Supplemental Online Content

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Supplement 3. Study manual

This supplemental material has been provided by the authors to give readers additional information about their work.

Study Manual for the REST trial

pRotective vEntilation with veno-venouS lung assisT in respiratory failure

Table of Contents

Abbreviations

AC:	Assist Control
APRV:	Airway Pressure Release Ventilation
APTTr:	Activated Partial Thromboplastin Time Ratio
ARDS:	Acute Respiratory Distress Syndrome
CO_2:	Carbon Dioxide
CRRT:	Continuous Renal Replacement Therapy
$ECCO_2R$:	Extracorporeal CO_2 Removal
ECLS:	Extracorporeal Life Support
ECMO:	Extracorporeal Membrane Oxygenation
HFOV:	High Frequency Oscillatory Ventilation
IBW:	Ideal Body Weight
NMB:	Neuromuscular Blockers
PPlat:	Inspiratory Plateau Pressure
PBW:	Predicted Body Weight
PC:	Pressure Control
PEEP:	Positive End Inspiratory Pressure
RR:	Respiratory Rate
SIMV:	Synchronised Intermittent Mandatory Ventilation
TEG:	Thromboelastography
SVC:	Superior Vena Cava
UPS:	Uninterruptible Power Supply
VC:	Volume Control
Vt:	Tidal Volume

1. Introduction

This document is intended to provide an overview of providing veno-venous extracorporeal CO_2 removal ($ECCO_2R$) therapy and ventilation management as part of the REST Trial. **The eligibility criteria for the REST trial are described in the study protocol.**

$ECCO_2R$ is an unproven therapy in hypoxaemic respiratory failure and its use is discouraged as a salvage therapy for standard care. The crossover and use of the device in the non-interventional arm will be considered a protocol violation. Persistent violations may result in termination of the trial at that site.

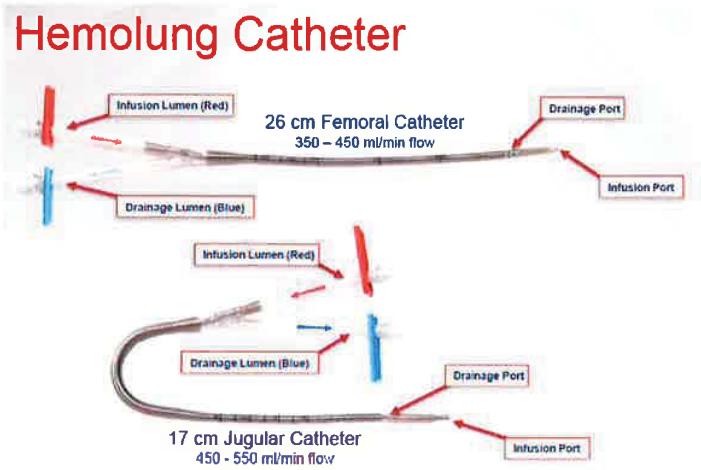
2. Equipment for $ECCO_2R$ system

The $ECCO_2R$ system used in the REST trial is the Alung Hemolung-RAS system. This is a relatively low-flow CO_2 removal system operating at blood flow rates of approximately 350-550 mL/min. The components of this system are the catheter, the cartridge and the controller:

2.1 Catheter

The Hemolung catheter is a 15.5F reinforced, dual lumen venous catheter, which can be inserted into the right internal jugular or any femoral vein. It is acceptable to rewire a pre-placed central line as an insertion technique if the team are confident it is correctly sited and can be undertaken aseptically. Two catheters of different shape, dimension and flow rate are available, depending on the approach used (Figure 1.). A curved 17cm catheter is used for right internal jugular approach and a longer 26cm straight catheter is used for femoral vein approach. **It is vital that the correct catheter be used for each approach.**

Figure 1. Hemolung Catheter

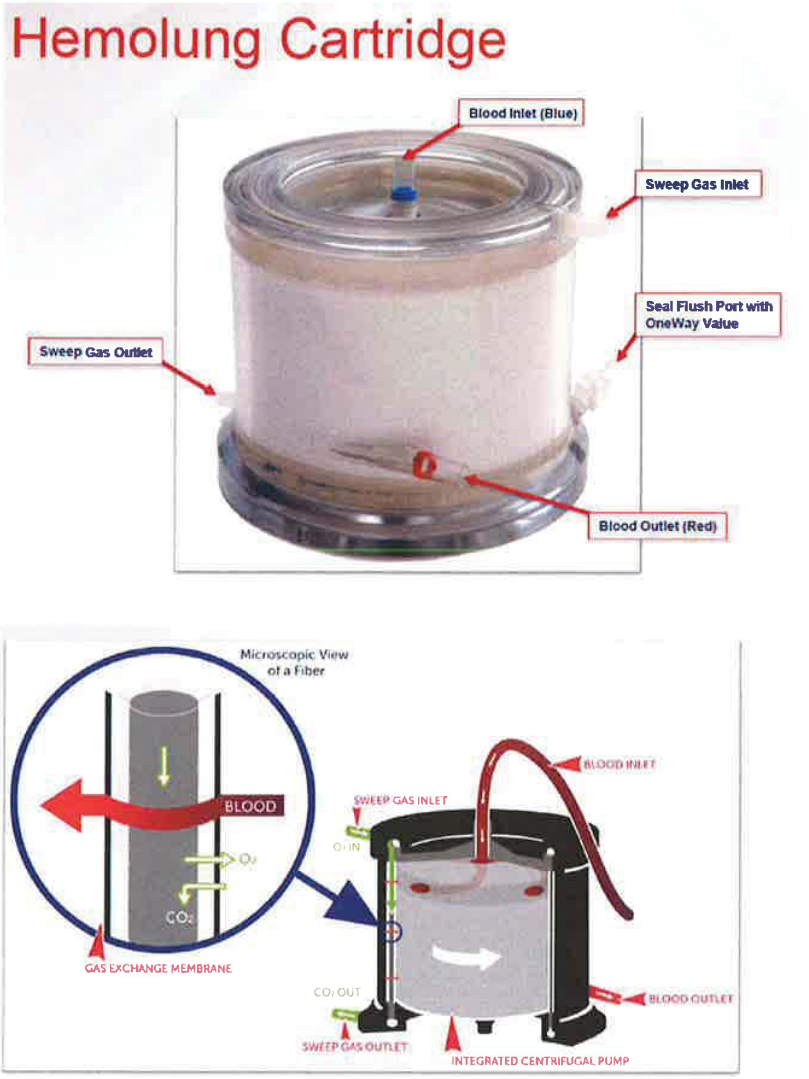


After cannulation, the patient is connected to the Hemolung circuit, which incorporates the circuit tubing, the Hemolung cartridge and a pump, operated by the Hemolung controller.

2.2 Cartridge

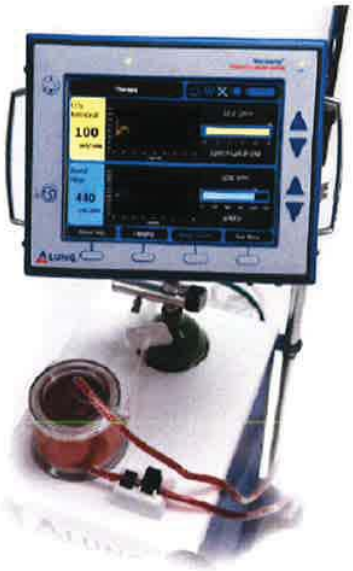
The Hemolung cartridge incorporates a gas exchange membrane with a centrifugal pump (Figure 2). Blood is pumped from the patient through the cartridge and "sweep gas" is attached to the gas exchange membrane with tubing at a gas flow rate of 0-10 L/min. CO_2 removal is achieved by running "sweep gas" (which for the purposes of the trial will be room air) through the centre of the hollow fibres in the cartridge while blood is circulated around the outside of the fibres (Figure 2). The set "Sweep Gas Flow Rate" determines the sweep gas flow and the "Blood Flow Rate" is determined by the pump speed i.e. revolutions per minute (RPM) of the centrifugal pump. The patients blood enters the cartridge at the top and leaves from the bottom side of the cartridge.

Figure 2 The Hemolung Cartridge



2.3 The Hemolung Controller

Figure 4 The Hemolung Controller



The Hemolung controller controls the pump speed (RPM) and sweep gas flow while providing real-time monitoring of CO_2 removal and blood flow, bubble detection and other operating alarms.

An infusion pump controls a continuous saline infusion to prevent the pump bearings from becoming damaged.

2.4 Theory of Operation

Venous blood is pumped via the catheter through the cartridge at a rate of 350-550 mL/minute and sweep gas is connected. CO_2 removal is determined primarily by the sweep gas flow rate but can also be affected by the blood flow rate and the patients venous CO_2.

