 6A.

[0033] **FIGS. 7A-7D** illustrate one embodiment of the presently disclosed floating ball check valve from different perspective viewing angles.

[0034] **FIGS. 8A-8D** illustrate one embodiment of the presently disclosed oral return catheters from different perspective viewing angles.

[0035] **FIGS. 9A-9C** illustrate one embodiment of the presently disclosed nasal masks from different perspective viewing angles.

[0036] **FIGS. 10A and 10B** illustrate one embodiment of the presently disclosed esophageal catheters from different perspective viewing angles.

[0037] **FIG. 11** illustrates the catheter placement and fluid flow according to one embodiment of the present disclosure.

[0038] **FIG. 12** illustrates one configuration for some embodiments with valves such as non fluid contacting pinch valves driven by external or internal inputs.

DETAILED DESCRIPTION OF THE INVENTION

[0039] The term “aerodigestive tract” refers to a complex of organs that, in total, make up the tissues and organs of the upper respiratory tract and the upper part of the digestive tract. The aerodigestive tract, as used herein, may include the lips and mouth, tongue, nose, throat, vocal cords, esophagus, stomach and/or trachea. The aerodigestive tract does not include the lungs. The phrase “introducing liquid into the aerodigestive tract” includes introducing liquids into any part of the aerodigestive tract, such as the nasal cavity, upper airway (nasal and oral cavity and pharynx), the nasal cavity and upper airway and

esophagus, or the nasal cavity and upper airway and esophagus and stomach, or any combination or sub-combination thereof.

[0040] The term “coupled” is defined as connected, although not necessarily directly, and not necessarily mechanically. Two items are “couplable” if they may be coupled to each other. Unless the context explicitly requires otherwise, items that are couplable are also decouplable, and vice-versa. One non-limiting way in which a first structure is couplable to a second structure is for the first structure to be configured to be coupled (or configured to be couplable) to the second structure.

[0041] The terms “a” and “an” are defined as one or more unless this disclosure explicitly requires otherwise.

[0042] The term “substantially” is defined as largely but not necessarily wholly what is specified (and includes what is specified; e.g., substantially 90 degrees includes 90 degrees, and substantially parallel includes parallel), as understood by a person of ordinary skill in the art. In any disclosed embodiment, the terms “substantially,” “approximately,” and “about” may be substituted with “within [a percentage] of” what is specified, where the percentage includes 0.1, 1, 5, and 10 percent.

[0043] The terms “comprise” (and any form of comprise, such as “comprises” and “comprising”), “have” (and any form of have, such as “has” and “having”), “include” (and any form of include, such as “includes” and “including”) and “contain” (and any form of contain, such as “contains” and “containing”) are open-ended linking verbs. As a result, a cooling device, or a component of a cooling device, that “comprises,” “has,” “includes” or “contains” one or more elements or features possesses those one or more elements or features, but is not limited to possessing only those elements or features. Likewise, a cooling method that “comprises,” “has,” “includes” or “contains” one or more steps possesses those one or more steps, but is not limited to possessing only those one or more steps. Additionally, terms such as “first” and “second” are used only to differentiate structures or features, and not to limit the different structures or features to a particular order.

[0044] In some embodiments, the devices of this disclosure (or components thereof) may be coupled or couplable (directly or indirectly) to an independent power source (e.g., a power source that provides power without being coupled to an electrical grid), such as, for example, a manual power source (e.g., rotating or reciprocating a handle, by depressing or extending a plunger, and the like), a chemical power source, a solar power source, and/or a

standalone electrical power source; and, in other embodiments, the devices of this disclosure (or components thereof) may be coupled or couplable (directly or indirectly) to a dependent power source (e.g., an electrical grid), such as with an outlet plug. In some embodiments, the primary power source of the devices of this disclosure (or components thereof) is an independent power source, and the devices (or components thereof) may be coupled or couplable (directly or indirectly) to a dependent power source as a secondary power source; and, in other embodiments, the primary power source of the devices of this disclosure (or components thereof) is a dependent power source, and the devices (or components thereof) may be coupled or couplable (directly or indirectly) to an independent power source.

[0045] The term “Disposable kit” is used to refer to the set of components in contact with the patient, e.g., a nasal mask, an esophageal catheter and oral return line and also those components in fluidic communication with the patient. The term also includes the Y connector used in initial filling in some embodiments.

[0046] The term “Tube set” refers to the parts of the disposable kit that are not the nasal mask, esophageal catheter and oral return line. These patient contacting parts are called “end effectors.” The tube set includes tubing, connectors, valves, clamps, etc. through which fluid is circulated.

[0047] The term “fluid aspiration” is used to refer to fluid from the aerodigestive tract entering the lungs of the patient. For instance, a collapse of the endotracheal tube cuff may allow fluid to enter the lungs if fluid is present proximal to the cuff.

[0048] The term “single fault” refers to an individual failure of a component used during the therapy described in this disclosure. An example of a single fault condition is an endotracheal tube cuff collapse.

[0049] The term “double fault” refers to two failures occurring during the therapy. An example of a double fault condition is an endotracheal tube cuff collapse in unison with a dislodgement of the oral return catheter.

[0050] The term “triple fault” refers to three failures occurring during the therapy. An example of a triple fault condition is an endotracheal tube cuff collapse in unison with a dislodgement of the oral return catheter in unison with a failure of at least one safety valve mechanism.

[0051] Turning to the figures, FIG. 1 illustrates one example of the present disclosure. FIG. 1 illustrates a system 100 for cooling the brain, comprising a tube set 104 and a pump,

e.g., 108 that is configured to receive a first portion of the tube set 112. A CPB roller pump 108 is illustrated, but other forms of pumps may be used such as other peristaltic pumps or centrifugal pumps. Some examples of potential pumps are described elsewhere in this disclosure.

5 [0052] The depicted embodiment also comprises a heat exchanger 116 configured to receive a second portion of the tube set. The portion of the tube set is enclosed within the heat exchanger between input point 120 and output point 124. Other heat exchangers may be used that do not fully enclose a segment of the tube set. In some embodiments, a heat exchanger may receive the tube set by enveloping or integrating with a portion of the cooling
10 circuit such that the fluid of the cooling circuit is isolated from the internal elements of the heat exchanger. In such embodiments, the portion of the cooling circuit that is received by the heat exchanger may comprise various geometries and/or materials to facilitate heat transfer between the cooling fluid and the heat exchanger elements. In other embodiments, the heat exchanger may receive the tube set via connections to one or more ports or fittings.
15 In some of these embodiments, the cooling fluid will be in direct contact with the internal elements of the heat exchanger. Such embodiments may provide more efficient cooling by removing intermediary materials that would otherwise isolate the cooling fluid from the heat exchanger cooling elements. Other embodiments may receive the tube set via connections to one or more fittings to a specialized heat exchanging conduit kit. Such conduit kits may be
20 configured to integrate with a heat exchanger while also maintaining isolation between the cooling circuit fluid and some or all of the heat exchanger elements. Such kits may be disposable and included as part of the tube set or may come separately with the capability of coupling with the tube set. Variations on the heat exchanger are described elsewhere in this disclosure. A reservoir of ice or an evaporative cooler such as zeolite may also be used in
25 place of a heat exchanger for short periods of time, such as transport from field to hospital.

[0053] The present disclosure also includes a nasal mask 128 configured to couple with the tube set (e.g., as shown in FIGS. 9A-9C) such that the tube set is in fluidic communication with a port in the nasal mask, where the port is configured to deliver fluid into the nasal cavity. The system presented in FIG. 1 also includes an esophageal catheter
30 132 configured to couple with the tube set (e.g., the tube set shown in FIGS. 10A-10B). The nasal mask and the esophageal catheter may be configured to introduce cooling fluid into the aerodigestive tract of a patient 136. In some embodiments, either or both of the nasal mask and the esophageal catheter may act as a dam to prevent leakage of cooling fluid from the

patient's nose. FIG. 1 also includes an oral return catheter 140 (e.g., the catheter shown in FIGS. 8A-8C) that is configured to remove fluid from the patient's oropharynx or other part of the patient's aero-digestive tract. The oral return catheter may comprise at least one port configured to couple with the tube set as shown at junction 144.

5 [0054] FIGS. 2 – 6A illustrate various embodiments and configurations for the present systems and methods. The different configurations are described throughout this disclosure.

[0055] For example, FIG. 2 illustrates an Initial Filling and Pre-chilling of Tube Set configuration. In this example, to fill the tube set 104 prior to attachment to a patient, the
10 nasal delivery tube 204 and esophagus delivery tube 208 are connected directly to the oral return tube 212 via a specialized connector, termed the pre-chill connector 216. A one liter full IV bag 220 is also connected to the tube set. Fluid is driven from the IV bag and into the tube set by the pump 108, while air is driven out of the tube set and into the IV bag. In this arrangement, the fluid path to the empty bag and the bypass line of the floating ball check
15 valve 224 are closed by clamps 228 and 232, respectively. Fluid may be circulated indefinitely in this arrangement, for instance as a means to pre-chill and/or de-air the fluid before a patient arrives. When the patient is ready for connection to the tube set, the pump is stopped and the pre-chill connector 216 is removed. The delivery tubes are then connected to the nasal mask and esophageal catheter. The return tube is connected to the oral return
20 catheter and mouth suction lines connected to the nasal, esophageal, and oral return catheters.

[0056] FIG. 13 shows an exemplary flow chart for operating embodiments like that shown in FIG. 2 for initial filling. In the method 1300 depicted in FIG. 13, filling is begun at step 1304 by attaching a nasal line, an esophageal line and a return line to connector section (e.g., quick connectors 236, 240, and 244 shown in FIG. 2). Later, in step 1308, a full or
25 partially full IV bag may be attached to act as source of saline or other cooling fluid (e.g., IV bag 220 shown in FIG. 2). Next, at step 1312, pinch clamps and/or valves are opened to allow source fluid to leave the IV bag and enter the cooling circuit. Then at step 1316, the pump (e.g., 108) is activated to circulate fluid through the cooling circuit. Observing the fluid path and tapping or pinching lines may be necessary to dislodge bubbles where they
30 appear, as shown in step 1320. Next, the chiller may be engaged to begin cooling fluids in the cooling circuit, as shown in step 1324. Once the cooling circuit is filled and substantially all air has been removed from the cooling circuit, step 1328 maybe performed. Here the

pump may be paused and clamps closed on each side of the pre-chill connector (e.g., 216 in FIG. 2) to prepare for connecting to the patient.

[0057] FIG. 3 illustrates an embodiment of a system in Normal Operation. During normal operation, the fluid-filled tube set is directly coupled to the patient via the nasal mask 128, esophageal catheter 132, and oral return catheter 140. Under positive pressure, fluid is pumped through the filter 148, the heat exchanger 116, and to the nasal catheter 128 and esophageal catheter 132. Using the same pump 108, the fluid is pulled (i.e., under negative pressure) from the oral return catheter 140 and through the floating ball check valve 224. Clamps 228, 232, 304, 308, and 312 are closed to prevent flow in the emptying line, and prevent bypass of the filter and floating ball check valve, but these may be opened to purge blockages (e.g., air or foam).

[0058] FIG. 14 shows an exemplary flow chart for operating embodiments like that shown in FIG. 3 for normal operation. In the method 1400 depicted in FIG. 14, normal operation may begin at step 1404 with verification of placement of the nasal mask (e.g., 128), esophageal catheter (e.g., 132), and the oral return catheter (e.g., 140). In the embodiment shown, step 1408 comprises connecting the nasal line of the tube set to the nasal mask, connecting the esophageal line to the esophageal lumen of the esophageal catheter, and connecting the return line to the oral return catheter. In step 1412, the circuit liquid level is observed as saline flows into the patient. In step 1416, clamps, e.g., 312, on an elevated IV bag are opened to allow flow into the cooling circuit. Fluid flow in the circuit may and/or on the incoming fluid from the IV bag may be measured with an inline drip chamber or other metering device. At step 1420, the liquid level in the patient's oral cavity is observed. In some embodiments, the clamps allowing fluid from the IV bag, e.g., 312, may be closed once the liquid level reaches roughly the level of the back molars or when the liquid level reaches the ports on the return line. At step 1424, the pump may be started or re-started. At step 1428, the bypass line of the safety check valve may be opened (e.g., clamp 232) and the exit line closed (clamp not shown) until the float is suspended. Next, the bypass line of the safety check valve (e.g., clamp 232) may be closed and the exit line clamp is opened. At this point, the system will enter steady state, but the fluid flow should be observed, as indicated in step 1436. Additional fluid may be added per method 1400 as appropriate.

[0059] FIG. 4 illustrates a configuration for the scenario of Flow Path After Safety Valve Engagement. When a loss of fluid occurs due to a leak (e.g., fluid aspiration in the lungs), the total volume of fluid in the fluid circuit will decrease. Therefore, the oral return

catheter 140 will draw in air instead of fluid from the patient. In this instance, the safety valve chamber traps the air recovered from the oral return catheter. Upon trapping of air, the safety valve, if it is a floating ball check valve closes via a floating ball check valve mechanism. Upon closure of the safety valve, the check valve 404 on the bypass fluid path 408 will open due to the creation of a large suction pressure between the pump head 412 and the safety valve 224. The fluid will no longer travel to the patient, and instead will travel through the check valve bypass loop 408. Note that a safety valve could also be created by one or more electronic level sensors on a reservoir or valve body positioned at a similar point on the return circuit with the sensor in communication with an electronic valve or pinch clamp. However, the reliability and low cost of the floating ball check valve are strong advantages, and this concept is emphasized here.

