Patient Selection Guide

EXTRACORPOREAL CO_2 REMOVAL WITH THE HEMOLUNG RAS

ALung Technologies, Inc.

2500 Jane Street, Suite 1
Pittsburgh, PA 15203 USA

ph: +1 412-697-3370
fax: +1 412-697-3376
email: sales@alung.com

www.alung.com

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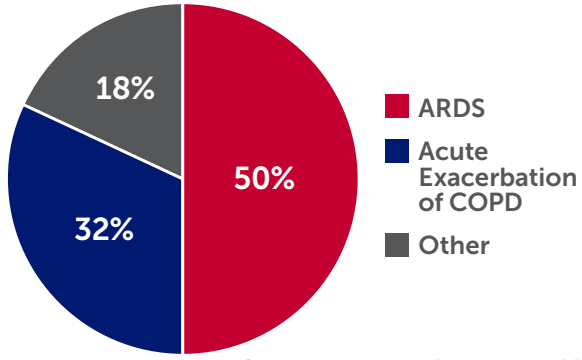
What is Respiratory Dialysis?

Respiratory Dialysis is a simple, minimally invasive approach to extracorporeal CO_2 removal ($ECCO_2R$), only available with the Hemolung Respiratory Assist System (RAS). Using blood flows of 350-550 mL/min, the Hemolung RAS removes 30-50% of metabolically produced CO_2, reducing ventilation requirements in patients who are either failing non-invasive ventilation or who are already invasively ventilated.

This patient selection guide is designed to assist physicians and nurses with maximizing the clinical benefit of Hemolung RAS therapy. The guide helps answer common questions, such as:

- **What are the indications for Hemolung therapy?**
- **How are appropriate patients for Hemolung therapy identified?**
- **When is the best time to initiate Hemolung therapy?**

How is the Hemolung RAS used?



Source: Hemolung Registry as of June 2015

Indications for Use:

The Hemolung RAS is approved for the following indications:

1) Patients with acute hypercapnic respiratory failure who are failing non-invasive ventilation, as an alternative to invasive mechanical ventilation. An example of such a case includes acute exacerbation of severe chronic obstructive pulmonary disease with failure and/or intolerance of non-invasive ventilation.

2) Patients who are invasively mechanically ventilated to allow the application of lung protective ventilation strategies. An example of such a case includes acute respiratory distress syndrome (ARDS).

Contraindications:

Patients with known sensitivity to heparin (e.g. history of heparin-induced thrombocytopenia). The Hemolung Cartridge membranes are coated with heparin and systemic anticoagulation is required when using the device.

Use of the Hemolung 15.5 Fr Femoral Catheter is contraindicated for patients with an inferior vena cava filter.

Hemolung RAS for COPD Patients

When should the Hemolung RAS be utilized during an acute exacerbation of COPD (AECOPD)?