Figure 5. Theory of Operation

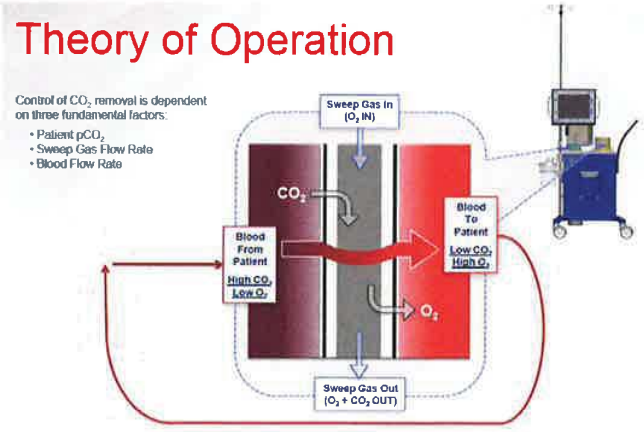


Figure 6. Bubble detector and flow sensor

3. Set-up of the circuit

If randomised to $ECCO_2R$, initial ventilator settings may be any mode not excluded in the study protocol. Initial recommended ventilator settings while you apply $ECCO_2R$ are as according to the ARDSNetwork ARMA trial. Target tidal volumes will be ≤ 6 mL/kg PBW, plateau pressure ≤ 30cmH_2O with PEEP level determined from the PEEP/FiO_2 table from the ARMA study (Appendix B and C). $ECCO_2R$ should ideally be initiated within 8 hours from randomisation. It is advisable to use neuromuscular blocking drugs if not already doing so to allow insertion of catheter, application of $ECCO_2R$ and initiation of lower tidal volume ventilation.

Priming the Hemolung Circuit

Before cannulation, the Hemolung should be primed for use.

Personnel should refer to Chapter 4 of the Hemolung RAS Training Workbook for priming and setup and have watched the Hemolung training videos "Setup and Priming" and "Starting and Managing Therapy".

Prime the Hemolung circuit in accordance with manufacturers instructions. A laminated quick reference guide will be attached to the console.

Important points to remember when priming the circuit:

- The priming solution should be heparinised saline (1u heparin / mL 0.9%NaCl)
- When replacing the soda lime column, make sure to reuse the endcaps.
- The recirculation bag must hang below the heparinised saline bag.
- Maintain sterility of the blood tubing with the sheath until catheter connection.
- Apply a small amount of petroleum jelly to the part of the tubing that sits in the blood flow sensor. **DO NOT** place petroleum jelly on the bubble detector section (Figure 6).
- Make sure connections are secure and that there are no leaks or air in the circuit. If air bubbles are found, guide them into the recirculation bag.
- Select **ROOM AIR** as the sweep gas source.

4. Insertion of Catheter

4.1 Personnel

An appropriately trained clinician (normally a consultant or senior ICU trainee) with the required competencies will insert the Hemolung catheter and this should be performed as a two-person procedure. Both clinicians must be familiar with the components of the Hemolung Catheter Insertion and Hemolung Setup. Personnel should refer to Chapter 4 Part 2 of the Hemolung RAS Training Workbook for catheter insertion and have watched the Hemolung training video "Hemolung Catheter Insertion".

The Hemolung cartridge and circuit must be set up and primed before catheter insertion to ensure rapid connection and avoid potential thrombus formation. Insert the Hemolung catheter in accordance with manufacturers instructions. A laminated quick reference guide will be attached to the console.

4.2 Procedure

It is recommended that all equipment for cannulation is stored in preparation for insertion in a designated box, tray or trolley.

It is **mandatory that ultrasound** is used to guide insertion of the catheter. These patients will normally be fully sedated and often receiving neuromuscular blocking drugs.

Patient preparation

- Site for catheter insertion chosen (Right Internal Jugular or Femoral Veins)
- Preliminary ultrasound scan for vessel patency and anatomical difficulty
- Excessive hair removal
- Selection of appropriate Hemolung catheter (femoral or jugular)
- Cardiovascular and respiratory stability with intra-arterial BP monitoring

Cannulation procedure

- Full asepsis i.e. gloves, gown, mask, hat, large bed drape with skin decontamination as per local policy. If using alcohol based solutions allow to fully dry and avoid contact with the circuit as it can degrade the circuit.
- Real-time ultrasound guided Seldinger technique
- Approach vessel at shallow angle to ensure straight path for the guidewire
- Once the guidewire is in place its position should be confirmed with ultrasound
- **Give 80 units/kg of intravenous heparin bolus (rounded to nearest 50 units) after guidewire insertion BEFORE dilatation.**
- Dilate skin and soft tissues with tapered dilator. **Shallow angle** will minimise risk of guidewire kinking or vessel trauma. Remove dilator and leave guidewire in place.
- Insert catheter and aspirate both lumens, demonstrating the free flow of blood
- Measure venous blood gas and ensure both lumens are flushed with 20mL heparinised saline (10 units/mL) after sampling ("rapid flush" technique).
- Chest X-ray is not necessary before $ECCO_2R$ initiation but can be considered if there are concerns regarding catheter position or

complication. Be aware that delays to initiating therapy may be associated with line thrombus.

- After catheter placement, withdraw the guidewire from the stylet. Remove the stylet from the catheter by unscrewing it from the priming adaptor and withdrawing. Close both slide clamps.
- Check catheter patency and remove any air by releasing each slide clamp in turn and aspirating and flushing. Blood should aspirate easily through both lumens. If either lumen exhibits excessive resistance to blood aspiration, rotate or reposition the catheter to obtain adequate blood flow. Each lumen should be flushed with 20 mL of heparinised saline before re-clamping.

5. Connecting tubing and Securing Catheter

5.1 Connecting Tubing

After catheter insertion you are ready to connect the circuit to the patient. Catheter should be connected to the Hemolung circuit and blood flow commenced as quickly as possible following insertion (see below). If a delay occurs in establishing extracorporeal blood flow then the catheter lumens should be flushed continuously to prevent clotting. Personnel should refer to Chapter 4 Part 3 connecting tubing to catheter in the Hemolung Training Workbook and have watched the video "Hemolung Catheter Insertion"

Connect the "TO PATIENT (Red)" Tubing Set to Catheter

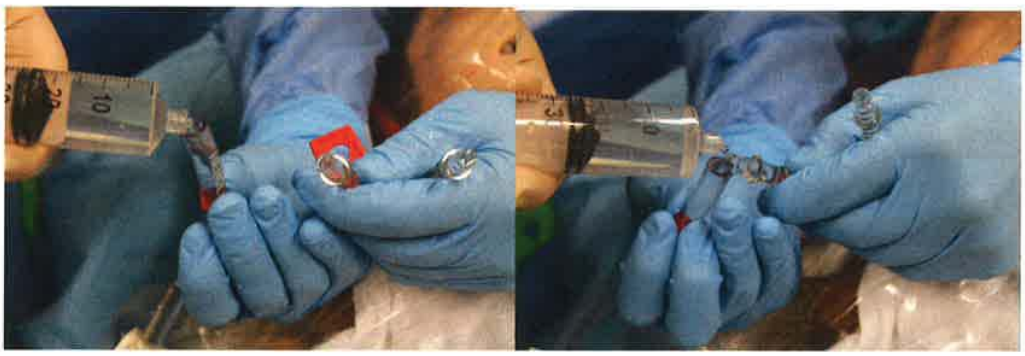
- Disconnect the TO PATIENT (RED) Tubing Set from the recirculation bag.
- Using a "wet-to-wet" technique (Figure 8), connect the tube to the red connector on the catheter. A wet-to-wet technique is whereby the two tubing ends are joined while a syringe of saline is used continuously to ensure there are no air bubbles present after connection.
- Ensure that the tubing is placed completely over the barb connector for a secure connection.

Connect "FROM PATIENT (Blue)" Tubing Set to Catheter

- Disconnect the FROM PATIENT (BLUE) Tubing Set from the Y-connector.
- Using a wet-to-wet technique, connect the tube to the blue connector on the Catheter.
- Ensure that the tubing is placed completely over the barb connector for a secure connection.

The plastic sheaths protecting the length of the blood tubes can be removed after successful connection

Figure 8. "Wet Join" between Hemolung catheter and circuit



5.2 Securing Catheter

Catheters are secured as follows:

Femoral

- For femoral catheter: secure cannula firmly with 1.0 silk suture placed on the plastic portion of the catheter. Place the lumens in the "Grip-Lok" device (Figure 9).

