Extracorporeal Blood Pathogen Removal with the Seraph 100

ExThera Medical

ICD-10-PCS Coordination & Maintenance Committee Meeting

March 19, 2024

Agenda

1. FDA Breakthrough Designations
2. Background
    a) High mortality in septic shock
    b) Major challenges in the treatment of sepsis
    c) Prevalence of antimicrobial resistance
3. Technology
    a) Natural affinity of pathogens for heparin
    b) Biomimetic action of the Seraph 100 filter
4. Procedure Description
5. Dosage and Documentation

The Seraph-100 Extracorporeal Pathogen Removal Filter

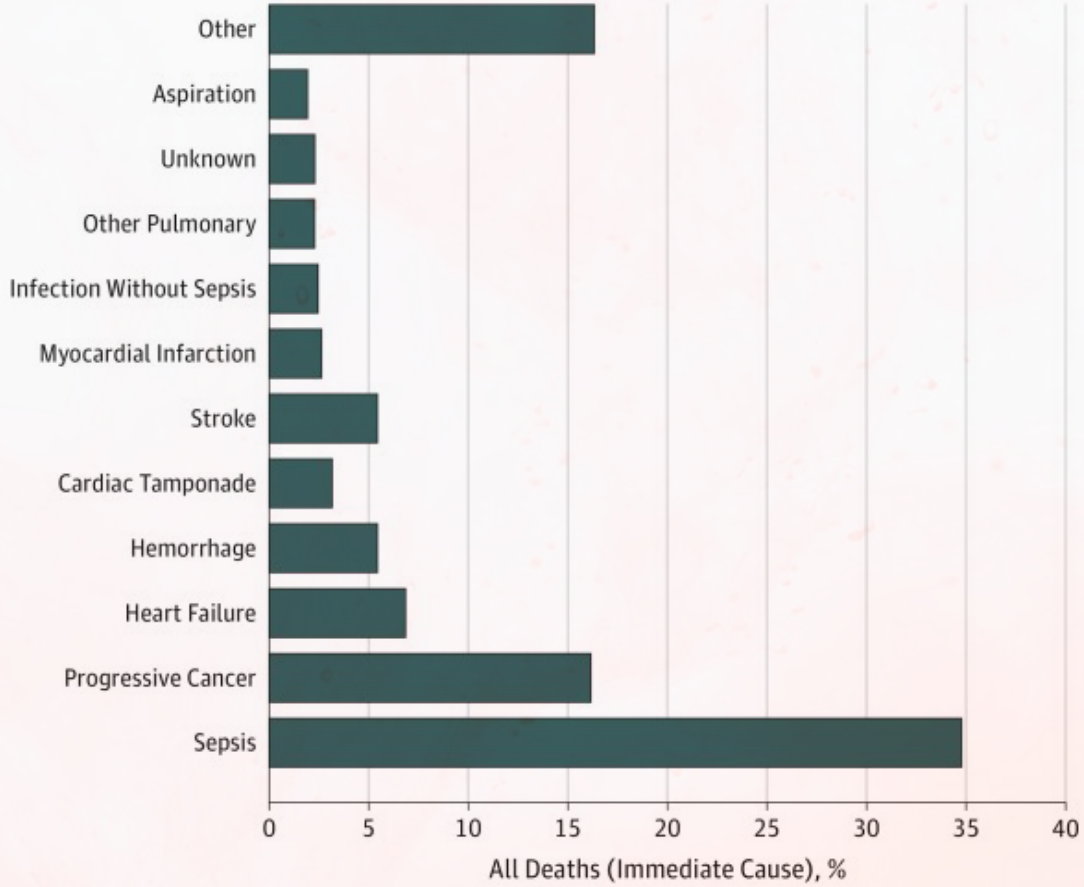
- Multiple FDA Breakthrough Designations
  - For patients with COVID-19 and moderate to severe acute respiratory distress syndrome (Q230839/S001)
  - Adjunctive treatment of patients with bacteremia in addition to antibiotics (Q171099)
- FDA Emergency Use Authorization: Over 2,500 Seraphs were used under the FDA's EUA (200165)

Sepsis is the leading cause of death in the US

Rhee C, Jones TM, Hamad Y, Klompas M, et al. for the CDC Prevention Epicenters Program

Brigham and Women's Hospital, Boston, MA
Harvard Medical School, Boston, MA
Duke University School of Medicine, Durham, NC

JAMA Network Open (2018)



Obtaining source control is the overarching principle for the treatment of sepsis

Broad spectrum antibiotics

Removal of infected lines

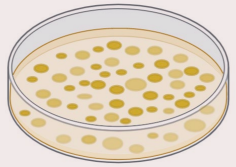
Surgical source control

Removal of pathogens from the blood

The Threat of Antibiotic Resistance is High

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Annually, antibiotic-resistant bacteria and fungi cause an estimated:

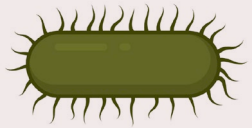


2,868,700
INFECTIONS

35,900 DEATHS

+

Clostridioides difficile is related to antibiotic use and antibiotic resistance:



223,900
CASES

12,800 DEATHS

Centers for Disease Control. Antibiotic Resistance Threats in the United States. 2019. https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