[0060] FIG. 15 shows an exemplary flow chart for operating embodiments like that shown in FIG. 4 when the safety check valve is triggered. In the method 1500 depicted in FIG. 15, the safety check valve (e.g., floating ball valve, 224, or 700) is observed. If the valve has been triggered (e.g., the ball has been seated to the bottom of the chamber) troubleshooting through path 1554 should be performed because a leak in the circuit may have occurred and the cause should be determined, as shown in step 1508. If it is determined that fluid has leaked into the lungs, then the cooling procedures may be stopped and the lungs may be suctioned before continuing, as shown in step 1512. Once the situation has been remediated or if otherwise safe to proceed, the cooling procedure may continue, as shown at step 1516, by re-setting the safety check valve. Where this valve is a floating ball valve, the lower exit of the valve is clamped until the ball floats. At this point, pumping may continue. Once the ball is floating, the exit clamp is opened. If the ball valve seals again or fluid leak from the cooling circuit is otherwise apparent, then therapy may be discontinued as shown in step 1520. If fluid is not leaking from the cooling circuit, then determine whether the delivery path is closed and find the cause as shown in step 1528. If an obstruction or occlusion is found in the cooling circuit at step 1532, remove the blockage. In some embodiments, the valves, such as the safety check valve or sensor driven pinch valve may need to be reset before continuing to step 1536 to resume normal operation.

[0061] FIG. 5 illustrates an example for emptying the system. To empty the tube set, the pump is used to drive fluid into an empty IV bag 504. To active this feature, the clamp (e.g., 228 in FIG. 2) on the emptying pathway is opened while the clamps 508 and 512 on the delivery pathways are closed. In some embodiments, the tube set 104; catheters 128, 132,

and 140; valves 224 and 404; and other parts (e.g., 148, 508, 512, 232, 228, 216, 304, 308, and 312) may be disposable. These parts and others may be presented as disposable kits for use in such cooling systems and methods. For example, a heat exchanger 116 and/or pump 108 may be fixed and/or re-usable assets that may engage with disposable tubing. This greatly reduces the cost and implementation of the disclosed methods and systems.

[0062] FIG. 16 shows an exemplary flow chart for operating embodiments like that shown in FIG. 5 for emptying the cooling circuit. In the method 1600 depicted in FIG. 16, cooling therapy is completed at step 1604 such that the clamp (e.g., 228) to an empty IV bag (e.g., 504) may be opened and clamps to the nasal catheter and esophageal catheter may be closed (e.g., clamps 508 and 512, respectively). At step 1608, the pump runs until no more fluid is entering the empty IV bag (e.g., 504). At this point, the pump may be stopped, as shown in step 1612. Then, all clamps in the system may be closed and the tubing set and/or catheters may be disconnected/removed from the patient in step 1616. In step 1620, suction may be applied to minimize residual fluid in the patients aerodigestive tract.

[0063] FIG. 6A illustrates one embodiment 600 of the present system with the Tube Set 604 arranged on an IV pole 608. In this layout, the pump 612 is located on the base of the IV pole and fluid is pumped vertically up the IV pole to the patient 616. The IV pole may be configured such that one side of the IV pole 620 houses the delivery pathway components and one side of the IV pole 624 houses the return pathway components. FIG. 6B is an expanded view of one embodiment of a filter (e.g., 148) in embodiment 600, such as that described in FIGS. 1-5 with reference to filter 148. FIG. 6C is an expanded view of one embodiment of the safety valve (e.g., 224) in embodiment 600, such as that described in FIGS. 1-5 with references to safety valve 224. FIG. 6D is an expanded view of one embodiment of the heat exchanger (e.g., 116) in embodiment 600, such as that described in FIGS. 1-5 with references to heat exchanger 116.

[0064] In some embodiments such as those shown in FIG. 6A, an IV pole is used to mount the disposable kit, with the source IV bag elevated relative to the remainder of the kit to facilitate liquid addition and de-airing. The kit is shown interfaced with a roller pump commonly found in hospitals, e.g., a Sorin S3. A heater/chiller is used to provide cooling to the heat exchanger in FIG. 6D but this is not shown here in FIG. 6A.

[0065] FIG. 6B illustrates a filter that may be positioned on the delivery side of the flow path just after the pump to minimize back pressure in the rest of the circuit. The filter

can be a 0.2 micron filter to prevent passage of microbes. A bypass or vent line may be attached to the filter to enable venting or passage of small air bubbles. The filter may also be more than one filter arranged in parallel or a series arrangement comprising one or more ‘pre filters’ of larger pore size and subsequent filters of smaller pore size. In this embodiment
5 hollow fiber filters are used because of their large filtration surface area and compact size.

[0066] FIG. 6C shows a floating ball check valve in place on the return side of the circuit. The valve accepts flowing fluid at the side port, while the body allows gravity to separate air (exiting the upper port) from liquid (exiting the lower port). If too much air accumulates in the valve body, the ball (not shown in FIG. 6C) will block the lower port.
10 The action of the pump will then create vacuum in the return side relative to the delivery side, slowing or stopping fluid delivery to the patient.

[0067] FIG. 6D shows a shell and tube heat exchanger positioned on the delivery side of the flow path. The heat exchanger in some embodiments, as shown here, is of shell and tube type but other types can also be used such as a plate heat exchanger. One side of the
15 heat exchanger—the “cooling side”—is in fluidic communication with a source of circulating cold fluid, such as a heater-cooler used in heart lung bypass operations. However, the heat exchanger could also be in communication with other forms of cooling such as thermoelectric device, a heat pipe, a chemical cold pack undergoing endothermic reaction, vortex tubes, or even a bucket of ice. The other side of the heat exchanger—the “the patient side”—is in contact
20 with the cold fluid delivered to the patient.

[0068] FIG. 7 illustrates one embodiment of a safety valve (e.g., safety valve 224 discussed in FIGS. 1-6). A safety valve may have an inlet port 712, an upper outlet port 716 preferentially for air and a lower outlet port 708 preferentially for liquids. When an air-liquid mixture enters through the inlet port, the chamber 704 preferentially separates the air from
25 the liquid, thus trapping the air in the chamber. A free floating ball or float 720 falls to seal 724 above the lower outlet port when insufficient liquid is present, thereby shutting down flow. The safety valve may be a floating ball check valve. For example, FIG. 7 illustrates a floating ball check valve 700 comprising a chamber 704 comprising a first port 708, a second port 712, and a third port 716. Also shown is a ball 720 that is configured to move within the
30 chamber, where the ball has a density that is greater than the density of air but less than the density of water. Also shown in this example is a seal 724 configured to seat the ball, where the seal is within the chamber and surrounds a perimeter 728 of the first port. The ball may be further configured to substantially block the first port when the ball is seated in the seal.

Also, the ball may be configured to permit fluid flow from the second port to the first port when the chamber is filled with a fluid.

[0069] In one exemplary embodiment, discussed with reference to FIG. 1, tubing is placed in a roller pump sized to provide 1 to 5 liters per minute of flow (depending on pump speed and tubing size). A Sorin S3 pump is an example of such a pump, but similar pumps are sold by Medtronic, Terumo and others for use in cardiopulmonary bypass. Examples of representative tubing sizes are 3/8", 1/2", 12 mm, etc. To deliver fluid to the patient, the pump pushes fluid through a filter and a heat exchanger. The fluid is subsequently divided, with one portion being directed toward the nasal cavity and the other directed toward the esophagus. Using the same pump, fluid returns from the patient via an oral return catheter, then passes through the floating ball check valve, and returns to the same pump inlet. To fill the tube set, a 1 liter full IV bag is coupled to the tube set on the return pathway. To empty the tube set, a 1 liter empty IV bag is coupled to the tube set on the delivery pathway. In this embodiment, pinch clamps are used as valves to change the flow path when needed to accomplish various functions described in subsequent figures.

[0070] FIGS. 8A-8D illustrate one embodiment of an oral return catheter 800 from various perspectives. Some embodiments of the oral return catheter include a blunt tip for positioning near or against the back of the throat (i.e., the oropharynx). At least 1 side inlet port may be used to suction fluid from the oral cavity. In some embodiments, two inlet ports are used to prevent "hickeying" against structures in the oral cavity. In FIG. 8, for example oral return catheter 800 to recover free-flowing fluid from an oral cavity during selective brain cooling, comprises a first channel 804 and a second channel 808, where the first channel is coupled to the second channel by an elbow 812. The example shown also comprises a first tip 816 on the first channel configured to couple to a catheter (not shown) and a second tip 820 on the second channel that is rounded. Other geometries are also possible to prevent hickeying or minimize trauma or impact if the return catheter makes contact with the aerodigestive tract. Additionally, some embodiments, such as that shown, may comprise an inlet port 824 located at a point between the second tip and the elbow, where the inlet port is in fluidic communication with the first and second channels. Also shown in this embodiment is a catch 828 located on an exterior surface 832 of the second channel, where the catch is configured to make contact with at least one of a patient's cheek, lip, or teeth to maintain the position of the inlet port within the patient's oral cavity.

[0071] FIGS. 9A-9C illustrate one embodiment of a Nasal Mask from various perspectives. A nasal mask may include soft silicone nostril pillows to create a fluid-tight seal at each nostril in order to allow introduction of fluid into the nasal cavity. An adjustable head strap may apply mild tension on each nostril to maintain the fluid-tight seals. FIG. 9 depicts, for example, a nasal mask 900 comprising a mask-body 904 comprising a first channel 908, a second channel 912, a first latch 916, and a second latch 920. As shown, the first channel may comprise a first opening 924 and a second opening 928 such that the first and second openings are connected by the first channel, and the first opening is configured to couple with a first catheter 932. In the depicted embodiment, the second channel also comprises a first opening 936 and a second opening 940 such that the first and second openings are connected by the second channel, and the first opening is configured to couple with a second catheter 944. In the depicted embodiment, the second opening of the first channel comprises a first pillow 948 that is configured to form a substantially water-tight seal with a first nostril of a patient and the second opening of the second channel comprises a second pillow 952 that is configured to form a substantially water tight seal with a second nostril of the patient. As shown, the first latch 916 and second latch 936 are configured to be connected to a strap 956 where the strap is configured to maintain the position of the first pillow relative to the first nostril and the strap is configured to maintain the position of the second pillow relative to the second nostril. The mask-body illustrated further comprises a joint 960 where the first and second channels are connected by the joint such that the position of the first and second channels may be configured to fit the patient's first and second nostrils (not shown).

[0072] FIGS. 10A and 10B illustrate one embodiment of an esophageal catheter and one cross sectional view of the esophageal catheter lumen, respectively. An esophageal catheter is used to introduce free flowing fluid into the esophagus while preventing fluid from entering the stomach. The depicted esophageal catheter shaft has 3 separate lumens: the esophageal or fluid lumen is used to introduce fluid into the esophagus, the gastric lumen is used to access the stomach when needed, and the gastric balloon lumen is used to inflate the gastric balloon. In the depicted cross section, the cooling fluid lumen cross section 1004 is 'bean shaped' to provide high flow in a relatively small diameter access catheter lumen. In embodiments where the fluid lumen is bean shape, fluid may continue to flow even when the catheter shaft is pinched. To prevent fluid from entering the stomach, the gastric balloon may be inflated in the stomach and held under traction against the lower esophageal sphincter.

FIG. 10 depicts one embodiment of an esophageal catheter 1000, comprising an access catheter 1008 comprising an access lumen 1012. Also shown, for example, are a fluid catheter 1016 comprising a fluid lumen 1004, a balloon catheter 1020 comprising a balloon lumen 1024, a gastric catheter 1028 comprising a gastric lumen 1032. As shown, the access lumen may contain at least a portion 1036 of a fluid lumen, a portion 1036 of the balloon lumen, and a portion 1036 of the gastric lumen. The fluid lumen may also comprise, for example, a first port 1040 and a second port 1044, the first port configured to couple with a catheter outside of a patient's body to receive cooling fluid for delivery to the patient's esophagus through the second port. The balloon lumen of the depicted embodiment also comprises a first port 1048 and a balloon 1052, the first port may be configured to couple with a catheter outside of a patient's body to receive a gas or liquid to inflate the balloon, where the balloon is configured to prevent cooling fluid in the esophagus from flowing into the stomach of the patient. The gastric lumen of the depicted embodiment comprises a first port 1056 and a second port 1060, where the first port configured to couple with a catheter outside of a patient's body, and where the second port is in fluidic communication with the patient's stomach.

[0073] FIG. 11 illustrates an example of catheter placements and fluid flow during "Normal Operation" according to some embodiments of this disclosure. During normal operation 1100, fluid is delivered into the patient's aerodigestive tract through the esophageal catheter (see, e.g., FIGS. 10A and 10B) and the nasal mask (see, e.g., FIGS. 9A-9C). Fluid is recovered through the oral return catheter (see, e.g., FIGS. 8A-8D). The gastric balloon 1052 on the esophageal catheter 1000 prevents fluid from entering the stomach. The cuff 1128 on the endotracheal tube 1132 prevents fluid from entering the lungs. Arrows 1108 show the direction of flow of cooling fluid 1124, entering at a nasal mask opening (e.g., 928) and esophageal lumen ports 1044a and 1044b. Fluid returns to the pump via catheter 1112 in the embodiment shown. Port 1120 maintains a breathing path for the lungs via port 1136, while cuff 1129 is controlled at port 1116. Fluid communication with the stomach is maintained via ports 1060 in catheter 1000.

[0074] FIG. 12 illustrates an example of some embodiments with valves such as non-fluid contacting pinch valves 1201, 1203, 1205, driven by external or internal inputs 1202, 1204, 1206. One or more valves may be located at any position in the circuit such that they will cause flow to divert away from the patient and into the bypass circuit 408 comprising the check valve 1250 when activated. Examples of inputs could be temperature or other

measurement 1202, a signal from a timer 1204, or a stop signal from a remote control, kill switch or voice command 1206. The valve 1201 may be in communication with a temperature probe in the patient and respond to a measurement of core temperature shutting off if temperature falls too low, for example. Or it may respond to a measurement of cooling fluid temperature and shut off if temperature gets too high. The valve 1203 could allow treatment to be discontinued automatically after a set period of time, while 1205 could stop treatment upon voice command or other signal. Other possibilities exist: one valve might accept multiple inputs such as patient brain temperature and heart rate. Further, the form of these inputs are merely exemplary and may be interchanged with one another, used in the alternative, or conjunctively.

D. EXAMPLES

[0075] Some examples of clinical and theoretical implementations of the present devices and methods are described below. These examples are illustrative of one embodiment only and are not meant to provide any limitations to the scope of this disclosure.

