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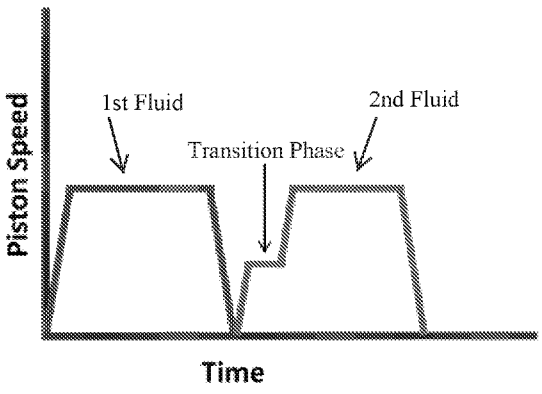

FIG. 7A

(57) Abstract: A method of delivering a multi-phase fluid injection to a patient via a fluid injector comprising two or more syringes includes injecting a first fluid of the fluid injection from at least a first syringe at a first predetermined flow rate, wherein the first fluid has a first viscosity; injecting an initial portion of a second fluid from at least a second syringe at an intermediate flow rate different than a second predetermined flow rate for a specified time, the second fluid having a second viscosity different from the first viscosity; and injecting a remaining portion of the second fluid of the fluid injection at a flow rate at the second predetermined flow rate. A fluid injector system configured for delivering a multi-phase fluid injection is disclosed.

SYSTEM AND METHOD HAVING TRANSITION PHASE IN MULTI-PHASE INJECTION PROTOCOL

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/552,494, titled "System and Method Having Transition phase in Multi-Phase Injection Protocol" and filed on 31 August, 2017, the disclosure of which is incorporated herein in its entirety.

BACKGROUND OF THE DISCLOSURE

Field of the Disclosure

[0002] The present disclosure relates generally to a system and method for controlling a fluid injector. More particularly, the present disclosure relates to a system and method for controlling the fluid injector utilizing a multi-phase injection protocol having a transition phase.

Description of Related Art

[0003] In many medical diagnostic and therapeutic procedures, a medical practitioner, such as a physician, injects a patient with one or more medical fluids. In recent years, a number of fluid delivery systems having injector-actuated syringes and fluid injectors for pressurized injection of fluids, such as a contrast solution (often referred to simply as "contrast"), a flushing agent, such as saline or Ringer's lactate , and other medical fluids have been developed for use in procedures such as angiography (CV), computed tomography (CT), ultrasound, magnetic resonance imaging (MRI), positron emission tomography (PET), and other imaging procedures. In general, these fluid delivery systems are designed to deliver a preset amount of fluid at a desired flow rate.

[0004] An actual flow rate (or delivered volume) of fluid that is delivered to the patient is targeted to be as close as possible to the desired flow rate (or desired volume). However, the actual performance of the fluid delivery system is a function of many factors due to overall impedance and capacitance of the fluid delivery system. In certain delivery procedures, impedance and capacitance of the fluid delivery system may cause a fluid flow over-rate, under-rate (or volume over- or under-delivery) from a desired flow rate (or desired volume), and fluctuations in fluid flow, particularly when transitioning from one fluid type to another fluid type.

[0005] While various approaches exist for characterizing the performance of a fluid delivery system and correlating the desired performance with actual performance in terms of

fluid flow rate and volume delivered, these approaches do not address the differences between desired and actual performance due to impedance and/or capacitance of the fluid delivery system in a comprehensive manner. As a result, existing approaches fail to address the under-delivery or over-delivery of fluid resulting from system impedance and/or capacitance. As a result, less than optimal injection boluses or volumes may result and/or operation of the fluid delivery system can result in relatively large amounts of wasted fluid.

SUMMARY OF DISCLOSURE

[0006] In one example of the present disclosure, a method of delivering a multi-phase fluid injection to a patient via a fluid injector comprising two or more fluid reservoirs is described. The method may comprise injecting a first fluid of the fluid injection from at least a first fluid reservoir, the first fluid having a first viscosity, wherein the first fluid is delivered to the patient at a first predetermined flow rate; injecting an initial portion of at least a second fluid of the fluid injection from at least a second fluid reservoir, the second fluid having a second viscosity different from the first viscosity, wherein the initial portion of the second fluid is delivered to the patient with a flow rate profile different from a second predetermined flow rate for a specified intermediate time interval; and injecting a remaining portion of the second fluid of the fluid injection at a flow rate at least equal to the second predetermined flow rate.

[0007] In specific embodiments the first viscosity is greater than the second viscosity. The first and second fluid may be a contrast medium, saline, Ringer's lactate, or other medical fluid. In particular embodiments, the first fluid may be selected from the group consisting of a contrast media, and a mixture of a specific ratio of the contrast media and saline or other flushing fluid such as water or Ringer's lactate, and wherein the second fluid may be selected from the group consisting of saline or other flushing fluid such as water or Ringer's lactate and a mixture of a second specific ratio of the contrast media and saline or other flushing fluid such as water or Ringer's lactate. According to certain aspects, the second predetermined flow rate may be substantially the same as the first predetermined flow rate.

[0008] According to various embodiments, the flow rate profile of the initial portion of the at least second fluid may be different than the first predetermined flow rate and/or the second predetermined flow rate. In certain embodiments, the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate lower than the first predetermined flow rate. In other embodiments, the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate that varies between zero and the first predetermined flow rate or the second predetermined flow rate over the specified

intermediate time interval. For example, the flow rate profile of the at least the initial portion may start at a lower flow rate and increase over the specified intermediate time interval, such increasing to the second predetermined flow rate by the end of the initial portion of the at least second fluid.

[0009] According to various embodiments of the methods described herein, injecting the initial portion of at least the second fluid may comprise injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval, wherein the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line to the patient before beginning the step of injecting the remaining portion of the second fluid, wherein the specified intermediate time interval is based on system architecture; a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the length of a catheter, the diameter of the catheter, the volume of the catheter and any combination thereof. In various embodiments of the methods, a volume of the initial portion of the second fluid of the fluid injection may be determined by one or more of a volume capacity of a fluid line, optionally including the catheter volume capacity, between the second fluid reservoir and the patient, a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, and an injection system compliance.

[0010] In specific embodiments, the methods may further comprise inputting by a system user the flow rate profile of the second fluid including the transition phase based at least in part on one or more parameters selected from the group consisting of a table of injection protocols, first phase flow rate, second phase flow rate, transition flow rate, catheter volume, catheter diameter, catheter length, volume of the fluid line between the fluid reservoir and the patient, diameter of the fluid line, length of the fluid line, viscosity of the first fluid, viscosity of the second fluid, temperature of the first fluid, temperature of the second fluid, programmed volume of the first fluid to be delivered, and programmed volume of the second fluid to be delivered. The tables may be prepared by a system manufacturer and programmed into a processor associated with the fluid injector system, may be developed independently by the system user or some other third party to be utilized with various injection protocols for the fluid injection system.

[0011] According to specific embodiments, the flow rate profile of the initial portion is selected to minimize flow rate deviations over the specified intermediate time interval. In

particular embodiments, the flow rate profile of the initial portion may be calculated based on the following equation:

$$Q(transition) = Q(programmed) - Q(adjusted)$$

wherein Q(transition) is a desired flow rate profile over a transition between the first fluid to at least the second fluid by adjusting the drive member movement (speed over distance) to control the fluid flow out of the catheter tip; Q(programmed) is a desired flow rate profile for the at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid results in a fluid flow rate from the catheter that is substantially similar to Q(programmed). In other embodiments, the flow rate profile of the initial portion may be calculated based on the following equation:

$$Q(t) = Q(p) - (C(1) - C(2))/t(t),$$

wherein Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a steady state system compliance during the first fluid phase, C(2) is a system compliance during the second fluid injection, and t(t) is a derived time for delivering the volume associated with the system compliance (C(2)). According to various embodiments, the system compliance during the first fluid injection comprises a first compliance factor associated with one or more of the first fluid reservoir, a first fluid delivery mechanism, and a tubing set in operative fluid communication the first fluid reservoir, and the system compliance during the second fluid injection comprises a second compliance factor associated with one or more of the second fluid reservoir, a second fluid delivery mechanism, and a tubing set in operative communication the second fluid reservoir. The system compliance of the first reservoir and/or the at least the second reservoir may be measured, for example using a flow sensor in the fluid path between the reservoir(s) and the catheter. Alternatively the one or both of the system compliance of the first reservoir and/or the at least the second reservoir may be may be predicted based on factors of the fluid injector, the first or second fluid reservoir, and the first or second fluid, respectively.

[0012] According to various embodiments of the present disclosure, first and second fluid reservoirs may be independently selected from the group consisting of a syringe, a peristaltic pump, and a compressible bag. In specific embodiments, the first fluid reservoir is a first syringe operatively connected to a first drive member of the fluid injector and at least the second fluid reservoir is at least a second syringe operatively connected to at least a second drive member of the fluid injector.

[0013] According to other embodiments, the present disclosure describes a fluid injector system for delivering a multi-phase fluid injection to a patient. The fluid injector system may comprise at least one first syringe configured to contain a first fluid of the multi-phase fluid injection, the first fluid having a first viscosity; at least one first drive member operatively connected with the at least one first syringe, the at least one first drive member being operable to dispense the first fluid of the multi-phase fluid injection; at least one second syringe configured to contain a second fluid of the multi-phase fluid injection, the second fluid having a second viscosity different from the first viscosity; at least one second drive member operatively connected with the at least one second syringe, the at least one second piston being operable to dispense the second fluid of the multi-phase fluid injection; a fluid line connected to the at least one first syringe and the at least one second syringe, and configured to deliver at least one of the first fluid of the multi-phase fluid injection from the at least one first syringe to the patient and the second fluid of the multi-phase fluid injection from the at least one second syringe to the patient; and a control device configured to control movement of the first drive member associated with the at least one first syringe and movement of the at least one second drive member associated with the at least one second syringe to control the delivery of the first fluid and the second fluid of the multi-phase fluid injection to the patient. The control device may be configured to control the first drive member to inject the first fluid at a first predetermined flow rate, to control the at least one second drive member to inject an initial portion of at least the second fluid of the fluid injection from the at least one second syringe at an intermediate flow rate profile different from a second predetermined flow rate for a specified intermediate time, and to inject a remaining portion of the second fluid at least equal to the second predetermined flow rate, wherein the second fluid has a second viscosity different from the first viscosity.

[0014] According to various embodiments, the first viscosity is greater than the second viscosity. The first and second fluid may be a contrast medium, a saline, Ringer's lactate, other flushing fluid, or other medical fluid. In particular embodiments, the first fluid may be selected from the group consisting of a contrast media, and a mixture of a specific ratio of the contrast media and saline, and wherein the second fluid may be selected from the group consisting of saline, Ringer's lactate, and a mixture of a second specific ratio of the contrast media and saline. According to certain aspects, the second predetermined flow rate may be substantially the same as the first predetermined flow rate.

[0015] In various embodiments of the fluid injector system, the first predetermined flow rate may be substantially the same as the second predetermined flow rate. In other embodiments, the flow rate profile of at least the initial portion of the at least second fluid may be delivered at a flow rate lower than the first predetermined flow rate, or the flow rate profile of at least the initial portion of the at least second fluid may be delivered at a flow rate that varies between zero and the first predetermined flow rate or between zero and the second predetermined flow rate over the specified intermediate time interval. According to certain embodiments, the first predetermined flow rate may be greater than the second predetermined flow rate.

[0016] According to various embodiments of the fluid injector system, control device may be configured to time an injection of the initial portion of at least the second fluid comprises injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval, wherein the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line to the patient before beginning the step of injecting the remaining portion of the second fluid, wherein the specified intermediate time interval is based on one or more of system architecture; a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the capacitance of the fluid line and an associated catheter, and any combination thereof.

[0017] According to certain embodiments of the fluid injection system, the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(\text{transition}) = Q(\text{programmed}) - Q(\text{adjusted})$$

wherein Q(transition) is a desired flow rate profile over a transition between the first fluid to at least the second fluid by adjusting the drive member movement (speed over distance) to control the fluid flow out of the catheter tip; Q(programmed) is a desired flow rate profile for the at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid results in a fluid flow rate from the catheter that is substantially similar to Q(programmed). According to specific embodiments, the intermediate time may be substantially question to the time that it takes for the remaining amount of the first fluid to be delivered out of the fluid line, for example by dividing the volume of the fluid line and catheter by the programmed flow rate.

[0017] According to other embodiments of the fluid injector system, the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(t) = Q(p) - (C(1) - C(2))/t(t),$$

wherein Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a steady state system compliance during the first fluid phase, C(2) is a system compliance during the second fluid injection, and t(t) is a derived time for delivering the volume associated with the system compliance (C(2)).

[0018] Various aspects of the system and method for controlling a fluid injector utilizing a multi-phase injection protocol having a transition phase are disclosed in one or more of the following numbered clauses:

[0019] Clause 1. A method of delivering a multi-phase fluid injection to a patient via a fluid injector comprising two or more fluid reservoirs, the method comprising: injecting a first fluid of the fluid injection from at least a first fluid reservoir, the first fluid having a first viscosity, wherein the first fluid is delivered to the patient at a first predetermined flow rate; injecting an initial portion of at least a second fluid of the fluid injection from at least a second fluid reservoir, the second fluid having a second viscosity different from the first viscosity, wherein the initial portion of the second fluid is delivered to the patient with a flow rate profile different from a second predetermined flow rate for a specified intermediate time interval or intermediate fluid volume; and injecting a remaining portion of the second fluid of the fluid injection at a flow rate at least equal to the second predetermined flow rate.

[0020] Clause 2. The method according to clause 1, wherein the first viscosity is greater than the second viscosity.

[0021] Clause 3. The method according to clause 1 or clause 2, wherein first fluid is selected from the group consisting of a contrast media, and a mixture of a specific ratio of the contrast media and saline, and wherein the second fluid is selected from the group consisting of saline and a mixture of a second specific ratio of the contrast media and saline.

[0022] Clause 4. The method according to any of clauses 1 to 3, wherein the second predetermined flow rate is substantially the same as the first predetermined flow rate.

[0023] Clause 5. The method according to any of clauses 1 to 4, wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate lower than the first predetermined flow rate.

[0024] Clause 6. The method according to any of clauses 1 to 5, wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate that

varies between zero and the second predetermined flow rate over the specified intermediate time interval.

[0025] Clause 7. The method according to any of clauses 1 to 6, wherein injecting the initial portion of at least the second fluid comprises injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval, wherein the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line to the patient before beginning the step of injecting the remaining portion of the second fluid, wherein the specified intermediate time interval is based on one or more of system architecture; a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the length of a catheter, the diameter of the catheter, the volume of the catheter and any combination thereof.

[0026] Clause 8. The method according to any of clauses 1 to 6, wherein a volume of the initial portion of the second fluid of the fluid injection is determined by one or more of a volume capacity of a fluid line between the second fluid reservoir and the patient, a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, and an injection system compliance.

[0027] Clause 9. The method according to any of clauses 1 to 8, , further comprising inputting by a system user the flow rate profile of the second fluid based at least in part on one or more parameters selected from the group consisting of a table of injection protocols, first phase flow rate, second phase flow rate, transition flow rate, catheter volume, catheter diameter, catheter length, volume of the fluid line between the fluid reservoir and the patient, diameter of the fluid line, length of the fluid line, temperature of the first fluid, temperature of the second fluid, viscosity of the first fluid, viscosity of the second fluid, programmed volume of the first fluid to be delivered, and programmed volume of the second fluid to be delivered.

[0028] Clause 10. The method according to any of clauses 1 to 9, wherein the flow rate profile of the initial portion is selected to minimize flow rate deviations over the specified intermediate time interval.

[0029] Clause 11. The method according to any of clauses 1 to 10, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(\text{transition}) = Q(\text{programmed}) - Q(\text{adjusted})$$

wherein Q(transition) is a desired flow rate profile at a transition between the first fluid to at least the second fluid; Q(programmed) is a desired flow rate profile for the first fluid and at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid a flow rate at a catheter tip is substantially similar to Q(programmed).

[0030] Clause 12. The method according to any of clauses 1 to 10, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(t) = Q(p) - (C(1) - C(2))/t(t),$$

wherein Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a steady state system compliance during the first fluid phase, C(2) is a system compliance during the second fluid injection, and t(t) is a derived intermediate time for for delivering the volume associated with the system compliance (C(2)).

[0031] Clause 13. The method according to clause 12, wherein the system compliance during the first fluid injection comprises a first compliance factor associated with one or more of the first fluid reservoir, a first fluid delivery mechanism, and a tubing set in operative fluid communication the first fluid reservoir, and the system compliance during the second fluid injection comprises a second compliance factor associated with one or more of the second fluid reservoir, a second fluid delivery mechanism, and a tubing set in operative communication the second fluid reservoir.

[0032] Clause 14. The method according to any of clauses 1 to 13, wherein the first fluid reservoir is a first syringe operatively connected to a first drive member of the fluid injector and at least the second fluid reservoir is at least a second syringe operatively connected to at least a second drive member of the fluid injector.