Extracorporeal Pathogen Removal procedure allows for early intervention before multi-system organ failure occurs

Extracorporeal Pathogen Removal Procedure

SERAPH® 100
MICROBIND AFFINITY BLOOD FILTER

Infection → Sepsis/ COVID-19 → Septic Shock Severe COVID-19 → Multi-System Organ Failure → Death

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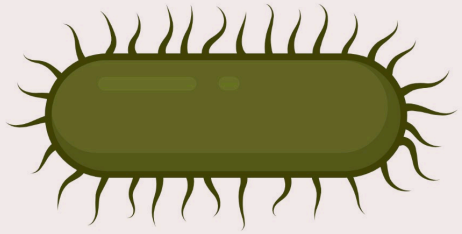
Intended Population for Extracorporeal Pathogen Removal Procedure

Extracorporeal Pathogen Removal Procedure

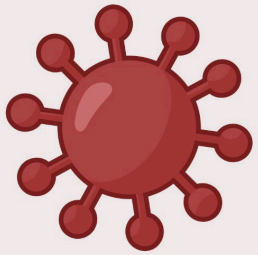
- **Diagnoses to address:** Severe sepsis (R65.2, R65.20) and septic shock (R65.21), ARDS (J80), Acute Respiratory Failure (J96.01)
- **Typical care setting:** Hospitalized ICU patients
- **Coder identification for performance of this procedure:** Procedure note entitled “Extracorporeal Pathogen Removal Procedure”

Seraph® 100 Microbind® Affinity Blood Filter

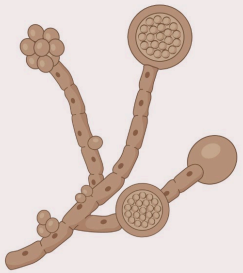
Broad Pathogen Binding Capacity



BACTERIA



VIRUSES



FUNGI

- Single use, disposable filter
- 3x9 inches in size
- 160 mL priming volume
- 40m^2 surface area
- Contains 0.3 mm heparin-endpoint attached beads

1. FDA Emergency Use Authorization: EUA200165 Instructions For Use (IFU) CP021 Rev A
2. Kielstein et al, Hemofiltration with Seraph 100® Microbind Affinity filter decreases SARS-CoV-2 nucleocapsid protein in critically ill…, Critical Care 25.1(2021):1-48.
3. Schmidt & Eden et al, In vitro elimination of anti-infective drugs by the Seraph 100 Microbind affinity blood filter, CKJ, 2020, vol 13, no. 3, 421-424
4. Chitty et al, A Multicenter Evaluation of Blood Purification with Seraph 100 Microbind Affinity Blood Filter for the Treatment of Severe COVID-19: A Preliminary Report, (2021)
5. Seffer et al, Heparin 2.0: A New Approach to the Infection Crisis, Bld Purification (2020); Jul 2, 1-7

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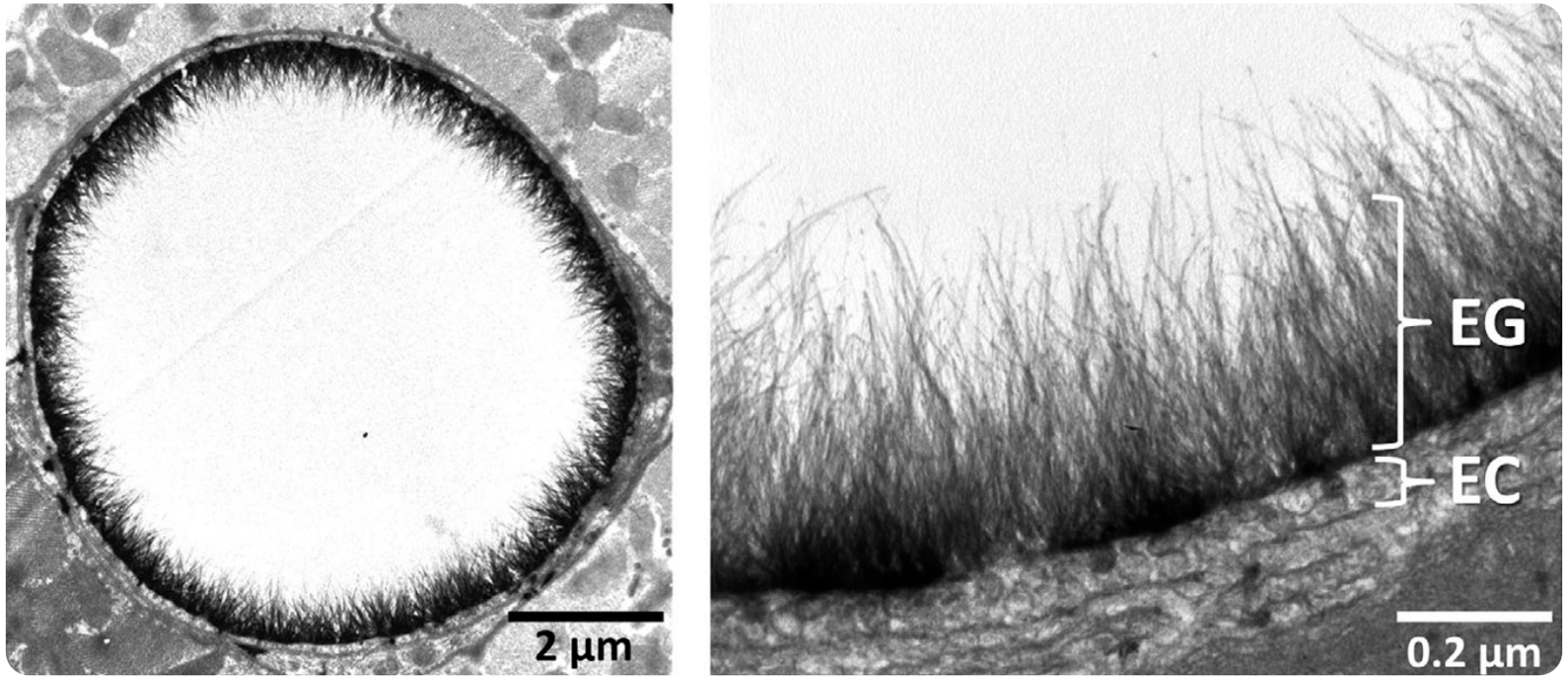
MICROBIND AFFINITY BLOOD FILTER

