Single Lumen Alternating Micro-Batch Hemodialfiltration (SLAMB-HDF):
A Device for Minimally Invasive Renal Replacement Therapy

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Abstract

Blood based renal replacement therapies (RRT) such as hemodialysis require access to the bloodstream and adequate blood flow to enable the requisite clearance. As such, nearly all RRT systems require two lumens enabling a blood circuit that pulls blood from one lumen or needle and returns via another lumen or needle. The proposed single lumen alternating micro-batch (SLAMB) technique utilizes a small single lumen to draw a ‘micro’ batch of blood into a single reservoir. In the reservoir, the ‘batch’ of blood is circulated at a high blood flow rate through a hemofilter or hemodialyzer enabling efficient small and middle molecule clearance. Thereafter, the ‘purified’ blood is returned to the patient and the cycle is repeated. Each batch is comprised of 20-300 cc of blood which is adjusted to the vascular access, hemodynamic status, and patient size. Up to 15 cycles can done per hour enabling this system to achieve a blood clearance level comparable to modern continuous RRT systems.

Since the system can function with a small-bore single lumen, this device can work with existing central lines allowing for less invasive vascular access. Because this system is small and relatively simple, SLAMB based systems are less expensive, smaller, and have improved portability. Lastly, a similar manual SLAMB-HF kit that requires no electricity or battery may be able to be developed at low cost (less than $25) for use in austere medical conditions thus expanding the availability of RRT for patients with AKI.
Introduction

Modern blood based renal replacement therapies (RRT) such as hemodialysis and hemofiltration require access to the blood compartment and adequate blood flow to enable the required clearance for the RRT prescription. As such, nearly all RRT systems require two lumens enabling an afferent and efferent limb to create a blood circuit that pulls blood from one lumen or needle and returns via another lumen or needle. Additionally, achieving high levels of solute clearance requires a high blood flow thereby necessitating large bore vascular access. As an example, in order to conduct a typical RRT treatment, a dual-lumen catheter with a diameter of 11-13 French, an arterio-venous graft, or a mature arterio-venous fistula is required. All of these vascular access types requires maintenance to assure patency and are associated with potential complications.

The device concept proposed in this technical note is a modernization of the first hemodialysis ever performed. The first successful hemodialysis procedure was performed utilizing a drum dialyzer wherein a sausage casing made of cellophane was wrapped around a cylinder which was immersed in a large drum filled with dialysate. (Figure 1). The patient was phlebotomized and the blood was placed into a jug with an anticoagulant (i.e. heparin). This ‘batch’ of blood was then placed into the sausage casing membrane and submerged into the dialysate thereby allowing a diffusive dialysis effect. After this procedure was completed, the dialyzed blood was drained into a second jug which was then transfused back into the patient. This procedure was repeated multiple times until an adequate clearance was achieved and this series of ‘drain-refill’ procedures comprised the first successful dialysis treatment(s).1

The treatment outlined above was cumbersome and took about 6 hours to complete. Therefore, an approach utilizing an afferent/efferent circuit was pursued to improve the efficiency of the treatment and this basic technique is still the basis of modern RRT. The device described below maintains the advantages but eliminates the cumbersome features of the initial batch concept by utilizing modern pump, scale, and filter technology.

Description

In order to operate the device, an intravascular catheter that is patent and can reliably withdraw up to 300 ml of blood is all that is required. The single lumen alternating micro-batch (SLAMB) technique utilizes a small single lumen to draw a ‘micro’ batch of blood into a single reservoir. (Figure 2) If the patient is not already anticoagulated, a small amount of anticoagulant (e.g. heparin, citrate) is added to the reservoir first. A small batch of blood ranging from 20 to 300 cc of blood is added to the reservoir. Once the blood is in the reservoir,
the blood is dialyzed and/or hemo-filtered at a high blood flow rate and a high dialysate flow rate for 1-3 minutes. The blood is recirculated back into the reservoir after it is dialyzed so the same blood can be reprocessed multiple times thus allowing rapid and high-efficiency clearance of solutes and ultra-filtration as needed. Once the blood is purified, the blood is returned to the patient along with an anticoagulant reversal agent if needed (i.e. protamine, calcium). This procedure is repeated until the desired level of clearance and ultra-filtration are achieved. The time for one full cycle (blood drawn in, hemodialfiltration, blood returned) is dependent on the size of the batch and the vascular access. Assuming a batch of 200 cc and a single lumen of a standard central line, the entire cycle would take 4-7 minutes allowing 8-15 batches per hour.

Results

Schematics and animation of the proposed SLAMB systems are shown in Figures 2,3, S1-S4. Clearance rates and times have been modeled and shown in Table 1 and S1. Table S2 and S3 outline the manual SLAMB dialysate and approximated costs, respectively.