[0076] *Compatibility with existing hospital equipment (e.g., for hospital use).* In some examples, the disposable kit is coupled to a single, readily available peristaltic (or roller) pump such as a Sorin S3, Sorin S5, or similar products from Medtronic and Terumo. Alternatively, the disposable kit may also be coupled to a single centrifugal pump or diaphragm pump or other pump having disposable fluid contacting parts such as the pumps used in heart lung bypass or dialysis procedures. For cooling and/or heating of the fluid, the disposable kit may be coupled to a single, readily available heater-cooler used for patient temperature management such as those used in heart lung bypass. Examples of heater-cooler manufacturers that may be used are Sorin (3T), Cincinnati Sub-zero (Hemotherm, Blanketrol), and Gaymar/Stryker (Medi-Therm). For arranging the tube set proximal to the patient, a standard IV pole may be used to optimally mount and organize the tube set components. The disposable kit interfaces with and may make use of equipment readily available in hospitals and more importantly leverages the many years of testing and experience that practitioners (perfusionists in particular) have with existing equipment. Moreover, operating the disposable kit with a single pump allows reduction of liquid volume required to cool the patient by removing the necessity for a fluid reservoir. Instead, all fluid can be contained within the disposable kit tubing itself. An in-line heat exchanger with a small priming volume is utilized to provide cooling of the fluid. In addition, a single-pump

arrangement reduces the footprint of the system – allowing the system to be optimally positioned closer to the patient and thus reducing dead-space fluid volume within long lengths of tubing. Single pump operation (as opposed to multiple pump operation) is enabled by balancing the resistances of the nasal and esophageal parallel flow paths and supported by the design of the oral return catheter. Refer to FIG. 6 for an example of this arrangement.

[0077] *Integrated pump, chiller, and disposable kit (e.g., for ambulance use).* In some examples, the disposable kit is integrated with a custom pumping and chilling device, as opposed to readily available equipment. A custom pumping and chilling device may be required in specialized situations – such as in an ambulance – where standard equipment does not exist or where size constraints do not allow for standard equipment. In this application, a custom pumping and chilling device may be coupled to the disposable kit. The custom device includes a single pumping functionality (optimally enabled by a roller pump or a centrifugal pump) and a single temperature control functionality.

[0078] *Integrated pump and disposable kit (e.g., for field use).* In other examples, the disposable kit is utilized in the field to provide therapy where electrical power may not be readily available. In this application, a custom portable battery-powered pumping device may be coupled to the disposable kit. If required, cooling is achievable via ice, Zeolite, or other non-electrical means.

[0079] *Setup of tube set and initial filling with fluid.* Gravity is employed to assist fluid flow through all or part the disposable kit in certain operations. The IV source bag should be elevated compared to the rest of the kit and the pump should be roughly at the level of the patient or lower. In addition, lengths of tubing from the IV mounting pole to the patient should be minimized. Refer to FIG. 6. The usual cooling fluid used with the disposable kit is normal saline solution (i.e., 0.9% sodium chloride solution), supplied by IV bag. The system is designed to fill from an elevated IV bag. A pre-chill connector, comprising a “Y” fitting and tubing, is used to substitute for the fluid path in the vicinity of patient during set up. In filling mode, the pump draws fluid out of the IV bag and circulates the fluid through the tube set. The air within the tube set is purged out of the tubing and is captured within the same IV bag. Using this technique, nearly the entire system may be assembled and made ready in parallel with preparation of the patient. The system may be held in this state until the patient is ready, and then the patient is connected by removing the pre-chill connector and connecting instead to the esophageal catheter, nasal mask, and oral return catheter on the patient. Rapid change over from filling to normal operation is made

possible by quick connections and valves arranged as shown in the drawings. See FIG. 2 for more details.

[0080] *Normal operation.* Once the patient is connected, normal operation may be continued for several hours or indefinitely. During normal operation the ‘single pump’ drives saline cooling fluid from the outlet line of the roller pump, through a filter and heat exchanger, and onward to the patient. The fluid flow is branched into at least two branches with at least one branch leading to the nasal cavity and one branch leading to the esophagus. The fluid is circulated in the patient’s esophagus and nasal cavity and recovered from the mouth by the oral return catheter. Suction from the oral return catheter is provided by placing it in fluidic communication with the ‘inlet’ line of the same pump, as shown in FIG. 1. Because the same pump is used to deliver and recover fluid from the patient, the fluid entering the patient at any moment in time during normal operation is roughly equal to the fluid leaving the patient at any moment in time. Valves or clamps are closed on the lines used for emptying the tube set and bypass lines of the filter and bypass line of the floating ball check valve to keep the cooling fluid along the desired flow path. The check valve is closed in this state. Refer to FIG. 3 for details of one embodiment of the fluid pathway.

[0081] *Emptying of tube set and disposal.* The system may be largely emptied in a tidy way by opening the emptying valve and closing the delivery valves on the nasal and esophageal lines to pump the spent fluid to an empty IV bag. Refer to FIG. 5 for details of one embodiment of the fluid pathway.

[0082] *Example of aspiration prevention via placement of the oral return catheter.* Loss of liquid, particularly into the lungs, is a risk of the device, or any other device employing fluids in the aerodigestive tract. If a failure of the endotracheal tube cuff occurs, fluid in the aerodigestive tract may enter the lungs (i.e., fluid aspiration). In this situation, the severity of fluid aspiration is mitigated by limiting the total fluid of volume that may potentially enter the lungs. In one example, the subject is supine (as in FIG. 11). In other examples, the subject may be tilted head-down such that his/her head is below his/her chest cavity. The oral return catheter is placed such that its inlet ports are located below the level of the glottis. In a supine or head-down position, the relative location of the inlet ports to the glottis is ensured by placing the oral return catheter tip directly in contact with the wall of the oropharynx (i.e., the back of the throat). The oral return catheter may be secured in place with a bite block positioned against the patient’s cheek, teeth, and/or gums. The bite block applies friction against the catheter shaft, preventing movement of the oral return catheter.

During an unexpected failure of the endotracheal tube cuff, the total amount of fluid that can enter the lungs is equal to the volume of fluid in the oral cavity that is above the level of the glottis. In some patients, this volume is up to 100 mL. That is, the steady-state fluid level in the patient's mouth will drop and will enter the patient's lungs until the fluid level in the patient's mouth equals the fluid level of the glottis. If the failure of the endotracheal tube cuff goes unnoticed by the clinician, the pump will continue to run and circulate fluid to and from the patient but no additional fluid will enter the patient's lungs. This phenomenon is because the same pump is being used to deliver and recover fluid from the patient (i.e., fluid in = fluid out) and because the inlet ports of the oral return catheter are positioned below the level of the glottis.

[0083] *Example of aspiration risk reduction using a safety valve.* In some cases a failure of the endotracheal tube cuff may occur without the oral return catheter in position to prevent aspiration. In this scenario, fluid in the aerodigestive tract will be allowed to enter the lungs (i.e., fluid aspiration) and will not be stopped by the position of the oral return catheter. Instead, the severity of this risk is mitigated with a safety valve in concert with a check valve. In this scenario, if fluid is lost from the circuit, the oral return catheter draws air, instead of fluid, into the tube set. The safety valve captures the air while allowing the fluid to pass through the tube set. When a sufficient volume of air is captured in the air-trap chamber of the safety valve, the floating ball will seal at the bottom of the chamber – effectively closing the safety valve. Upon closure of the safety valve, a large suction pressure will be generated by action of the roller pump almost immediately between the safety valve and the roller pump, causing the check valve to open. With the safety valve closed and the check valve opened, the fluid is no longer able to be delivered to the patient and is instead pumped through the check valve, establishing a bypass loop. This state is readily detectable by observation of flow indicators (e.g., paddle wheels and/or the like) in the nasal and esophageal lines, as well as an audible change in the sound of the pump. A flow indicator may also be placed on the bypass flow loop near the check valve to aid observation of flow through the bypass loop. Detection is also aided if all or part of the tube set is translucent or transparent enough to observe bubbles in the fluid path. The fluid level in the patient's mouth and the circuit around the floating ball check valve may be set such that the floating ball check valve engages at various levels of fluid loss, at 400 mL, 300 mL, 200 mL or even 150 mL. A volume of 150 mL is of special interest as this volume is known to be less than

the total volume remaining in the lungs on average after a routine bronchoscopy or bronchoalveolar lavage.

[0084] *Limiting aspiration without safety valve or oral return catheter.* In the event that a failure of the endotracheal tube cuff occurs simultaneously without positioning of the oral return catheter and a failure of the safety valve mechanism. In this scenario, a significant portion of the total contents of fluid in the disposable kit may enter the lungs. However, the small total volume of the disposable kit (< 1 liter optimally) is less than that deliberately introduced in some medical procedures such as bronchoalveolar lavage (BAL) which mitigates the severity of this risk. Aspiration risk may also be reduced or eliminated in all scenarios by tilting the patient such that liquid level in the oral cavity is below the elevation of the endotracheal tube cuff.

[0085] *Safety valve.* A representative example of a robust and effective safety valve, a floating ball check valve is shown in FIG. 7. The valve housing has an inlet port and two outlet ports – an upper port meant to vent air when required and a lower port for normal flow of liquid during normal operation. The density of the floating ball is chosen to be greater than air and less than water. A ball of solid polypropylene is used in one example, but hollow balls of other biocompatible materials may be used to provide greater or lesser buoyancy. FIG. 7 shows the parts of the floating ball check valve. The air-trap chamber functions to separate air from fluid within the chamber, allowing the fluid to pass through while capturing the air within the chamber. It is important to note that the function of this valve may also be accomplished using a small reservoir and an electronic level sensor. Proximity of the safety valve to patient minimizes response time and maximizes effectiveness of this strategy.

[0086] *Oral return catheter.* The oral return catheter has a rounded tip and ‘side ports’ to recover fluid from the patient’s mouth. The side ports are located such that the fluid is removed from the oral cavity at a height that is lower than the height of the glottis. Optimally, there exists more than 1 side port in order to prevent ‘hickeying’ or other suction-related injury. The side ports also function to allow the catheter tip to be flexible to prevent excessive pressure being applied to the oropharynx wall. FIG. 8 shows one embodiment of the oral return catheter.

[0087] *Nasal mask.* One embodiment of a ‘nasal mask’ for this system is shown in FIG. 9. The essential functions of the nasal mask are to provide a liquid-tight connection to the nostrils without placing excessive pressure on the surrounding tissue. Soft silicone nasal

‘cones’ or ‘pillows’ are used to interface with the nostrils. An adjustable head strap is coupled to the nasal pillows in order to apply mild tension to maintain a fluid-tight seal at each nostril. Tubing is directly coupled to each nasal pillow in order to deliver fluid to each nostril. The nasal pillows, tubing, and associated connectors are designed to match the fluid flow resistance of the esophageal catheter.

[0088] *Esophageal catheter.* The intended purpose of the esophageal catheter, as shown in FIG. 10, is to deliver fluid into the esophagus while preventing fluid from entering the stomach. In the depicted embodiment, the esophageal catheter has 3 lumens – a first lumen that leads to a balloon, a second lumen leading to distal holes for stomach access, and a lumen with a “bean shaped” cross section for introduction of cold saline to proximal holes that terminates above the gastric balloon. The esophageal catheter is placed by a physician. Placement may be verified by introducing air in the gastric lumen and listening for bubbling in the stomach (i.e., auscultation). In the event that confirmation of placement is desired, some embodiments comprise metallic (e.g., platinum) marker rings may be visualized by XRAY, fluoroscopy, or other radiologic means. Two radio opaque marker rings on one side (proximal or distal) of the balloon and one radio opaque marker ring on the opposite side are the preferred configuration. Once the gastric balloon is verified to be in the stomach, the balloon is inflated and the esophageal catheter is placed under traction to create a fluid tight seal at the gastroesophageal junction.

[0089] In one preferred embodiment the system, a peristaltic pump also commonly called a roller pump is placed to interface with the tubing of the disposable kit as shown in FIG. 1. This positioning of the pump is advantageous because it allows the roller pump pressure to drive fluid through both the filter and heat exchanger. The choice of peristaltic pump is advantageous as it does not contact the fluid being pumped and does not require any parts to interface with the fluid other than the tubing contacting the fluid itself. The peristaltic pump is also advantageous because it may pump liquid, air, or a mixture of the two. This makes it particularly suitable for de-airing the tube set before it is connected to the patient- note that air ‘leaving’ the circuit is actually simply rising to the top of the filling bag in some embodiments, which may contain variable volume because it is flexible. The tubing is usually 0.5 inch inner diameter at the tubing segment interfacing with the peristaltic pumps but inner diameter between 0.375 inch and 0.75 inch will work well. Smaller diameters may not be as desirable because they require the pump to run at higher RPM and also introduce additional flow resistance according to the Hagen-Poiseuille law. The filter may be positioned

either before, as shown in FIG. 1, or after the entrance to the bypass loop containing the check valve. If the filter is positioned before the check valve, a small diameter bypass line around the filter should be used to prevent over pressure in case of filter clog or overpressure. The check valve and filter bypass are important when a peristaltic pump is used because the resistance to flow of this arrangement will result in a relatively high pressure (typically between 2 and 20 psi) on the delivery side of the system when paired with a peristaltic pump (in contrast a centrifugal pump will simply deliver a smaller flow rate) the pressure is intended to be larger than the variance in pressure caused by differences between nasal and esophageal flow paths in the patient. Said differently the tube set resistance may be designed to be dominant and so enabling roughly equal flow rates in two (or more) branches of the disposable kit when it is connected to the patient. In this particular example balance would be between the nasal, and esophageal lines. When the tube set is connected to the pre-chill Y connector, which functions as a placeholder in lieu of the patient, the peristaltic pump runs as saline is added to the circuit from the full IV bag (this is typically a one liter bag as shown in FIG. 1 but larger volumes may be used or multiple smaller bags applied). The key features are that the bag or bags are flexible (to accommodate returning air) and elevated so that gravity assists in filling the circuit. Note that a drip chamber or other metering device may be incorporated into the circuit to track the precise volume used in filling the circuit. The heat exchanger may be chosen to be of a size that the temperature of the patient contacting circuit is closely coupled (within 10 degrees C when removing 300 watts or less from the patient circuit) to that of the fluid in the chiller circuit, allowing the chiller temperature control to control the temperature of the fluid in the disposable kit during use. The return of fluid from the patient is driven by the suction of the inlet side of the peristaltic pump. The use of a peristaltic pump here is advantageous in that the volumetric flow rate of the return is match by the volumetric flow rate of the delivery side of the pump, thus the 'single pump' concept with volumetric matching of fluid delivery and fluid recovery helps promote a stable fluid circuit without excessive operator intervention.