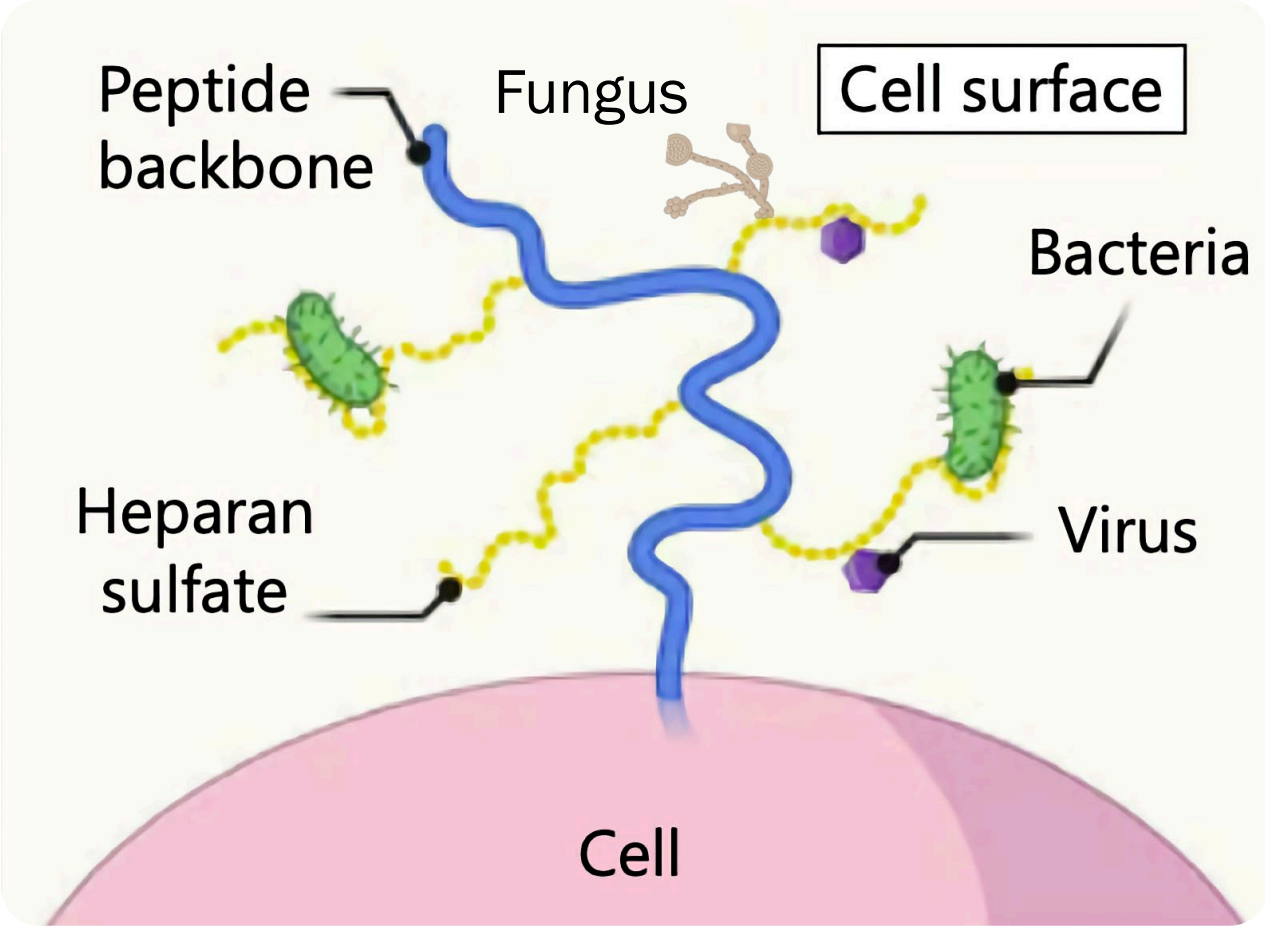
Mechanism of Action: The Endothelial Glycocalyx