Discussion

A concept known as ‘Single Needle Dialysis’ was proposed by Kopp and colleagues in 1972 and this type of RRT has been utilized since that time with varying degrees of enthusiasm.2, 3 Currently, there are two single-needle devices are available in Europe, the Dialog iQ (Braun) and FMC 5008 (Fresenius), both of which have vastly improved the original concept.4 The Dialog iQ and the FMC 5008 are offer the benefit of a single needle, yet maintain the familiar arterial and venous circuit through which blood is dialyzed and utilize a large gauge needle (14 or 15 gauge) or large-bore central line. The Dialog iQ and FMC 5008 systems can both perform an intermittent therapy albeit with reduced efficiency compared to standard intermittent machines.2, 4 These devices are good options for patients who can only tolerate a single needle, but can have significant recirculation. In addition to the above systems, a device called the Newcastle Infant Dialysis and Ultrafiltration System (NIDUS) has been developed for neonates that utilizes a single lumen system, comprised of two reservoirs made up of two low volumes syringes in order to conduct precise hemofiltration. The NIDUS system is designed specifically for low-weight children.5

The SLAMB-HDF system builds on these initial concepts and is designed for larger patients, a longer duration of therapy, and would be better suited for continuous renal replacement therapy (CRRT), aquapheresis, slow continuous ultrafiltration (SCUF), periodic intermittent renal replacement therapy (PIRRT), nocturnal dialysis, and/or daily home dialysis. There are multiple advantages to the proposed SLAMB-HDF technique over current dual lumen RRT
systems. First, this technique can occur via a small single lumen catheter (i.e. one lumen of a standard triple-lumen central line or a small single needle) potentially easing the burden of vascular access in both acute and chronic patients. Second, since the blood is held in a reservoir and recirculated, this system disentangles the usual need of large vascular access and high blood blow to achieve high middle molecule and protein-bound uremic toxin clearance. Third, since the blood is held in a reservoir this system can also utilized for hemoperfusion, aquapheresis, and other extra-corporeal therapeutics. Fourth, since blood batches are small and anticoagulated, a small hemofilter can be utilized thus decreasing the cost. Fifth, the small batch and small filter can allow for a small device that takes up less space and increases portability. Sixth, the IV access attached to the SLAMB device can also be used to administer regular IV medications while performing RRT - this is possible because the device had 3 cycles: (1) withdraw blood (2) process blood (3) ‘return blood’ phases. (Figures S1-S3) Thus, during the ‘process blood’ and ‘return blood’ phase, a separate IV pump synchronized to the SLAMB device can continue to administer other of IV medications and pause infusion during the ‘withdraw blood’ phase. In essence, a patient with an existing central line can have RRT initiated without the loss of that lumen for giving other medications. Seventh, the absence of a dual-lumen catheter precludes the inefficiencies due to blood recirculation. Lastly, the batch size can be customized for the size and severity of illness of the patient. Theoretically, having smaller amount of blood leave the circulation should decrease the hemodynamic instability often seen when a RRT session is initiated.

However, there are some disadvantages to the proposed system. First, the small batches preclude this device for being used for a standard intermittent RRT session as the time for the push/pull and dialysis/hemofiltration to occur would take too long to generate the requisite clearance over the short period of time (e.g. 3-4 hours). Second, due to the batching systemic anticoagulation or ‘regional’ anticoagulation is required which may be inappropriate in some patients.

**SLAMB-HF for Use in Austere Conditions**

A simpler version of this device that utilizes only hemofiltration is shown in Figure 3. In this system, the blood from the patient is drawn into the reservoir along with a small amount of anticoagulant and hemofiltration fluid (sterile crystalloid or similar hemofiltration fluid). The reservoir is then rapidly hemo-filtered and then the blood is returned to the patient. Because this system does not require high-flow pumps and relies exclusively on hemofiltration, the overall system is small and requires only three small pumps and one gravity scale. (Figure 3) This low-power system can run on a battery and its capacity to work with a small single lumen catheter makes it appealing in places where full nephrology services are not available. The
overall cost for this simple minimally invasive system would be less than 1,000 dollars per machine and can utilize known standard technology making maintenance and repair inexpensive and tractable.

A fully manual syringe mode of the SLAMB-HF system is shown in Figure S4. Though this system is labor intensive, it is ‘powered’ manually with two 50 cc syringes, six 3-way stopcocks, one hemofilter, two bags, and IV tubing. This manual version of the SLAMB-HF system does not require any electricity and would have a total cost of less than 25 dollars per kit. While not ideal, a combination of 1-liter D5/NS and 4 liters Hartmann’s solution (i.e. lactated ringers) make an adequate hemofiltration solution to manage uremia, acidemia, and hyperkalemia (Table S2). Since these sterile IV fluids are inexpensive and widely available a simple manual SLAMB-HF machine coupled with these fluids could allow for adequate RRT for patients with AKI who are likely to recover renal function (i.e. rhabdomyolysis). The manual SLAMB would require training in order to be implemented properly, but the technical operation is simple and could be taught to a combat medic, nurse, or other skilled healthcare professional thus expanding the availability of RRT. An example where this might be useful is in the immediate aftermath of an earthquake. Many earthquake survivors suffer crush injury an associated rhabdomyolysis with severe AKI. The provision of RRT could prove lifesaving in many of these patients. An inexpensive RRT system that can be deployed with low-cost IV fluids and does not require power may be advantageous. In addition, the placement of a peritoneal catheter or a double-lumen catheter can be challenging in austere environments as both require technical expertise. Since the SLAMB systems require more modest vascular access, RRT may be more feasible and safer with this system in an austere environment. The ISN has initiated the 0by25 program and if the manual SLAMB-HF system is developed and deployed, it may improve the availability of RRT for patients with AKI and mitigate otherwise preventable deaths.6