[0033] Clause 15. A fluid injector system for delivering a multi-phase fluid injection to a patient, the fluid injector system comprising: at least one first syringe configured to contain a first fluid of the multi-phase fluid injection, the first fluid having a first viscosity; at least one first drive member operatively connected with the at least one first syringe, the at least one first drive member being operable to dispense the first fluid of the multi-phase fluid injection; at least one second syringe configured to contain a second fluid of the multi-phase fluid injection, the second fluid having a second viscosity different from the first viscosity; at least one second drive member operatively connected with the at least one second syringe, the at least one second piston being operable to dispense the second fluid of the multi-phase fluid injection; a fluid line connected to the at least one first syringe and the at least one second

syringe, and configured to deliver at least one of the first fluid of the multi-phase fluid injection from the at least one first syringe to the patient and the second fluid of the multi-phase fluid injection from the at least one second syringe to the patient; and a control device configured to control movement of the first drive member associated with the at least one first syringe and movement of the at least one second drive member associated with the at least one second syringe to control the delivery of the first fluid and the second fluid of the multi-phase fluid injection to the patient, wherein the control device is configured to control the first drive member to inject the first fluid at a first predetermined flow rate, to control the at least one second drive member to inject an initial portion of at least the second fluid of the fluid injection from the at least one second syringe at an intermediate flow rate profile different from a second predetermined flow rate for a specified intermediate time or intermediate fluid volume, and to inject a remaining portion of the second fluid at least equal to the second predetermined flow rate, wherein the second fluid has a second viscosity different from the first viscosity.

[0034] Clause 16. The fluid injector system according to clause 15, wherein the first viscosity is greater than the second viscosity.

[0035] Clause 17. The fluid injector system according to clause 15 or clause 16, wherein the first predetermined flow rate is substantially the same as the second predetermined flow rate.

[0036] Clause 18. The fluid injector system according to any of clauses 15 to 17, wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate lower than the first predetermined flow rate, or wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate that varies between zero and the first predetermined flow rate or the second predetermined flow rate over the specified intermediate time interval.

[0037] Clause 19. The fluid injector system according to any of clauses 15 to 18, wherein the control device is configured to time an injection of the initial portion of at least the second fluid comprises injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval, wherein the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line to the patient before beginning the step of injecting the remaining portion of the second fluid, wherein the specified intermediate time interval is based on system architecture; a capacitance of at least one of the first fluid

reservoir and the second fluid reservoir, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the length of a catheter, the diameter of the catheter, the volume of the catheter and any combination thereof.

[0038] Clause 20. The fluid injection system according to any of clauses 15 to 19, wherein the first fluid is selected from the group consisting of a contrast media, and a mixture of a specific ratio of the contrast media and saline, and wherein the second fluid is selected from the group consisting of saline and a mixture of a second specific ratio of the contrast media and saline.

[0039] Clause 21. The fluid injection system according to any of clauses 15 to 20, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(\text{transition}) = Q(\text{programmed}) - Q(\text{adjusted})$$

wherein Q(transition) is an desired flow rate profile at a transition between the first fluid to at least the second fluid; Q(programmed) is a desired flow rate profile for the first fluid and at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid a flow rate at a catheter tip is substantially similar to Q(programmed).

[0040] Clause 22. The fluid injection system according to any of clauses 15 to 20, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(t) = Q(p) - (C(1) - C(2))/t(t),$$

wherein Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a system compliance during the first fluid injection, C(2) is a system compliance during the second fluid injection, and t(t) is a derived intermediate time for delivering the volume of the initial portion of the second fluid of the fluid injection.

[0041] These and other features and characteristics of the present disclosure, as well as the methods of operation and functions of the related elements of structures and the combination of parts and economies of manufacture, will become more apparent upon consideration of the following description and the appended claims with reference to the accompanying drawings, all of which form a part of this specification, wherein like reference numerals designate corresponding parts in the various figures. It is to be expressly understood, however, that the drawings are for the purpose of illustration and description only.

BRIEF DESCRIPTION OF THE DRAWINGS

[0042] **FIG. 1** is a perspective view of a fluid delivery system according to an example of the present disclosure;

[0043] **FIG. 2** is a cross-sectional view of a syringe configured for use with the fluid delivery system of **FIG. 1**;

[0044] **FIG. 3** is a perspective view of a fluid delivery system according to another example of the present disclosure;

[0045] **FIG. 4** is a cross-sectional view of a syringe configured for use with the fluid delivery system of **FIG. 3**;

[0046] **FIG. 5** is a perspective view of a fluid delivery system according to another example of the present disclosure;

[0047] **FIG. 6** is a front perspective view of a multi-use disposable system configured for use with the fluid delivery system of **FIG. 5**;

[0048] **FIG. 7A – 7I** illustrate several embodiments of flow profiles including transition phases by control of a motor speed of the fluid delivery system during a multi-phase injection;

[0049] **FIG. 8** is a chart comparing a measured flow rate of a multi-phase fluid injection at a phase transition to a measured flow rate of the multi-phase injection at a transition phase;

[0050] **FIG. 9** is a step diagram for determining the derivation of steady state pressure for the second phase of a multi-phase fluid injection;

[0051] **FIG. 10** is an exemplary lookup table for deriving restriction and a steady state pressure for a multi-phase fluid injection;

[0052] **FIG. 11** is an exemplary graphed equation for deriving the steady state pressure for a multi-phase fluid injection;

[0053] **FIG. 12** is a graphical representation of a surface corresponding to a compliance equation for calculating capacitance;

[0054] **FIG. 13** illustrates a general workflow for determining the an injection protocol including a transition phase according to an embodiments; and

[0055] **FIG. 14** illustrates a specific implementation of an injection protocol including a transition phase for an injector as illustrated in **FIG. 5**.

DETAILED DESCRIPTION

[0056] As used in the specification and the claims, the singular form of "a", "an", and "the" include plural referents unless the context clearly dictates otherwise.

[0057] For purposes of the description hereinafter, the terms "upper", "lower", "right", "left", "vertical", "horizontal", "top", "bottom", "lateral", "longitudinal", and derivatives thereof shall relate to the disclosure as it is oriented in the drawing figures.

[0058] Spatial or directional terms, such as "left", "right", "inner", "outer", "above", "below", and the like, are not to be considered as limiting as the invention can assume various alternative orientations.

[0059] All numbers used in the specification and claims are to be understood as being modified in all instances by the term "about". The term "about" means a range of plus or minus ten percent of the stated value.

[0060] Unless otherwise indicated, all ranges or ratios disclosed herein are to be understood to encompass any and all subranges or subratios subsumed therein. For example, a stated range or ratio of "1 to 10" should be considered to include any and all subranges between (and inclusive of) the minimum value of 1 and the maximum value of 10; that is, all subranges or subratios beginning with a minimum value of 1 or more and ending with a maximum value of 10 or less, such as but not limited to, 1 to 6.1, 3.5 to 7.8, and 5.5 to 10.

[0061] The term "at least" means "greater than or equal to".

[0062] The term "includes" is synonymous with "comprises". "Comprises" includes "consisting of", and "consisting essentially of".

[0063] When used in relation to a syringe and/or a plunger, the term "proximal" refers to a portion of a syringe and/or a plunger nearest a fluid injector when a syringe and/or a plunger is oriented for connecting to a fluid injector. The term "distal" refers to a portion of a syringe and/or a plunger farthest away from a fluid injector when a syringe and/or a plunger is oriented for connecting to a fluid injector. The term "radial" refers to a direction in a cross-sectional plane normal to a longitudinal axis of a syringe, a plunger, and/or a piston extending between proximal and distal ends. The term "circumferential" refers to a direction around an inner or outer surface of a sidewall of a syringe, a plunger, and/or a piston. The term "axial" refers to a direction along a longitudinal axis of a syringe, a piston, and/or a piston extending between the proximal and distal ends. The term "open" when used to refer to a fluid delivery component means that the system is in fluid connection with an outlet, for example through a nozzle or the open end of a tubing component or catheter. In an open system, fluid flow may be constrained, for example by forcing a fluid through a small diameter fluid path where flow may be determined by physical parameters of the system and the fluid, such as tubing diameter, fluid path constrictions, applied pressure, viscosity, etc. The term "closed" when

used to refer to a fluid delivery component means that the system is not in fluid connection with an outlet, for example where fluid flow is stopped by a valve, such as a stopcock, high crack pressure valve, pinch valve, and the like. As used herein the term "slack" means mechanical slack, including a clearance or lost motion in a mechanism caused by gaps between parts, compression of mechanical components under applied load (such as by applied pressure), deflection of mechanical components under applied load (such as by applied pressure), that results in a delay of pressurized delivery of a fluid from a fluid injection after application of force.

[0064] It is to be understood that the disclosure may assume alternative variations and step sequences, except where expressly specified to the contrary. It is also to be understood that the specific devices and processes illustrated in the attached drawings, and described in the following specification, are simply exemplary embodiments of the disclosure. Hence, specific dimensions and other physical characteristics related to the examples disclosed herein are not to be considered as limiting.

[0065] Characterizing an impedance of a fluid delivery system to minimize a difference between desired and actual fluid delivery system performance requires consideration how energy from an energy source is used in or moves through the system. The energy output or loss from the fluid delivery system may be in the form of heat losses through frictional forces or of work done on the fluid delivery system. For example, some of the energy carried by the pressurized fluid as it is delivered under pressure through a catheter is lost through resistive, frictional, or dissipative heating of the fluid. Additionally, pressurized delivery of fluid can also increase the potential energy of the system in terms of an increase in overall volume of system components or compressive forces on system components, as discussed herein. Furthermore, the kinetic energy of pressurized fluid moving through the fluid delivery system can affect the overall performance of the fluid delivery system. For example, inertial forces of moving contrast material and expansion of the containers and/or tubing associated with the system may cause a phase lag between movement of the syringe plunger within the injector syringe and movement of contrast material out of the catheter and into the patient.

[0066] Due to high injection pressures, which may be on the order of 1,200 psi in some angiographic procedures, there may be an expansion, deflection, or compression of various components of the fluid delivery system, such as the syringes, tubing connected to the patient, and components of the fluid injector, such that there may be a volume of fluid in the syringe and tubing in excess of the desired quantity selected to be delivered in the injection

procedure. Such increase in the quantity of fluid occurs due to system capacitance. Total system capacitance (also referred to as compliance or elasticity) represents the amount of fluid (i.e., change in volume, such as excess volume) that is captured in the swelling of the components of the fluid delivery system. In general, capacitance is directly correlative to injection pressure and directly correlative to pressurized fluid volume of contrast medium and saline in the syringes, for example, the greater the volume the greater the inner surface area of the syringe that may be expanded. In other words, capacitance increases with an increase in injection pressure and an increase in volume of fluid in the syringes. Total system capacitance is inherent to each fluid delivery system and depends on a plurality of factors beyond pressure and volume of fluid remaining in the system, including, without limitation, injector construction, mechanical properties of materials used to construct the syringe, plunger, pressure jacket surrounding the syringe, and fluid lines delivering the fluid to the patient, size of the syringe, plunger, pressure jacket, diameter of tubing or other orifices through which the fluid must pass under pressure, and fluid properties, such as temperature, viscosity, and density.

[0067] In some fluid delivery systems, such as fluid delivery systems having two or more syringes each independently driven by a piston of the fluid injector, where two or more different fluids having different properties, such as viscosities, temperature, and/or density, are independently stored in the two or more syringes, fluid flow rates may fluctuate during delivery procedures having multiple phases where a delivery of a first fluid having first properties is followed by a delivery of a second fluid having second properties different from the first properties. In such delivery procedures, an overall fluid flow rate at a transition between the delivery of the first fluid and the delivery of the second fluid may vary or fluctuate due to differences in stored pressures in the fluid delivery system and fluid flow dynamics between the two fluids. For example, viscous fluids may require higher applied pressures to achieve comparable fluid flow rates relative to less viscous fluids. Accordingly, a first delivery phase using the first fluid having a relatively high viscosity, such as contrast, may require a higher applied pressure to achieve a target flow rate than a second delivery phase using the second fluid having a relatively low viscosity compared to the first fluid, such as saline. During injections where a first phase of an injection with the first fluid is followed by a second phase of the injection with the second fluid, this difference in pressure necessary to achieve target flow rates for the two different fluids may result in undesired fluctuations in the overall flow rate during the transition between the first phrase and the second phase.

[0068] In closed systems, where fluid flow from the at least one syringe may be closed by a stopcock or other flow control member, equalization of syringe capacitance between multiple syringes is prevented and capacitance is stored in the closed syringe, thereby potentially affecting the flow rates of the subsequent fluid delivery from that syringe. In addition, residual first fluid in a fluid line must be pushed out of the line by the second fluid, which in certain situations may require a higher pressure than a desired pressure until the first fluid is purged. At the transition between the delivery of the first fluid to the delivery of the second fluid, the higher-than-desired pressure may result in an increase in flow rate of the second fluid as the last of the first fluid exits the fluid line, particularly in injections where the first fluid is more viscous than the second fluid. For example, as illustrated in **FIG. 8**, the dotted lines illustrates the fluid flow rate fluctuations observed at the transition from a highly viscous fluid for several desired programmed flow rates, such as a contrast media which can range from 2.0 to 30.0 cP (at 20°C), to a lower viscosity fluid, such as saline having a viscosity of 1.0 to 1.5 cP (at 20°C). These undesired fluctuations of flow rate may result, for example, in variations and inaccuracies of delivery of fluid volumes and potentially problems with bolus consistency and, ultimately, image quality when contrast agents are being injected. Accordingly, there is a need in the art for improved control of fluid delivery from a fluid injector. There is a further need for improved systems and methods for limiting fluid flow fluctuations in fluid injections having at least one transition between the delivery of fluids having different physical properties.

[0069] According to various embodiments, the present disclosure provides methods for delivering a multi-phase fluid injection to a patient via a fluid injector, such as delivering a fluid injection protocol with an imaging contrast agent and a saline flush, including defined mixtures of contrast and saline. The fluid injector may include two or more fluid reservoirs, such as reservoirs selected from the group consisting of a syringe, a compressible bag, a peristaltic pump, and various combinations thereof, such as at least one syringe and at least one peristaltic pump. In specific embodiments, the fluid injector may include a first syringe and a second syringe. In other embodiments, the fluid injector may include a first syringe, a second syringe, and a third syringe. In certain embodiments, the syringe may be a rolling diaphragm type syringe. The method may include injecting a first fluid of the fluid injection from at least a first fluid reservoir where the first fluid having a first viscosity and where the first fluid is delivered to the patient at a first predetermined flow rate, which may be a constant flow rate or a ramped flow rate. In certain embodiments, the first fluid may be a

contrast agent, a saline, or a defined mixture of contrast agent and saline. In specific embodiments, the first fluid may be a contrast agent or a defined mixture of contrast agent and saline.

[0070] The method may further include injecting an initial portion of at least a second fluid of the fluid injection from at least a second fluid reservoir at a flow rate selected to minimize fluid flow fluctuations at the transition, as describe herein, where the second fluid has a second viscosity which is different from the first viscosity of the first fluid. In certain embodiments, the first fluid may have a viscosity that is greater than the viscosity of the second fluid, for example where the first fluid is a contrast agent and the second fluid is saline. In other embodiments, the first fluid may have a viscosity that is less than the viscosity of the second fluid. In still other embodiments, the first fluid may have a viscosity that is substantially the same as the viscosity of the second fluid. Viscosity of the fluid may vary according to the amount of a dissolved solute per volume of solvent (i.e., a fluid with a higher concentration of dissolved solute will be more viscous than a fluid with a lower concentration of the dissolved solute). According to the various embodiments herein the initial portion of the second fluid may be delivered to the patient with a flow rate profile different from a second predetermined flow rate for a specified intermediate time interval, while the remaining volume of the second fluid (i.e., after the initial portion) may be delivered to the patient at the second predetermined flow rate. In various embodiments, the second predetermined flow rate is substantially the same as the first predetermined flow rate. As used herein, the term "substantially the same" when referring to a second value means ranging from -10% to 10% (i.e., ranging from 10% less than to 10% greater than) of the first value. In specific embodiments, the flow rate profile of the initial portion of the second fluid include a flow rate lower than the first predetermined flow rate. For example, the flow rate of the initial portion of the second fluid may be from 0% to 100% of that of the second predetermined flow rate or of that of the first predetermined rate.

[0071] In other embodiments, the flow rate of the initial portion of the at least second fluid may be delivered at a flow rate that varies over the specified intermediate time interval. For example, in one embodiment, the intermediate flow rate may vary by slowly ramping from 0 mL/sec up to the second predetermined flow rate over the specified intermediate time interval. In other embodiments, the intermediate flow rate may vary by slowly ramping from 0 mL/sec up to a transitional flow rate over the specified intermediate time interval, where the transitional flow rate is less than at least one of the first predetermined flow rate and the

second predetermined flow rate. According to other embodiments where the intermediate flow rate comprises a ramp from 0 mL/sec to at least one of the first predetermined flow rate, the second predetermined flow rate, and the transitional flow rate, the intermediate time may start during the injection of the first fluid at the first predetermined flow rate and continue on past the end of the injection of the first fluid to before the injection of the second fluid at the second predetermined flow rate (i.e., at the end of the specified intermediate time).

[0072] In other embodiment, the intermediate flow rate may be input by a system user the flow rate profile of the second fluid based at least in part on one or more parameters selected from the group consisting of a of a table of injection protocols, first phase flow rate, second phase flow rate, transition flow rate, catheter volume, catheter diameter, catheter length, volume of the fluid line between the fluid reservoir and the patient, diameter of the fluid line, length of the fluid line, temperature of the first fluid, temperature of the second fluid, viscosity of the first fluid, viscosity of the second fluid, programmed volume of the first fluid to be delivered, and programmed volume of the second fluid to be delivered. For example, the intermediate flow rate may be manually input by a system user base at least in part on one or more predetermined factors. Examples of predetermined factors may be provided from or derived from a predetermined table of factors, such as one or more tables containing one or more of a listing of pressures, volumes, flowrates, formula equations, and combinations of any thereof which can be reviewed or utilized to determine or calculate the intermediate flow rate. In certain embodiments, the user may recall the one or more tables from a processor memory and/or display the one or more tables on a screen associated with the injector. In another embodiment, the injector processor may automatically recall the tables from memory and calculate a suggested intermediate flow rate based on various injection parameters. Other potential flow profiles for the first and/or second fluid phase are described in detail in **FIGS. 7A-7I**.