- A matrix lining the vascular endothelium, regulates vascular permeability
- Pathogens bind to *heparan sulfate* proteoglycans which facilitates initial pathogen attachment and promotes infection

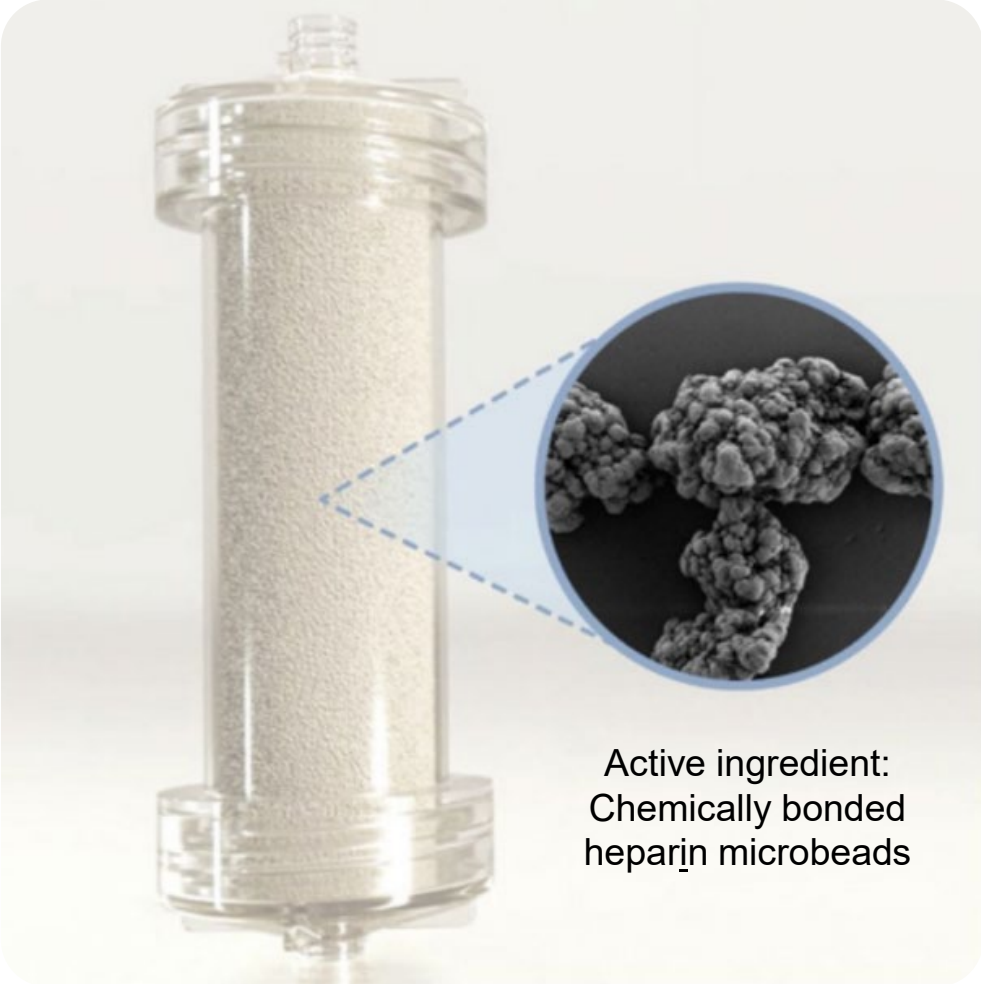
Biddle C. Like a slippery fish, a little slime is a good thing: the glycocalyx revealed. AANA J. 2013 Dec;81(6):473-80. PMID: 24597010
Bartlett et. Al., Heparan Sulfate Proteoglycans in Infection, in: Pavao M. (eds) Glycans in Diseases and Therapeutics. Biology of Extracellular Matrix. Springer, 2011

Pathogens have a natural affinity to heparan sulfate on the lining of blood vessels/endothelium in our body