Jugular

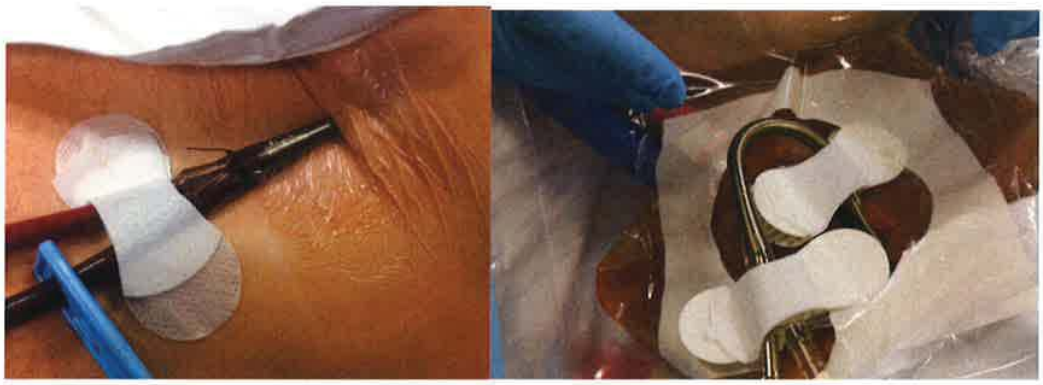
- For the internal jugular catheter, the suture is required at the catheter hub. Place the body and hub of the catheter in the two "Grip-Lok" devices (Figure 10).

General

Ensure that hard plastic components (e.g. clamps) are padded to prevent skin pressure injury.

- Dress according to local policy with semipermeable dressing (Figure 9).

Figure 9. Femoral Hemolung Catheter Secured with Sutures and Grip-Lok



6. Starting $ECCO_2R$ Therapy

After catheter insertion and connecting the tubing you are ready to start the blood pump and commence $ECCO_2R$. Personnel should refer to Chapter 4 Part 4 Starting the blood pump and Chapter 5 Managing therapy and using RAS in the Hemolung Training Workbook. Personnel should also have watched the Hemolung training video "Starting and managing Therapy"

Ensure:

- Check for air in the circuit
- Check for secure connections
- Seal flush is running at 30 mL/hr
- All clamps are open
- Lock the console wheels.

Initiation of $ECCO_2R$ Therapy

After connecting the primed extracorporeal circuit to the catheter, therapy is initiated by:

- Enter the "Main Therapy screen" (Figure 10)
- Turn on the pump by pressing "Start Therapy" function key
- Press and hold the pump start/stop button. This initiates the flow of blood through the extracorporeal circuit and sweep gas to pass through the Cartridge membranes.
- The Hemolung Cartridge will initially operate at the default pump speed (500 RPM) and sweep gas flow rate (1 L/min).
- Visually inspect the system for leaks, air; ensure clamps are released.
- Once established on $ECCO_2R$, pump speed should be slowly increased (over a few minutes if cardiovascular stable) immediately using the lower arrow keys until blood flow plateaus and does not increase with further increases in RPM. (should be in the range of 1100 – 1400 RPM)
- Higher pump speed will not always generate higher blood flow. Catheter can lodge against vessel wall due to negative pressure.
- Blood flow is typically in the range of 350-550 mL/min. Set pump speed to lowest setting (RPM) that achieves maximum blood flow (mL/min)
- To avoid over revving and causing haemolysis be careful not to increase pump speed once blood flow plateaus.
- Wait for 20 minutes with maximum blood flow as a stabilisation period before moving to CO_2 removal and ventilator adjustments detailed in chapter 7.
- An Arterial Blood Gas (ABG) should be taken at this stage.

Figure 10. Initiating Therapy on the Hemolung Console

From the last catheter connection screen, press the Start Therapy Function Key to enter Therapy Mode. You will be prompted with this screen. Press and hold the Pump Start/ Stop Key on the Hemolung Controller to initiate/resume therapy.

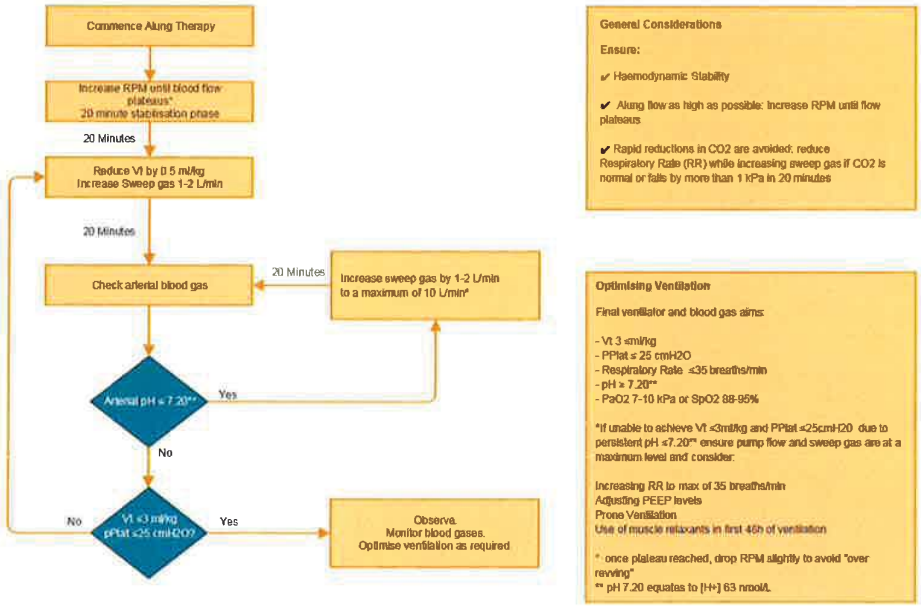
7. Ventilator and $ECCO_2R$ Settings During Trial

Following a 20 minute stabilisation period, tidal volumes should be reduced in tandem with increases in sweep gas flow rate slowly over 2 hours while the patient is carefully monitored. A description of how the ventilator and $ECCO_2R$ settings should be achieved is summarised in Figure 11 on the next page. It may be possible to achieve maximum CO_2 removal and tidal volume reduction over a shorter time period. If pH < 7.20 at any stage then respiratory rate can be increased to a maximum of 35 breaths per minute as tolerated. I:E ratio should remain 1:1-1:2. If the arterial pH is < 7.20 and RR is maximally tolerated up to 35/min then no further tidal volume reductions are recommended. Once ventilation goals are achieved and stabilised on $ECCO_2R$ blood gases should usually be checked every 4-6 hours or following any significant events or change in management.

The aim is to achieve the following goals:

- tidal volume of ≤ 3mL/kg PBW
- Pplat < 25cmH_2O
- Sweep gas 10
- Respiratory Rate < 35 per minute
- pH > 7.20
- PaO_2 7-10 kPa (SpO_2 88-95%)

Figure 11. Adjusting $ECCO_2R$ Settings to Achieve Ventilator Goals



§The timings on this flow chart are as a guide only. Sweep gas flow and tidal volume may be adjusted more rapidly with an aim of 3ml kg^{-1} as the clinical condition of the patient permits.

8. Anticoagulation Management

All patients on $ECCO_2R$ should be systemically anticoagulated with intravenous heparin unless contraindicated (active bleeding, anticipated or recent surgery, thrombocytopenia). An APTTr of 1.5-2.0 will be targeted for the duration of therapy. Heparin infusions can be adjusted according to local policy.

Management of Life Threatening Bleeding

If there is high risk of bleeding (e.g. planned or recent surgery) the following parameters should also be targeted: Platelets >80; Fibrinogen > 2.0.

In the case of life threatening bleeding (either from catheter insertion site or elsewhere), inform responsible consultant and stop heparin. Blood component therapy (Cryoprecipitate, Platelets, fresh frozen plasma) should be given as to achieve the following targets: Platelets >80; Fibrinogen > 2.0, APTTr <1.5, INR <1.5. Tranexamic Acid administration (1g intravenously 6th hourly) should be considered. Source control (surgery, endoscopy, interventional radiology) should be considered as appropriate.

If high risk or active bleeding, consider use of Thrombelastograph (TEG) to guide therapy if available.

The Hemolung can continue to operate without heparin infusion with increased risk of the circuit clotting. Ongoing bleeding may necessitate discontinuation of $ECCO_2R$ therapy.

Heparin-induced thrombocytopaenia and thrombosis (HITT)

An isolated fall in platelets is common and not diagnostic. Advice from haematology is advised. Patients unable to have systemic heparin are excluded from this trial. If any patient develops HITT while in this trial specialist advice should be sought from a hematologist and the study team should be contacted. $ECCO_2R$ therapy should be discontinued.