[0073] In various embodiments, injecting the initial portion of at least the second fluid may include injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval. In certain embodiments, the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line and into the patient before beginning the step of injecting the remaining portion of the second fluid, for example at the second predetermined flow rate. The specified intermediate time interval maybe based on one or more different factors. For example, the specified intermediate time interval may be selected

at least partially base on features of the fluid injector system architecture. For example, the fluid injector system architecture may include features of the drive system of a first pressurization feature and/or a second pressurization feature, such as a motor, gearing, and other mechanical features of a first and/or a second drive system associated with a first pressurization feature and/or a second pressurization feature, respectively Examples of such pressurization features include, but are not limited to, features of a motorized piston based drive members for reversibly moving one or more plunger of one or more syringe, features of a motorized peristaltic pump based drive system, and mechanical features of a clam-shell compression feature for a compressible bag based system. Upon pressurization of various mechanical components, compression of the mechanical components may result in an amount of slack where the pressurization force is not immediately converted to fluid flow due to compression of and/or strain on mechanical components, such as gearing and drive components of the fluid injector that apply the pressure. Another factor may include a capacitance of at least one of system architecture, a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, pressure and/or flow rate of the first fluid, pressure and/or flow rate of the second fluid, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the length of a catheter, the diameter of the catheter, the volume of the catheter and any combination thereof. Other factors may include expansion of the fluid reservoirs, such as syringes and tubing such that there may be an increased volume of fluid in the syringe and tubing in excess of the desired quantity selected to be delivered in the injection procedure. Such increase in the volume of fluid in the fluid reservoir or tubing occurs due to increased system capacitance (i.e., increased fluid volume capacity). Total system capacitance is inherent to each fluid delivery system and depends on a plurality of factors beyond pressure and volume of fluid remaining in the system, including, without limitation, fluid properties (such as viscosity, temperature, etc.), injector construction, mechanical properties of materials used to construct the syringe or reservoir, plunger, pressure jacket surrounding the syringe, fluid lines delivering the fluid to the patient, size of the syringe, plunger, pressure jacket, diameter of tubing or other orifices through which the fluid must pass under pressure, and fluid properties, such as temperature, viscosity, and density. System capacitance may result in discrepancies between programed fluid volume delivery and actual volume delivery. For example, when beginning a pressurized fluid delivery, initial pressurization may result in swelling of system components under fluidized

pressure and/or compression of mechanical components under force, rather than delivery of a corresponding fluid volume to a patient.

[0074] According to various embodiments, the first fluid may be a contrast media, such as a CT contrast agent, a CV contrast agent, an MRI contrast agent, a PET radioactive contrast agent, an ultrasound contrast, or combinations of any thereof. In other embodiments, the first fluid may be a dual flow mixture of a first specified ratio of a contrast agent, as described herein, and the second fluid, such as saline or other flushing fluid, such as Ringer's lactate. In still other embodiments, mixtures of three or more fluids are contemplated, wherein the fluids comprise a specified ratio of at least one contrast agent, saline, and a third medical fluid (such as a second contrast agent or other medical fluid). According to various embodiments, the second fluid may be a medical flushing agent (such as saline or water) or a mixture of a contrast agent and the flushing agent, wherein the mixture has a second specified ratio of the contrast and the flushing agent that is different than the first specified ratio. According to certain embodiment, the first specified ratio of contrast to flushing fluid and/or the second specified ratio of contrast to flushing may vary over the course of an injection protocol. For example, in a dual flow contrast injection of the first fluid at a first specified ratio, the injected first fluid may start at an 80:20 ratio of contrast to saline and ramp to a 20:80 ratio of contrast to saline over at least a portion of the injection time of the first fluid. In another example, the second fluid may include a dual flow ramp at the second specified ratio, where the injected second fluid is injected over the remaining time and may start at a 10:90 specified ratio of contrast agent to saline and ramp to a 0:100 specified ratio of contrast to saline. According to other embodiments, the initial portion of the second fluid may be injected as a specified dual flow ratio of the first fluid and the second fluid over the specified intermediate time. In still other embodiments, the initial portion of the second fluid may be injected at a ramp from a specified intermediate dual flow ratio of the first fluid and the second fluid to a second specified intermediate dual flow ratio of the first fluid and the second fluid over the specified intermediate time. One of skill in the art, reading the current disclosure, will understand that the ratios of the first fluid and the second fluid that are used in the dual flow portions of the injections may be any ratio of the first and second fluid, and the specific ratios detailed herein are for reference only. All other potential ratios are within the scope of the invention. In other embodiments, the volume of the initial portion of the second fluid of the fluid injection may be determined by one or more of a volume capacity of

a fluid line between the second fluid reservoir and the patient, a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, and an injection system compliance

[0075] According to various embodiments herein, the flow rate profile of the initial portion is selected to minimize flow rate deviations over the specified intermediate time interval. For example, as illustrated in **FIG. 8**, fluid transitions from a fluid having a first viscosity to a fluid having a second, different viscosity may result in fluid flow fluctuations or other deviations from the intended fluid flow rate over the specified intermediate time interval. For examples, in certain embodiments when the fluid flow transitions from a more viscous first fluid to a less viscous second fluid, flow fluctuations may be observed since the second fluid must be pressurized to a greater pressure than necessary to push the remaining first fluid from the fluid path into the patient at the first predetermined flow rate. As soon as the last of the more viscous fluid exits the fluid path, the increased pressure on the second less viscous fluid may result in sudden fluctuations of fluid velocity of the second fluid exiting the fluid path. By appropriate selection of a flow rate for the initial portion of the second fluid, for example where the flow rate is less than the first predetermined flow rate and the second predetermined flow rate, as described herein, the sudden increase in fluid velocity of the second fluid exiting the fluid path may be reduced, minimized, or substantially eliminated.

[0076] According to various embodiments, the flow rate and/or the flow rate profile of the initial portion of the second fluid may be calculated using an equation that takes into account one or more of various factors described herein to provide a calculated transition flow rate selected to minimize any fluctuations or deviations in the fluid flow rate of fluid entering the patient at the transition from the first fluid to the second fluid. According to certain embodiments, the flow rate and/or flow rate profile of the initial portion based on equation (1):

$$Q(\text{transition}) = Q(\text{programmed}) - Q(\text{adjusted}) \quad (1)$$

According to equation (1), (transition) is a desired flow rate profile over a transition between the first fluid to at least the second fluid by adjusting the drive member movement (speed over distance) to control the fluid flow out of the catheter tip; Q(programmed) is a desired flow rate profile for the at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid results in a fluid flow rate from the catheter that is substantially similar to Q(programmed). According to specific embodiments, the intermediate time may be substantially question to the time that it takes for the remaining amount of the first fluid to

be delivered out of the fluid line, for example by dividing the volume of the fluid line and catheter by the programmed flow rate. To avoid fluctuations in the fluid flow, the equation values are selected so that Q(transition) results in a flow rate substantially similar to Q(programmed).

[0077] According to other embodiments, the flow rate and/or flow rate profile of the initial portion based on equation (2):

$$Q(t) = Q(p) - (C(1) - C(2))/t(t) \quad (2)$$

According to equation (2), Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a steady state system compliance during the first fluid phase, C(2) is a system compliance during the second fluid injection, and t(t) is a derived time for delivering the volume associated with the system compliance (C(2)). According to various embodiments, the system compliance during the first fluid injection comprises a first compliance factor associated with one or more of the first fluid reservoir, a first fluid delivery mechanism, and a tubing set in operative fluid communication the first fluid reservoir, and the system compliance during the second fluid injection comprises a second compliance factor associated with one or more of the second fluid reservoir, a second fluid delivery mechanism, and a tubing set in operative communication the second fluid reservoir. The system compliance of the first reservoir and/or the at least the second reservoir may be measured, for example using a flow sensor in the fluid path between the reservoir(s) and the catheter. Alternatively the one or both of the system compliance of the first reservoir and/or the at least the second reservoir may be may be predicted based on factors of the fluid injector, the first or second fluid reservoir, and the first or second fluid, respectively. According to these embodiments, the system compliance during the first fluid injection comprises a first compliance factor associated with one or more of the first fluid reservoir, a first fluid delivery mechanism, and a tubing set and catheter in operative fluid communication the first fluid reservoir, and the system compliance during the second fluid injection comprises a second compliance factor associated with one or more of the second fluid reservoir, a second fluid delivery mechanism, and a tubing set and catheter in operative communication the second fluid reservoir, including pressure applied to each fluid reservoir and volume of fluid remaining in each fluid reservoir. Alternatively, the capacitance of a fluid injector and associated components may be at least partially measured optically, for example by measuring swelling of a fluid reservoir, compression of mechanical components

and plunger features, and deflection of system components under pressure, by comparing the relaxed state to the pressurized state.

[0078] As described herein, in specific embodiments of the fluid injector and methods, the first fluid reservoir may be a first syringe operatively connected to a first drive member of the fluid injector and at least the second fluid reservoir may be at least a second syringe operatively connected to at least a second drive member of the fluid injector.

[0079] For example, according to certain embodiments, fluid injector system for delivering a multi-phase fluid injection to a patient may comprise at least one first syringe and at least one second syringe. The at least one first syringe may be configured to contain a first fluid of the multi-phase fluid injection where the first fluid has a first viscosity and the injector may include at least one first drive member operatively connected with the at least one first syringe where the at least one first drive member is operable to dispense the first fluid of the multi-phase fluid injection. The at least one second syringe may be configured to contain a second fluid of the multi-phase fluid injection where the second fluid has a second viscosity different from the first viscosity and the injector may include at least one second drive member operatively connected with the at least one second syringe where the at least one second piston being operable to dispense the second fluid of the multi-phase fluid injection. The injector may further include a fluid line that is fluidly connected to the at least one first syringe and the at least one second syringe, and configured to deliver at least one of the first fluid of the multi-phase fluid injection from the at least one first syringe to the patient and the second fluid of the multi-phase fluid injection from the at least one second syringe to the patient. In various embodiments, the injector system may include a third syringe, and in other embodiments may include other fluid delivery mechanisms such as one or more peristaltic pumps and/or one or more compressible reservoirs. According to various embodiments, the first syringe and the at least second syringe may be part of a closed system, wherein the first syringe and the at least second syringe are configured to be independently isolated from the remainder of the fluid path, for example by a valve, stopcock, or other feature that can selectively and reversibly isolate one or both of the first and at least second syringe from the fluid path. According to other embodiments, the first syringe and/or the at least second syringe may be part of an open system, wherein one or both of the first syringe and the at least second syringe are configured to be in fluid communication with the fluid path during the injection procedure. Various embodiments of the fluid injector may include a control device configured to control movement of the first drive member associated with the

at least one first syringe and movement of the at least one second drive member associated with the at least one second syringe to control the delivery of the first fluid and the second fluid of the multi-phase fluid injection to the patient. For example, the control device may be configured to control the first drive member to inject the first fluid at a first predetermined flow rate, to control the at least one second drive member to inject an initial portion of at least the second fluid of the fluid injection from the at least one second syringe at an intermediate flow rate profile different from a second predetermined flow rate for a specified intermediate time, and to inject a remaining portion of the second fluid at least equal to the second predetermined flow rate, wherein the second fluid has a second viscosity different from the first viscosity. According to various embodiments, the control device, such as a processor, may be configured to operate the fluid injector to independently open and close the fluid connectivity of the first and/or second syringe with the remainder of the fluid path.

[0080] With reference to **FIG. 1**, a fluid injector **10** (hereinafter referred to as "injector **10**"), such as an automated or powered fluid injector, is adapted to interface with and actuate one or more syringes **12** (hereinafter referred to as "syringe **12**"), which may be filed with a fluid **F**, such as contrast media, saline solution, or any desired medical fluid. The injector **10** may be used during a medical procedure to inject the medical fluid into the body of a patient by driving a plunger **14** of each syringe **12** with a drive member, such as piston **19** (shown in **FIG. 2**), such as linear actuator or a piston element. The injector **10** may be a multi-syringe injector having two, three or more syringes, wherein the several syringes **12** may be oriented in a side-by-side or other relationship and may be separately actuated by respective drive members/pistons **16** associated with the injector **10**. In examples with two or more syringes, for example, arranged in a side-by-side or other relationship and filled with two different fluids, the injector **10** may be configured to deliver fluid from one or both of the syringes **12**, sequentially or concurrently. According to one embodiment, the fluid injector **10** may be a dual head injector having two syringes **12a** and **12b**, a first syringe **12a** for delivering a contrast media or other medical fluid and a second syringe **12b** for delivering saline or other medically approved flushing agent to flush the contrast media to the patient. In other embodiments, the fluid injector **10** may have three syringes **12**, a first and second syringe for delivering one or two different contrast media or other medical fluid and a third syringe for delivering saline or other medically approved flushing agent to flush the contrast media to the patient. According to various embodiments, the fluid injector **10** may be configured to deliver the contrast and saline separately (e.g., delivering a specific volume saline over a

specific time followed by delivering a specific volume of contrast over a specific time, followed by a second volume of saline over a specified time to flush the contrast media from the tubing into the patient). According to various embodiments, the fluid injector **10** may be configured to deliver the contrast and saline separately or as a mixture (e.g., delivering a specific volume saline over a specific time followed by delivering a specific volume of contrast or a specified ratio of contrast and saline (i.e., in a "dual flow" process) over a specific time, followed by a second volume of saline over a specified time to flush the contrast media from the tubing into the patient). A technician may program a specific injection protocol into the injector (or use a pre-written protocol) to deliver the desired volumes of saline, contrast, specific ratios of contrast and saline mixtures, etc., at a desired flow rate, time, and volume for each solution. The fluid injector **10** may have at least one bulk fluid source (not shown) for filling the syringes **12a,b** with fluid and in certain embodiments, the fluid injector **10** may have a plurality of bulk fluid source, one for each of the plurality of syringes, for filling each of the plurality of syringes with the desired fluid.

[0081] A fluid path set **17** may be in fluid communication with each syringe **12** to place each syringe in fluid communication with a catheter for delivering the fluid **F** from each syringes **12** to a catheter (not shown) inserted into a patient at a vascular access site. In certain embodiments, fluid flow from the one or more syringes **12** may be regulated by a fluid control module (not shown) that operates various valves, stopcocks, and flow regulating structures to regulate the delivery of the saline solution and contrast to the patient based on user selected injection parameters, such as injection flow rate, duration, total injection volume, and ratio of fluids from the syringes **12**, including specific ratios of each fluid in a dual flow injection protocol.

[0082] With reference to **FIG. 2**, the drive member **19**, such as a reciprocally driven piston moved by a motor **31**, may be configured to extend into and from the respective syringe port **13** through an opening in the front end of the injector housing. In fluid injector embodiments comprising a plurality of syringes, a separate drive member/piston **19** may be provided for each syringe **12**. Each drive member/piston **19** is configured to impart a motive force to at least a portion of the syringe **12**, such as the plunger **14** or a distal end of a rolling diaphragm syringe (for example, as described in PCT/US2017/056747; WO 2016/172467; and WO 2015/164783, the disclosures of which are incorporated herein by this reference). The drive member or piston **19** may be reciprocally operable via electro-mechanical drive components such as a ball screw shaft driven by the motor **31**, a voice coil actuator, a rack-and-pinion

gear drive, a linear motor, a linear actuator, and the like. The motor **31** may be an electric motor.

[0083] Examples of suitable front-loading fluid injectors **10** are disclosed in U.S. Patent Nos. 5,383,858; 7,553,294; 7,666,169; 9,173,995; 9,199,033; and 9,474,857; and in PCT Application Publication No. WO 2016/191485 and WO 2016/112163, the disclosures of which are incorporated by reference in their entirety.

[0084] Having described the general structure and function of specific embodiments of the fluid injector **10**, an embodiment of syringe **12** configured for use with the injector **10** will now be described with reference to **FIG. 2**. The syringe **12** generally has a cylindrical syringe barrel **18** formed from glass, metal, or a suitable medical-grade plastic. The barrel **18** has a proximal end **20** and a distal end **24**, with a sidewall **119** extending therebetween along a length of a longitudinal axis **15** extending through a center of the barrel **18**. In some examples, the distal end **24** may have a conical shape that narrows in a distal direction from the cylindrical barrel **18**. A nozzle **22** extends from the distal end **24**. The barrel **18** has an outer surface **21** and an inner surface **23** with an interior volume **25** configured for receiving the fluid therein. The proximal end **20** of the barrel **18** may be sealed with the plunger **14** that is reciprocally movable through the barrel **18** by reciprocal movement of the corresponding piston **19** or drive member. The plunger **14** forms a liquid-tight seal against the inner surface **23** of the barrel **18** as the plunger **14** is advanced moved through the barrel **18**.

[0085] With continued reference to **FIG. 2**, the proximal end **20** of the syringe **12** is sized and adapted for being removably inserted in a syringe port **13** of an injector **10** (shown in **FIG. 1**). In some examples, the proximal end **20** of the syringe **12** defines an insertion section **30** that is configured to be removably inserted into the syringe port **13** of the injector **10** while the remaining portion of the syringe **12** remains outside of the syringe port **13**.

[0086] The syringe **12** may be made of any suitable medical-grade plastic or polymeric material, desirably a clear or substantially translucent plastic material. The material of the syringe **12** is desirably selected to meet the required tensile and planar stress requirements, water vapor transmission, and chemical/biological compatibility. Exemplary syringes suitable for use with the injector **10** depicted in **FIG. 1** are described in United States Patent Nos. 5,383,858; 6,322,535; 6,652,489; 9,173,995; and 9,199,033, the disclosures of which are all incorporated by reference in their entirety.