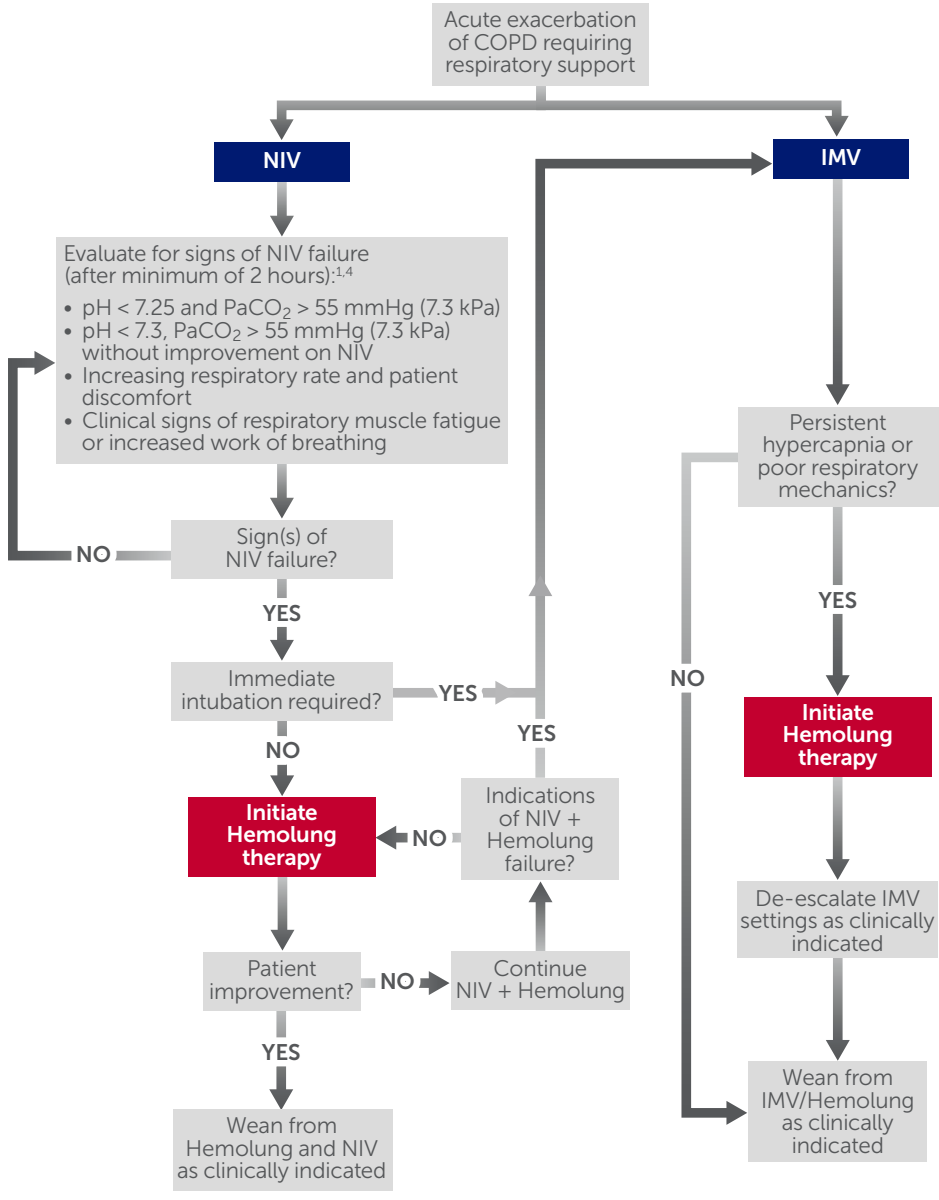
The Hemolung RAS can be used to correct hypercapnia and respiratory acidosis for COPD patients failing non-invasive ventilation, or to improve ventilator management for COPD patients who are invasively mechanically ventilated. Early initiation of Hemolung therapy can help prevent intubation and mechanical ventilation.[1] Avoidance of IMV is associated with reduced mortality and morbidity in AECOPD.[2,3]

Clinical benefits: Respiratory Dialysis during AECOPD[5-7]

- Avoid intubation and mechanical ventilation
- Rapidly correct hypercapnia and acidosis
- Relieve dyspnea
- Reduce work of breathing
- Patient remains awake and mobile, with increased quality of life

Patient selection: Respiratory Dialysis during AECOPD

- Failing NIV
  - pH < 7.25 and $PaCO_2$ > 55 mmHg (7.3 kPa)
  - pH < 7.3, $PaCO_2$ > 55 mmHg (7.3 kPa) without improvement on NIV
  - Increasing respiratory rate and patient discomfort
  - Clinical signs of respiratory muscle fatigue or increased work of breathing
- Invasively mechanically ventilated
  - Clinical signs of poor respiratory mechanics (dynamic hyperinflation, requirements for high pressures or minute volumes)

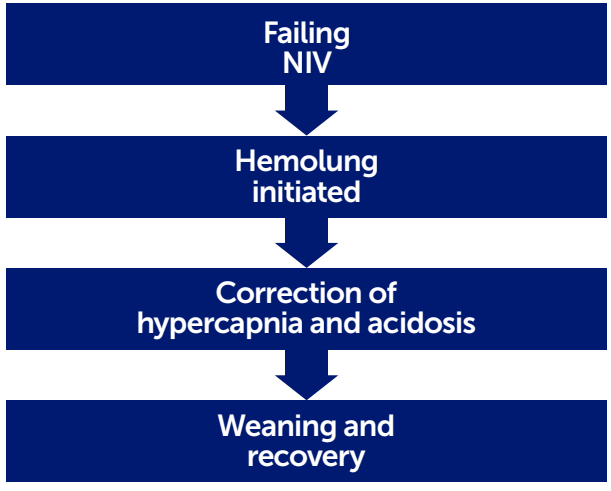


Abbreviations:
AECOPD: Acute exacerbation of chronic obstructive pulmonary disease
IMV: Invasive mechanical ventilation
NIV: Noninvasive ventilation