[0090] Another preferred embodiment is an 'ambulance' version of the system that is optimized for compact foot print. In this embodiment a large chiller is not used, but rather an ice bath, chemical cold pack, or evaporative cooling system such as a zeolite system may be used to remove heat from the patient contacting saline. Further reduction of foot print may be accomplished using a peristaltic pump without the precision and accuracy of in-hospital pumps. Still further reduction of foot print may be accomplished by using a centrifugal or

gear pump with disposable fluid contacting parts. These arrangements will be less effective than peristaltic pumps with respect to delivery pressure, priming, and suction for fluid recovery, but some of these limitations may be mitigated by positioning the pump lower than the patient. Centrifugal and gear pump based arrangements may be favored in an ambulance environment because their size advantages may offset performance limitations. If the patient may be positioned in an inclined or “Trendelenburg” posture at a 10-20 degree angle below flat horizontal, the liquid challenge to the endotracheal cuff may be lessened or removed, and thus the floating ball check valve is not needed if the patient may be sufficiently tilted. If a centrifugal or gear pump is used, overpressure is unlikely to develop and so the check valve may not be needed.

[0091] The claims are not intended to include, and should not be interpreted to include, means-plus- or step-plus-function limitations, unless such a limitation is explicitly recited in a given claim using the phrase(s) “means for” or “step for,” respectively.

CLAIMS

1. A system for cooling the brain, comprising:
 - a tube set;
 - a pump configured to receive a first portion of the tube set;
 - a heat exchanger configured to receive a second portion of the tube set;
 - a nasal mask configured to couple with the tube set such that the tube set is in fluidic communication with a port in the nasal mask, where the port is configured to deliver fluid into the nasal cavity;
 - an esophageal catheter configured to couple with the tube set;
 - an oral return catheter where the oral return catheter is configured to remove fluid from a patient's oropharynx and where the oral return catheter comprises at least one inlet port configured to couple with the tube set.
2. The system of claim 1, where the heat exchanger is in fluidic communication with the tube set.
3. A nasal mask comprising:
 - a mask-body comprising a first channel, a second channel, a first latch, and a second latch;
 - the first channel comprising a first opening and a second opening such that the first and second openings are connected by the first channel, and the first opening is configured to couple with a first catheter;
 - the second channel comprising a third opening and a fourth opening such that the third and fourth openings are connected by the second channel, and the third opening is configured to couple with a second catheter;
 - wherein the second opening comprises a first pillow that is configured to form a substantially water-tight seal with a first nostril of a patient;
 - wherein the fourth opening comprises a second pillow that is configured to form a substantially water tight seal with a second nostril of the patient;
 - wherein the first latch and second latch are configured to be connected to a strap where the strap is configured to maintain the position of the first pillow

relative to the first nostril and the strap is configured to maintain the position of the second pillow relative to the second nostril.

4. The nasal mask of claim 3, where the mask-body further comprises a joint where the first and second channels are connected by the joint such that the position of the first and second channels are configurable to fit the patient's first and second nostrils.
5. A floating ball check valve comprising:
 - a chamber comprising a first port, a second port, and a third port;
 - a ball or float that is configured to move within the chamber, where the ball or float has a density that is greater than the density of air but less than the density of water;
 - a seal configured to seat the ball or float, where the seal is within the chamber and surrounds a perimeter of the first port;
 - where the ball or float is further configured to substantially block the first port when the ball is seated in the seal; and
 - where the ball or float is configured to permit fluid flow from the second port to the first port when the chamber is filled with a fluid.
6. A floating ball check valve comprising:
 - a chamber comprising a first port, a second port, and a third port;
 - a ball or float that is configured to move within the chamber, where the ball has a density that is greater than the density of air but less than the density of water;
 - a seal configured to seat the ball or float, where the seal is within the chamber and surrounds a perimeter of the first port;
 - where the ball or float is further configured to substantially block the first port when the ball is seated in the seal; and
 - where the ball or float is configured to permit fluid flow from the second port to the first port when the chamber is filled with a fluid.
7. An oral return catheter to recover free-flowing fluid from an oral cavity during selective brain cooling, comprising:

a first channel and a second channel, where the first channel is coupled to the second channel by an elbow fitting with an internal angle between 15 and 180 degrees;

a first tip on the first channel configured to couple to a catheter;

a second tip on the second channel that is rounded;

an inlet port located at a point between the second tip and the elbow, where the inlet port is in fluidic communication with the first and second channels.

8. The oral return catheter of claim 7, further comprising:

a catch located on an exterior surface of the second channel, where the catch is configured to make contact with at least one of a patient's cheek, lip, or teeth to maintain the position of the inlet port within the patient's oral cavity.

9. An esophageal catheter, comprising:

an access catheter comprising an access lumen;

a fluid catheter comprising a fluid lumen;

a balloon catheter comprising a balloon lumen;

a gastric catheter comprising a gastric lumen;

where the access lumen contains at least a portion of a fluid lumen, a portion of the balloon lumen, and a portion of the gastric lumen;

where the fluid lumen comprises a first port and a second port, the first port configured to couple with a catheter outside of a patient's body to receive cooling fluid for delivery to the patient's esophagus through the second port;

where the balloon lumen comprises a first port and a balloon, the first port configured to couple with a catheter outside of a patient's body to receive a gas or liquid to inflate the balloon, where the balloon is configured to prevent cooling fluid in the esophagus from flowing into the stomach of the patient;

where the gastric lumen comprises a first port and a second port, where the first port configured to couple with a catheter outside of a patient's body, and where the second port is in fluidic communication with the patient's stomach.

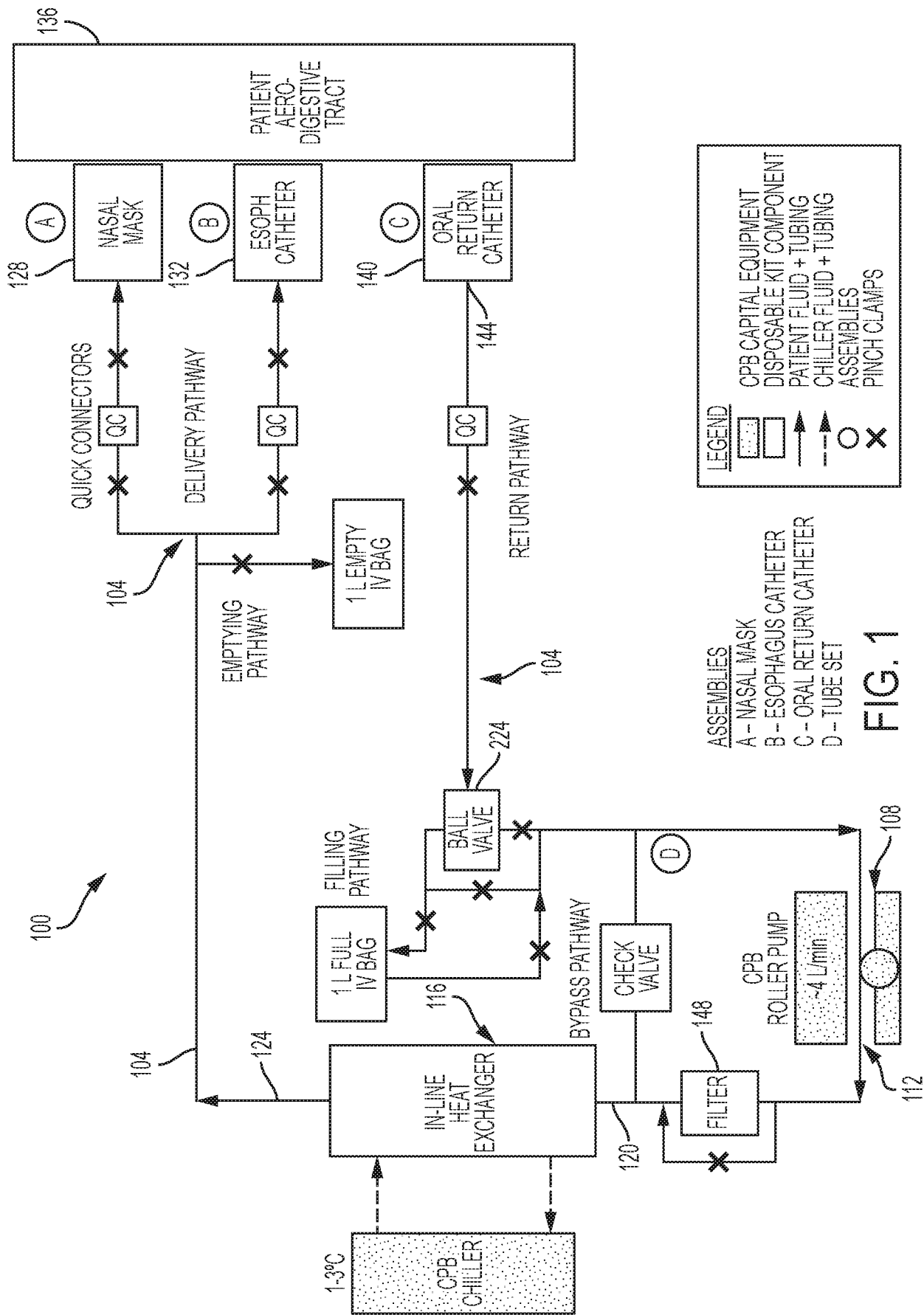
10. The esophageal catheter of claim 9, containing one or more radiopaque markers such as platinum rings to enable verification of placement.
11. A device for cooling the brain, comprising: an interface for mechanically coupling a single pump to a fluid circuit where the pump is configured to move chilled fluid toward a patient through a branched pathway with at least one branch to deliver fluid to the nose via a nasal mask and to deliver fluid to the esophagus via at least one esophageal catheter; and where the device is configured to recover fluid from the oral cavity by action of the pump.
12. The device of claim 11, where the heat exchanger is placed in thermal communication with a heating or chilling device.
13. The device of claim 11, including an automated shut-off feature triggered by loss of circulating fluid.
14. The system of claim 11 further comprising a pinch valve valve actuated by measurement, timer, switch, or command.
15. The device of claim 13, where the automated shut off device is a floating ball check valve.
16. The device of claim 15, further including a check valve.
17. The device of claim 15, further including at least one fluid bypass loop.
18. The device of claim 11, where fluid addition is accomplished from an elevated IV bag.
19. The device of claim 11, where fluid removal is accomplished by pumping into an IV bag.
20. The device of claim 11, where a “Y” fitting and quick connects are used as a place holder for the patient during set up.
21. A system to limit fluid aspiration when circulating free-flowing fluid to the aerodigestive tract, including a return catheter, a delivery catheter, and a single pump to circulate fluid to the delivery catheter and from the return catheter.
22. The system of claim 21, where the return catheter has fluid inlet ports located below the fluid level of the glottis.
23. The system of claim 21, where fluid aspiration is limited to less than 200 mL.

24. The system of claim 21, where a safety valve is coupled distally to said return catheter.
25. The system of claim 21, where the safety valve is actuated by buoyancy.
26. The system of claim 21, where the safety valve is actuated electronically.
27. The system of claim 24, where the safety valve is a floating ball check valve comprising a chamber configured to separate air and liquid recovered from the return catheter; the safety valve further comprising a floating element configured to be suspended during ordinary operation; where the floating element is further configured to close the safety valve when insufficient liquid is present in the chamber.
28. The system of claim 27, where a check valve opens a bypass fluid pathway upon the closure of said safety valve.
29. Methods to limit fluid aspiration when circulating free-flowing fluid to the aerodigestive tract, including placement of a return catheter and a delivery catheter, and operation of a single pump to circulate fluid to the delivery catheter and from the return catheter.
30. The methods of claim 29, where the return catheter has fluid inlet ports that are placed below the fluid level roughly level with the glottis.
31. The methods of claim 29, where the subject is supine.
32. The methods of claim 29, where the subject is tilted head-down.
33. A nasal mask to deliver free-flowing fluid into the nasal cavity for selective brain cooling, comprising a nostril pad through which fluid is delivered into a nostril, a head strap, and tubing coupling the nostril pad to a fluid delivery pump.
34. The nasal mask of claim 33, comprising a second nostril pad through which fluid is delivered into a second nostril, and tubing coupling the second nostril pad to a fluid delivery pump.
35. The nasal mask of claim 33, comprising a second nostril pad configured to substantially block a second nostril.
36. An esophageal catheter to deliver free-flowing fluid into the esophagus for selective brain cooling and to prevent fluid from entering the stomach, comprising an esophagus lumen, a gastric lumen, a gastric balloon, and a connection manifold.

37. The esophageal catheter of claim 36, where the gastric balloon is constructed from a compliant material.
38. The esophageal catheter of claim 37, where the compliant material comprises at least one of natural rubber, polyisoprene, silicone, or polyurethane.
39. The esophageal catheter of claim 36, where the esophagus lumen is shaped as a circle, oval or bean shape.
40. The esophageal catheter of claim 36, where the connection manifold includes a connection for application of traction.
41. Methods to deliver free-flowing fluid into the esophagus for selective brain cooling and to prevent fluid from entering the stomach, comprising placement of an esophageal catheter, inflation of a gastric balloon, and application of traction to the esophageal catheter.
42. Methods of claim 41, where the gastric balloon traction is at least 0.5 lbs.
43. An oral return catheter to recover free-flowing fluid from the oral cavity for selective brain cooling, comprising least 1 fluid inlet port and a rounded tip.
44. The oral return catheter of claim 43, where the fluid inlet port is no more than 3 cm from the rounded tip.
45. The oral return catheter of claim 43, where the fluid inlet port is no more than 2 cm from the rounded tip.
46. A method for filling and de-airing the tube set with fluid such as saline, comprising attachment of an elevated, saline containing source IV bag that is full or partially full to the tube set and use of a removable connector section as a place holder for the patient.
47. The method of claim 46, comprising use of a pump to circulate fluid such as saline through the tube set and connector section during the filling and de-airing operations.
48. The method of claim 46, where a chiller or other heat sink is engaged to cool liquid in the tube set and connector section before connection to the patient.
49. The method of claim 46, where the tube set is arranged on a board or pole so that the source IV or Full IV bag is elevated relative to at least one of: the pump interface, filter, and heat exchanger.