[0087] In some examples, such as shown in **FIG. 3**, the injector **10** may be configured for receiving and retaining a pressure jacket **32** within each syringe port **13** of the injector **10**.

While **FIGS. 1** and **3** illustrate fluid injectors **10** with two syringe ports **13**, which for the injector **10** shown in **FIG. 3** each having a corresponding pressure jacket **32**, other examples of the fluid injector **10** may include a single syringe port **13** and optionally, a corresponding pressure jacket **32** or more than two syringe ports **13** with an optional corresponding number of pressure jackets **32**. In embodiments comprising pressure jackets, each pressure jacket **32** may be configured to receive a syringe, such as a syringe for an angiographic (CV) procedure, or a rolling diaphragm syringe **34** (suitable examples of which are described in described in PCT/US2017/056747; WO 2016/172467; and WO 2015/164783). A fluid path set, similar to the fluid path set **17** shown in **FIG. 1**, may be fluidly connected with a discharge end of each rolling diaphragm syringe **34** for delivering fluid from the syringes **34** through tubing connected to a catheter, needle, or other fluid delivery connection (not shown) inserted into a patient at a vascular access site. According to various embodiments, the syringe **12** or **34** may be a pre-filled syringe, i.e., the syringe may be prefilled with a medical fluid, such as a contrast agent or saline, when provided by the syringe manufacturer. According to certain embodiments, the pre-filled syringe may be required to be spiked or otherwise punctured at the discharge end prior to an injection procedure to allow fluid to be expelled from the syringe into a fluid line to the patient, as described herein.

[0088] With reference to **FIG. 4**, the rolling diaphragm syringe **34** generally includes a hollow body **36** defining an interior volume **38**. The body **36** has a forward or distal end **40**, a rearward or proximal end **42**, and a flexible sidewall **44** extending therebetween. The proximal end **42** may be configured to act as piston to pressurize the syringe interior to draw in or expel fluid therefrom, as described herein. The sidewall **44** of the rolling diaphragm syringe **34** defines a soft, pliable or flexible, yet self-supporting body that is configured to roll upon itself, as a "rolling diaphragm", under the action of the a drive member or piston of the fluid injector **10**. The drive member/piston **19** may be configured to releasably engage a drive member engagement portion **52** at the proximal end **42** of the rolling diaphragm syringe **34** (examples of which are described in PCT/US2017/056747). In operation, the sidewall **44** is configured to roll such that its outer surface is folded and inverted in a radially inward direction as the drive member/piston **19** moves the proximal end **42** in a distal direction and unrolled and unfolded in the opposite manner in a radially outward direction as the drive member/piston **19** retract the proximal end **42** in a proximal direction.

[0089] With continued reference to **FIG. 4**, the rearward or proximal portion of the sidewall **44** connects to a closed end wall **46**, and a forward or distal portion of the sidewall

44 defines a discharge neck **48** opposite the closed end wall **46**. The closed end wall **46** may have a concave shape to facilitate the initiation of the inversion or rolling of the sidewall **44**, enhance mechanical strength of the closed end wall **46**, and/or to provide a receiving pocket to receive a distal end of drive member/piston **19**. For example, the closed end wall **46** may define a receiving end pocket for interfacing directly with a similarly-shaped distal end of the drive member/piston **19**. In some examples, at least a portion of the drive member/piston **19** may be shaped to substantially match the shape of the closed end wall **46** or, alternatively, pressure from the drive member/piston **19** as it is moved distally may conform the end wall **46** to substantially match the shape of at least a portion of the drive member/piston **19**.

[0090] The end wall **46** may have a central portion **50** having a substantially dome-shaped structure and a drive member engagement portion **52** extending proximally from the central portion **50**. The drive member engagement portion **52** is configured for releasably interacting with a corresponding engagement mechanism on the drive member/piston **19** of the fluid injector **10**, for example as the drive member/piston is retracted. The rolling diaphragm syringe **34** may be made of any suitable medical-grade plastic or polymeric material, desirably a clear or substantially translucent plastic material. The material of the rolling diaphragm syringe **34** is desirably selected to meet the required tensile and planar stress requirements, water vapor transmission, and chemical/biological compatibility.

[0091] With reference to **FIG. 5**, a fluid injector **10** is shown in accordance with another example of the present disclosure. The injector **10** has a housing **54** that encloses various mechanical drive components, electrical and power components necessary to drive the mechanical drive components, and control components, such as electronic memory and electronic control devices used to control operation of reciprocally movable pistons (not shown). The fluid injector **10** further has a multi-patient disposable system (MUDS) **56** that is removably connectable with the fluid injector **10**. The MUDS **56** has one or more syringes or pumps **58**. In some aspects, the number of syringes **58** corresponds to the number of pistons on the fluid injector **10**. In some examples, such as shown in **FIG. 6**, the MUDS **56** has three syringes **58a-58c** in a side-by-side arrangement. Each syringe **58a-58c** has a bulk fluid connector **60** for connecting to a respective bulk fluid source (not shown) via a MUDS fluid path **62**. The MUDS fluid path **62** may be formed as a flexible tube with a spike element at its terminal end that connects to the bulk fluid connector **60**. Injector **10** and the corresponding MUDS **56** as illustrated in **FIG. 5** are described in detail in WO 2016/112163, the disclosure of which is incorporated herein by this reference.

[0092] The MUDS **56** may comprise one or more syringes or pumps **58a-58c**. In some aspects, the number of syringes **58** corresponds to the number of drive members/pistons on the fluid injector **10**. In some examples, such as shown in **FIGS. 5** and **6**, the MUDS **56** has three syringes **58a-58c** arranged in a side-by-side arrangement. Each syringe **58a-58c** has a bulk fluid connector **60** for connecting to a respective bulk fluid source (not shown) via a MUDS fluid path **62**. The MUDS fluid path **62** may be formed as a flexible tube that connects to the bulk fluid connector **60** having a spike element at its terminal end.

[0093] With reference to **FIG. 6**, the MUDS **56** has a frame **64** for supporting the one or more syringes **58a-58c**. The syringes **58a-58c** may be removably or non-removably connected to the frame **64**. Each syringe **58a-58c** has an elongated, substantially cylindrical syringe body. Each syringe **58a-58c** has a filling port **66** in fluid communication with the MUDS fluid path **62** for filling the syringe **58a-58c** with fluid from a bulk fluid source. Each syringe **58a-58c** further has a discharge outlet or conduit **68** at the terminal portion of its distal end. The discharge outlet **68** of each syringe **58a-58c** is in fluid communication with a manifold **70**. A valve **72** is associated with each discharge outlet **68** and is operable between a filling position, where the filling port **66** is in fluid communication with the syringe interior while the discharge outlet **68** is in fluid isolation from the syringe interior, and a delivery position, where the discharge outlet **68** is in fluid communication with the syringe interior while the filling port **66** is in fluid isolation from the syringe interior. The manifold **70** has a fluid pathway that is in fluid communication with each syringe **58a-58c** and with a fluid outlet line **74** in fluid communication with a port **76** configured for connecting to a single use fluid path element (not shown) for delivering fluid to the patient.

[0094] In various embodiments, for fluid injector **10**, for example any of the fluid injectors shown in **FIGS. 1**, **3**, and **5**, the motor **31** (**FIG. 2**) provides the motive force to reciprocally drive the drive member/piston **19** in a distal direction and discharges fluid within the syringes **12, 34** or MUDS **56**. The motor **31** may have drive components, such as gears and shafts, that are operatively connected to the drive member/piston **19** to reciprocally move the drive member/piston **19**. Each motor **31** must be calibrated to correlate its operating characteristics, such as input current or output torque, to a flow rate or pressure and tolerances associated therewith. As described herein, calibration may be desirable to compensate for any variations or out of specification behavior from any of the different components of the fluid injectors **10**, such as any variations in motor performance characteristics, particularly in fluid injectors with two or more syringes driven by two or more motors. For example, conversion of motor

input torque for one motor **31** to an injector output pressure may be different for another motor **31**. This variation may be further compounded by variations in tolerances of the drivetrain of the fluid injector **10**. The accuracy of flow rate or pressure in a fluid injector **10** is directly correlative to a system and method used to calibrate the motor **31.**

[0095] According to one example of the present disclosure, the fluid injector **10** discussed above with respect to **FIGS. 1-6** may be configured to perform a multi-phase fluid injection which includes an injection of a first fluid **F1** during a first phase, followed by an injection of a second fluid **F2** during a second phase. During the first phase, the first fluid **F1** is injected from at least a first syringe, for example the syringe **12a** of **FIG. 1** or one of the syringes **58b** and/or **58c** of **FIGS. 5-6**. During the second phase, the second fluid **F2** is injected from at least a second syringe, for example the syringe **12b** of **FIG. 1** or syringe **58a** of **FIGS. 5-6**. Hereinafter, the first and second syringes will be discussed with reference to **FIGS. 5-6**, and will thus be referred to as the first syringe **58b** and the second syringe **58a**. However, it is to be understood that the systems and methods described herein are equally applicable to any of the syringes **12a-12b** of **FIG. 1**, an injector with two or more rolling diaphragm syringes **34** as illustrated in in **FIGS. 3-4**, or any other set of least two syringes in a fluid injection system.

[0096] The first fluid **F1** of the first syringe **58b** and the second fluid **F2** of the second syringe **58a** may be different fluids, such as medical fluids having different properties, such as different viscosities. Alternatively the first fluid **F1** and the second fluid **F2** may be the same fluid, for example medical fluid but at different concentrations or temperatures, or the same fluid being delivered at a different flow rate. For example, the first and second fluids **F1, F2** may have one or more of a different viscosity, temperature, and/or density. In one example of the present disclosure, the first fluid **F1** may be contrast media, as described herein, having a first viscosity and the second fluid **F2** may be saline having a second viscosity which is typically lower than the first viscosity. In certain embodiments, the fluid injector may have a third syringe **58c**, which may contain a third fluid **F3** that may be the same or different that the first fluid **F1** and second fluid **F2**. For example, **F3** may be a contrast media, which may be the same as first fluid **F1** or **F3** may be a different contrast agent than **F1**, or **F3** may be the same contrast type as **F1** but at a different concentration than **F1**. During the first phase of the multi-phase injection, the first fluid **F1**, i.e. contrast, may be injected from the first syringe **58b** at a first predetermined flow rate programmed into the injector **10**. Delivery of the first fluid **F1** at the first predetermined flow rate is achieved by

applying a pressure to the first fluid **F1** in the first syringe **58b**, such as by driving the plunger of the first syringe **58b** with the piston **19**, where the necessary applied pressure to achieve the desired first predetermined flow rate is a function of the first viscosity of the first fluid **F1**. Because of the generally higher viscosity of the contrast of the first fluid **F1**, higher applied pressures are generally required to achieve a predetermined flow rate compared to the necessary applied pressure to achieve the same flow rate for a fluid with a lower viscosity, such as saline. Following the first phase of the multi-phase injection, the second phase includes injection of the second fluid **F2**, i.e. saline, from the second syringe **58a**. The second predetermined flow rate of the second fluid **F2** may be the same as, greater than, or lower than the first predetermined flow rate of the first fluid **F1**. In fluid injections where the first and second predetermined flow rates are targeted to be the same, due to the differences between the first viscosity of the first fluid **F1** and the second viscosity of the second fluid **F2**, the pressure required to deliver the second fluid **F2** may differ from the pressure required to deliver the first fluid **F1**. In the present example, the pressure applied to the first fluid **F1**, i.e. contrast media, is generally higher than the pressure applied to the second fluid **F2**, i.e. saline, in order to obtain the same flow rate. In other examples, the second predetermined flow rate of the second fluid **F2** may be different than the first predetermined flow rate of the first fluid **F1**, yet the pressures necessary to achieve the predetermined flow rates of the first fluid **F1** and the second fluid **F2** may still be different.

[0097] Regardless of the predetermined flow rates of the first fluid **F1** and the second fluid **F2**, applying the pressure necessary to achieve the second predetermined flow rate of the second fluid **F2** during the second phase may result in undesired fluctuations in the actual flow rate at the catheter tip of the fluid path set **17** due to the difference in the pressures applied during the first phase and the second phase of the multi-phase injection. In particular, during an initial portion of the second phase, undesirable fluctuations may occur in the actual flow rate as a result of the residual first fluid **F1** in the fluid path set **17** being pushed out or purged from the fluid delivery system by the second fluid **F2**. Because of the residual more viscous first fluid **F1** remaining in the fluid path set **17**, a higher pressure may result in the less viscous second fluid **F2** being ejected from the second syringe **58b** while ejecting the residual first fluid. However, once substantially all of the residual first fluid exits the fluid path set **17**, the higher pressure that is applied to the less viscous second fluid **F2** may result in an undesired fluctuations in the flow rate of the second fluid **F2** as it exits the catheter. The present disclosure presents methods to minimize the effect of any fluid transition, such as

described herein. Additionally, in open fluid delivery systems, such as the fluid injector **10** described herein with reference to **FIGS. 1-2**, in which the first syringe **12a** and the second syringe **12b** are in fluid communication during the multi-stage injection, equalization of the capacitances of the first syringe **12a** and the second syringe **12b** may contribute to undesired fluctuations in the actual flow rate.

[0098] According to embodiments, in order to mitigate undesirable fluctuations in the actual flow rate, and in order to more precisely match the actual flow rate to the predetermined flow rate, an initial portion of the second phase may be a transition phase in which the pressure applied to the second fluid **F2** in the second syringe **58a** is reduced while the residual first fluid **F1** is purged from the fluid delivery system.

[0099] The transition phase of the multi-stage injection is performed by the electronic control devices responsible for controlling the movement of the piston **19** within the second syringe **58a** to dispense the second fluid **F2** from the second syringe **58a**. Movement of the piston **19** is controlled via actuation of motor, such as motor **31** shown in **FIG. 2**, responsible for moving the piston **19** within the second syringe **58a** to apply pressure to the second fluid **F2**. **FIGS. 7A** to **7I** illustrate various non-limiting embodiments of flow rate profiles for injection of a first fluid in a first phase and a second fluid, during a transition phase and during a remaining phase utilizing the methods described herein to reduce fluid fluctuations during the transition phase. As shown in **FIG. 7A**, in accordance with various example of the present disclosure, the electronic control devices operate the motor **31** at a speed to inject the first fluid **F1**, for example from the first syringe **12a** or **58b** during the first phase at a first predetermined flow rate programmed into the injection **10**. After injection of the first phase is completed, the electronic control devices operate the motor **31** at a lower speed (thereby reducing the pressure at which the second fluid **F2** is delivered) during the transition phase, i.e. the initial portion of the second phase, to inject the second fluid **F2** from the second syringe **12b** or **58a** to the patient at a flow rate lower than a second predetermined flow rate for the second phase. After this transition phase is completed, the electronic control devices may operate the motor **31** at a speed to inject the remaining of the second fluid **F2** at the second predetermined flow rate, completing the multi-stage injection. With reference to **FIG. 7B**, the transition phase comprises a long ramp where injection of the second fluid ramps from a zero flow rate (zero piston speed) starting substantially concurrently with the first phase injection of the first fluid and ramps to a piston speed sufficient to provide the second predetermined flow rate after completion of the injection of the first phase. With

reference to **FIG. 7C**, the flow profile shows an extended cross-over ramp transition phase injection protocol, where the motor speed for the first fluid phase is ramped down to zero while the motor speed of the second fluid during the transition phase is ramped up to the second predetermined flow rate. With reference to **FIG. 7D**, a transition phase is illustrated having a ramping transition phase that starts substantially when the motor speed of the first phase is substantially zero. **FIGS. 7E** and **7F** illustrate a transition phases having a programmed motor speed that quickly starts at the second predetermined flow rate, then includes an optimized downward ramp when the second fluid is calculated to reach the end of the catheter, followed by a ramp back to the second predetermined phase after a the flow of the first fluid is calculated or estimated to have completed been expelled. In **FIG. 7E**, the transition phase ramp to the second predetermined flow rate begins prior to the end of the first phase, whereas **FIG. 7F** illustrates and embodiment where the transition phase ramp to the second predetermined flow rate begins after the first phase injection. With reference to **FIG. 7G**, a step-wise ramp of the second fluid motor speed and flow rate during the transition phase is illustrated. The step-wise ramp of motor speed may increase until the second predetermined flow rate is reached. With reference to **FIG. 7H**, the motor speed of the first fluid phase drive member is decreased to an intermediate speed during the transition phase and once the first motor speed reaches substantially zero, the motor speed of the second fluid phase drive member is increased to an intermediate speed during the transition phase and then is increased to a speed associated with the second predetermined flow rate. **FIG. 7I**, includes intermediate speed during the transition phase for both the first fluid phase and the second fluid phase, similar to **FIG. 7H**, having overlapping timing of the decrease and increase of the first and second injector motor, respectively, during the transition phase. The duration of the injection of the transition phase may be determined, for example, by calculating the time necessary to flow the volume of the residual first fluid **F1** from the fluid path set, which may generally be calculated as the fluid volume of the fluid path set.

[00100] According to a particular example of the present disclosure, the electronic control devices are programmed to set the reduced flow rate of the transition phase in accordance with equation (2):

$$Q(t) = Q(p) - (C(1) - C(2))/t(t) \qquad (2)$$

In Equation 2, Q(t) is the reduced flow rate of the multi-phase fluid injection during the transition phase. Q(p) is the second predetermined flow rate of the injection during the second phase; C(1) is a steady state system capacitance (compliance) of the first phase

determined during the injection of the first phase; C(2) is a system capacitance (compliance) of the second phase; and t(t) is a derived time for delivering the volume associated with the system compliance (C(2)). In some examples, C(2) and/or t(t) may be obtained from a lookup table or derived from an equation. In other examples, C(2) and t(t) may be obtained or derived in real time by the injector **10**.