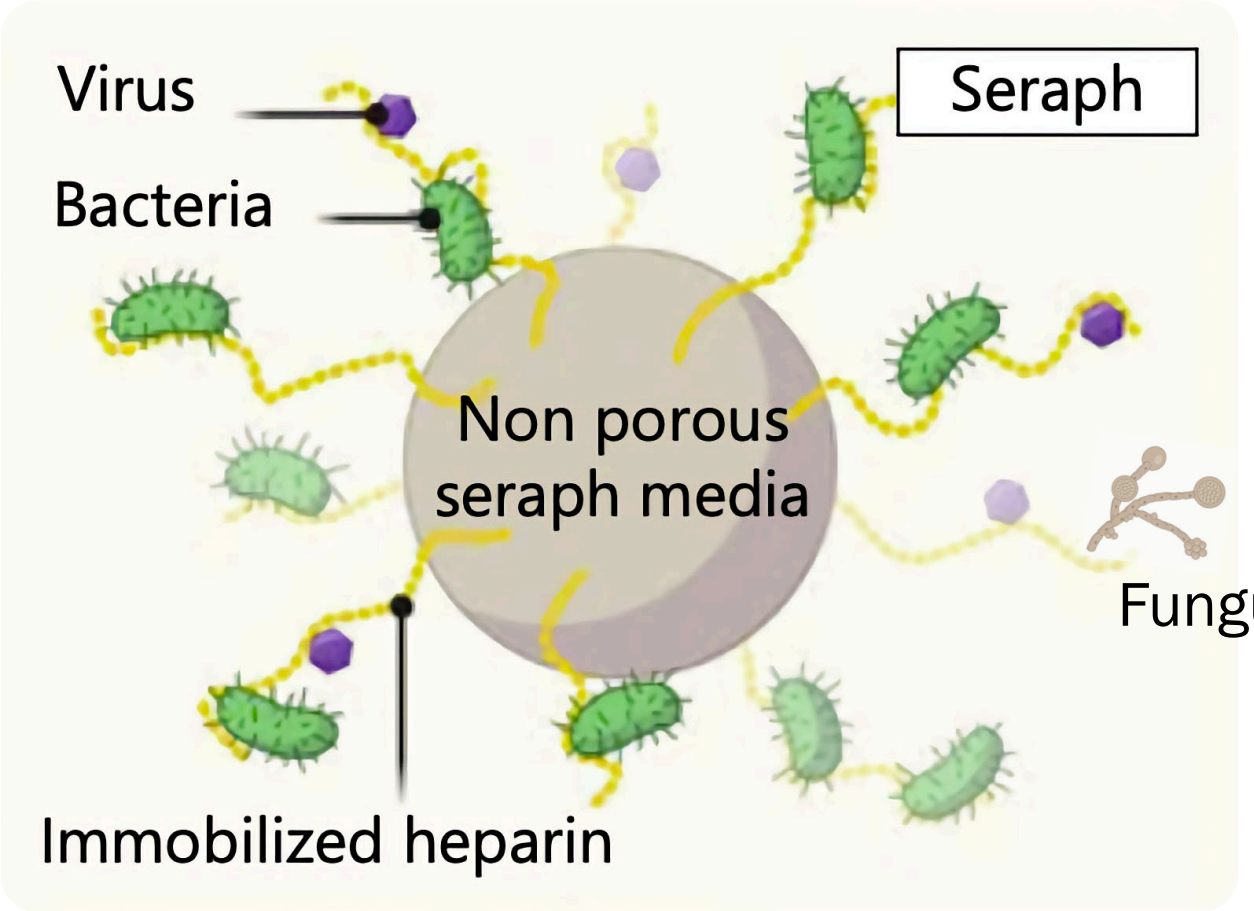


Adapted from Seffer et al, Heparin 2.0: A New Approach to the Infection Crisis, Bld Purification (2020); Jul 2, 1-7

Biomimetic action of the Seraph 100's heparin beads enables extracorporeal removal of pathogens from the circulation



Active ingredient:
Chemically bonded
heparin microbeads



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Adapted from Seffer et al, Heparin 2.0: A New Approach to the Infection Crisis, Bld Purification (2020); Jul 2, 1-7

SERAPH 100
MICROBIND AFFINITY BLOOD FILTER

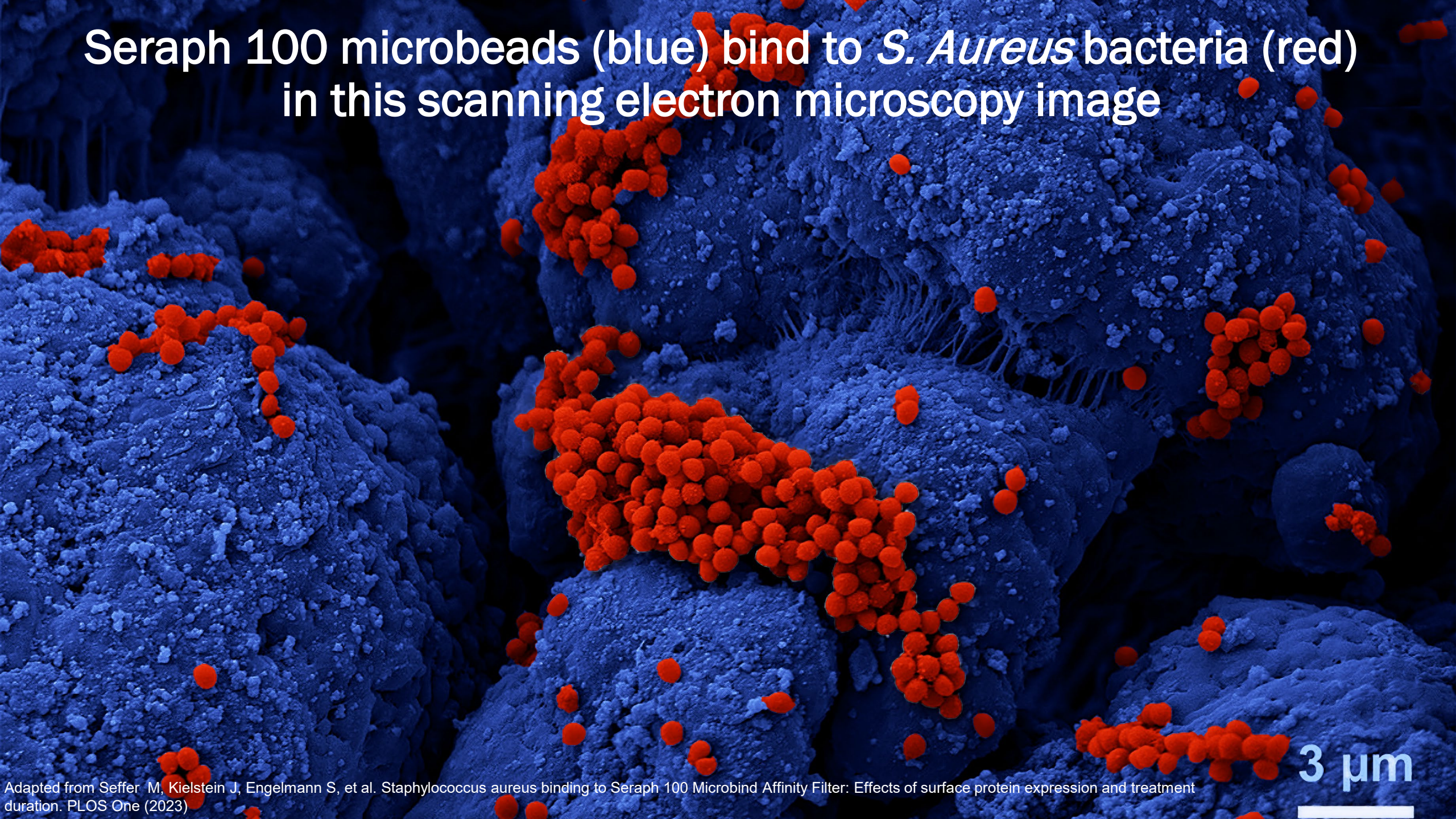
Seraph 100 Adsorbs Across a Broad Therapeutic Spectrum

