Claims

1. A closed-loop citrate anticoagulation system for use with a continuous-renal-replacement-therapy (CRRT) circuit, the system comprising:

   a) a first ion-selective electrode (ISE) sensor positioned in the extracorporeal bloodline downstream of a hemofilter and configured to generate a signal proportional to post-filter ionised-calcium concentration;

   b) a second ISE sensor positioned in a venous-return line and configured to generate a signal proportional to systemic ionised-calcium concentration;

   c) a first electronically-controlled infusion pump fluidly coupled to a source of trisodium-citrate and arranged to infuse citrate upstream of the hemofilter;

   d) a second electronically-controlled infusion pump fluidly coupled to a source of calcium-chloride solution and arranged to infuse calcium downstream of the hemofilter; and

   e) a microcontroller in communication with the first and second sensors and the first and second pumps, the microcontroller executing a feedback-control algorithm that (i) maintains the post-filter ionised-calcium concentration between about 0.25 mmol L^{-1} and 0.35 mmol L^{-1} by adjusting the citrate-infusion rate and (ii) maintains the systemic ionised-calcium concentration between about 1.0 mmol L^{-1} and 1.2 mmol L^{-1} by adjusting the calcium-chloride-infusion rate.

2. The system of claim 1, wherein each ISE sensor comprises a calcium-selective polymer membrane doped with ETH-129 ionophore, a solid-contact transducer layer comprising PEDOT:PSS, and an on-chip Ag/AgCl reference electrode.

3. The system of claim 2, wherein each sensor further comprises an integrated platinum resistance-temperature detector that provides temperature compensation of the ion-selective membrane potential.

4. The system of claim 1, wherein the first and second infusion pumps are contained in a single disposable cartridge that further includes a MEMS thermal mass-flow sensor providing real-time verification of delivered flow.

5. The system of claim 4, wherein the disposable cartridge comprises a non-volatile memory that stores at least a cartridge identifier, solution concentration, and cumulative infused volume, and wherein the microcontroller writes incremental usage data to the memory and disables the corresponding pump when a preset dose ceiling is reached.

6. The system of claim 1, wherein the feedback-control algorithm comprises two cascaded proportional–integral–derivative (PID) sub-loops that are updated at intervals of five seconds or

less.

7. The system of claim 1, wherein the feedback-control algorithm further comprises a model-predictive control routine that anticipates systemic calcium changes resulting from changes in citrate dose and pre-emptively commands compensatory adjustments to the calcium-chloride-infusion rate.

8. The system of claim 1, wherein the microcontroller automatically ramps the calcium-chloride-infusion rate from zero to a maintenance value over a predetermined ramp interval when the systemic ionised-calcium concentration falls below a low-threshold value, and thereafter maintains the infusion at the maintenance value until the systemic concentration re-enters a target band.

9. The system of claim 1, further comprising safety logic that halts the citrate-infusion pump and maintains or increases the calcium-chloride-infusion pump to a maintenance rate when either sensor detects ionised-calcium below 0.20 mmol L^{-1} post-filter or below 0.80 mmol L^{-1} systemically.

10. The system of claim 9, wherein the safety logic, upon halting citrate infusion, automatically initiates or prompts systemic heparin anticoagulation as a backup therapy.

11. The system of claim 1, wherein the sensors are connected to the microcontroller by a dual-redundant I^2C bus that supports hot-swap detection, 16-bit part-type broadcasting, address negotiation, and watchdog timeouts that place the pumps in a maintenance-drip mode if any sensor is silent for more than one second.

12. The system of claim 1, wherein the microcontroller records every sensor reading, pump-rate command, alarm, and mode transition in a tamper-resistant audit log.

13. The system of claim 1, wherein the microcontroller enforces hardware-limited maximum infusion rates for the citrate and calcium pumps that cannot be overridden by software commands.

14. The system of claim 1, wherein the first and second sensors are factory-calibrated and further calibrated in situ by exposure to two calibration solutions at start-up.

15. The system of claim 14, wherein during operation the microcontroller periodically cross-checks the first and second sensor outputs to detect drift and, if drift is detected, adjusts calibration offsets or triggers an alarm.

16. The system of claim 1, wherein the citrate infusion solution is 4 % (w/w) trisodium-citrate and the calcium infusion solution is 5 % (w/v) calcium-chloride in saline.

17. The system of claim 1, wherein each infusion pump has a maximum rate that is hardware-limited to prevent infusion of citrate in excess of 600 mL h^{-1} or calcium-chloride in excess of 120 mL h^{-1}.

18. The system of claim 1, wherein the citrate and calcium-chloride infusion lines each include a one-way check valve to prevent backflow of blood into the infusion lines.

19. The system of claim 1, wherein the infusion pumps are gear pumps driven by brushless-DC motors with Hall-effect sensors that provide independent verification of motor rotation.

20. The system of claim 1, wherein the system is mechanically keyed so that the citrate cartridge can occupy only a pre-filter bay and the calcium cartridge can occupy only a post-filter bay.

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21. A method of providing regional anticoagulation during CRRT, the method comprising:

    i) measuring post-filter ionised-calcium concentration with a first solid-state sensor;

    ii) measuring systemic ionised-calcium concentration with a second solid-state sensor;

    iii) infusing trisodium-citrate upstream of a hemofilter at a rate adjusted in response to the post-filter ionised-calcium measurement to maintain the post-filter ionised-calcium concentration in a first target range;

    iv) infusing calcium-chloride downstream of the hemofilter at a rate adjusted in response to the systemic ionised-calcium measurement to maintain the systemic ionised-calcium concentration in a second target range; and

    v) automatically halting citrate infusion and maintaining at least a maintenance rate of calcium-chloride infusion when either ionised-calcium measurement falls below a safety threshold.

22. The method of claim 21, further comprising ramping the calcium-chloride-infusion rate from zero to a maintenance value over a ramp period of 30- to 60 minutes when the systemic ionised-calcium concentration is below the second target range.

23. The method of claim 21, wherein steps iii) and iv) are performed by executing a cascaded PID control loop at a cycle time of no more than five seconds.

24. The method of claim 21, wherein cumulative infused volumes of trisodium-citrate and calcium-chloride are stored in a non-volatile memory on corresponding disposable reagent cartridges, and further comprising disabling infusion when a cartridge-specific dose ceiling is reached.

25. The method of claim 21, further comprising logging each sensor measurement, pump command, alarm event and safety-state transition in an immutable audit log.

26. The method of claim 21, further comprising, upon detection of a sensor fault, placing both infusion pumps in a fixed maintenance-drip mode until the fault is cleared or a clinician intervenes.

27. The method of claim 21, further comprising transmitting a command to an external CRRT console to switch from citrate to systemic heparin anticoagulation when citrate infusion is halted due to a safety condition.

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28. A disposable reagent cartridge for use in the system of claim 1, the cartridge comprising:

    a) a first flexible pouch containing a trisodium-citrate solution;

    b) a second flexible pouch containing a calcium-chloride solution;

    c) first and second gear-type micro-pumps fluidically coupled to the respective pouches;

    d) a MEMS thermal mass-flow sensor positioned downstream of each pump; and

    e) a non-volatile memory device electrically connected to a cartridge backplane, the memory device storing cartridge identity, solution concentration and cumulative delivered volume, the memory device configured to prevent pump activation when a preset volume limit is reached.

29. The cartridge of claim 28, further comprising mechanical keys that prevent installation of the cartridge into an incorrect pump bay.

30. The cartridge of claim 28, wherein each pump outlet contains a unidirectional valve and a coloured optical fiducial that is read by a photodiode in the pump bay to confirm reagent class before pump activation.