50. A method for cooling of a patient comprising removing a section of a pre-chilled liquid circuit and connecting at least one end of the open circuit to at least one point of fluid deliver and connecting one point of the open circuit to at least one point of fluid recovery from the patient.
51. A method for setting a floating ball check valve comprising opening the highest outlet and closing the lowest outlet of the floating ball check valve by means of a clamp or valve until the ball or float floats, and then opening the lowest outline and opening the highest outlet.
52. The method of claim 50, where additional fluid is added to the circuit to displace air volume in the patient's aerodigestive tract and patient contacting end effector and connectors introduced to complete the disposable kit.
53. The method of claim 50, where visual flow indicators such as paddlewheels, are used to monitor flow rates in fluid delivery lines.
54. The method of claim 50, where a visual flow indicator is used to monitor flow in the bypass pathway, thereby signifying flow through the check valve.
55. A method to stop fluid delivery to a patient without stopping motion of the pump driving said fluid in the tube set, yet keeping pressures lower than safe limits of the tube set, by providing an alternative fluid path comprising a pressure sensitive check valve.
56. The method of claim 55, where elevated pressure on the delivery side, i.e. the portion of the flow path containing fluid moving toward the patient, is used to open the pressure sensitive check valve.
57. The method of claim 55, where decreased pressure or vacuum on the return side, i.e. the portion of the flow path containing fluid moving away from the patient, is used to open the check valve.
58. The method of claim 55, where both increased pressure on the delivery side, i.e. the portion of the flow path containing fluid moving toward the patient and decreased pressure on the return side, i.e the portion of the flow path containing fluid moving away from the patient are used to open the check valve.
59. The method of claim 55, where a pinch valve or clamp is used to block the delivery flow path resulting in elevated pressure in the delivery flow path when actuated.

60. The method of claim 55, where a floating ball check valve is used to block the return flow path resulting in reduced pressure in the return flow path when actuated.
61. The method of claim 55, where a pinch valve or clamp is used to block the return flow path resulting in reduced pressure in the return flow path when actuated.
62. A method of removing cooling fluid from the tubing set, comprising opening a clamp leading to an IV bag connected to the delivery side of the circuit while closing clamps or valves on both the nasal and esophageal lines to prevent fluid delivery to the patient, while continuing to run the pump.



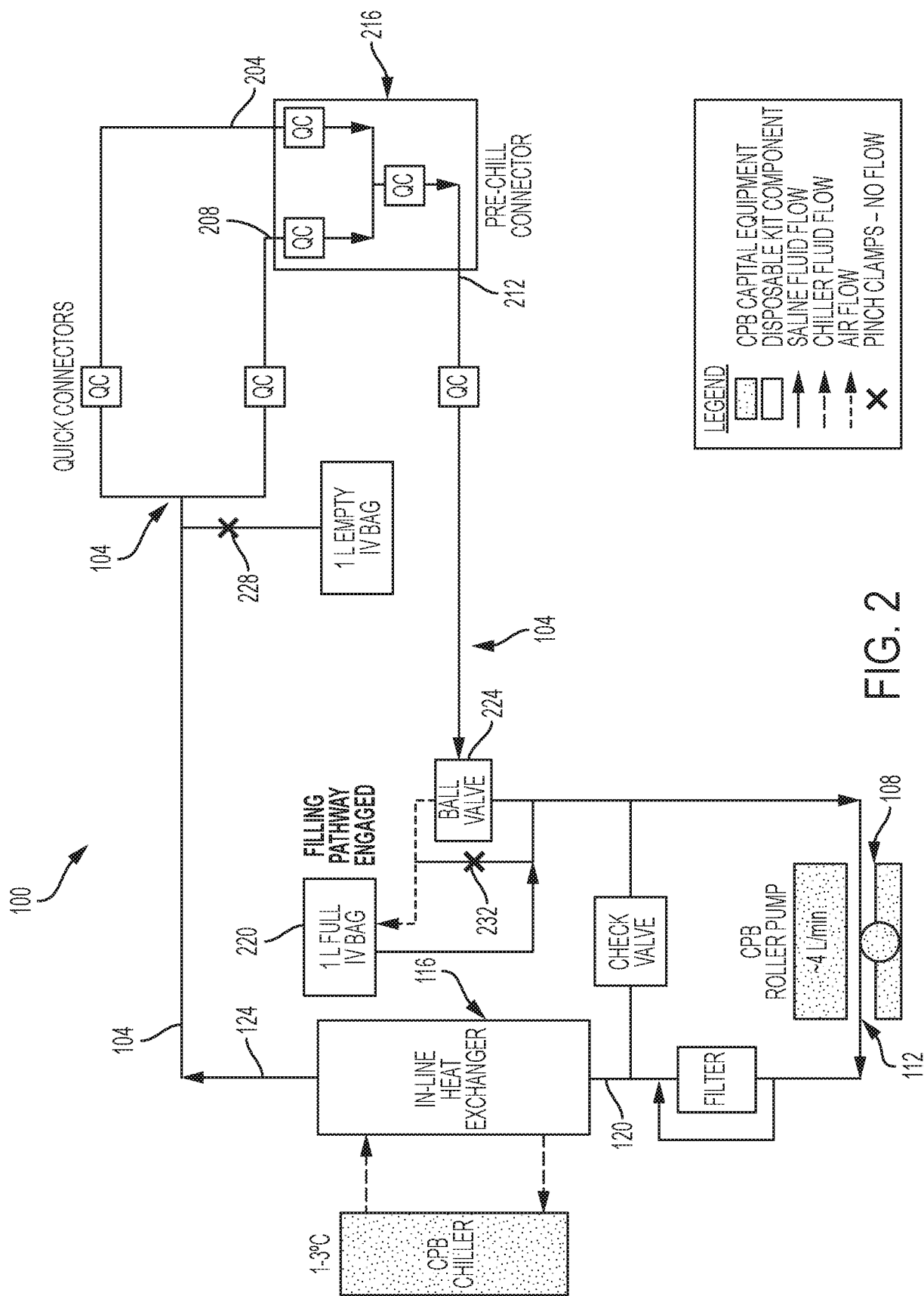
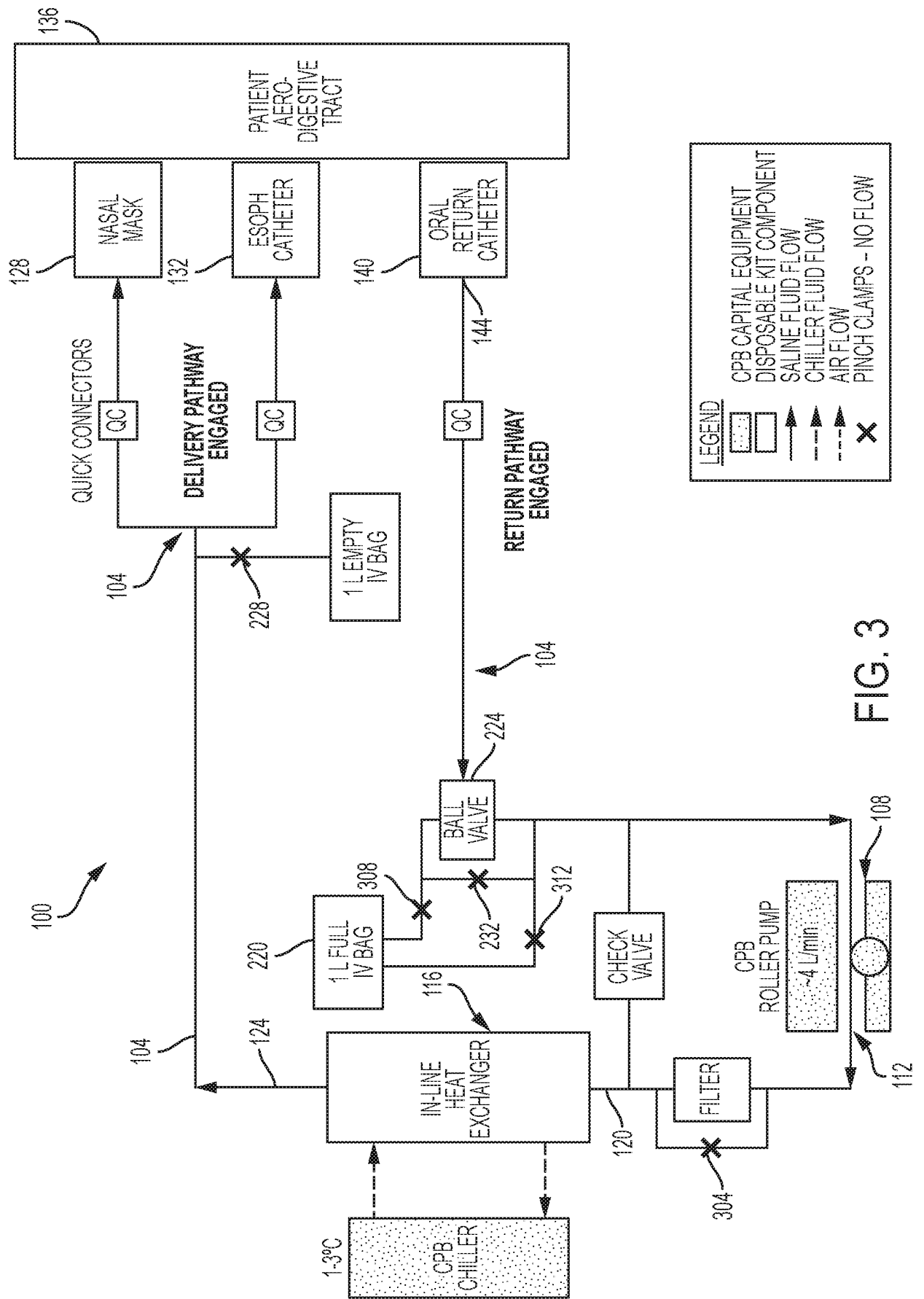
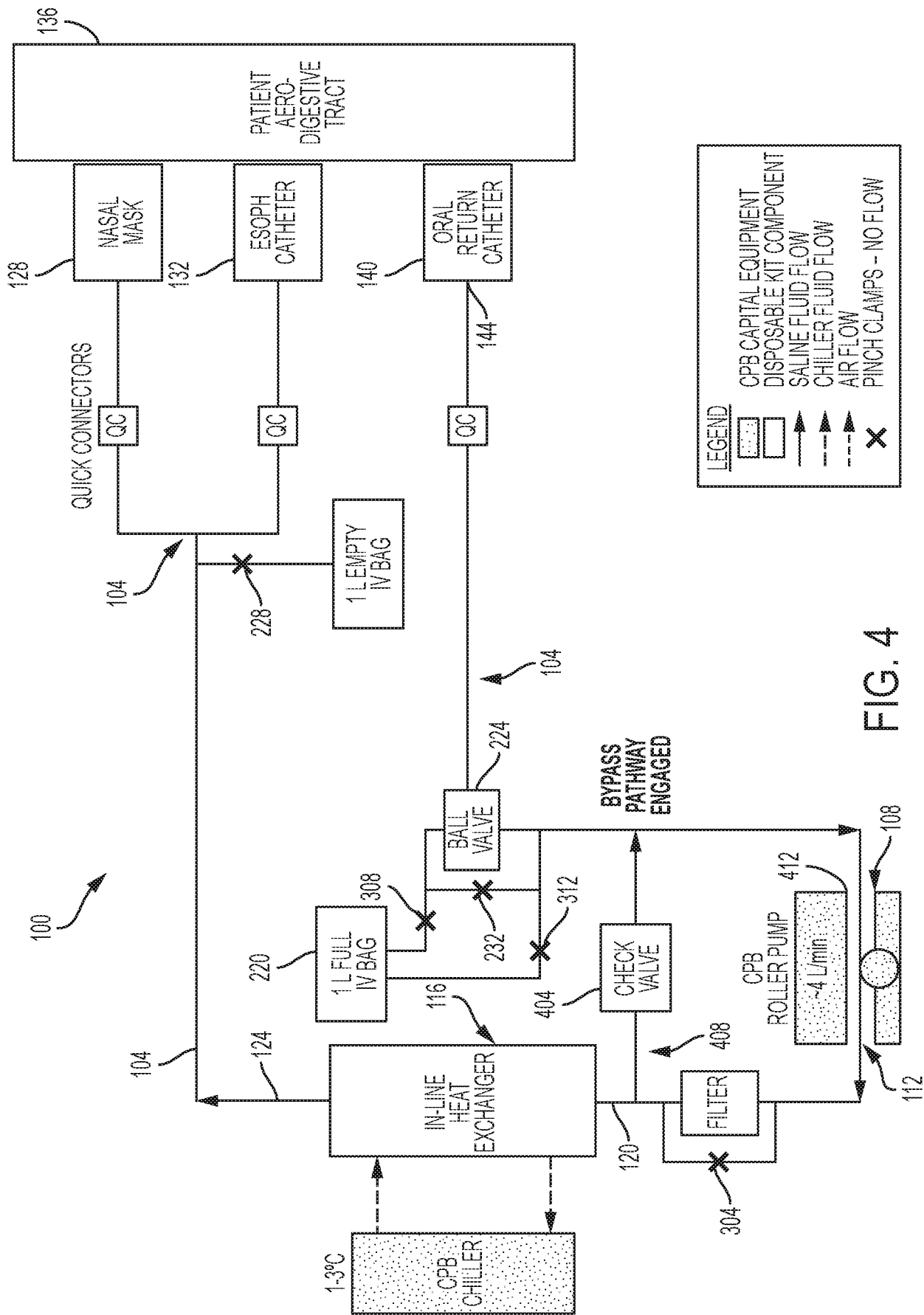