In vitro Bacteria Binding (Drug-Resistant)	Calculated Maximum Reduction in 4 hr. @ 300 mL/min
K. *pneumoniae* (CRE)	>99.9 %
E. *coli*	>99.9 %
E. *coli* (CRE)	>99.9 %
E. *faecalis*	>99.9 %
MRSA	>99.9 %
E. *faecalis* (VRE)	>99.9 %
P. *aeruginosa*	>99.9 %
S. *pyogenes*	>99.9 %
S. *marcescens*	>99.9 %
S. *aureus*	>99.9 %
Methicillin-Resistant S. *epidermidis*	>99.9 %
S. *epidermidis*	>99.9 %
E. *faecium*	>99.9 %
S. *pneumoniae*	>99.9 %
K. *pneumoniae*	99.70%

In vitro Bacteria, virus, toxin, and DAMP Binding	Calculated Maximum Reduction in 4 hr. @ 300 mL/min
A. *baumannii*	>99.9 %
HSV-1 and HSV-2	>99.7 %
Ebola	>99.7 %
Zika	>99.7 %
Adenovirus	>99.7 %
CMV	>99.7 %
SARS-CoV-2	>99.7 %
C. *albicans*	>99.7 %
S. *Aureus* α-*hemolysin*	>99.7 %
B. *anthracis*	>99.7 %
Protective Antigens	>99.7 %
Heparin-Binding Protein	>99.7 %
Histone H4	>99.7 %

Seffer et al, Heparin 2.0: A New Approach to the Infection Crisis, Bld Purification (2020); Jul 2, 1-7

Seraph 100 microbeads (blue) bind to *S. Aureus* bacteria (red) in this scanning electron microscopy image



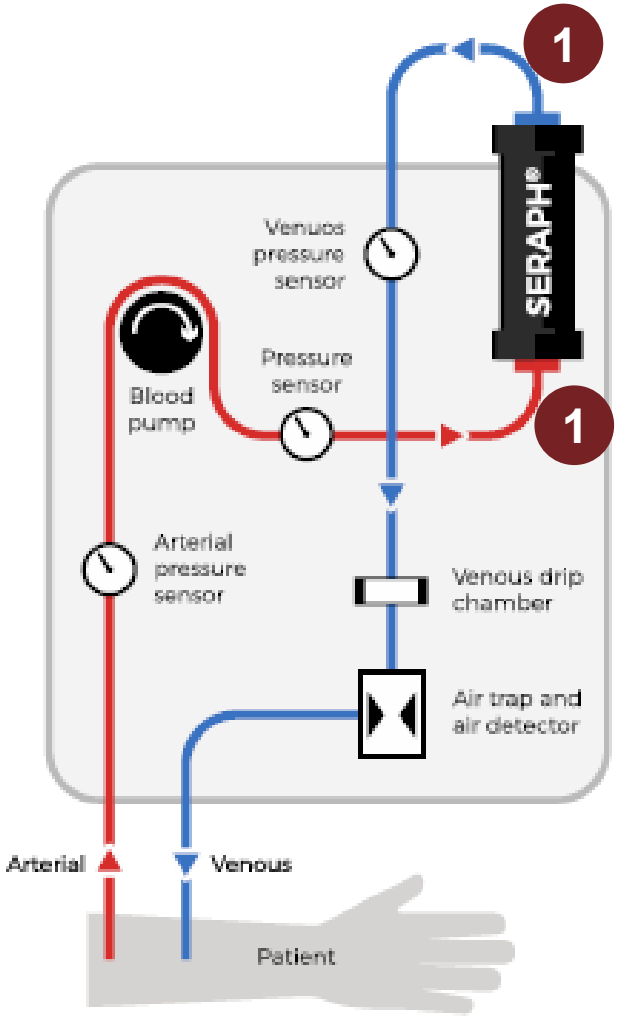
Adapted from Seffer M, Kielstein J, Engelmann S, et al. Staphylococcus aureus binding to Seraph 100 Microbind Affinity Filter: Effects of surface protein expression and treatment duration. PLOS One (2023)