[00101] The method performed through the execution of equation (2) to calculate the reduced flow rate Q(t) during the transition phase utilizes knowledge of the system capacitance of the different phases (C(1) and C(2)) along with the transition time t(t), and the programmed flow rate of the less-viscous second phase Q(p), i.e., the predetermined flow rate. Inputs to the calculations include real-time pressure of the first fluid **F1** of the first phase (P1), the derived pressure of the second fluid **F2** of the second phase (P2), the derived time of transition t(t) of the transition phase, and the pre-injection volume (X2) during the second phase.

[00102] The pressure of the second phase (P2) and the time of transition t(t) of the transition phase may be derived according to the step diagram of **FIG. 9**. In particular, the first predetermined flow rate of the first fluid **F1**, in this example contrast media, is used to determine how the transition phase flow rate Q(t) is calculated. If the first predetermined flow rate of the first fluid **F1** is less than or equal to a threshold value, in this example 5 mL/s, the transition phase flow rate Q(t) is calculated by measuring the steady state pressure during injection of the first fluid **F1**, approximating the catheter gauge, and using the catheter gauge approximation to estimate the steady state pressure of the second fluid **F2**. In particular, the estimated steady state pressure of the second fluid **F2** may be derived from the a table or other calculation based on the measured steady state pressure of the first fluid **F1** as illustrated by the exemplary, non-limiting lookup table shown in **FIG. 10**, which provides values for system features such as rate, contrast pressure, saline pressure, and catheter size. Using the steady state pressure of the first fluid **F1** and the estimated steady state pressure of the second fluid **F2**, respectively, the system capacitance during the first phase C(1) and the system capacitance during the second phase C(2) may be calculated as described hereinafter with particular reference to **FIG. 12**. The transition phase flow rate Q(t) may then be calculated from equation (2).

[00103] Where the predetermined flow rate of the first fluid **F1** is greater than the threshold value, in this example 5 mL/s, the transition phase flow rate Q(t) is calculated by assuming a gauge of the catheter, calculating the estimated steady state pressure of the second

fluid **F2**, and calculating the system capacitance during the second phase C(2). The estimated steady state pressure of the second fluid **F2** may be derived from an equation such the exemplary, non-limiting equation shown in **FIG. 11**, showing the pressure of the second fluid **F2** as a function of flow rate for a known catheter size. The system capacitance during the second phase C(2) may be calculated as described hereinafter with particular reference to **FIG. 12**. The transition phase flow rate Q(t) may then be calculated from equation (2).

[00104] The transition phase is timed to deliver a volume necessary to fill the fluid path set **17**, which in some examples may be from 5 mL to 20 mL, depending on the tubing inner diameter and length, for example approximately 12 mL, with the second fluid **F2** at the beginning of the second phase at the reduced flow rate. This allows for the residual first fluid **F1** in the fluid path set to be pushed through the fluid path set **17** and the catheter at a lower flow rate and exit the fluid path set **17** and the catheter without generating undesirable fluctuations in the actual flow rate at the catheter. After the transition phase is completed, the injection of the second phase of the fluid **F** is returned to the predetermined programmed flow rate Q(p) of the second phase for delivery of the remaining volume of the second phase programmed by the operator.

[00105] Equation (2) may be utilized in accordance with the following steps: (1) P1 is measured during the first phase, this pressure should be measured either at a steady state or a predetermined amount of time prior to the transition to the second phase; (2) P2 is derived from a table or formula using as inputs the parameters of the second phase (i.e., second fluid **F2** being used, predetermined flow rate of the second phase, catheter gauge, etc.); (3) P1 and X2 are input into the capacitance equation discussed herein to derive the volume from capacitance during the first phase; (4) P2 and X2 are input into the capacitance equation to derive the volume from capacitance during the second phase; (5) equation (1) is executed to solve for the reduced flow rate of the transition phase Q(t); and (6) the protocol is modified to deliver the transition phase at the reduced flow rate Q(t) for a volume necessary to fill the fluid path set **17**, and return to the predetermined flow rate Q(p) after completion of the transition phase.

[00106] According to certain embodiments, the capacitance equation may be shown graphically in **FIG. 12**. The capacitance properties of one exemplary fluid injector result in an under-delivery according to the following equation (3):

$$z^{-1} = a + bx^{0.5} + \frac{c}{y^{0.5}} \qquad (3)$$

wherein z is the under-delivered volume (which may be measured in any appropriate volume unit such as in milliliters ("mL")); y is the pressure (which may be measured in any appropriate pressure unit, such as in pounds per square inch ("psi")); x is the volume of fluid in the at least one syringe at the time of injection, and *a, b,* and *c* are constants for the particular surface. For example, in the surface depicted in FIG. 12, a = 0.097795815, b = -0.014798654, and c = 11.030418. When the under-delivered volume of fluid is determined thusly, the fluid to be injected into a patient may be corrected for and increased by the appropriate amount to compensate for the volume lost due to capacitance and impedance of the fluid injector and/or fluid. The fluid injector can overdrive the piston by the distance calculated to deliver the predicted volume that is under-delivered (i.e., z) to ensure an accurate injection dose of the fluid to the patient. The value "z" may be referred to as a "correction volume." P1 and X1 are substituted into equation (3) for y and x, respectively, to obtain the correction volume of the first phase, which is substituted for (C1) of equation (2). P2 and X2 are substituted into equation (3) for y and x, respectively, to obtain the correction volume for the second phase, which is substituted for (C2) of equation (2).

[00107] **FIG. 8** is a chart illustrating the effect of utilizing the above-described transition phase on the measured flow rate of the patient catheter end of the fluid path set **17** during the transition between the first and second phases of the multi-phase fluid injection. The dashed lines represent various baseline injection flow rates, during which no transition phase was implemented. As a result, a significant increase in the measured flow rate, which correlates to a buildup of fluid pressure at the catheter, is seen at the catheter end of the fluid path set **17** during the transition from the first phase to the second phase. The solid lines represent the same flow rates as the dashed lines, but include a transition phase according to embodiments herein during an initial portion of the second phase of the multi-stage injection. As can be appreciated by a comparison of the corresponding dashed and doted lines, the implementation of a transition phase greatly reduces the measured fluctuation in flow rate at the catheter end of the fluid path set **17**.

[00108] **FIG. 13** illustrates a general workflow for an injection protocol including a transition phase according to various embodiments of the present disclosure. As shown in **FIG. 13**, step **1310** includes input of the desired flow profile for an injection, including a first predetermined flow rate for a first fluid and in certain embodiments a second predetermined flow rate for a second fluid. The injection is started **1320** and the injector determines at step **1330** whether the first injected fluid phase is to be followed by a subsequent second injected

fluid phase. If the injector processor determines that the first injected phase is not followed by a second fluid phase, the injector completes the injection of the first phase **1340** and then ends the injection **1350**. Alternatively, if the injector processor determines that the first injected phase is scheduled to be followed by a second fluid phase, the injector then assesses the compliance of the currently injected first fluid phase **1360** and, based on that assessment predicts the compliance of the subsequent second fluid phase **1370**, for example based on the various system components associated with the second fluid reservoir and the characteristics of the first and second fluids. Once the compliance is predicted, the fluid injector processor then calculates the appropriate adjustment to the flow rate for an initial portion of the second fluid phase injection **1380** and determines the flow rate adjustment which is used to alter the flow rate of the initial portion of the second fluid phase is to be injected. The injector then adjusts the flow profile of the initial portion of the second fluid phase **1390** to the calculated values and injects the initial portion of the second fluid at the calculated flow rate for the intermediate specified time. A feedback loop may then occur where the injector processor returns to step **1320** and starts the injection of the second fluid phase at the second predetermined flow rate after completion of the injection of the initial portion of the second fluid over the transition phase. As the protocol continues, the injector then determines if any additional phases are to be injected (i.e., subsequent contrast phases, dual flow phases, or saline phases) or if the injection protocol can be completed after injection of the second phase.

[00109] **FIG. 14** illustrates a workflow for an injection protocol including a transition phase according to a specific embodiment of the present disclosure, for example the injector shown in **FIG. 5**. As shown in **FIG. 14**, step **1410** starts the first injection phase injecting the first fluid at a first predetermined pressure. The injector may measure the pressure of the first fluid in the first phase in step **1415** and calculate the compliance of the first phase **1440**. Based on the measured pressure of the first fluid phase, the injector processor may approximate the pressure that the second fluid **1420** that will provide the transition phase flow rate and the second predetermined flow rate that second fluid is to be injected at, for example by reference to a data lookup table, such as shown in **FIG. 11**. Alternatively the injector processor may calculate the pressure that the second fluid **1420** to provide the transition phase flow rate and the second predetermined flow rate by a process as shown in **FIG. 9** along with the appropriate equation or surface plot. Once the second pressure is approximated, the injector may utilize this value along with detailed information on the

capacitance features of the second fluid reservoir, fluid path, and the second drive mechanism of the injector and features of the second fluid to calculate the compliance of the second fluid phase **1425**. The injector processor may then determine whether the second fluid phase compliance is greater than the first fluid phase compliance in step **1430**. If the second fluid phase compliance is greater than the first fluid phase compliance then the injector will determine that no flow rate adjustment is required for the initial portion of the second phase **1435** and start the injection of the second fluid phase at the second predetermined flow rate. Alternatively, if the calculations of compliance of the second fluid phase indicate there is a significant difference between the second fluid phase compliance and the first fluid phase compliance **1455**, the delta between the compliance values is determined and based on the difference may be utilized to determine the intermediate flow rate for the initial portion of the second fluid phase **1460** and determine the necessary intermediate specified time period or injection volume to clear the first fluid from the fluid path/catheter, start the injection of the second fluid at the intermediate corrected flow rate **1465** and inject at the intermediate flow rate over the intermediate specified time period, and after the end of the volume delivery over the intermediate specified time period, increase the flow rate of the second fluid to the second predetermined flow rate **1470**.

[00110] According to other embodiments of the workflow illustrated in **FIG. 14**, once the step of measuring the pressure of the first fluid phase **1415** is performed, the injector may utilize the pressure value along with detailed information on the capacitance features of the first fluid reservoir, fluid path, and the first drive mechanism of the injector and features of the first fluid to calculate the compliance of the first fluid phase **1440**. The calculated compliance of the first fluid phase may be directly used to guide the approximation of the pressure in the second fluid phase **1420** and/or may be used to determine the flow rate of the first fluid phase **1445**, for example to ensure that the value is substantially equal to the expected first predetermined flow rate. In other embodiments, the calculated value of the compliance of the second fluid phase **1450** and this value along with the value for the calculated compliance of the first fluid phase **1440** may be fed into step **1455** to determine the delta or difference between the calculated compliances for the first fluid phase and the second fluid phase. The described workflows are exemplary and non-limiting, as there are other workflows within the scope of the present disclosure which provide values for the first fluid and second fluid flow rates, the initial flow rate of the second fluid, the intermediate specified time for the initial flow rate of the second fluid, the compliance associated with injection of

the first fluid, the compliance associated with the injection of the second fluid, and other necessary values to provide an injection protocol having a fluid transition portion that does not include any significant fluctuations in overall fluid flow.

[00111] As discussed above, after the transition phase is completed, injection of the remaining portion of the second phase is resumed at the second predetermined flow rate for the second fluid. According to an alternative example of the present disclosure, the remaining portion of the second phase is injected at a flow rate faster than the predetermined flow rate in order compensate for the effect of the slower transition phase on the total injection time for injecting both phases to the patient.

[00112] Although the disclosure has been described in detail for the purpose of illustration based on what is currently considered to be the most practical and preferred examples, it is to be understood that such detail is solely for that purpose and that the disclosure is not limited to the disclosed examples, but, on the contrary, is intended to cover modifications and equivalent arrangements. For example, it is to be understood that the present disclosure contemplates that, to the extent possible, one or more features of any example can be combined with one or more features of any other example.

THE INVENTION CLAIMED IS:

1. A method of delivering a multi-phase fluid injection to a patient via a fluid injector comprising two or more fluid reservoirs, the method comprising:

injecting a first fluid of the fluid injection from at least a first fluid reservoir, the first fluid having a first viscosity, wherein the first fluid is delivered to the patient at a first predetermined flow rate;

injecting an initial portion of at least a second fluid of the fluid injection from at least a second fluid reservoir, the second fluid having a second viscosity different from the first viscosity, wherein the initial portion of the second fluid is delivered to the patient with a flow rate profile different from a second predetermined flow rate for a specified intermediate time interval or intermediate fluid volume; and

injecting a remaining portion of the second fluid of the fluid injection at a flow rate at least equal to the second predetermined flow rate.

2. The method of claim 1, wherein the first viscosity is greater than the second viscosity.

3. The method of claim 1 or 2, wherein the first fluid is selected from the group consisting of a contrast media, and a mixture of a specific ratio of the contrast media and saline, and wherein the second fluid is selected from the group consisting of saline and a mixture of a second specific ratio of the contrast media and saline.

4. The method of any one of claims 1 to 3, wherein the second predetermined flow rate is substantially the same as the first predetermined flow rate.

5. The method of any one of claims 1 to 4, wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate lower than the first predetermined flow rate.

6. The method of any one of claims 1 to 5, wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate that varies between zero and the second predetermined flow rate over the specified intermediate time interval.

7. The method of any one of claims 1 to 6, wherein injecting the initial portion of at least the second fluid comprises injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval, wherein the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line to the patient before beginning the step of injecting the remaining portion of the second fluid, wherein the specified intermediate time interval is based on system architecture; a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the length of a catheter, the diameter of the catheter, the volume of the catheter and any combination thereof.

8. The method of any one of claims 1 to 6, wherein a volume of the initial portion of the second fluid of the fluid injection is determined by one or more of a volume capacity of a fluid line between the second fluid reservoir and the patient, a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, and an injection system compliance.

9. The method of any one of claims 1 to 8, further comprising inputting by a system user the flow rate profile of the second fluid based at least in part on one or more parameters selected from the group consisting of a table of injection protocols, first phase flow rate, second phase flow rate, transition flow rate, catheter volume, catheter diameter, catheter length, volume of the fluid line between the fluid reservoir and the patient, diameter of the fluid line, length of the fluid line, temperature of the first fluid, temperature of the second fluid, viscosity of the first fluid, viscosity of the second fluid, programmed volume of the first fluid to be delivered, and programmed volume of the second fluid to be delivered.

10. The method of any one of claims 1 to 9, wherein the flow rate profile of the initial portion is selected to minimize flow rate deviations over the specified intermediate time interval.

11. The method of any one of claims 1 to 10, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(\text{transition}) = Q(\text{programmed}) - Q(\text{adjusted})$$

wherein Q(transition) is a desired flow rate profile at a transition between the first fluid to at least the second fluid; Q(programmed) is a desired flow rate profile for the first fluid and at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid a flow rate at a catheter tip is substantially similar to Q(programmed).

12. The method of any one of claims 1 to 10, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(t) = Q(p) - (C(1) - C(2))/t(t),$$

wherein Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a steady state system compliance during the first fluid phase, C(2) is a system compliance during the second fluid injection, and t(t) is a derived time for delivering the volume associated with the system compliance (C(2)).

13. The method of claim 12, wherein the system compliance during the first fluid injection comprises a first compliance factor associated with one or more of the first fluid reservoir, a first fluid delivery mechanism, and a tubing set in operative fluid communication the first fluid reservoir, and

the system compliance during the second fluid injection comprises a second compliance factor associated with one or more of the second fluid reservoir, a second fluid delivery mechanism, and a tubing set in operative communication the second fluid reservoir.

14. The method of any one of claims 1 to 13, wherein the first fluid reservoir is a first syringe operatively connected to a first drive member of the fluid injector and at least the second fluid reservoir is at least a second syringe operatively connected to at least a second drive member of the fluid injector.

15. A fluid injector system for delivering a multi-phase fluid injection to a patient, the fluid injector system comprising:

at least one first syringe configured to contain a first fluid of the multi-phase fluid injection, the first fluid having a first viscosity;

at least one first drive member operatively connected with the at least one first syringe, the at least one first drive member being operable to dispense the first fluid of the multi-phase fluid injection;

at least one second syringe configured to contain a second fluid of the multi-phase fluid injection, the second fluid having a second viscosity different from the first viscosity;

at least one second drive member operatively connected with the at least one second syringe, the at least one second piston being operable to dispense the second fluid of the multi-phase fluid injection;

a fluid line connected to the at least one first syringe and the at least one second syringe, and configured to deliver at least one of the first fluid of the multi-phase fluid injection from the at least one first syringe to the patient and the second fluid of the multi-phase fluid injection from the at least one second syringe to the patient; and

a control device configured to control movement of the first drive member associated with the at least one first syringe and movement of the at least one second drive member associated with the at least one second syringe to control the delivery of the first fluid and the second fluid of the multi-phase fluid injection to the patient,

wherein the control device is configured to control the first drive member to inject the first fluid at a first predetermined flow rate, to control the at least one second drive member to inject an initial portion of at least the second fluid of the fluid injection from the at least one second syringe at an intermediate flow rate profile different from a second predetermined flow rate for a specified intermediate time or intermediate fluid volume, and to inject a remaining portion of the second fluid at least equal to the second predetermined flow rate, wherein the second fluid has a second viscosity different from the first viscosity.