FIG. 2





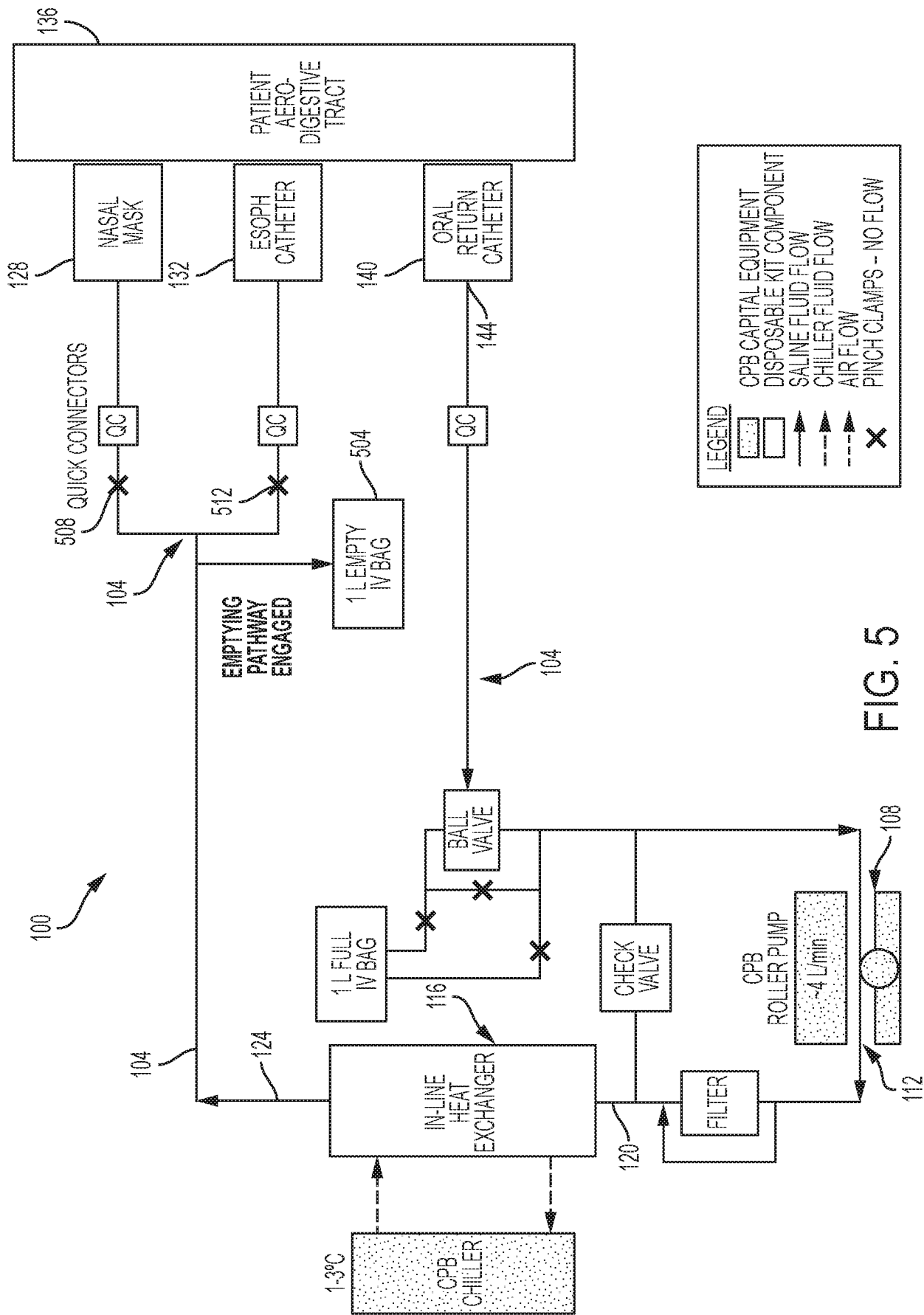
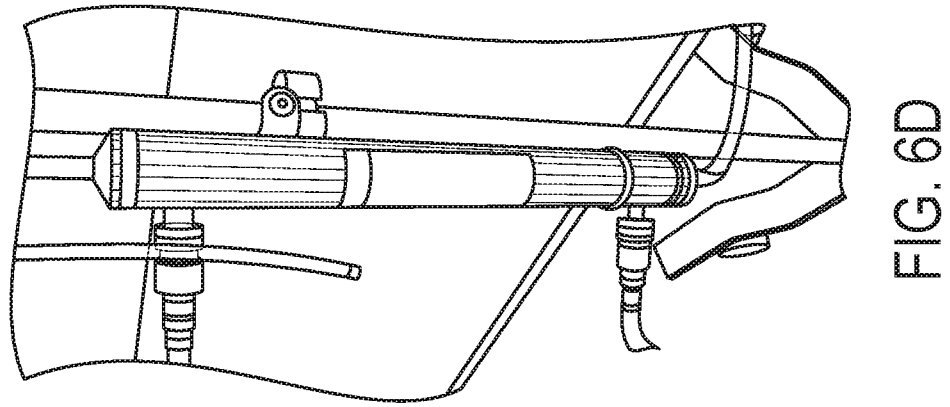
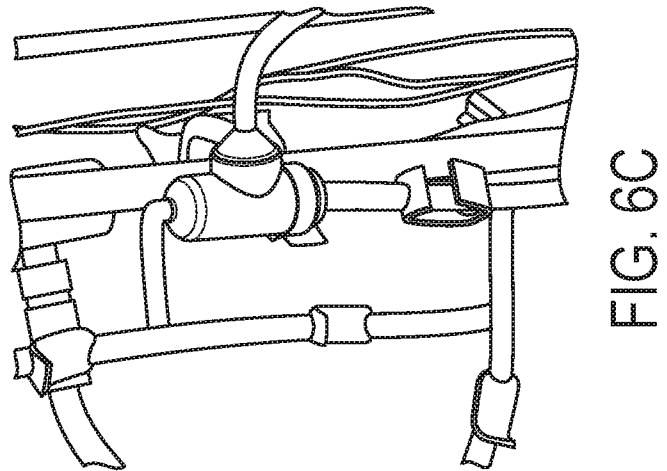
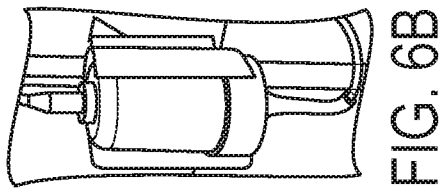
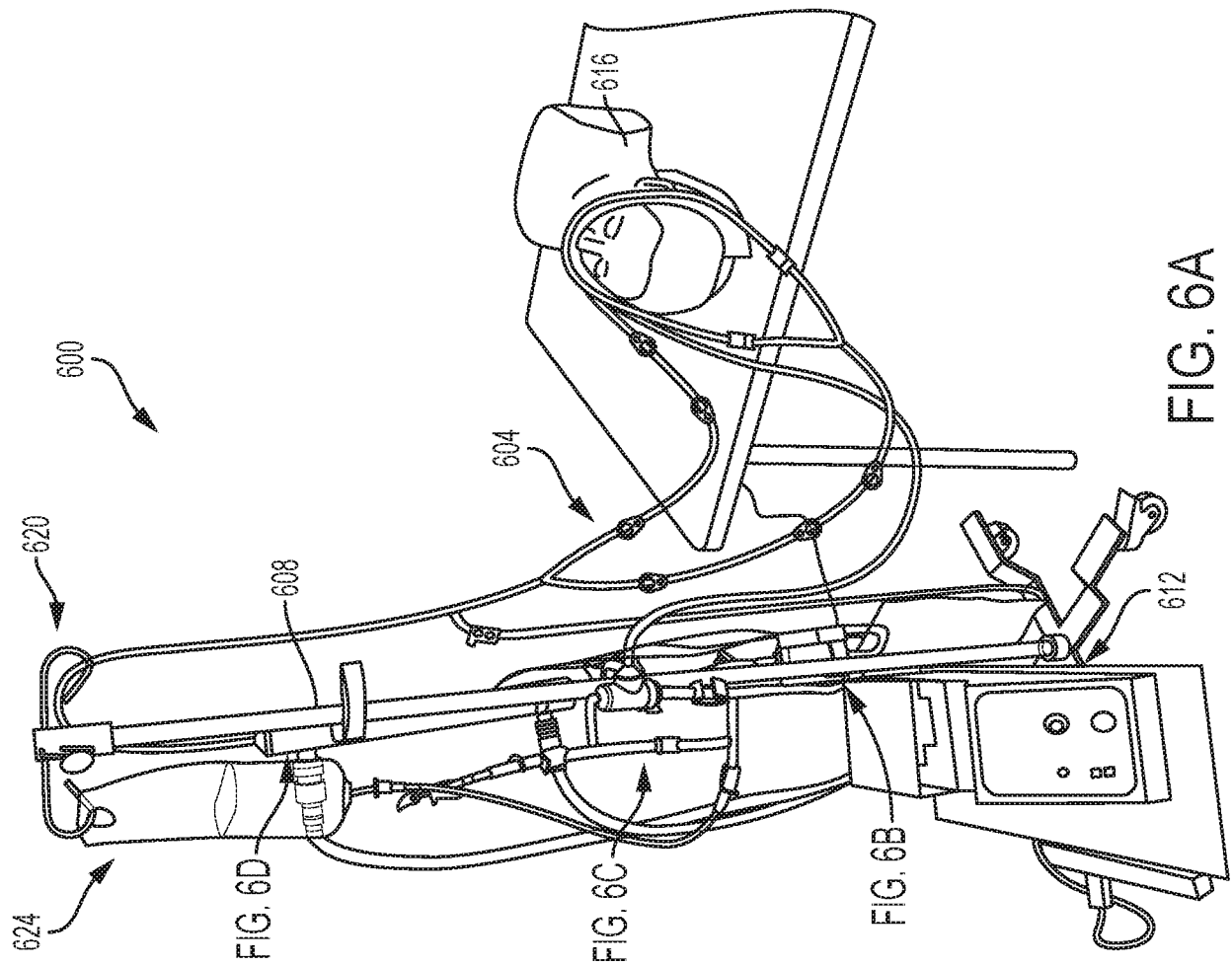