Extracorporeal Pathogen Removal Procedural Steps (1 & 2)

Step 1: Connection of both ports of the Seraph 100 to a blood pump

Step 2: Priming the system to remove all air from the Seraph and blood pump lines

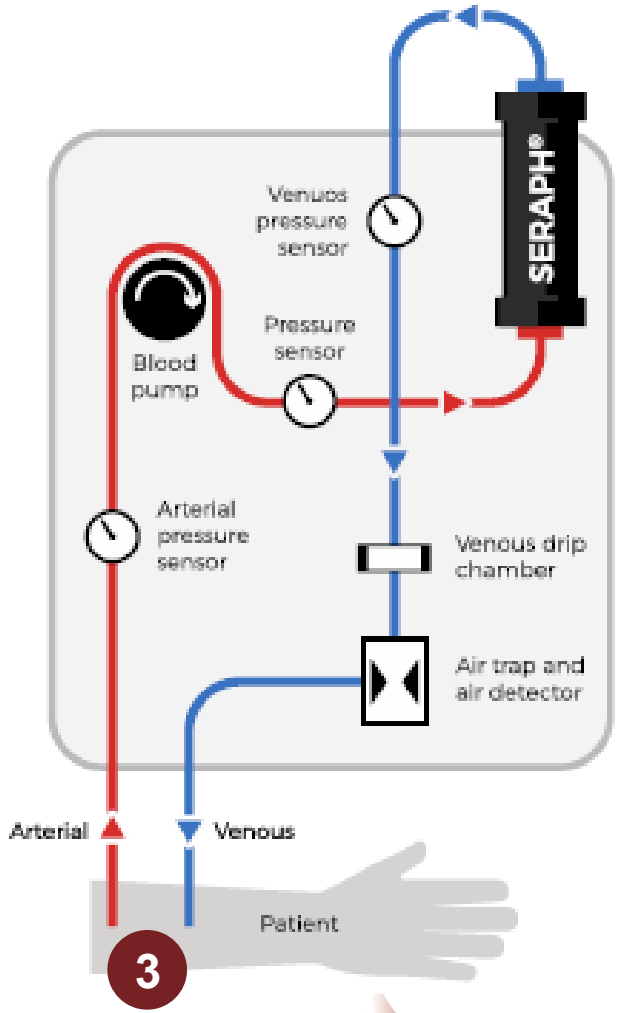
Description: The Extracorporeal Pathogen Removal procedure can be initiated by attaching the inflow port of the Seraph 100 to the arterial limb of a blood pump capable of delivering a blood flow rate between 50-450 mL/min. The outflow port of the Seraph 100 is then connected to the venous limb of the blood pump, and the entire system is primed with normal saline to remove all of the air from the tubing.



Extracorporeal Pathogen Removal Procedural Steps (3)

Step 3: Connection of the arterial/venous lines of the blood pump system to the arterial/venous lines of a large bore access catheter

Description: Once the system is primed, the arterial line of the blood pump is connected to the arterial end of a large bore access catheter, and the venous line of the blood pump is connected to the venous end of the same access catheter.

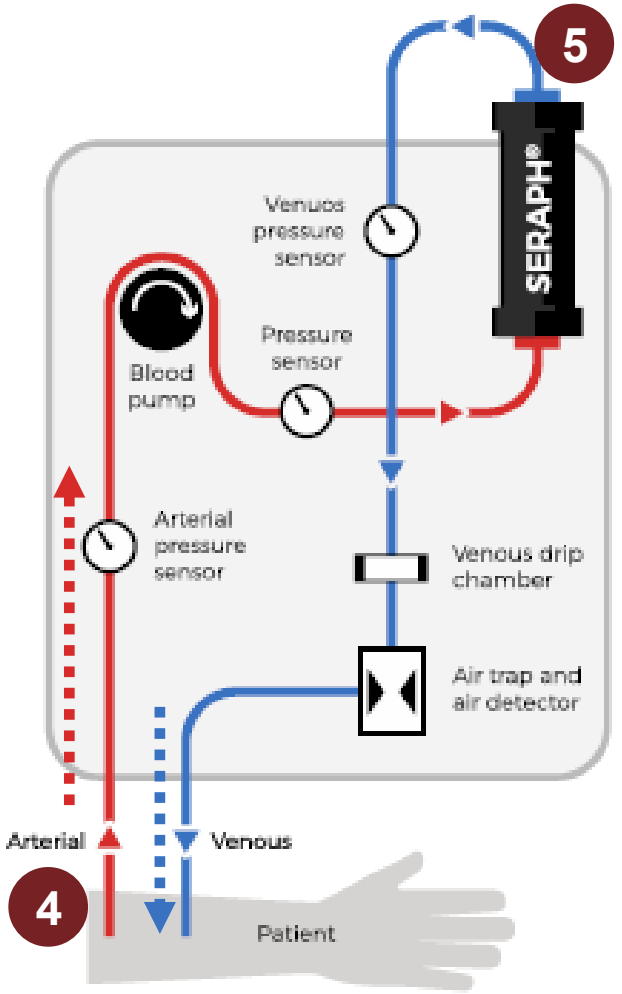


Extracorporeal Pathogen Removal Procedural Steps (4 & 5)