9. Staffing and Maintenance while on Hemolung

9.1 Medical and Nursing Staff – General Principles

- Patients will receive standard therapy as per local policy while they are in ICU
- All patients in the REST trial must have decisions pertaining to $ECCO_2R$ management undertaken by physicians and nurses who have undertaken appropriate training in the use of the Hemolung system.
- An ICU consultant with appropriate training and experience in $ECCO_2R$ should review patients daily.
- The nursing requirements specific to the patient on $ECCO_2R$ are primarily related to the nursing responsibilities of maintaining a safe environment, continuous monitoring and pressure area care.
- Responsibility of the technical maintenance of the $ECCO_2R$ circuit (including changes to circuit gas/blood flows) lies with appropriately trained medical and nursing staff.
- Patients on $ECCO_2R$ can be rolled and moved for chest x-rays, prone ventilation, procedures and for pressure area assessment. However, a Hemolung trained nurse or physician must be present to ensure that no tension is transmitted to the catheter and that the circuit tubing is not kinked and to designate a staff member to co-ordinate the move. Moves should only be undertaken when staffing levels are appropriate (unless there is an urgent patient need).
- No procedures should be performed on an $ECCO_2R$ patient without the consent of the ICU consultant.
- If a surgical procedure is required while on the Hemolung, the heparin infusion should be discontinued until it can safely be recommenced. It is possible for patients to go to theatre with the Hemolung running but this should be discussed with the local PI, the surgical team and if necessary a member of the study team. In some circumstances it may be more appropriate to discontinue Hemolung therapy prior to surgery. In the event that the Hemolung is discontinued temporarily for a surgical procedure, the device should be reprimed and left in re-circulation mode, and the catheter flushed with heparinised saline and clamped.

For a more detailed account of Nursing Care, see section 12.

9.2 Criteria for Replacement of Hemolung Cartridge

The Hemolung should be discontinued after 7 days. If there is a decision by the treating physician that the Hemolung RAS therapy should last for longer than 7 days, the Cartridge may require replacement and, therefore, must be monitored for signs of reduced performance. This will be outside of the protocol and form part of clinical care. The following criteria are provided for determining the need for cartridge replacement:

1. If rate of CO_2 removal falls below 50 mL/min **AND** cannot be explained by:
   a. Reduced sweep gas flow (< 7 L/min)
   b. Reduction/correction of arterial $PaCO_2$ (Note: magnitude of CO_2 removal is directly proportional to partial pressure of CO_2 in the blood; a hypercapnic patient will have a high rate of CO_2 removal by the Hemolung, but as the Hemolung increases CO_2 ventilation and $PaCO_2$ begins to decrease, so will the rate of Hemolung CO_2 removal. This is expected.)
   c. Acceptable and minor reductions in blood flow which will occur transiently due to patient fluid volume
2. If circuit blood flow falls below 350 mL/min **AND** cannot be revived by:
   a. Inspection of controller RPM setting (should be in the range of 1100 – 1400 RPM);
   b. Inspection of circuit for pinching, bending, or twisting of tubing;
   c. Repositioning of patient;
   d. Minor (< 1 cm) adjustment of catheter position;
   e. Increase in patient fluid volume, if low.
3. If severe hemolysis is indicated by observed hematuria and/or plasma free hemoglobin > 40 mg/dL, **AND** cannot be resolved within 2 hours by:
   a. Identifying and correcting pinching or severe bends in circuit tubing;
   b. Repositioning of patient and/or catheter (< 1 cm);
   c. Alternative sources (e.g. kinked or damaged infusion lines, dialysis catheters/systems);
   d. Cessation or dilution of recently administered RBCs.

10. Weaning $ECCO_2R$

After at least 48 hours of $ECCO_2R$ and lower tidal volume ventilation the patient will be assessed daily to determine whether the following 3 criteria to progress to $ECCO_2R$ weaning have been met:

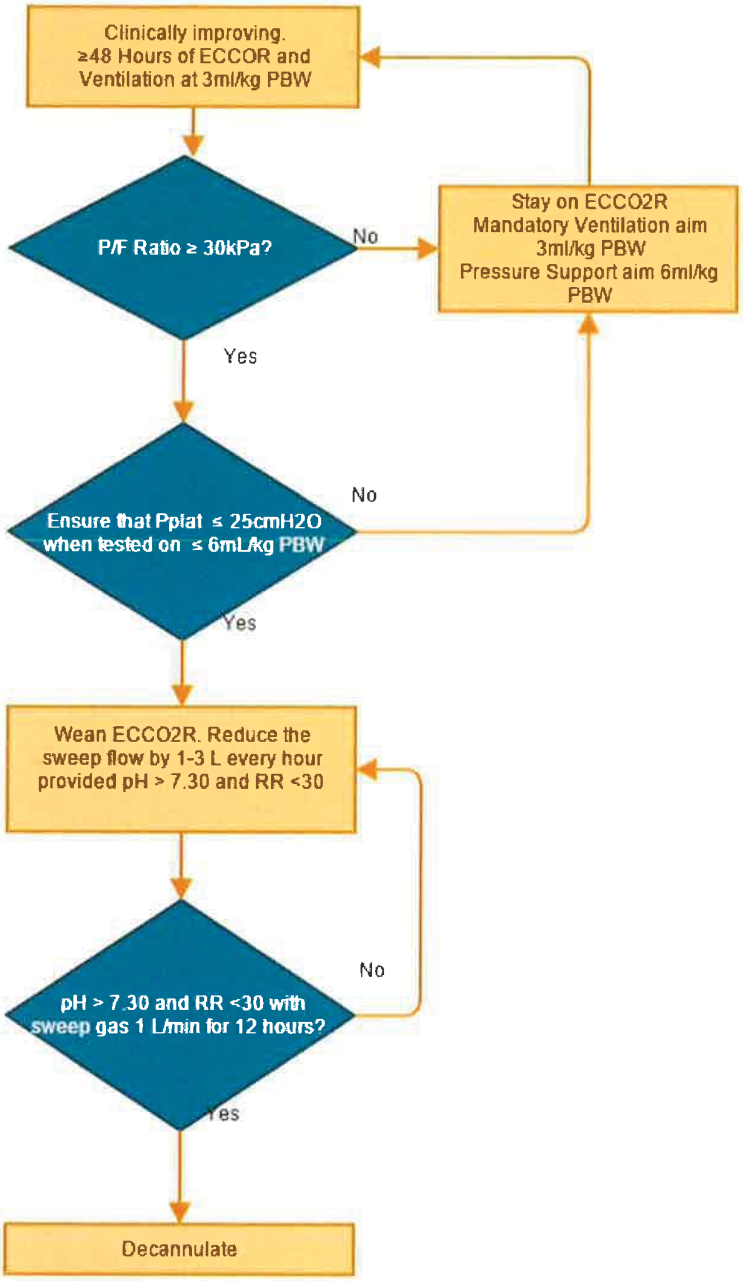
1. Signs of clinical improvement of the underlying condition e.g. an improvement in chest radiograph appearance or a reduction in the PEEP level required to maintain acceptable oxygenation after the establishment of $ECCO_2R$.
2. PaO_2 / FiO_2 ratio ≥ 30kPa
3. Plateau pressure ≤ 25cmH_2O when mechanically ventilated with a short trial of Vt 6 mL kg^{-1} PBW **(Be aware of the risk of hypocapnia due to increased minute volume, this may be mitigated by reduction in respiratory rate)**

Once the above weaning criteria are met then $ECCO_2R$ is weaned as per Figure 12. Aim to reduce the sweep gas flow by 1 L/min every hour. It may be possible to achieve sweep gas reduction over a shorter time period. Following 12 hours of sweep gas flow at 1 L/min and an acceptable gas exchange, therapy is ended and decannulation should follow as detailed in **Section 11.**

If the above three weaning criteria are not all met on daily assessment then $ECCO_2R$ should be continued for a maximum of 7 days aiming for tidal volumes of ≤ 3mL/kg PBW in mandatory ventilation or Vt ≤ mL kg^{-1} PBW if using pressure support ventilation. It is recognised that at this stage that spontaneous breath tidal volumes may be difficult to limit even with minimal pressure support.

An overview of the weaning process is outlined in Figure 11. The aim is to continue lung protective ventilation regardless of whether mandatory ventilation (MV) or pressure support ventilation is being used, i.e. Vt ≤ 6 mL kg^{-1} PBW if spontaneous ventilation mode (pressure support) and Vt ≤ 3mL/kg PBW if mandatory mode.

Figure 12. Overview of weaning process for $ECCO_2R$



*The timings on this flow chart are as a guide only. Sweep gas flow and tidal volume may be adjusted more rapidly as the clinical condition of the patient permits.