FIG. 5



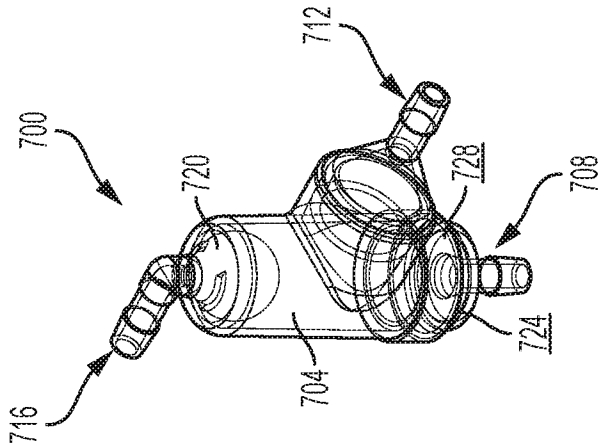


FIG. 7A

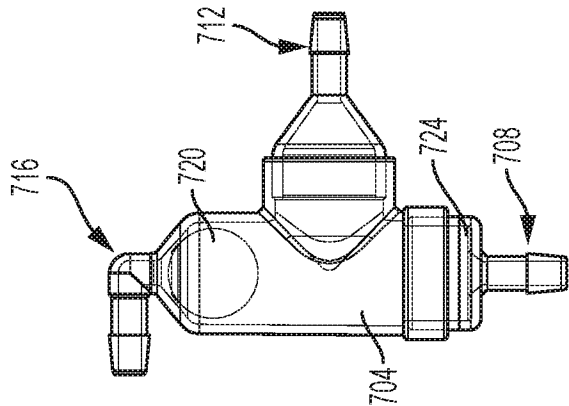


FIG. 7B

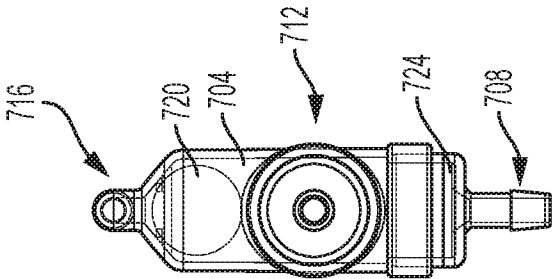


FIG. 7C

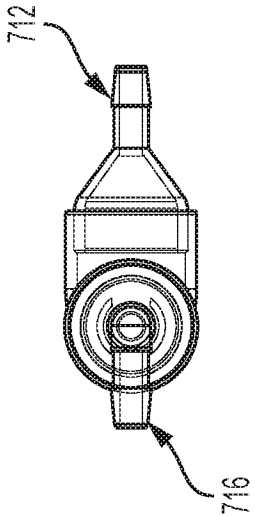
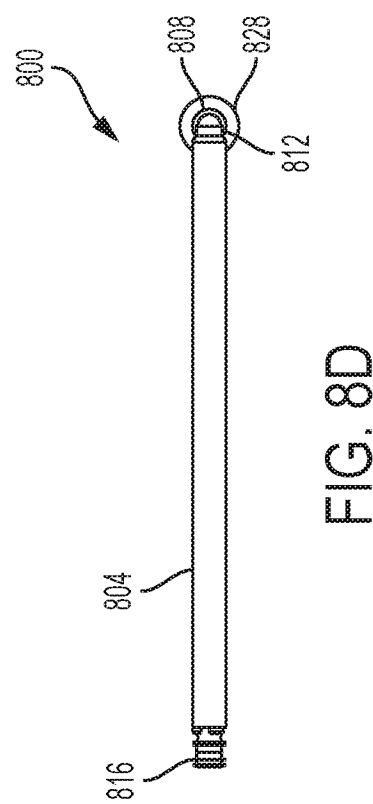
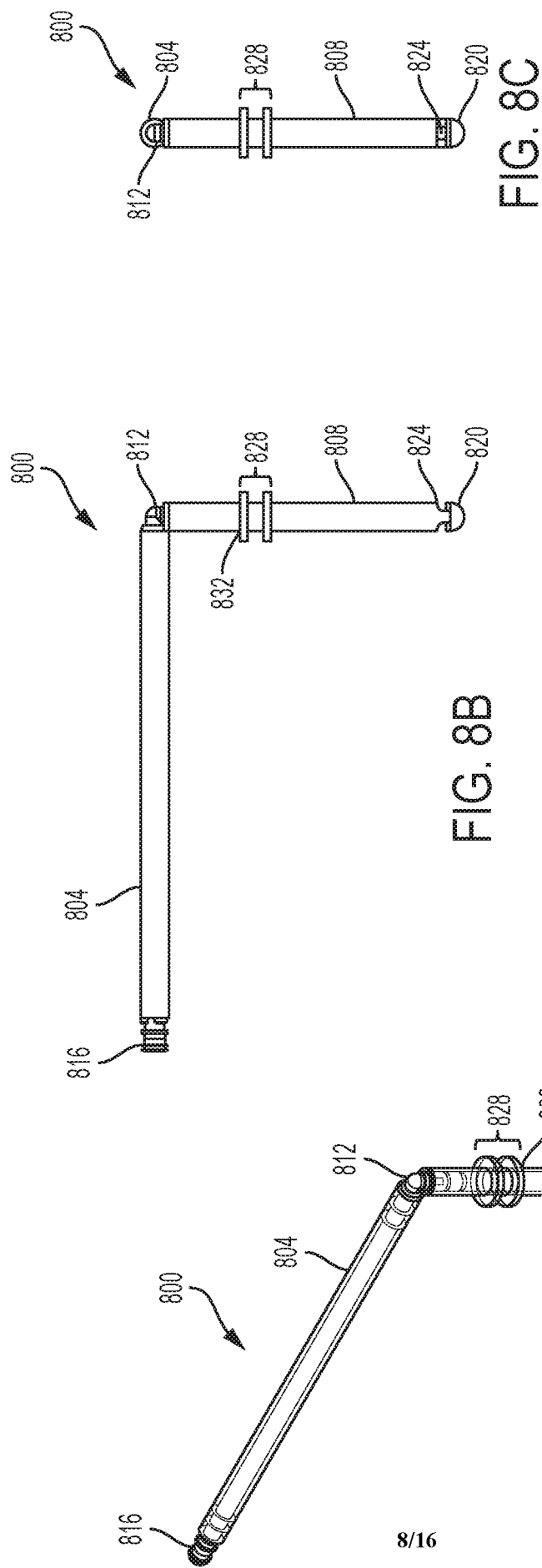