16. The fluid injector system of claim 15, wherein the first viscosity is greater than the second viscosity.

17. The fluid injector system of claim 15 or 16, wherein the first predetermined flow rate is substantially the same as the second predetermined flow rate.

18. The fluid injector system of any one of claims 15 to 17, wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate lower than the first predetermined flow rate, or

wherein the flow rate profile of at least the initial portion of the at least second fluid is delivered at a flow rate that varies between zero and the second predetermined flow rate over the specified intermediate time interval.

19. The fluid injector system of any one of claims 15 to 18, wherein the control device is configured to time an injection of the initial portion of at least the second fluid comprises injecting the initial portion of at least the second fluid at an intermediate flow rate lower than the second predetermined flow rate over the specified intermediate time interval, wherein the specified intermediate time interval is selected to allow a residual portion of the first fluid to pass through a fluid line to the patient before beginning the step of injecting the remaining portion of the second fluid, wherein the specified intermediate time interval is based on system architecture; a capacitance of at least one of the first fluid reservoir and the second fluid reservoir, a length of the fluid line, a diameter of the fluid line, a volume of the fluid line, the length of a catheter, the diameter of the catheter, the volume of the catheter and any combination thereof.

20. The fluid injection system of any one of claims 15 to 19, wherein the first fluid is selected from the group consisting of a contrast media, and a mixture of a specific ratio of the contrast media and saline, and wherein the second fluid is selected from the group consisting of saline and a mixture of a second specific ratio of the contrast media and saline.

21. The fluid injection system of any one of claims 15 to 20, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(\text{transition}) = Q(\text{programmed}) - Q(\text{adjusted})$$

wherein Q(transition) is a desired flow rate profile at a transition between the first fluid to at least the second fluid; Q(programmed) is a desired flow rate profile for the first fluid and at least the second fluid; and Q(adjusted) is a necessary adjustment of the flow rate of the second fluid so that Q(transition) at the transition between the first fluid and at least the second fluid a flow rate at a catheter tip is substantially similar to Q(programmed).

22. The fluid injection system of any one of claims 15 to 20, wherein the flow rate profile of the initial portion is calculated based on the following equation:

$$Q(t) = Q(p) - (C(1) - C(2))/t(t),$$

wherein Q(t) is the intermediate flow rate, Q(p) is the second predetermined flow rate, C(1) is a steady state system compliance during the first fluid phase, C(2) is a system compliance during the second fluid injection, and t(t) is a derived time for delivering the volume associated with the system compliance (C(2)).