Case study:
Hemolung RAS during AECOPD

- 59 year old male admitted to the hospital with AECOPD.
- Despite high level NIV support, the patient developed hypercapnia with increasing dyspnea, tachycardia and disorientation.
- $ECCO_2R$ was implemented using the Hemolung RAS to avoid intubation and IMV.
- Within 30 minutes of initiating $ECCO_2R$, the patient's respiratory distress began to diminish, and his condition continued to improve throughout the course of Hemolung therapy (Table 1).
- The patient was weaned off the Hemolung after 4.5 days, and ultimately discharged to home 7 days later.

Read the entire case report at ALung.com



	pH	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	HCO_3^- (mmol/L)
Pre-$ECCO_2R$	7.31	63	68	33
Post-$ECCO_2R$				
4 hours	7.43	58	75	30
1 day	7.43	55	78	32
2 days	7.45	52	91	30
3 days	7.47	48	83	29
4 days	7.48	49	91	31

Table 1. Changes in pH, blood gases and bicarbonate over the 4 day course of Hemolung RAS therapy.

Goals achieved:

- Avoided intubation and IMV
- Corrected hypercapnia and respiratory acidosis
- Lung recovery facilitated

> "The very early application of this technique in patients with...chronic obstructive pulmonary disease exacerbations may prevent the need for mechanical support"

Del Sorbo L, et al. Crit Care Med (2010) 38:S555

Hemolung RAS for ARDS Patients

When should the Hemolung RAS be utilized during ARDS?

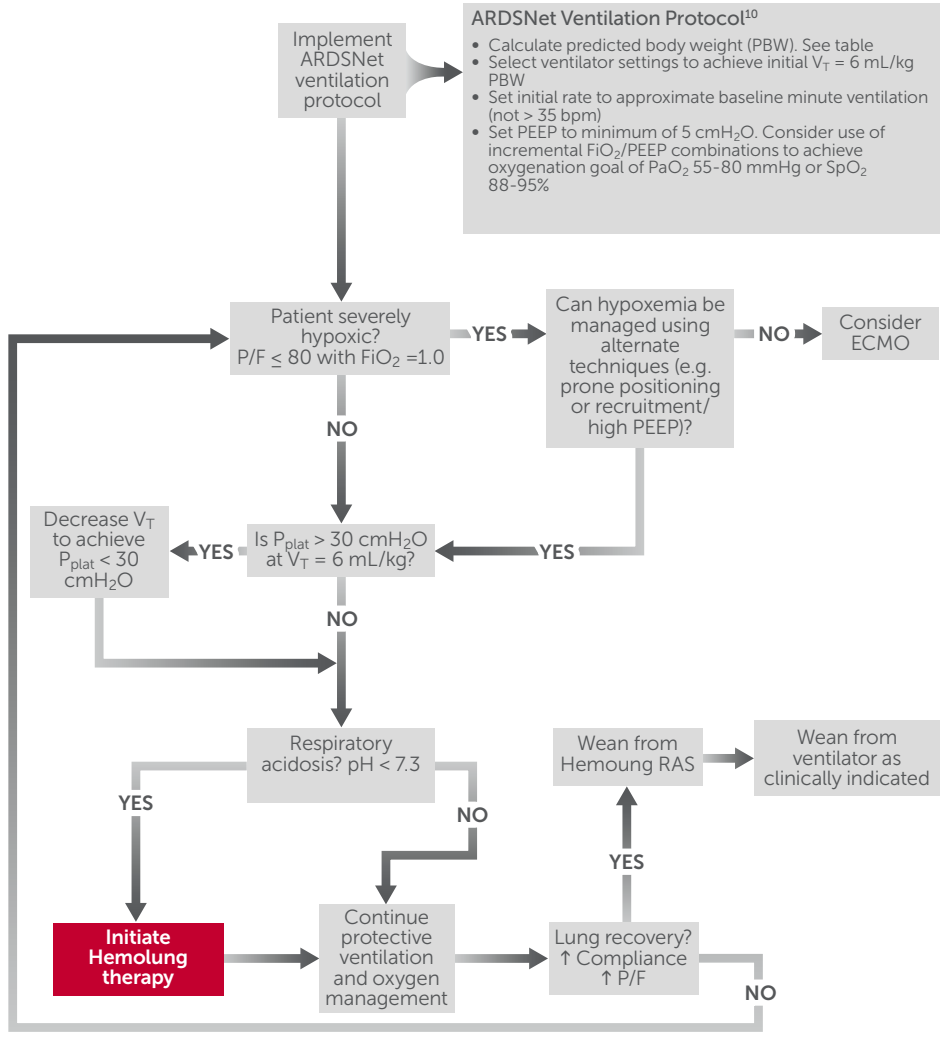
The Hemolung RAS can be used in conjunction with IMV to facilitate protective and ultra-protective ventilation strategies for patients presenting with ARDS without refractory hypoxemia. Extracorporeal CO_2 removal using the Hemolung RAS safely allows reduction in tidal volumes, inspiratory pressures and respiratory rates while maintaining safe $PaCO_2$ and pH levels.