FIG. 7D



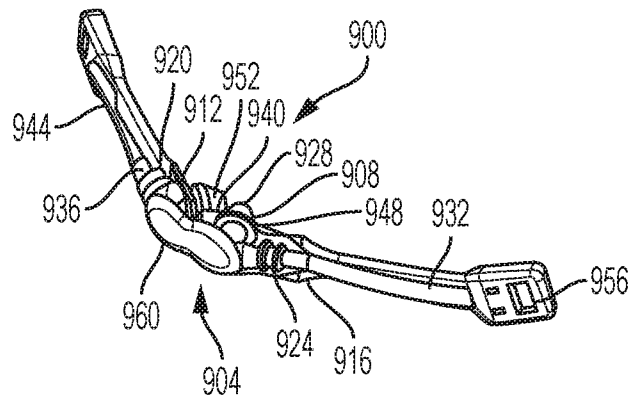


FIG. 9A

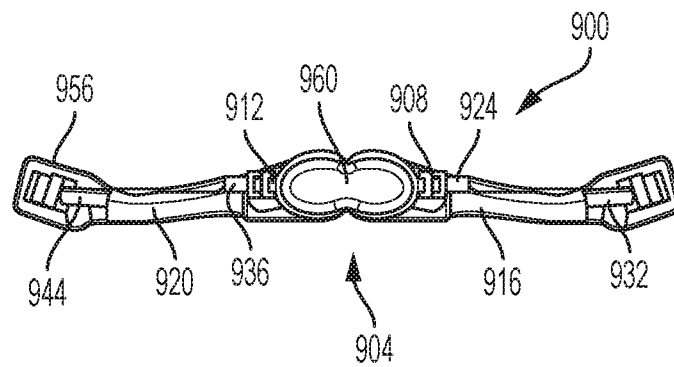


FIG. 9B

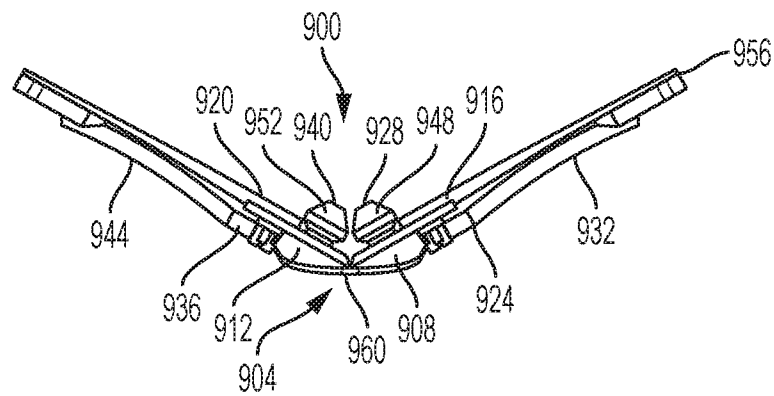


FIG. 9C

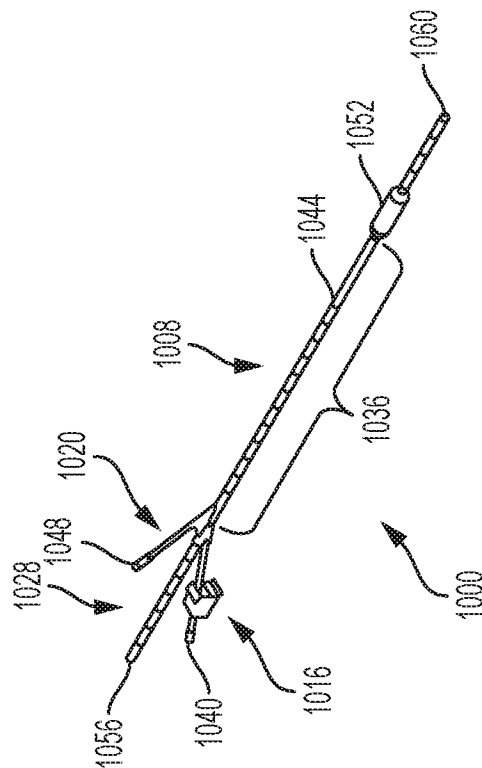


FIG. 10A

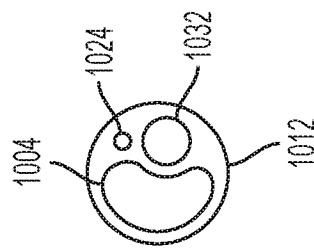


FIG. 10B

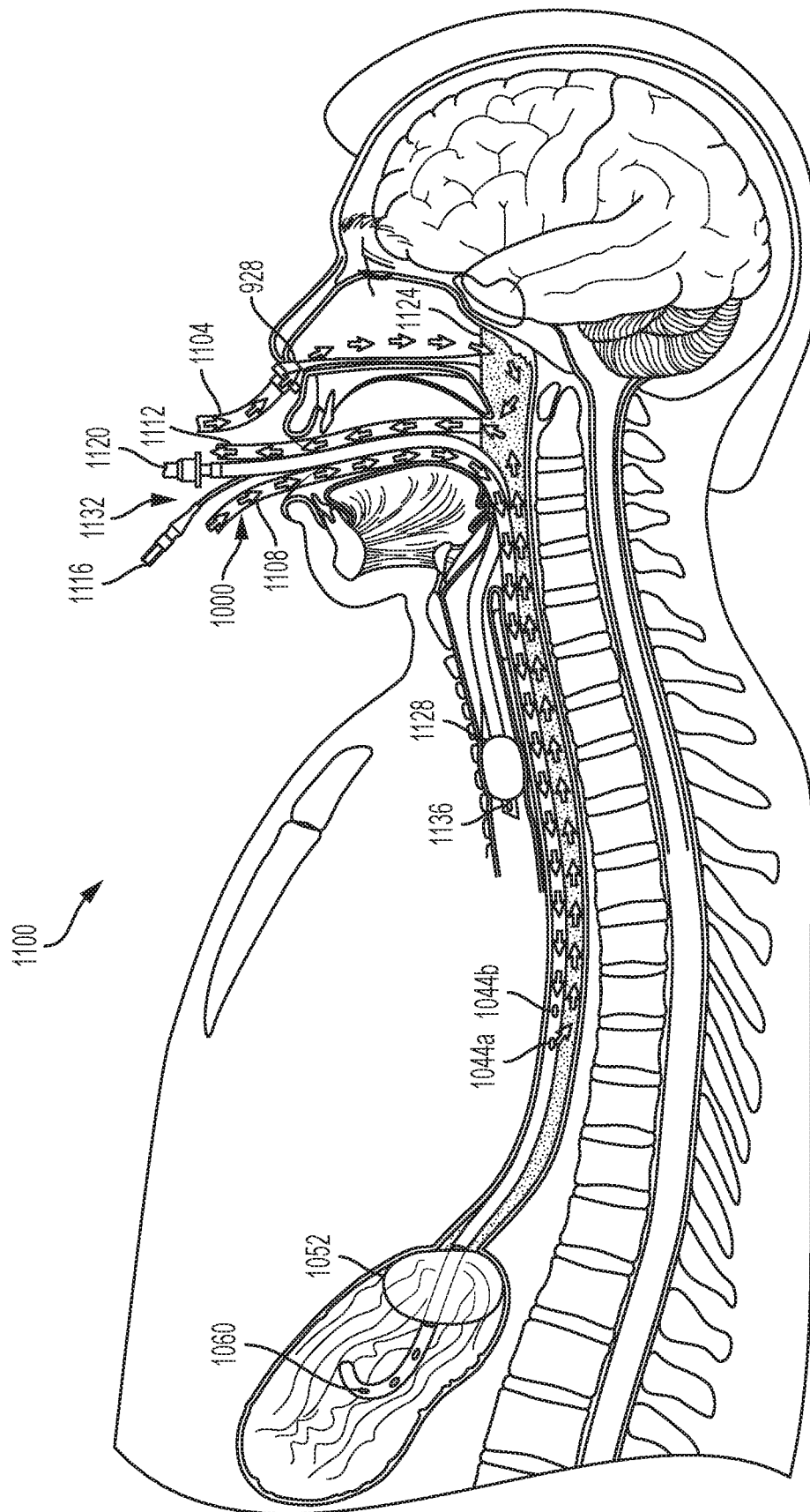


FIG. 11

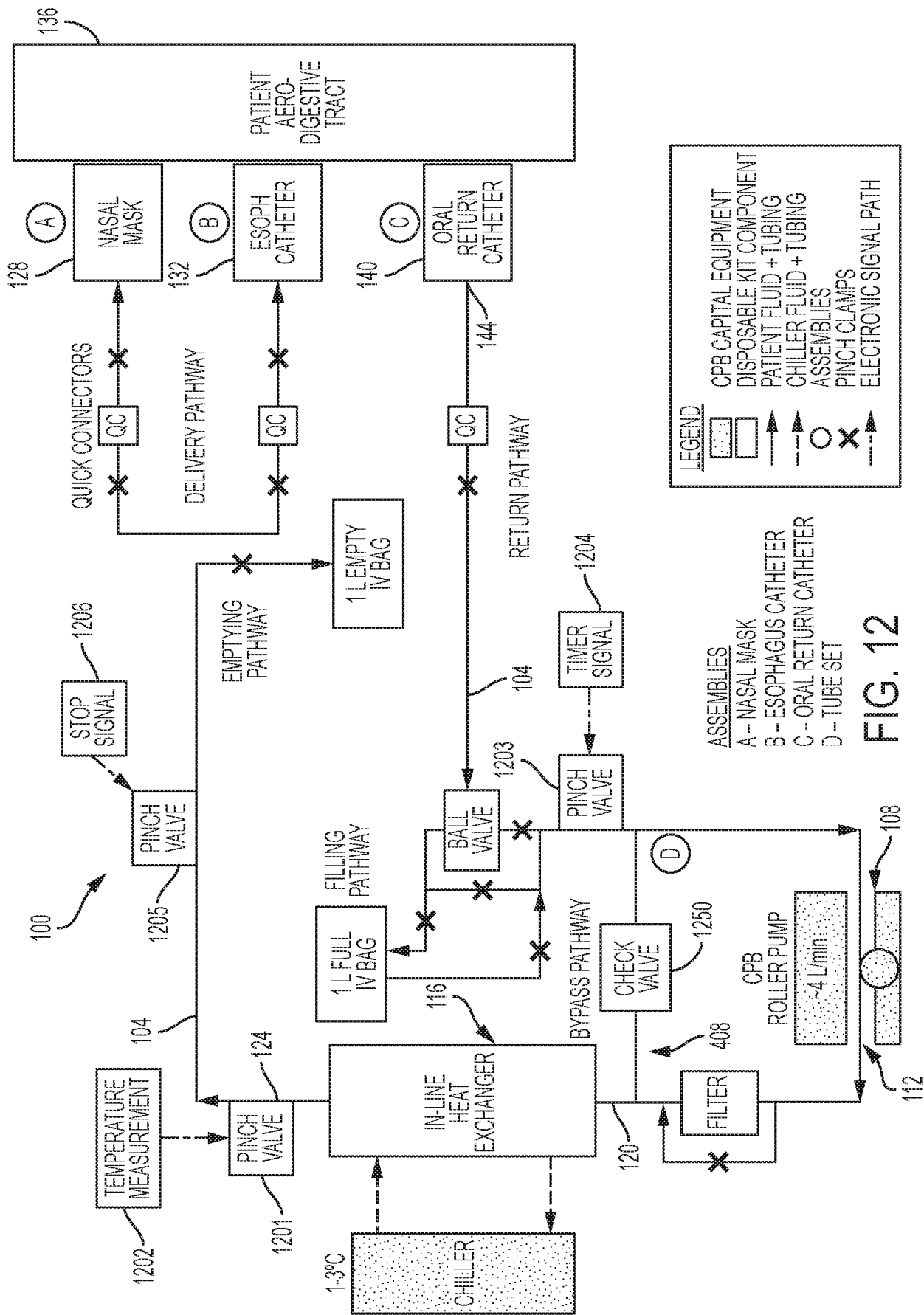


FIG. 12

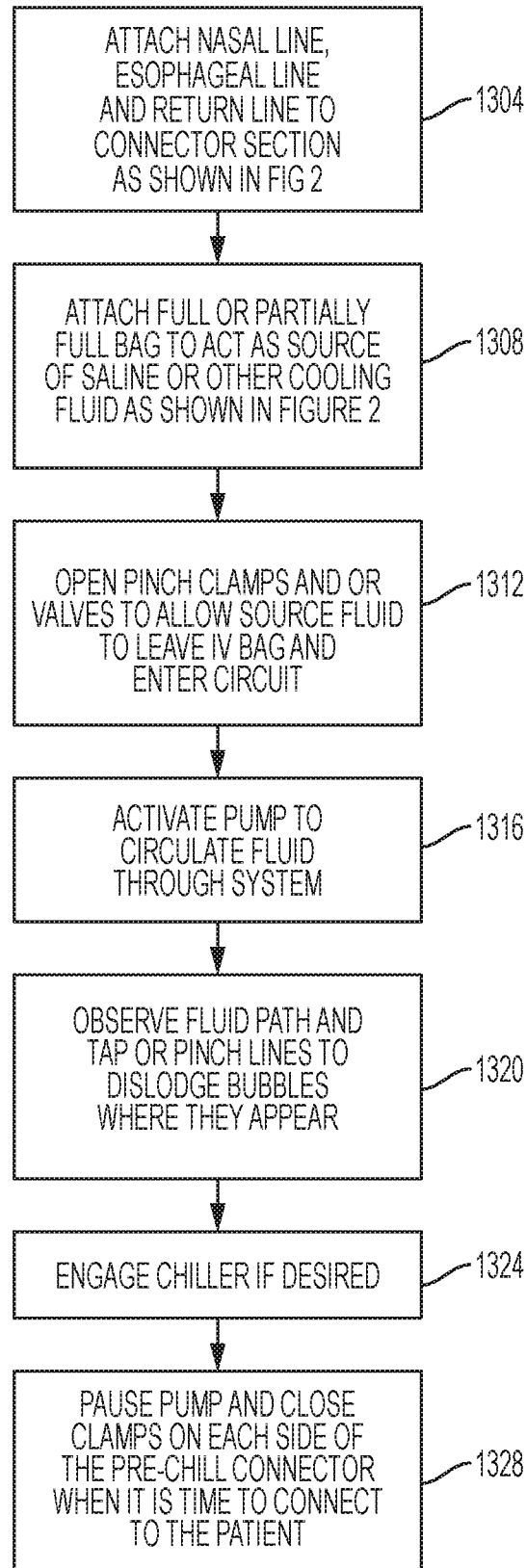
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FIG. 13

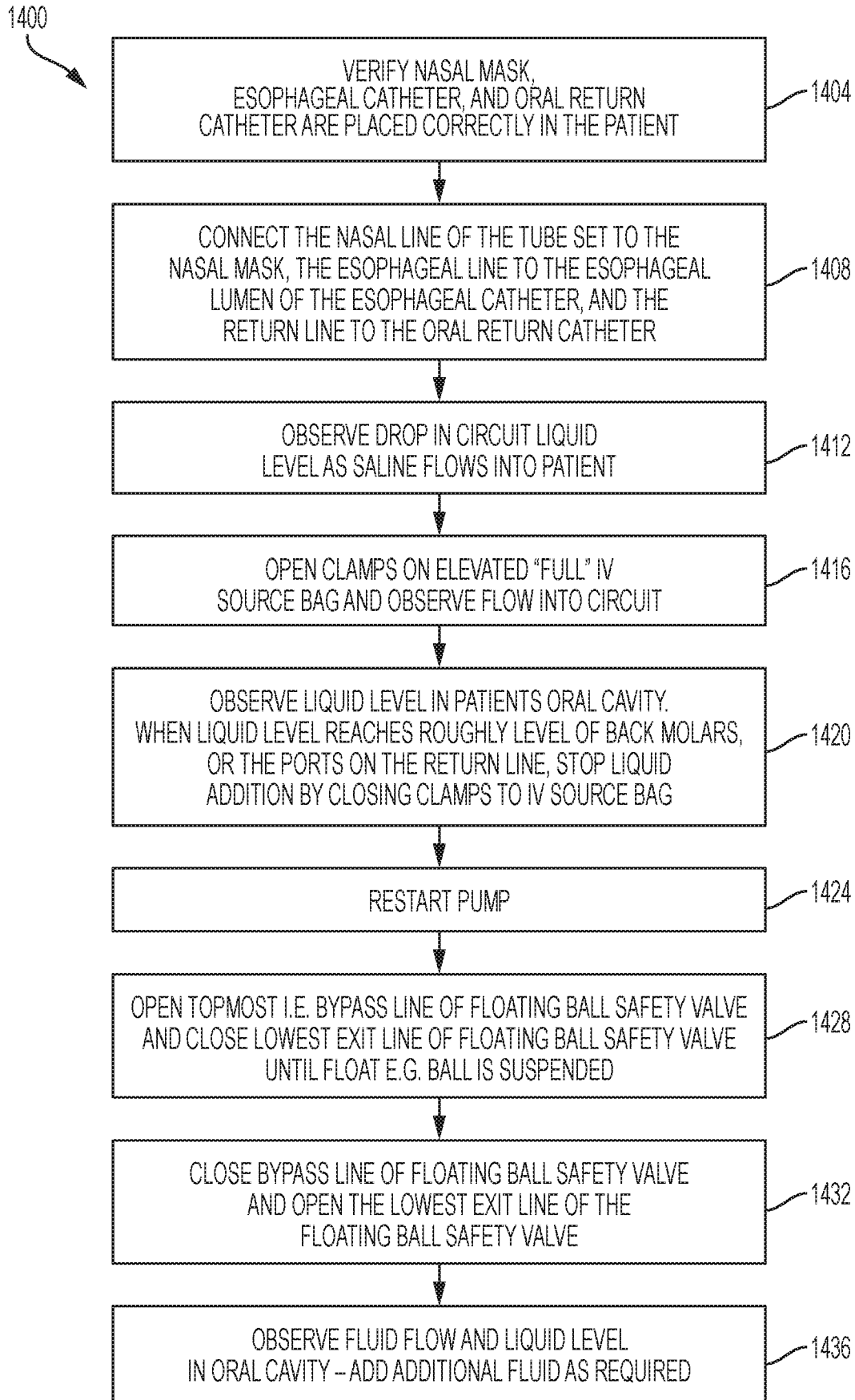


FIG. 14

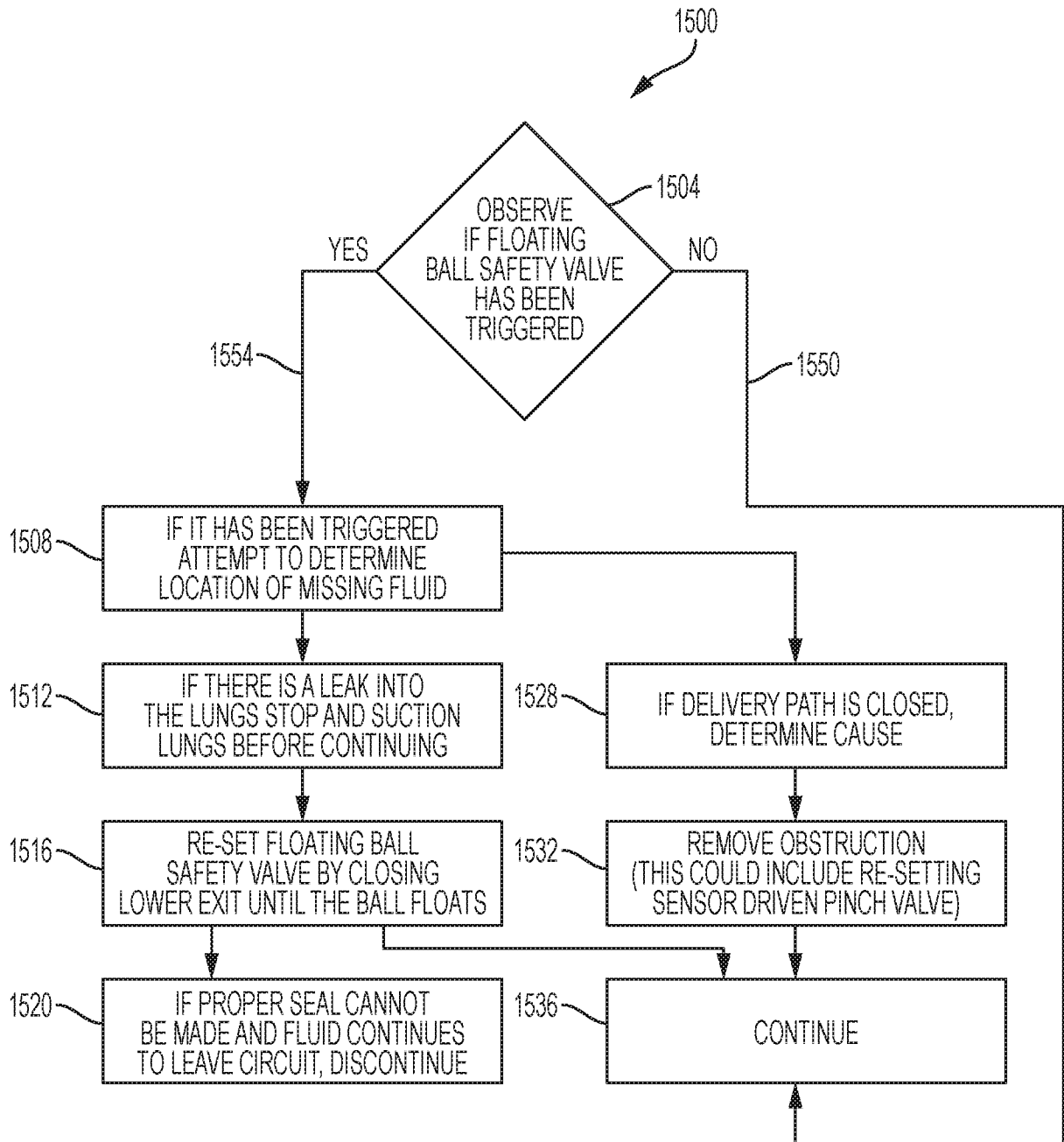


FIG. 15

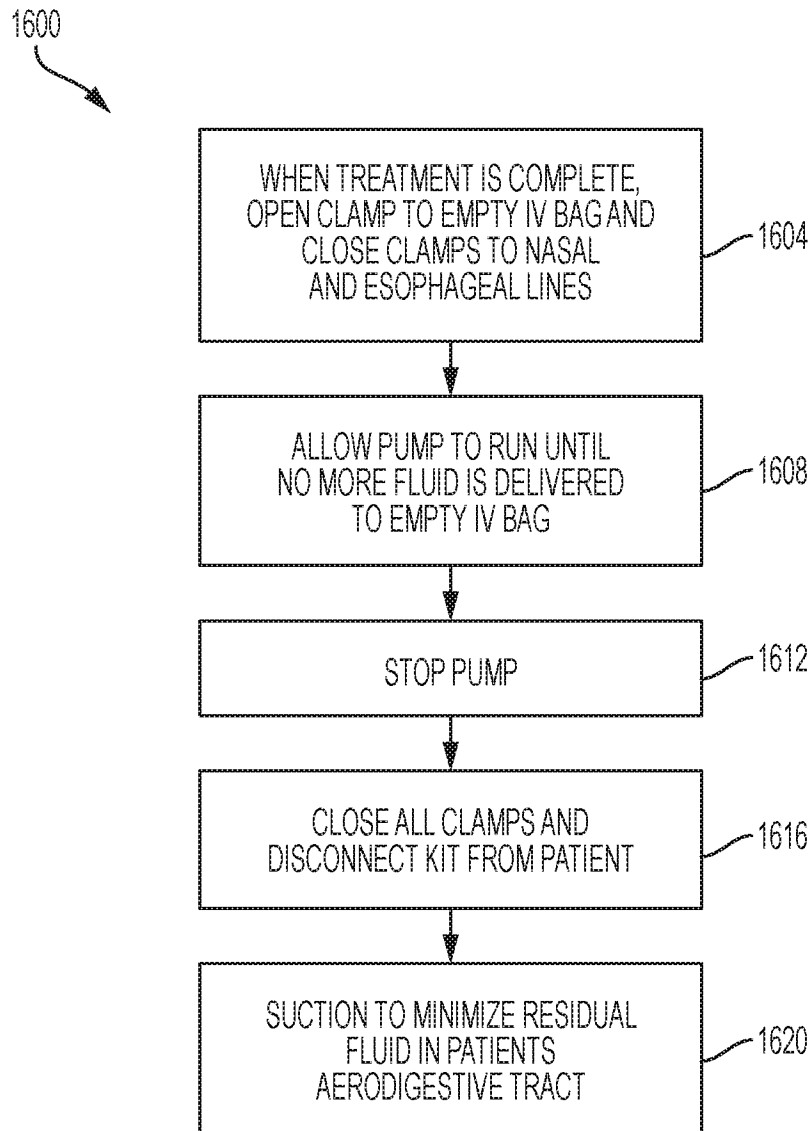


FIG. 16