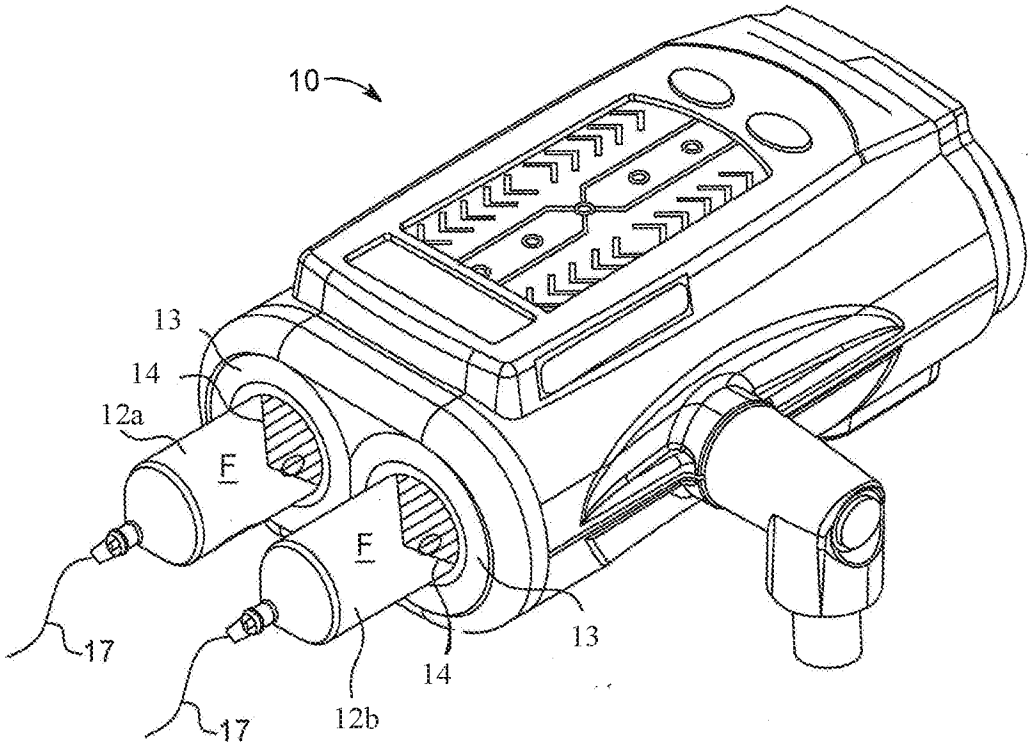

FIG. 1

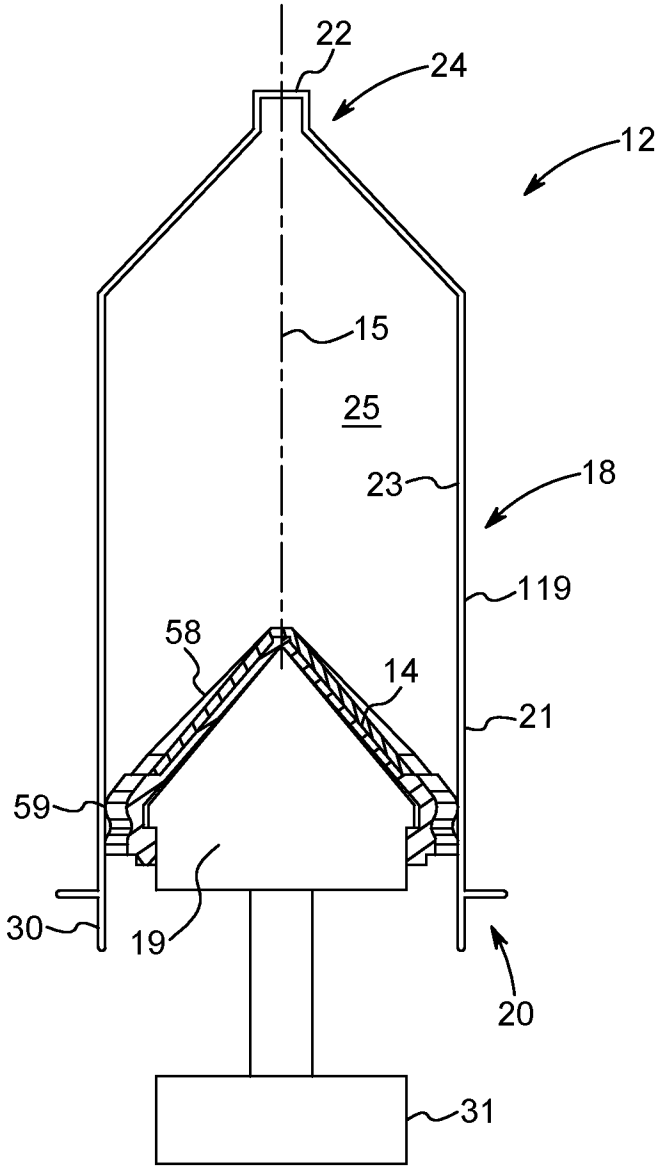

FIG. 2

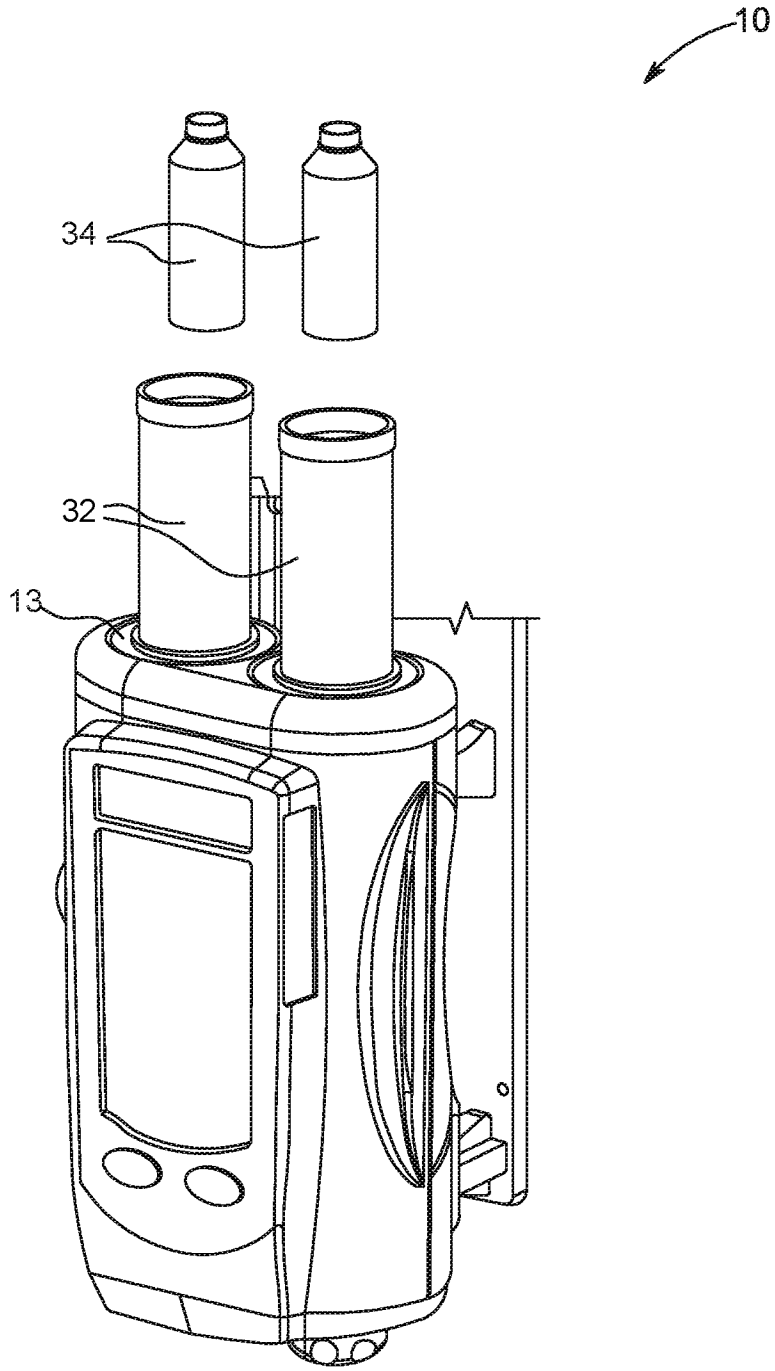

FIG. 3

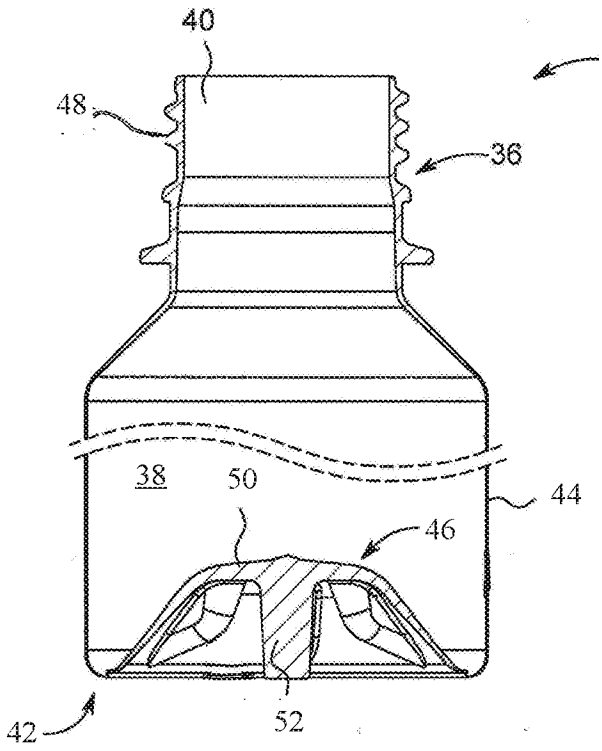

FIG. 4

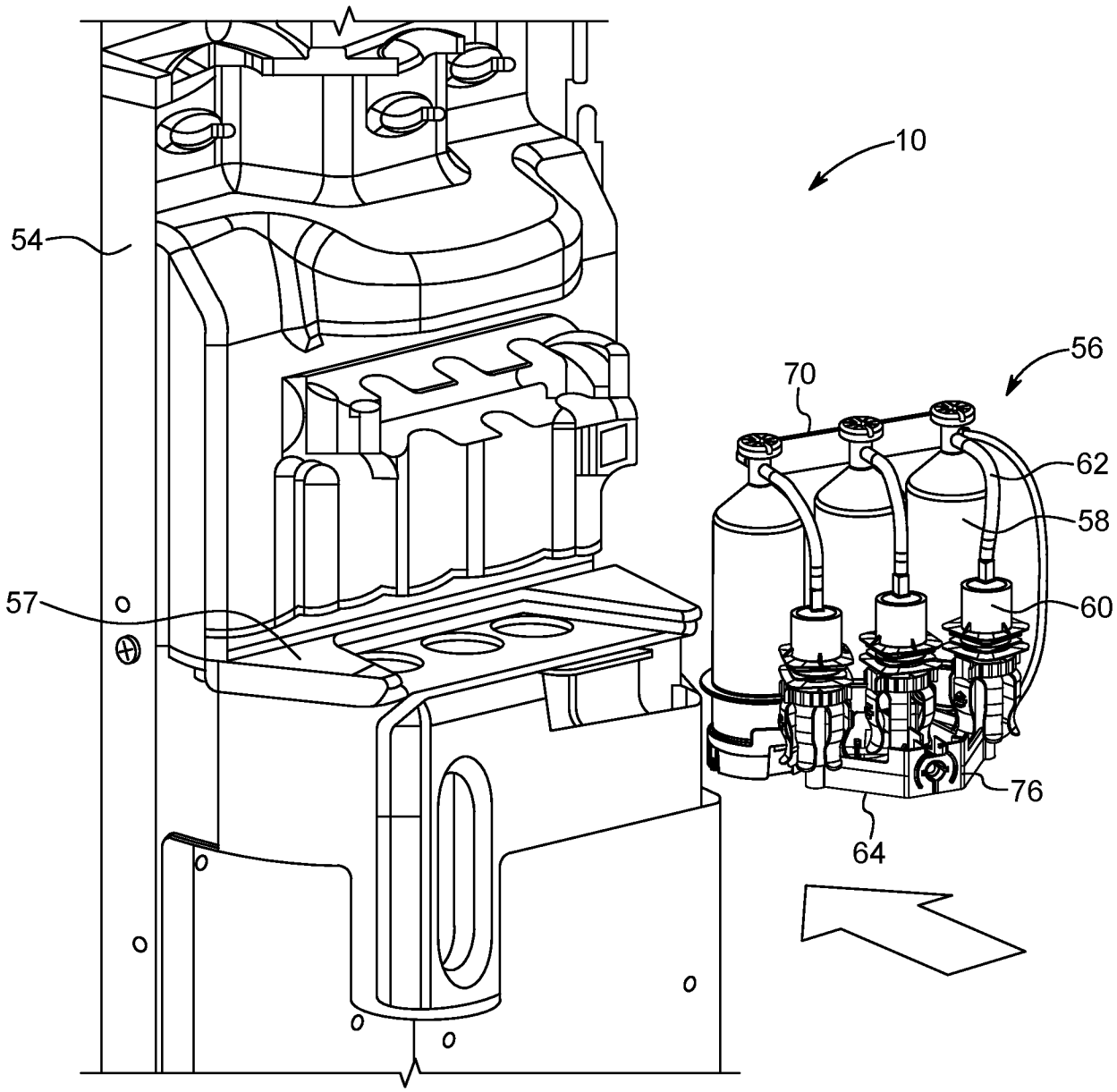

FIG. 5

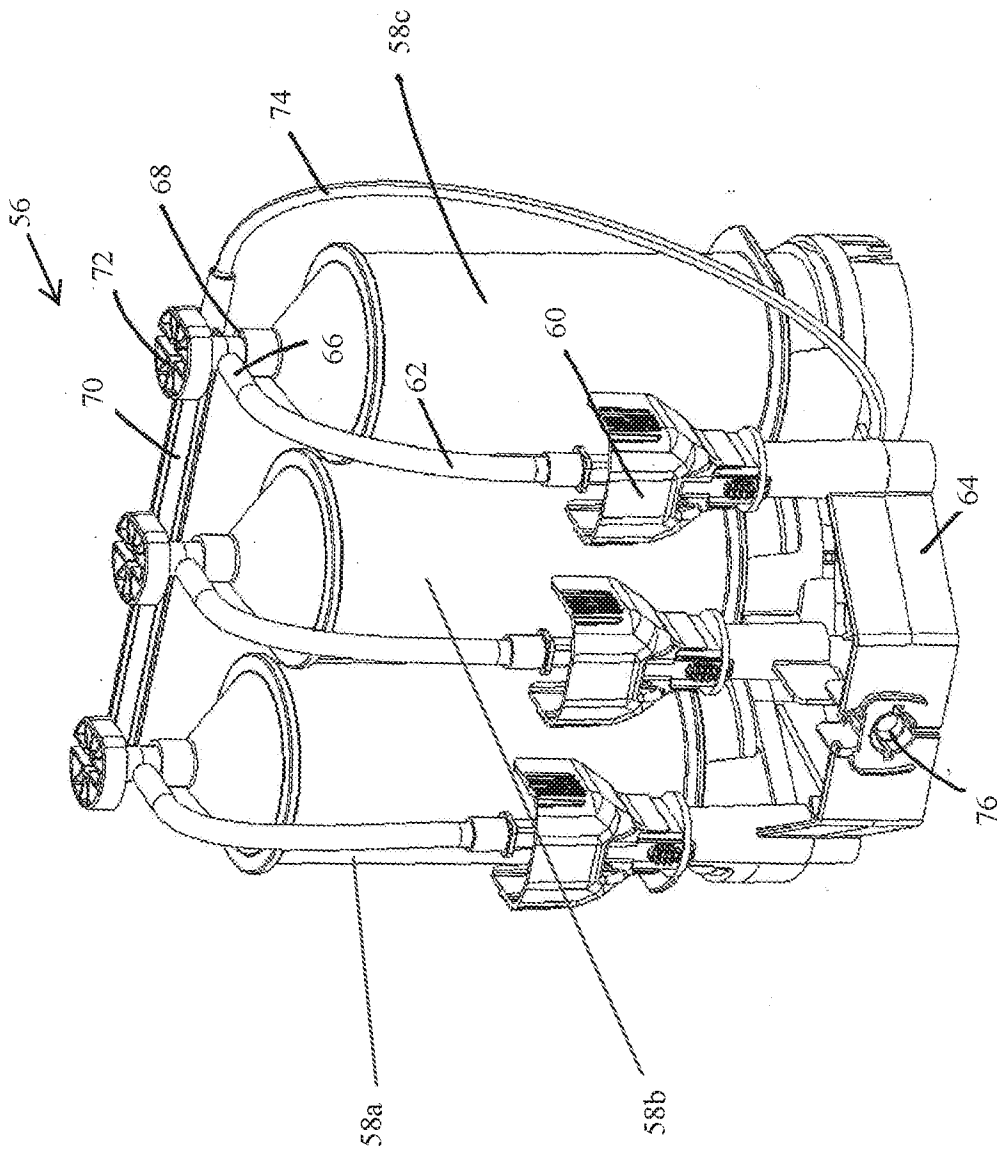

FIG. 6

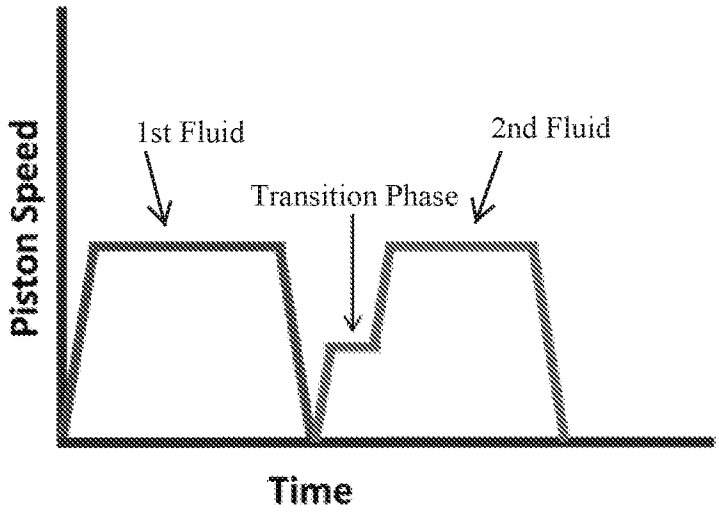

FIG. 7A

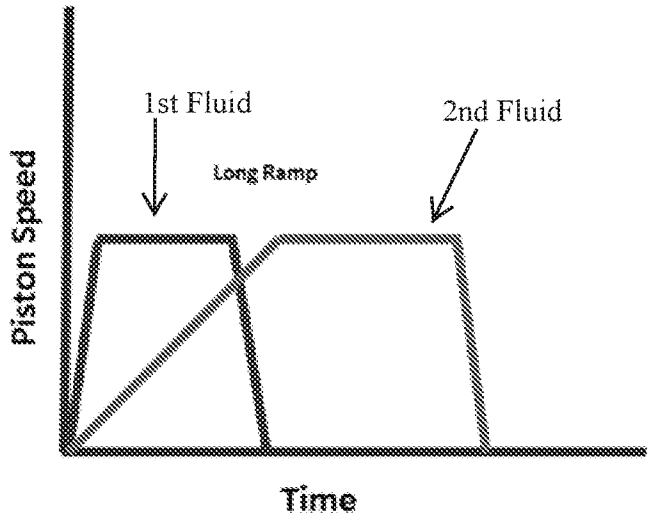

FIG. 7B

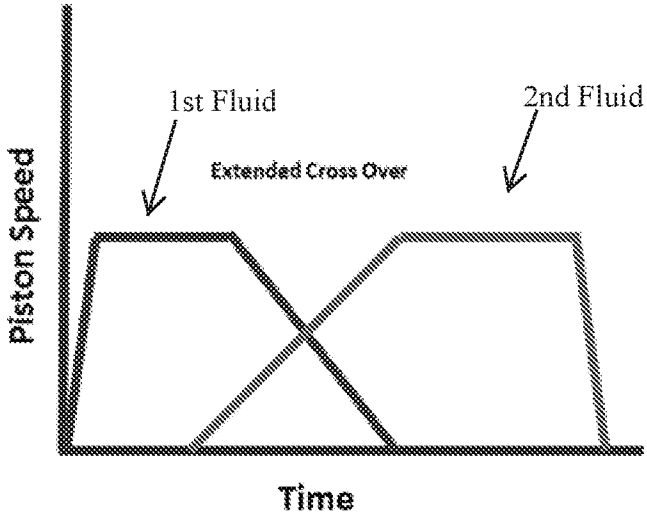

FIG. 7C

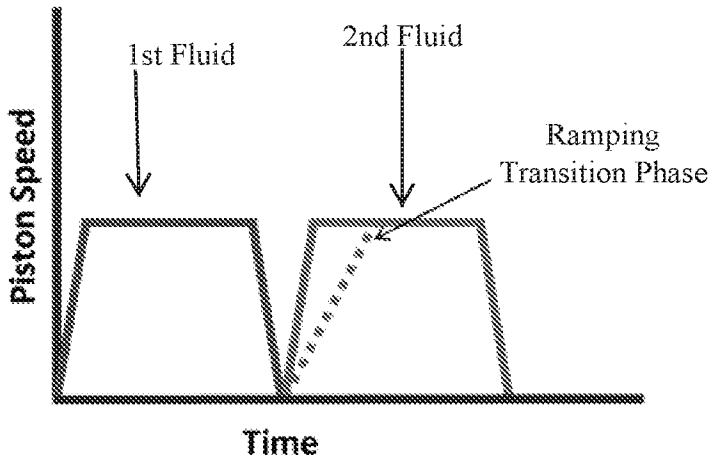

FIG. 7D

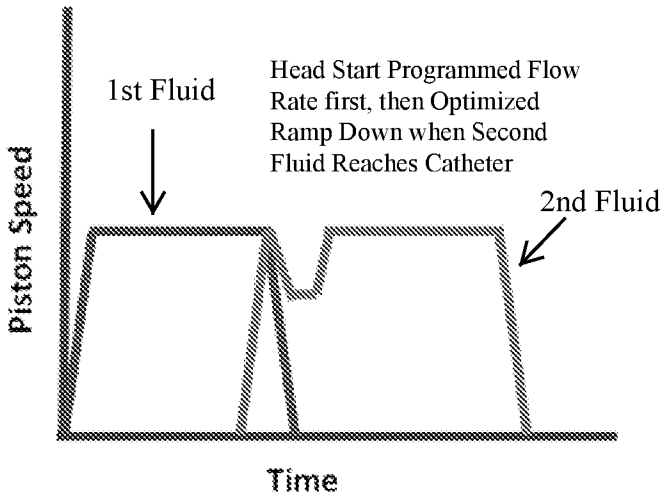

FIG. 7E

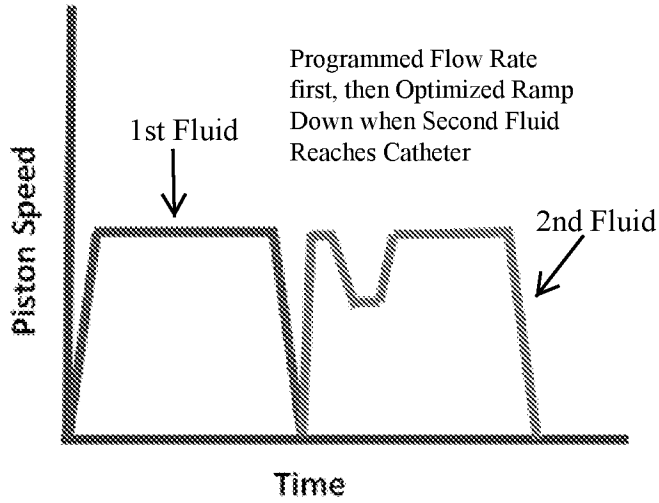

FIG. 7F

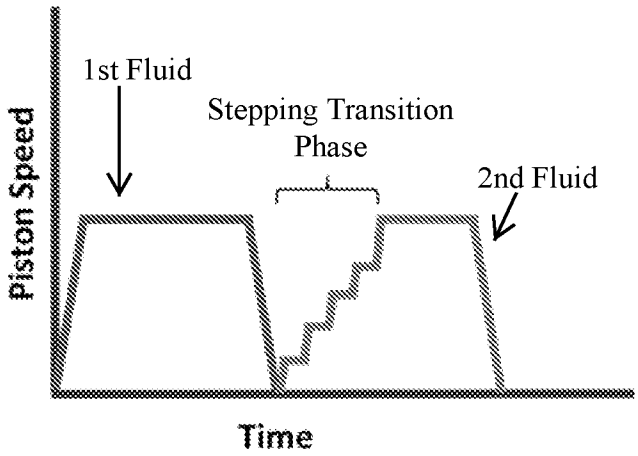

FIG. 7G

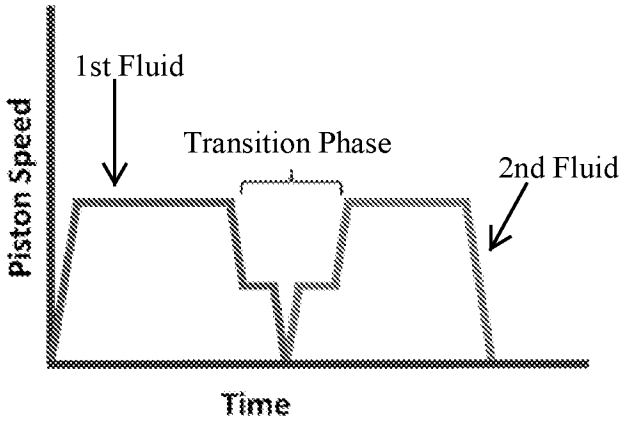

FIG. 7H

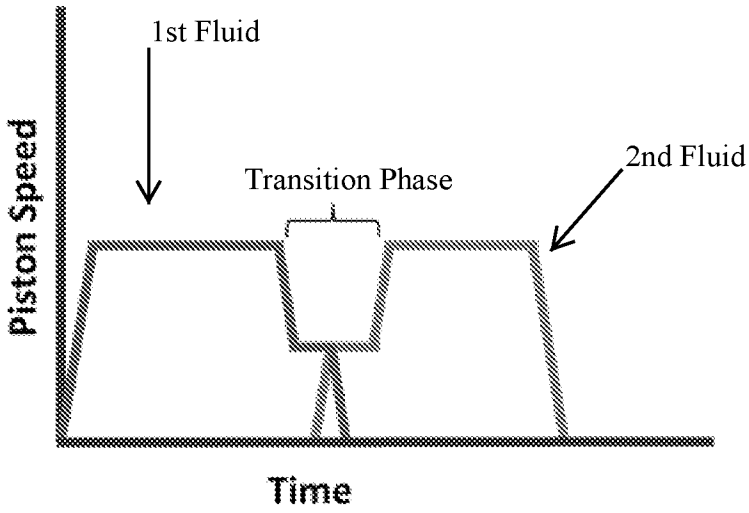
1st Fluid
Transition Phase
2nd Fluid
Piston Speed
Time

FIG. 7I

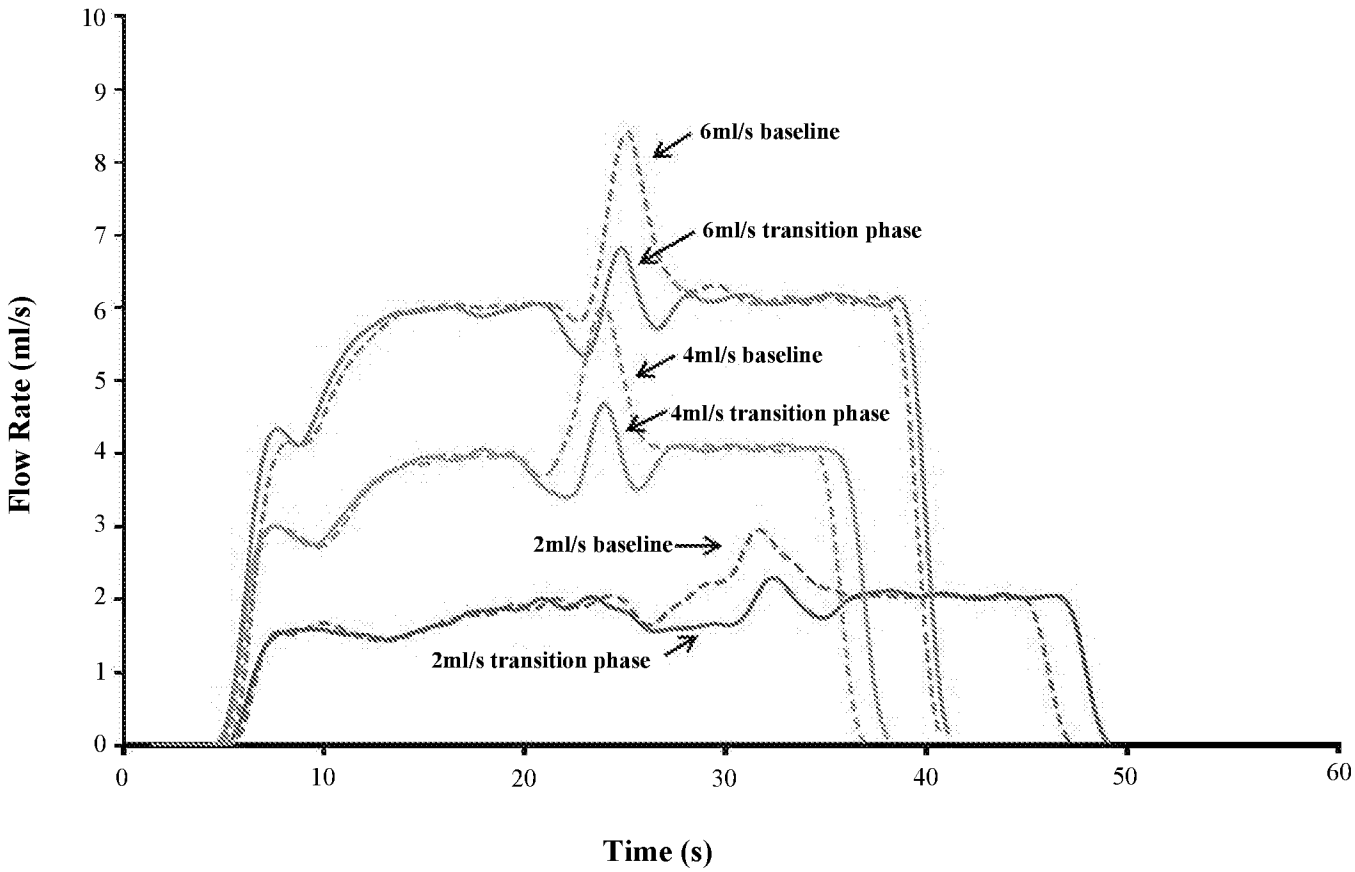
Flow Rate (ml/s)
Time (s)
6ml/s baseline
6ml/s transition phase
4ml/s baseline
4ml/s transition phase
2ml/s baseline
2ml/s transition phase
0
1
2
3
4
5
6
7
8
9
10
0
10
20
30
40
50
60