Dose, Intravenous Access, and Anticoagulation Considerations

In general, the cycle time and therefore total dose of RRT requires an adequate intravenous access. A standard double-lumen dialysis catheter of 11 Fr (each lumen of 5-5.5 Fr) can run a Qb of 200-300 ml/min. Thus, a single lumen catheter of at least 5 Fr can easily allow batches of 200-250 ml to be drawn into the SLAMB in 1 minute and returned in 1 minute. Single pass urea clearance in hemodialysis ranges between 85-90%, thus a batch of 200-250 ml can then be (re)cycled at 200-400 ml/min within the reservoir for 2-3 minutes to achieve 90-95% clearance.7 Therefore, a conservative estimate of the total cycle time with a single-lumen catheter of Fr is as follows: 5 minutes (1 minute ingress, 2-3 minutes of clearance, 1 minute blood return) which would allow 12-15 cycles per hour. If the urea distribution is assumed to be the same as total body water, the standard CRRT dose 20 ml/kg/hr equates to a Kt/V of 0.8.8 Modeling of
different SLAMB prescriptions are shown in Table 1. In the above example, a 75 kg patient
dosed with a SLAMB prescription of 200cc batch, 5-minute cycle time, 0 ml of ultrafiltrate
would achieve a Kt/V of 0.8 in 14.8 hours. If smaller/longer intravenous access where utilized
thus extending the cycle time, the time to achieve a Kt/V would be extended. In this example, if
the ingress/egress of blood from the device were extended to 9 minutes (3 minutes cycling, 3
minutes for ingress and 3 minutes for egress) a catheter would need to be able to enable a Qb
flow at least 67 ml/min and a Kt/V of 0.8 could be achieved in 24 hours.

Since the SLAMB system utilizes small batches that are resident in a reservoir, some element of
anticoagulation is a prerequisite. However, the amount of anticoagulant (i.e. heparin/sodium
citrate) per ml of blood to enable the batch operation is yet not known. Future research in the
development of this proposed system will need to be done to understand the anticoagulation
dosing parameters.

Conclusion

A SLAMB-HDF platform is a concept that may allow RRT to be conducted with a single and small
vascular access. Systems based on this design are simpler than current RRT systems which
make them less expensive, lighter, and more portable thus increasing the options for patients
who require RRT.

Disclosures
LSC reports submitting patents on the SLAMB design and concept

Funding
None

Acknowledgements
The author would like to thank David Askenazi, Pat Brophy, Stuart Goldstein, Lui Forni, and
Samir Patel for their constructive critiques and advice.

Author Contributions
L Chawla: Conceptualization; Data curation; Supervision; Writing - original draft; Writing -
review and editing
References

Table 1, SLAMB Dosing Models Based on Various Prescriptions

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<tr>
<th>Batch Size (ml)</th>
<th>Total Cycle Time (minutes)</th>
<th>Reservoir Cycle Time (minutes)</th>
<th>Time to Achieve Dose of 20 cc/kg/HR (hours)</th>
<th>IV Access Minimum Flow Rate Requirement (ml/min)</th>
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Legend: The dosing models assumes a 75 kg subject, no ultra-filtration, and that the distribution of urea is the same as the total body water. Dose goal is Kt/V of 0.8 (equivalent to 20 cc/kg/hr for 24 hours). Gray shaded area shows SLAMB prescriptions that would likely be utilized in for critically ill patients. Blue Shaded areas show prescriptions that could be used for home dialysis.
Figure Legends

Figure 1, Picture of a Patient Being Treated with a Kolff Drum Dialyzer

Figure 2, Configuration of the SLAMB-HDF
This configuration can do hemodialysis and hemofiltration alone in addition to hemodiafiltration

Figure 3, Configuration of SLAMB-HF
Simplified SLAMB designed for HF only. This configuration only requires 3 pumps.
SLAMB-HDF System Diagram

- **Hemofiltration Fluid**
- **Dialysate Pump**
- **Effluent Pump**
- **Blood Pump**
- **Gravity Scale**
- **Dialyzer**
- **Dialysate Supply**
- **Blood/Fluid Pump**
- **Anticoagulant**
- **Anticoagulant reversal agent**
- **Air Detector**
- **Flow Valve**
- **Pressure Gauge**
- **0.2 micron filter**
- **Heater**
- **Blood Pump**
- **Blood Leak Detector**
- **Effluent Pump**