11. Ending therapy and Decannulation

Once the responsible consultant has decided that $ECCO_2R$ can be discontinued (see above) decannulation should be undertaken. The A-Lung can be run with minimal or

no flow until a safe and appropriate time to decannulate the patient. There is 260mL of blood in the circuit so prior to decannulation blood "rinse back" may be carried out to return the blood to the patient if no thrombosis is suspected. Please refer to A-Lung manual for the "rinse back" procedure and ensure staff have watched the video "Ending Therapy". There is a quick reference guide to "ending therapy with blood rinse back" attached to the console

The process for removal of the Hemolung catheter is as follows:

- Cease heparin for 2 hours
- Reduce the RPM on the pump over a couple of minutes then Stop pump
- Clamp both lumens of the Hemolung catheter
- Clamp both blood tubes approximately 15cm from the catheter connection
- The use of a deep vertical mattress suture(s) at the insertion site may be considered
- Remove drainage catheter with direct pressure over the insertion site
- Close mattress suture(s) if appropriate
- Maintain digital pressure for 30 minutes after catheter removal (do not use a femstop device).
- After 30 minutes of direct finger pressure the insertion site should be observed for bleeding.
- Following this the insertion site should be observed every 15 minutes for 4 hours post removal. The area should NOT be covered over by a sheet during this time.
- The mattress suture will need to be removed at 7 days, ensure this is documented in patient notes.

12. Nursing Care while on $ECCO_2R$

12.1 Maintaining a Safe Environment

The following standards of nursing care should be met for patients on the Hemolung.

NURSING INTERVENTION	RATIONALE
$ECCO_2R$ patients must be have a 1:1 bedside nurse: patient ratio. In addition, a nurse who has undertaken requisite training in Hemolung operation should be available on the unit 24/7 and should be present for any procedures requiring movement of the patient. Observations of the Hemolung should be performed hourly for the first 24 hours and then 2 hourly. Continuously monitor the patient for signs and symptoms of fluid imbalance, abnormal laboratory values, infection/sepsis, bleeding, thrombocytopenia, hemolysis, or other complications related to extracorporeal support systems.	The trained Hemolung nurse can provide support for the bedside nurse ensuring the safe management of the patient and the Hemolung circuit. Frequency of observations to maintain safe monitoring of patient, ventilation and operation of the Hemolung system.
Safety checks performed on commencement of shift to include: • Hemolung plugged into UPS plug • Check blood pump flow rate • Check sweep flow rate • Hemolung cartridge inspection • Check patient's position and cannula sites • Check distal pulses and peripheral perfusion • Pump access line movement (shaking, swinging or still) • Check that all tubing is in the correct position to prevent kinks restrictions.	Ensure Hemolung settings are correct and minimise the risk of circuit failure. Identify problems with patient perfusion, catheter, circuit or cartridge at an early stage.
The $ECCO_2R$ patient must NOT be left unattended at any time. Relief for breaks should be arranged so that a suitably experienced member of staff is monitoring the patient and Hemolung at all times.	Minimise risk of accidental decannulation or other system failure.

12.2 Monitoring the Patient/Circuit

NURSING INTERVENTION	RATIONALE
Hemolung Flow Rate To be monitored continuously with circuit lines and membrane gas exchanger for any clot formation Document hourly for the first 24 hours then 2 hourly with RPM setting for trend monitoring Any drop in blood flow to be reported immediately and managed promptly (as per $ECCO_2R$ complications).	Blood flow through the Hemolung circuit is essential for maintenance of gaseous exchange and haemodynamic stability Immediately.
$ECCO_2R$ sweep flow rate To be monitored continuously. Document hourly for the first 24 hours then 2 hourly. Secure and label gas flow connections to membrane gas exchanger Ensure gas outlet is free from obstruction. Ensure correct sweep flow is given as prescribed. Regular ABGs	Any disruption to sweep flow will have significant effects on the patient's stability and should therefore be identified and managed immediately
Inspection of Hemolung cartridge Perform once per shift looking for clot formation	Visible clots on the inflow side of the membrane may give an indication that the set is clotting
CO_2 Clearance Record CO_2 clearance hourly for the first 24 hours then 2 hourly.	A sustained decrease in CO_2 extraction over time may indicate cartridge or circuit problems.
Haemodynamic Status Patient haemodynamic status should be monitored hourly.	Changes in haemodynamic status may affect both respiratory and circuit performance
Catheter Inspect catheter once per shift, for oozing of blood, and maintenance of secure dressings	Significant blood loss may occur from the catheter site. Dressings maintain catheter position and prevent infection.
Vascular Observation of Limbs (lower if femoral catheter used, upper if jugular catheter) Once per shift and should include limb temperature, colour and peripheral pulses.	Venous catheters may lead to DVT formation.

Change the sweep gas vacuum canister every 24 hours	Must be changed daily to ensure adequate sweep gas flow.
Ensure that the seal flush is connected and volume administered is recorded	The seal flush is used to provide an infusion of saline at 30 mL/hr to provide a continuous flush of the blood pump seal. An infusion pump controls a continuous saline infusion to prevent the pump bearings from becoming damaged.
Perform safety checks once per shift (settings, circuit/line/canister inspection). Monitor for leaks, cracks, vibrations, air, or other system failures.	To ensure the safe monitoring of the including management of circuit emergencies

12.3 Patient Positioning, Patient Care and Pressure Area Care

NURSING INTERVENTION	RATIONALE
All activities of nursing care involving the movement of the patient must be done with at least two nurses, one of who should be trained in use of the Hemolung.	Prevention of disruption of the circuit or accidental decannulation.
Patients should be positioned to optimise ventilation, $ECCO_2R$ blood flow rates and safety. Head of the bed may be elevated to 30 degrees	To improve respiratory and circuit function.
All moves are to be performed with nursing staff knowledgeable in $ECCO_2R$ immediately available in the unit	So any issues can be addressed immediately

13. Complications

Although fortunately rare, emergency complications involving the $ECCO_2R$ circuit can be serious and demand immediate responses. They are largely preventable.

Possible complications are: low flow; bleeding; accidental decannulation; air embolism; membrane failure.

13.1 Low Flow

Definition: A reduction in flow through the circuit e.g. an absolute blood flow of less than 0.25L/min.

Effect: Hypercapnoea; membrane thrombosis; possible air embolus.

Causes: Hypovolaemia; increased intra-abdominal or intrathoracic pressure; circuit kink; circuit thrombosis.

Prevention: Adequate circulating volume. Ensure that circuit not kinked or obstructed. Ensure adequate anticoagulation.

Response: Ensure that the circuit is unobstructed. Assess abdomen to exclude raised intra-abdominal pressure. Give a volume challenge. Ensure that circuit not thrombosed (visual inspection and assess CO_2 extraction). Ensure APTTr within target range.

13.2 Bleeding

Definition: Bleeding from any source

Effect: Loss of blood and circulating volume

Causes: Anticoagulation; catheter insertion sites; other potential bleeding sites. Accidental decannulation (partial or complete).

Prevention: Ensure patient not over-anticoagulated; where possible, avoid invasive procedures whilst on $ECCO_2R$. Catheter care on turns, positioning etc.

Response: Contact $ECCO_2R$ consultant to assess catheter position. Reduce or cease heparin following discussion with consultant. Consider surgical and imaging options. Consider tranexamic acid and desmopressin (DDAVP). Consider ceasing $ECCO_2R$.

13.3 Decannulation

Definition: This is the accidental removal of the Hemolung catheter

Effect: Hypercapnia, blood loss.

Causes: tension on circuit, accidental dislodgement on turning or positioning.

Prevention: Secure catheter; adequate numbers of trained staff on turning or positioning; circuit care on positioning or turning. A designated person should ensure that lines remain free during patient manoeuvres

Response: Call for help. Clamp the circuit proximal to the disconnected catheter. Apply pressure to the catheter insertion site. Adjust the ventilator settings to compensate for loss of support. Contact ICU Consultant. Consider replacement of circulating volume if indicated.

13.4 Circuit Air Embolism

Definition: This is the introduction of air into the $ECCO_2R$ circuit

Effect: Introduction of air embolus into the patient. Hypoxaemia and circulatory collapse if large.

Causes: Introduction of air into the circuit via the catheter insertion site or via the membrane gas exchanger.

Prevention: Only $ECCO_2R$ trained consultants to perform $ECCO_2R$ catheter insertion. Care with circuit and catheter on patient movement (as outlined above).

Response: Clamp both arms of the catheter. Call for help. Contact ICU Consultant. Assign roles for concurrent patient and circuit management.