FIG. 8

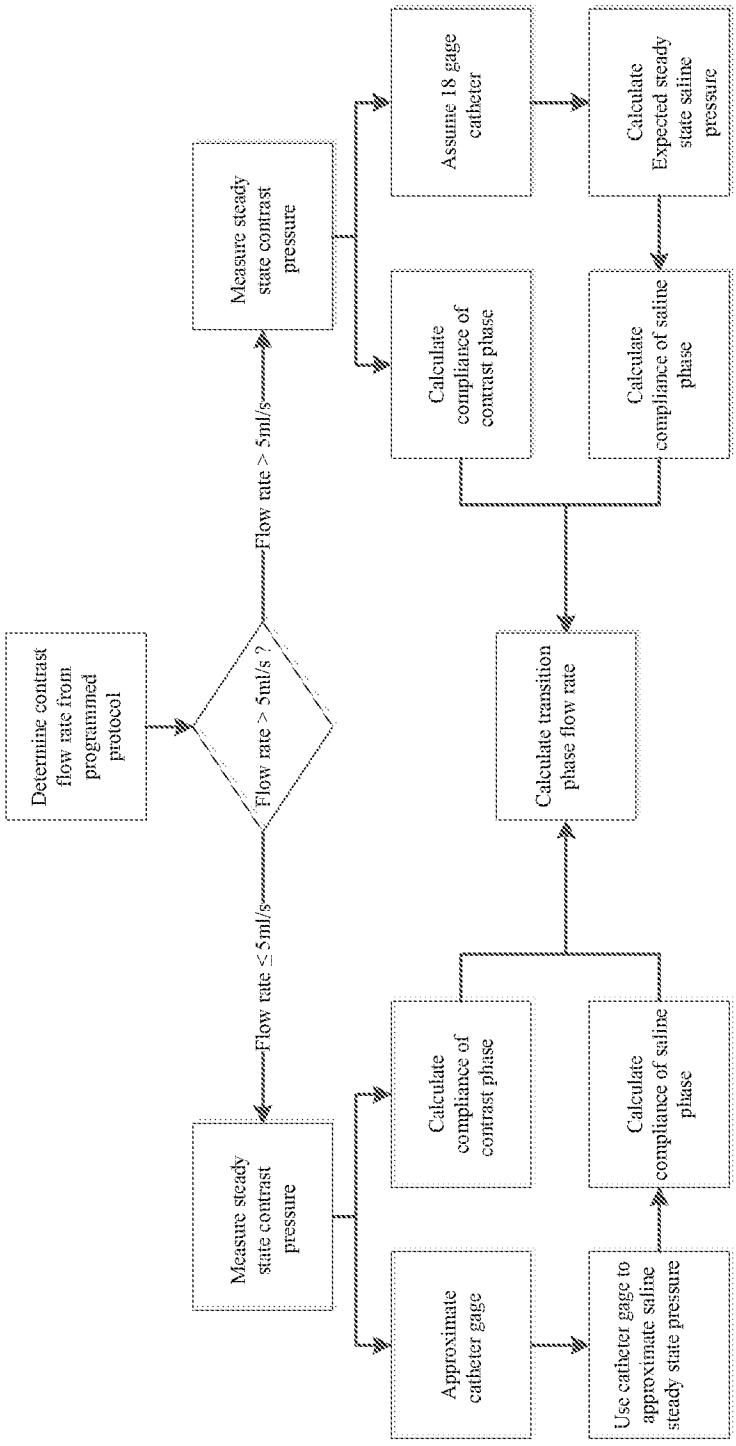
Determine contrast flow rate from programmed protocol
Flow rate > 5ml/s ?
Flow rate > 5ml/s
Flow rate ≤ 5ml/s
Measure steady state contrast pressure
Assume 18 gage catheter
Calculate Expected steady state saline pressure
Calculate compliance of contrast phase
Calculate compliance of saline phase
Calculate transition phase flow rate
Measure steady state contrast pressure
Approximate catheter gage
Use catheter gage to approximate saline steady state pressure
Calculate compliance of contrast phase
Calculate compliance of saline phase

FIG. 9

First Phase Flow Rate (mL/s)	First Phase Pressure (kPa)	Scaling Factor (Catheter Gauge)	Second Phase Flow Rate (mL/s)	Second Phase Predicted Pressure (kPa)
1	0	18	1	62
1	207	18	1	62
1	483	18	1	62
1	758	24	1	103
1	1034	24	1	103
1	1310	24	1	103
1	1586	24	1	103
1	1862	24	1	103
2	0	18	2	103
2	276	18	2	103
2	552	18	2	103
2	827	24	2	241
2	1103	24	2	241
2	1379	24	2	241
2	1655	24	2	241
2	1931	24	2	241
3	69	18	3	145
3	345	18	3	145
3	621	18	3	145
3	896	18	3	145
3	1172	24	3	448
3	1448	24	3	448
3	1724	24	3	448
3	1999	24	3	448
4	138	18	4	186
4	414	18	4	186
4	689	18	4	186
4	965	18	4	186
4	1241	18	4	186
4	1517	24	4	724
4	1793	24	4	724
4	2068	24	4	724
5	207	18	5	241
5	483	18	5	241
5	758	18	5	241
5	1034	18	5	241
5	1310	18	5	241
5	1586	18	5	241
5	1862	24	5	1351

FIG. 10

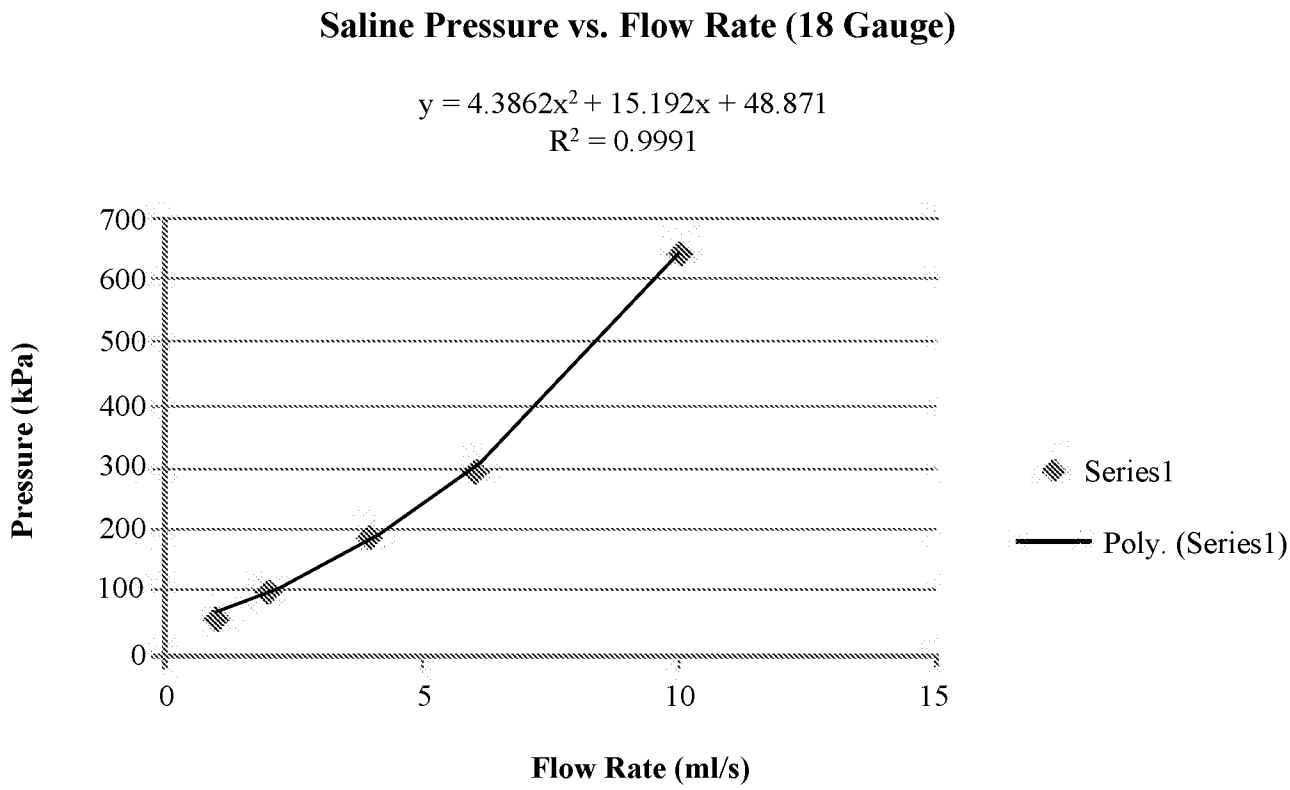
Saline Pressure vs. Flow Rate (18 Gauge)
y = 4.3862x² + 15.192x + 48.871
R² = 0.9991
Pressure (kPa)
700
600
500
400
300
200
100
0
0
5
10
15
Flow Rate (ml/s)
Series1
Poly. (Series1)

FIG. 11

System Compliance Characterization

Rank 7 Eqn 302461977 $z^{-1} = a+b/x^{0.5}+cy^{0.5}$

$r^2 = 0.98825093$ DF Adj $r^2 = 0.98800951$ FitStdErr = 0.19467277 Fstat = 6182.3152

a = 0.11422056 b=10.39086

c = -0.014863432

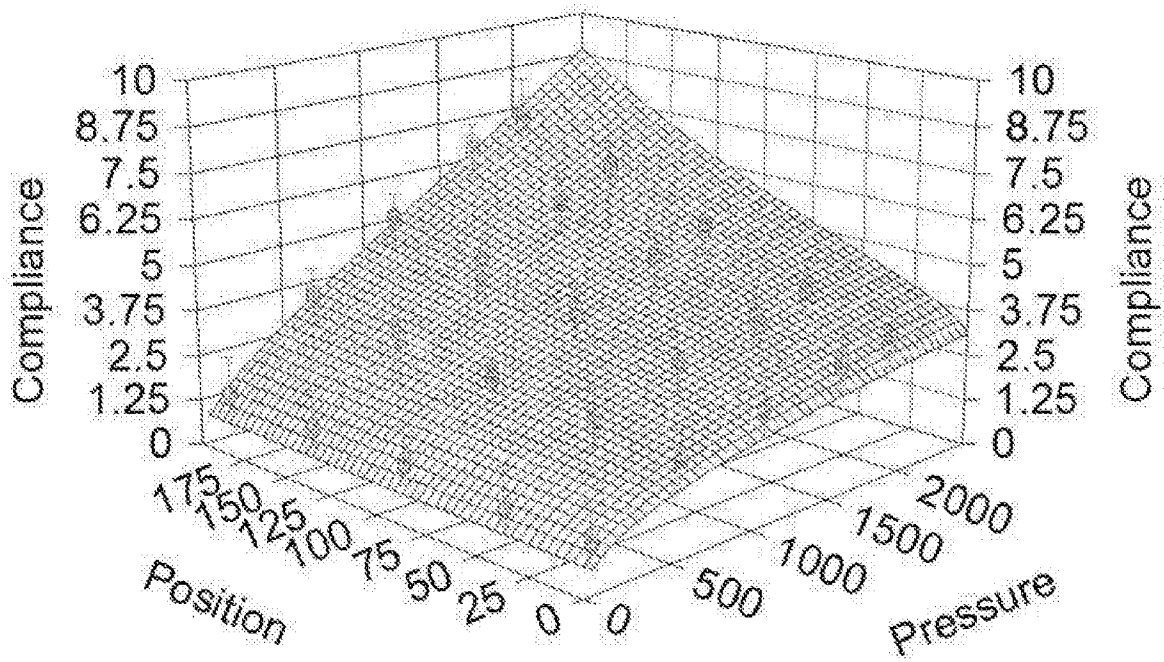

FIG. 12

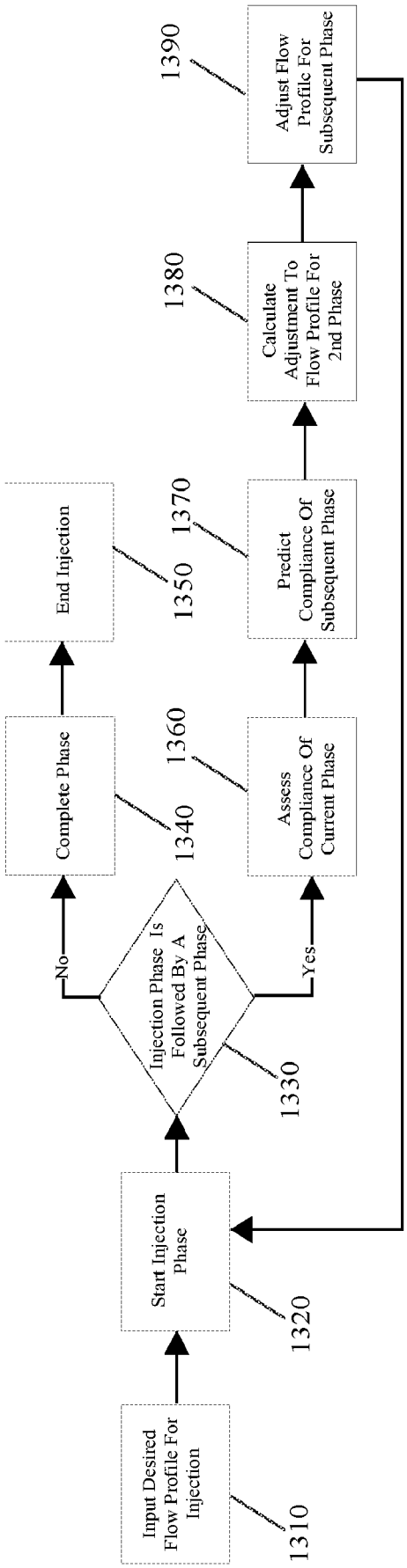
Input Desired Flow Profile For Injection
1310
Start Injection Phase
1320
Injection Phase Is Followed By A Subsequent Phase
1330
No
Yes
Complete Phase
1340
End Injection
1350
Assess Compliance Of Current Phase
1360
Predict Compliance Of Subsequent Phase
1370
Calculate Adjustment To Flow Profile For 2nd Phase
1380
Adjust Flow Profile For Subsequent Phase
1390
General Workflow

FIG. 13

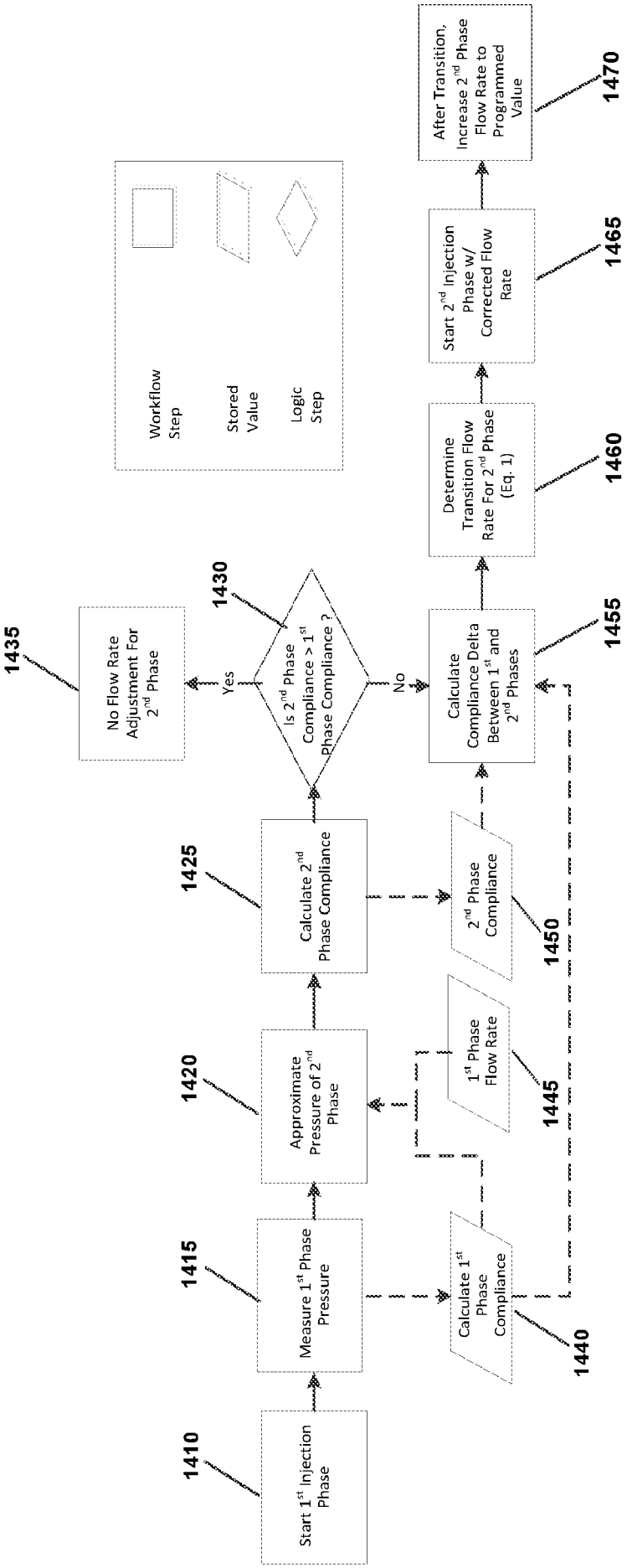
Workflow Step
Stored Value
Logic Step
Start 1st Injection Phase
1410
Measure 1st Phase Pressure
1415
Calculate 1st Phase Compliance
1440
1st Phase Flow Rate
1445
Approximate Pressure of 2nd Phase
1420
Calculate 2nd Phase Compliance
1425
2nd Phase Compliance
1450
Is 2nd Phase Compliance > 1st Phase Compliance ?
1430
Yes
No
No Flow Rate Adjustment For 2nd Phase
1435
Calculate Compliance Delta Between 1st and 2nd Phases
1455
Determine Transition Flow Rate For 2nd Phase (Eq. 1)
1460
Start 2nd Injection Phase w/ Corrected Flow Rate
1465
After Transition, Increase 2nd Phase Flow Rate to Programmed Value
1470

FIG. 14

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/048282

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/14 A61M5/168 A61M5/142
ADD.

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/007116 A1 (ZATEZALO DOUG [US] ET AL) 17 January 2002 (2002-01-17) figures 1, 2, 4, 5 paragraph [0022]	1-22
X	US 2013/245604 A1 (KOUYOUMJIAN GAREN [GB] ET AL) 19 September 2013 (2013-09-19) figures 1A, 15, 21, 22, 40-42 paragraphs [0118], [0200], [0268] - [0296]	1-22
A	US 2016/317738 A1 (CROSS DAVID [GB] ET AL) 3 November 2016 (2016-11-03) the whole document	1-22
A	US 2011/021978 A1 (MARTIN JAMES F [US] ET AL) 27 January 2011 (2011-01-27) the whole document	1-22

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
14 November 2018	23/11/2018

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/048282

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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A	GB 2 497 375 A (SANOFI AVENTIS DEUTSCHLAND [DE]) 12 June 2013 (2013-06-12) the whole document -----	1-22

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