Step 4: Initiation of treatment by starting extracorporeal blood flow through a blood pump

Step 5: Exposure of the patient's blood to the Seraph 100 adsorption media

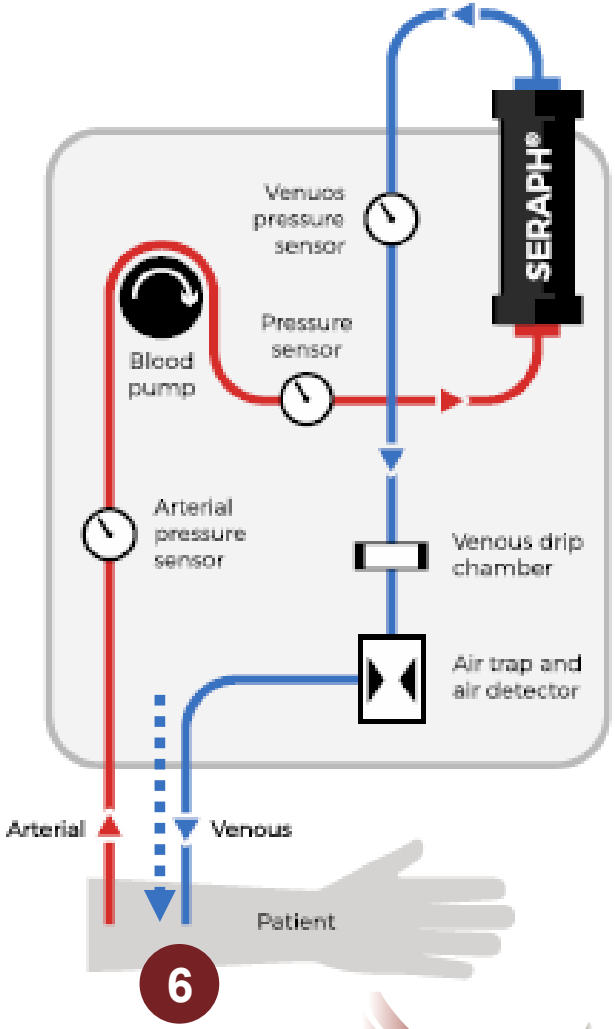
Description: Treatment is initiated by starting the extracorporeal pump and slowly increasing the blood pump speed to achieve a blood flow rate of 50-450 mL/min. The increase in flow must be performed slowly and in conjunction with intensive monitoring of the patient's arterial blood pressure to make sure that hypotension, shock, and cardiovascular collapse do not occur when initially starting this extracorporeal procedure. Furthermore, the arterial and venous pressures on the blood pump must be monitored carefully to detect and correct for any flow restrictions and inappropriate pressure readings in the circuit. Once a steady state blood flow has been reached, the treatment time may be extended for up to 24 hours in order to optimize sufficient exposure of the patient's blood to the Seraph 100 adsorption media.



Extracorporeal Pathogen Removal Procedural Steps (6)

Step 6: Termination of treatment by returning extracorporeal blood flow back to the patient when the procedure is complete.

Description: When the treatment is complete, the blood that is in the extracorporeal circuit must be returned back to the patient in order to prevent hypotension and unnecessary wastage of the patient's blood from occurring. A blood rinseback procedure is performed, whereby the pump is first briefly paused. The arterial limb of the circuit is disconnected from the patient's access catheter and connected to a bag of normal saline. This therefore prevents any additional blood from entering the extracorporeal circuit. The blood pump is then resumed at a low flow rate of ~50mL/min and the remaining blood in the extracorporeal circuit is then rinsed back to the patient through the venous limb of the circuit. When the venous limb is clear of the patient's blood, the pump is stopped, and the venous limb of the circuit is disconnected from the patient, thus terminating the Extracorporeal Pathogen Removal procedure.



Dosage and Documentation

- The administration of the Extracorporeal Pathogen Removal procedure will be documented in the medical record by recording the hourly blood flow rate through the Seraph filter. This will allow the clinician to calculate the total volume of blood filtered by the device, which is how the Extracorporeal Pathogen Removal procedure is dosed.
- To optimize sufficient exposure of the patient's blood to the Seraph 100 adsorption media, please refer to table below for recommended procedure duration according to the blood flow rate:

Blood Flow Rate	Procedure Duration
450 mL/min	3 hours
400 mL/min	4 hours
350 mL/min	5 hours
300 mL/min	6 hours
250 mL/min	7 hours
200 mL/min	8 hours
50-100 mL/min	10 to < 24 hours