Patient Management: Resuscitate A, B and C with 100% O_2 and ventilation support (increase minute ventilation as required). Consider positioning patient head down in left lateral position and advancing CVC line into right atrium to aspirate air. Identify source of air.

Circuit Management: Stop pump and discontinue therapy. Discard circuit.

13.5 Membrane gas exchanger failure

Definition: Over time thrombus may build up in the membrane. It is not unusual to have some thrombus in the cartridge, particularly at points of turbulent flow.

Effect: Rise in $PaCO_2$ despite constant minute ventilation, increased sweep gas flow and pump speed. Overall reduction in flow through cartridge.

Causes: Thrombus, increase in biofilm, low blood flow.

Prevention: Ensure adequate anticoagulation. Ensure that the tubing is unobstructed. Ensure adequate pump speed. Monitor CO_2 removal and alert medical staff if sustained reduction over time.

Response: Change the cartridge or circuit. Contact ICU Consultant.

APPENDIX A - Complete list of anticipated adverse events and their mitigation

Event	Description	Definition	Mitigation
Access site contamination	Contamination of access site.		The Hemolung System requires only a single access site, which reduces the number of access sites. The catheter will be inserted employing the UK care bundle for insertion and maintenance of central venous catheters.
Acute Kidney Injury	Abnormal kidney function.	Abnormal kidney function requiring dialysis (include hemofiltration) in patients who did not require this procedure prior to Hemolung RAS therapy initiation, or a rise in serum creatinine greater than 3 times baseline for greater than 48 hours.	Initiate medical treatment.
Air embolism	Entry of gas into the vasculature. This may occur during catheter insertion or during therapy due to fibre leak, tubing connector failure, cracked housing, breach of blood/air interface, or console failure.	Entry of gas into the vasculature that results in severe neurologic injury, cardiovascular collapse, or death.	Standard blood aspiration techniques and Trust protocols regarding the care and removal of central venous access will be employed. The veno-venous design minimises risk associated with air embolism, since catheter is inserted into vein only. Sweep gas pathway under vacuum prevents possibility of air embolism from fibre failure. Low and limited vacuum at the blood inlet, coupled with a centrifugal pump design that limits the maximum vacuum, and vertical pump position with impeller on top, that traps the air at the top impeller and stops the pump from pumping, are all safety features of the design. Controller will alarm due to signal from bubble detector and shutdown in a safe mode. If this occurs, the device can be replaced by the clinician.

Event	Description	Definition	Mitigation
Arterial puncture with needle during insertion	Incorrect insertion of needle during insertion of catheter resulting in artery being punctured instead of vein.	An arterial puncture requiring surgical intervention as treatment.	The protocol mandates the use of real-time ultrasound to locate the vein, and mandates that experienced personnel with the appropriate training will insert the catheter. If inadvertent arterial puncture occurs then the needle will be removed and local pressure applied.
Arteriovenous fistula.	Abnormal connections or passageways between an artery and vein.	Abnormal connections or passageways between an artery and vein.	Initiate medical treatment. If unresolved, discontinue therapy.
Battery Empty	Controller running on battery and battery is completely depleted	A controller failure resulting in inadequate, life-threatening failure of respiratory support.	Controller displays battery status. Controller will alarm for low battery when 20% battery power remains. Plug in controller to continue therapy.
Bleeding at the insertion site	Blood loss from placement site sufficient to require blood transfusion or surgical/catheter intervention.	> 100mLs blood loss from placement site sufficient to require blood transfusion or surgical/catheter intervention. Assessed by the investigator.	The insertion site will be examined and additional stitches / local pressure applied. If the bleeding is unresolved and excessive, then therapy will be discontinued and formal surgical repair of the catheter insertion site undertaken
Blood loss (Excessive) due to disconnection from return blood path	Excessive blood loss due to disconnection to return blood path	Excessive blood loss due to disconnection to return blood path	Controller detects disconnection and stops flow. Alarm sounds. Hemolung RAS utilizes tight barbed connectors to prevent disconnection. IFU recommends proper connection of tubing, locking castors to prevent pulling on tubing. Initiate medical management.
Blood pressure decrease (Hypotension)	Low blood pressure due to commencement of therapy.	Systolic blood pressure of below MAP 60 mmHg during the first two hours of therapy for more than 15 minutes.	Careful upregulation of the blood flow rate is mandated in the Protocol. Initiate medical treatment.
Brachial Plexus Injury	Ipsilateral neurologic deficit in upper arm secondary to catheter placement in internal/external jugular vein		Catheters are placed using real-time ultrasound and experienced operators.

Event	Description	Definition	Mitigation
Bradycardia (low heart rate)	Heart rate below 40 BPM during therapy	Heart rate below 40 BPM during therapy	Monitor heart rate (HR). If HR <40 BPM for greater than 2 minutes, initiate medical treatment. If unresolved, discontinue treatment.
Breach of device / environment barrier	A breach in connection of tubing. This could lead to bleeding or infection.		Investigators and nurses will be trained in the proper connection of tubing, connectors, and maintaining sterility. The system is designed to be seamLess with robust alarms and connections.
Cardiac Arrhythmias	Any documented arrhythmia requiring defibrillation or cardioversion.	Any documented arrhythmia that results in clinical compromise.	Medical management of arrhythmia, consider discontinuation of therapy if arrhythmia is recalcitrant.
Catheter and/or Blood Circuit Occlusion	Occlusion of the catheter and/or blood circuit due to thrombus formation. Reduced blood flow and CO_2 removal may result. Increased risk of thromboembolism.	A Catheter and/or Blood Circuit Occlusion resulting in inadequate, life-threatening respiratory support.	Hemolung device is coated with covalently bonded heparin to minimise thrombus formation. Protocol provides instruction regarding the anticoagulation protocol. Catheter size limits embolism. Any thrombus on the inflow side will be captured by fibre mat. Junctions are designed to be smooth to minimise potential for thrombus formation. The exchange of the device and/or the re-siting of the access catheter will be considered.
Catheter related blood stream infection or cellulitis at insertion area	A positive culture from the skin and/or tissue surrounding the catheter insertion site, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis. Contamination of access site may lead to an infection at the access site. Excessive movement of the catheter can cause trauma to the access site and increase risk of infection	A positive culture from the skin and/or tissue Hemolung catheter, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis.	Accessories included in catheter kit for sterile insertion (e.g., drape, antiseptic swab, etc.). IFU directions for aseptic technique. All catheters will be inserted by experienced personnel with appropriate competencies.

Event	Description	Definition	Mitigation
CO_2 removal--excessive	Excessive CO_2 removal causing tetanus and hypocalcaemia	Excessive CO_2 removal resulting in tetanus	Protocol for titration of therapy.
Chylothorax	Chyle leak or chylothorax, a type of pleural effusion, resulting from lymphatic fluid (chyle) accumulating in the pleural cavity.	Chyle leak or chylothorax, a type of pleural effusion, resulting from lymphatic fluid (chyle) accumulating in the pleural cavity.	Initiate medical management.
Device Malfunction	Failure of one or more of the components of the Hemolung System which either directly causes or could potentially induce a state of inadequate respiratory support, but does not include thrombus formation, or haemolysis, or any other biological response to the treatment (see Thrombus Formation event).	Failure of one or more of the components of the Hemolung System which either directly causes or could potentially induce a state of inadequate, life-threatening respiratory support or death.	Controller will alarm for a variety of malfunctions. When those alarms represent a safety concern for the patient, the controller will shutdown in a safe mode. The controller will be replaced by the back up one held on-site if the patient has not met weaning criteria.
Disseminated intravascular coagulation (DIC)	Disseminated intravascular coagulation is a disorder in which the proteins that control blood clotting become abnormally active. Small blood clots form that can cut off blood supply to organs. Once clotting proteins are consumed or used up, patients are at risk for serious bleeding.	Disseminated intravascular coagulation is a disorder in which the proteins that control blood clotting become abnormally active. Small blood clots form that can cut off blood supply to organs. Once clotting proteins are consumed or used up, patients are at risk for serious bleeding.	Initiate medical management. Discontinuation of therapy should be considered.
Endocarditis	Inflammation of the heart's inner lining. May be caused by a catheter related infection.	Inflammation of the heart's inner lining. May be caused by a catheter-related infection. Endocarditis requiring IV antibiotic therapy in the hospital.	Medical management
Exit Site Necrosis	At the catheter exit site due to injury		Medical management
External leak in gas pathway	A leak in the gas pathway to the device reducing CO_2 removal.	A leak in the gas pathway to the device reducing CO_2 removal resulting in inadequate, life-threatening respiratory support.	Controller will alarm and indicate low CO_2 removal. The console can be replaced and tubing checked for connections.

Event	Description	Definition	Mitigation
Extravasation	Infusion of blood into the tissue surrounding the accessed vessel due to retraction of the catheter, misplacement of the catheter, or perforation of the vessel.	Infusion of blood into the tissue surrounding the accessed vessel due to retraction of the catheter, misplacement of the catheter, or perforation of the vessel requiring surgical intervention for treatment.	Insertion and securing of the catheter by an experienced operator.
Failure of controller to provide sweep gas	Patient would receive insufficient respiratory support due to controller failure.	A controller failure resulting in inadequate, life-threatening respiratory support.	Controller will alarm. The controller will be replaced by the back up one held on-site.
Haemorrhage not related to insertion site bleeding.	Excessive external or internal bleeding not related to insertion site.	Within any 24 hours period, > 1U packed red blood cells (PRBC) required	The APTTr activities will be measured regularly and the heparin infusion titrated in accordance with the results. If uncontrolled internal bleeding occurs then the heparin infusion will be reduced. The patients haemoglobin will be supported by the appropriate use of allogenic blood products.
Haematoma	A mass of clotted blood (most likely to occur at the catheter insertion site)	A mass of clotted blood (most likely to occur at the catheter insertion site) requiring medical or surgical treatment.	This will be managed at the discretion of the attending clinician.
Haemothorax	A collection of blood in the space between the chest wall and the lung (the pleural cavity). Risk of haemothorax exists primarily during use of the jugular catheter.	A collection of blood in the space between the chest wall and the lung (the pleural cavity). Risk of haemothorax exists primarily during use of the jugular catheter.	Insertion and securing of the catheter by an experienced operator. It will be managed at the discretion of the attending clinician
Haemolysis	A plasma-free haemoglobin value that is greater than 40 mg.dL^{-1}, in association with clinical signs associated with haemolysis (e.g. anaemia, low haematocrit, hyperbilirubinaemia, raised LDH). Haemolysis related to documented non-device-related causes (e.g. transfusion or drug) is excluded from this definition	A plasma-free haemoglobin value that is greater than 40 mg.dL^{-1}, in association with clinical signs associated with haemolysis (e.g., anaemia, low haematocrit, hyperbilirubinaemia, raised LDH). Haemolysis related to documented non-device-related causes (e.g. transfusion or drug) is excluded from this definition.	All known contributors to haemolysis have been evaluated and optimised, RPM has been minimised, surfaces have been smoothed, non haemolytic materials utilised. The revolutions per minute of the device are controllable. Plasma free haemoglobin will be assayed if haemolysis suspected during therapy. The device may be replaced/removed if haemolysis is high.

Event	Description	Definition	Mitigation
Heparin Induced Thrombocytopenia (HIT)	Reduction in the number of platelets due to the administration of heparin (an anticoagulant), or use of heparin coated medical device. Can be associated with an increased risk of thrombosis. Excludes the expected fall in platelets associated with $ECCO_2R$	A reduction of platelets due to the administration of heparin requiring the infusion of any replacement blood products as treatment.	Monitor platelet count during therapy. If platelet count drops below 50 x $10.L^{-1}$; or platelet count < 50 x $100.L^{-1}$ in conjunction with >50% decrease from baseline; check for heparin induced thrombocytopenia (HIT) antibodies (HIT Type II) measured by serotonin release assay. If detectable, stop heparin. Discontinue Hemolung.
Hepatic dysfunction	An increase in any two of the following hepatic laboratory values (total bilirubin, AST, ALT) to a level greater than three times the upper limit of normal for the hospital during Hemolung therapy	An increase in any two of the following hepatic laboratory values (total bilirubin, AST, ALT) to a level greater than three times the upper limit of normal for the hospital during Hemolung therapy	Initiate medical management.
Hydrothorax	A collection of water or serous fluid in the space between the chest wall and the lung (the pleural cavity). Risk of hydrothorax exists primarily during use of the jugular catheter.		Insertion and securing of the catheter by an experienced operator. It will be managed at the discretion of the attending clinician
Hypothermia - primarily through extracorporeal circulation	Hypothermia could occur due to heat loss resulting from water evaporation from the blood through the fibre/blood interface.	Water evaporation from the blood through the fibre/blood interface resulting in life-threatening hypothermia below 35C	The patient's temperature should be monitored regularly as per standard care. Forced air blankets or similar will be used to maintain normothermia if indicated.
In flow blood path disconnected during use	Air enters circuit due to disconnection of inflow during use	Entry of gas into the vasculature secondary to air entering the circuit, that results in severe neurologic injury, cardiovascular collapse, or death	Controller detects disconnect and stops flow. Alarm sounds. The Hemolung System utilises robust connections to prevent disconnection. IFU recommends proper connection of tubing, locking castors to prevent pulling on tubing. Remove air from circuit and restart therapy

Event	Description	Definition	Mitigation
Interference between the Hemolung catheter and other indwelling devices	Compromised function of Hemolung catheter and/or indwelling devices	Compromised function of Hemolung catheter and/or indwelling devices resulting in inadequate, life-threatening respiratory support and/or medical support from other indwelling devices.	No indwelling catheter will be placed at the site of the Hemolung catheter insertion.
Intolerance reaction to catheter or blood circuit	A reaction by the body to contact with the foreign materials comprising the blood circuit including the catheter, tubing, and gas exchanger.	Severe (systolic systemic pressure <80 mmHg) and prolonged (>5 min) on therapy commencement unless device is stopped.	This will be managed by discontinuation of therapy and appropriate administration of intravenous fluids and vasoconstrictors.
Kink in tubing	Kink in tubing reducing or stopping blood flow	Kink in tubing reducing or stopping blood flow leading to inadequate, life-threatening respiratory support.	Controller will alarm due to low blood flow. The Directions for Use recommend locking console wheels to prevent console from rolling over tubing. The tubing is designed to be kink resistant.
Laceration or perforation of vessels	Laceration or perforation of the vessels. Risk exists primarily during insertion of the catheter.	An injury to a blood vessel requiring surgical repair.	All catheters will be inserted by experienced personnel. These will be managed by appropriate surgical techniques.
Loss of AC power.	Loss of Hemolung therapy due to loss of AC power.	Loss of Hemolung Therapy due to loss of AC power resulting in inadequate, life-threatening respiratory support.	Controller switch over to battery backup as well as continuously report condition of batteries. If the uninterruptible power supply fails, then the controller will alarm and be replaced.
Low power (brownout)	Reduction or loss of Hemolung therapy due to low power	Reduction or loss of Hemolung Therapy due to low power resulting in inadequate, life-threatening respiratory support.	System uses power conditioner with uninterruptible power supply. If this fails, then the controller will alarm and be replaced.
Myocardial infarction or coronary insufficiency	The clinical suspicion and diagnosis of myocardial infarction or coronary insufficiency		Initiate medical management,

Event	Description	Definition	Mitigation
Pericardial Fluid Collection, no Cardiac Tamponade	Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage. No clinical signs of tamponade. Can be caused by perforation of the right atrium during insertion of the catheter.	Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage.	All catheters will be inserted by experienced operators using real-time ultrasound. The complication will be managed by appropriate surgical or percutaneous drainage.
Pericardial Fluid Collection, with Cardiac Tamponade	Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage. With clinical signs of tamponade (e.g. increased central venous pressure and decreased cardiac output). Can be caused by perforation of the right atrium during insertion of the catheter.	Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage.	All catheters will be inserted by experienced operators using real-time ultrasound. The complication will be managed by appropriate surgical or percutaneous drainage.
Pleural Effusion	Excess fluid that accumulates between the two pleural layers, the fluid-filled space that surrounds the lungs.	Excess fluid that accumulates between the two pleural layers, the fluid-filled space that surrounds the lungs.	Initiate medical management.
Pneumothorax	Presence of air in the space between the chest wall and the lung (the pleural cavity).		This will be managed by appropriate drainage of the pneumothorax.
Pneumomediastinum	Presence of air in the mediastinum		Initiate medical management
Pulmonary embolism	Presence of a clot in a major pulmonary artery	Evidence of a large clot in a first, or second order pulmonary artery on CT angiography	This is unlikely in the presence of anticoagulation and will be managed by on-going anticoagulation
Right Heart Failure	Symptoms and signs of persistent right ventricular dysfunction.	Symptoms and signs of persistent right ventricular dysfunction not due to tamponade, ventricular arrhythmias or pneumothorax requiring right ventricular assist device, nitric oxide or inotropic agents.	Initiate medical management.

Event	Description	Definition	Mitigation
Shock	A life threatening medical condition as a result of insufficient blood flow throughout the body, including but not limited to hypovolaemic or septic shock.	A life threatening medical condition as a result of insufficient blood flow throughout the body, including but not limited to hypovolaemic or septic shock.	Initiate medical management. Discontinuation of therapy may be considered.
Stroke (Haemorrhagic/thrombotic) or transient ischaemic attack.	Any new, temporary or permanent, focal or global neurological deficit ascertained by a standard neurological examination.	Any new, temporary or permanent, focal or global neurological deficit ascertained by a standard neurological examination (administered by a neurologist or other qualified physician and documented with appropriate diagnostic tests and consultation note). The examining physician will distinguish between a transient ischemic attack (TIA), which is fully reversible within 24 hours (and without evidence of infarction), and a stroke, which lasts longer than 24 hours (or less than 24 hours if there is evidence of infarction).	This will be managed at the discretion of the attending clinician.
Subcutaneous emphysema	The presence of air in the subcutaneous tissues.		Initiate medical management.
Severe Thrombocytopenia, Non-HIT related	Reduction in the number of platelets due to deposition and consumption within the blood circuit. Severe thrombocytopenia is defined as a platelet count drop below $20{,}000.mm^{-3}$. Can be associated with an increased risk of thrombosis.		Monitor platelet count during therapy. If platelet count drops below $50 \times 10.L^{-1}$, or platelet count < $100.L^{-1}$ in conjunction with >50% decrease from baseline; check for heparin induced thrombocytopenia (HIT) antibodies (HIT Type II) measured by serotonin release assay. If detectable, stop heparin. In these settings therapy should be stopped.
Tachycardia	Heart rate could increase during therapy	HR > 140 beats per minute (BPM) for > 2 minutes	Monitor the heart rate. If it exceeds 140 BPM for more than 2 minutes, initiate medical management. If unresolved, discontinue therapy.

Event	Description	Definition	Mitigation
Thoracic Duct Injury	Injury to the thoracic duct during insertion of the jugular catheter may result in the leakage of chylous fluid.		All catheters will be inserted by experienced operators using real-time ultrasound. The complication will be managed by appropriate surgical or medical therapies.
Thromboembolism, arterial non-cns	An acute systemic arterial perfusion deficit in any non-cerebrovascular organ system due to thromboembolism confirmed by one or more of the following: 1) standard clinical and laboratory testing, 2) operative findings, and/or, 3) autopsy findings. This definition excludes neurological events.	An acute systemic arterial perfusion deficit in any non-cerebrovascular organ system due to thromboembolism confirmed by one or more of the following: 1) standard clinical and laboratory testing, 2) operative findings, and/or, 3) autopsy findings. This definition excludes neurological events.	Initiate medical management.
Thromboembolism, Venous Event or vascular obstruction of the Hemolung catheter	Evidence of venous thromboembolic event (e.g. deep vein thrombosis, pulmonary embolism) by standard clinical and laboratory testing	Evidence of venous thromboembolic event (e.g. deep vein thrombosis, pulmonary embolism) by ultrasound or pulmonary CT angiography (respectively)	Only catheters appropriate to the vessel size will be used.
Transposed connection of blood tubing	Increased level of recirculation in blood vessel and reduced gas exchange.	Increased level of recirculation in blood vessel and reduced gas exchange resulting in inadequate, life-threatening respiratory support.	The tubing is colour coded to prevent transposed connection of tubing.
Ventricular thrombosis			Initiate medical management.

APPENDIX B –Predicted Body Weight Guide

Males: **PBW = IBW (kg) = 50 + 0.91 (height (cm) – 152.4)**

HEIGHT cm	PBW Male	3 ml/kg	3.5 ml/kg	4 ml/kg	4.5 ml/kg	5 ml/kg	5.5 ml/kg	6 ml/kg
154	51	154	181	206	232	257	284	309
156	53	160	187	213	240	266	294	320
158	55	165	193	220	248	275	304	331
160	57	171	200	228	257	285	314	341
162	59	176	206	235	265	294	324	352
164	61	182	212	242	273	303	334	363
166	62	187	219	250	281	312	344	374
168	64	193	225	257	289	321	354	385
170	66	198	232	264	298	330	364	396
172	68	204	238	271	306	339	374	407
174	70	209	244	279	314	348	384	418
176	71	214	251	286	322	357	394	429
178	73	220	257	293	330	366	404	440
180	75	225	263	300	339	376	414	451
182	77	231	270	308	347	385	424	462
184	79	236	276	315	355	394	434	473
186	81	242	283	322	363	403	444	483
188	82	247	289	330	371	412	454	494
190	84	253	295	337	379	421	464	505
192	86	258	302	344	388	430	474	516
194	88	264	308	351	396	439	484	527
196	90	269	314	359	404	448	494	538
198	91	274	321	366	412	457	504	549
200	93	280	327	373	420	467	514	560
202	95	285	333	381	429	476	524	571
204	97	291	340	388	437	485	534	582
206	99	296	346	395	445	494	544	593
208	101	302	353	402	453	503	554	604
210	102	307	359	410	461	512	564	614
212	104	313	365	417	470	521	574	625
214	106	318	372	424	478	530	584	636
216	108	324	378	432	486	539	594	647
218	110	329	384	439	494	548	604	658
220	112	335	391	446	502	558	614	669

Females: **PBW = IBW (kg) = 45.5 + 0.91 (height (cm) – 152.4)**

HEIGHT cm	PBW Female	3 ml/kg	3.5 ml/kg	4 ml/kg	4.5 ml/kg	5 ml/kg	5.5 ml/kg	6 ml/kg
154	47	141	165	188	212	235	259	282
156	49	146	171	195	220	244	269	293
158	51	152	178	202	228	253	279	304
160	52	157	184	210	236	262	289	314
162	54	163	190	217	245	271	299	325
164	56	168	197	224	253	280	309	336
166	58	174	203	232	261	289	319	347
168	60	179	209	239	269	298	329	358
170	62	185	216	246	277	308	339	369
172	63	190	222	253	286	317	349	380
174	65	195	229	261	294	326	359	391
176	67	201	235	268	302	335	369	402
178	69	206	241	275	310	344	379	413
180	71	212	248	282	318	353	389	424
182	72	217	254	290	326	362	399	435
184	74	223	260	297	335	371	409	446
186	76	228	267	304	343	380	419	456
188	78	234	273	312	351	389	429	467
190	80	239	280	319	359	399	439	478
192	82	245	286	326	367	408	449	489
194	83	250	292	333	376	417	459	500
196	85	256	299	341	384	426	469	511
198	87	261	305	348	392	435	479	522
200	89	266	311	355	400	444	489	533
202	91	272	318	363	408	453	499	544
204	92	277	324	370	417	462	509	555
206	94	283	330	377	425	471	519	566
208	96	288	337	384	433	480	529	577
210	98	294	343	392	441	490	539	587
212	100	299	350	399	449	499	549	598
214	102	305	356	406	458	508	559	609
216	103	310	362	414	466	517	569	620
218	105	316	369	421	474	526	579	631
220	107	321	375	428	482	535	589	642

APPENDIX C – PEEP Ladder

PEEP/FiO_2 Combinations

FiO_2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
PEEP (cmH_2O)	5	5-8	8-10	10	10-14	14	14-16	18-24

Version 4.0	Authors
Date: 17th December 2019	M Gillies, N Barrett, S Finney, J McNamee, D McAuley, K Daly

APPENDIX D – Example Timeline for Initiation of Therapy

Time	Sweep Gas Flow L/min	Tidal Volume mL/kg	ABG
0	1	6	YES
10min			
20min	3	5.5	YES
30min			
40min	5	5	YES
50min			
60min	7	4.5	YES
70min			
80min	9	4	YES
90min			
100min	10	3.5	YES
110min	10		
120min	10	3	YES
130min	10		
140min	10	3	YES
150min	10		
160min	10	3	YES
170min	10		
180min	10	3	YES

APPENDIX E – Heparin Dosing

When administering the 80 units/kg dose of heparin following guide-wire insertion the bolus dose may be reduced (e.g. 2500 units) at the discretion of the treating clinician if there is perceived to be an increased bleeding risk such as a deranged coagulation system. The maximum bolus dose should be in the range 5000 to 7000 units. This is to avoid over anticoagulation when calculated doses are excessive. Obese and morbidly obese patients have a larger blood volume than normal weight patients due to the additional vasculature required to perfuse the excess adipose tissue although the blood volume of adipose tissue is less than lean tissue.The continuous infusion of unfractionated heparin after this initial bolus dose should then follow your unit guidelines.

When dosing unfractionated heparin for obese patients the *actual patient weight* should be used to calculate the dose. This may be best guessed if not available. Please note that this differs from the tidal volume calculation which use *ideal body weight*.