Clinical benefits: Respiratory Dialysis during ARDS[8,9]

- Facilitate lung protective and ultra-protective ventilation strategies
- Maintain safe pH and $PaCO_2$ levels
- Reduce ventilator induced lung injury
  - Barotrauma
  - Volutrauma
  - Systemic inflammatory response

Patient selection: Respiratory Dialysis during ARDS

- Unable to control pH and $PaCO_2$ using ARDSNet ventilation
- Tidal volumes < 6 mL/kg desired to meet lung protective goals



Abbreviations:
P/F: partial pressure of arterial oxygen (PaO_2) / fraction of inspired oxygen (FiO_2)
PEEP: positive end expiratory pressure
V_T: tidal volume
P_{plat}: plateau pressure
PBW: predicted body weight

How is protective and ultra-protective ventilation implemented?

- Adherence to the use of low tidal volume ventilation at the initial onset of IMV improves survival in ARDS.[11]
- Application of $ECCO_2R$ with the Hemolung RAS in conjunction with IMV can help safely titrate ventilator settings to protect the lungs and reduce the risk of ventilator induced lung injury.
- This table displays predicted body weights (PBW) and associated tidal volumes based on the ARDSNet protocol[10] for protective (6 mL/kg PBW) and ultra-protective (3 mL/kg PBW) ventilatory strategies.

ARDSNet Predicted Body Weight (PBW) and Tidal Volumes

MALE					FEMALE				
Height (in)	Height (cm)	PBW (kg)	Protective V_T (mL) (6mL/kg PBW)	Ultra-Protective V_T (mL) (3mL/kg PBW)	Height (in)	Height (cm)	PBW (kg)	Protective V_T (mL) (6mL/kg PBW)	Ultra-Protective V_T (mL) (3mL/kg PBW)
59.1	150	48	287	143	55.1	140	34	205	103
60.2	153	51	303	152	56.3	143	37	222	111
61.4	156	53	320	160	57.5	146	40	238	119
62.6	159	56	336	168	58.7	149	42	254	127
63.8	162	59	352	176	59.8	152	45	271	135
65	165	61	369	184	61	155	48	287	144
66.1	168	64	385	193	62.2	158	51	304	152
67.3	171	67	402	201	63.4	161	53	320	160
68.5	174	70	418	209	64.6	164	56	336	168
69.7	177	72	434	217	65.7	167	59	353	176
70.9	180	75	451	225	66.9	170	62	369	185
72	183	78	467	234	68.1	173	64	385	193
73.2	186	81	483	242	69.3	176	67	402	201
74.4	189	83	500	250	70.5	179	70	418	209
75.6	192	86	516	258	71.7	182	72	435	217
76.8	195	89	533	266	72.8	185	75	451	225
78	198	91	549	274	74	188	78	467	234
79.1	201	94	565	283	75.2	191	81	484	242

PBW (male) = 50 + 0.91 x (cm of height - 152.4)
PBW (female) = 45.5 + 0.91 x (cm of height - 152.4)

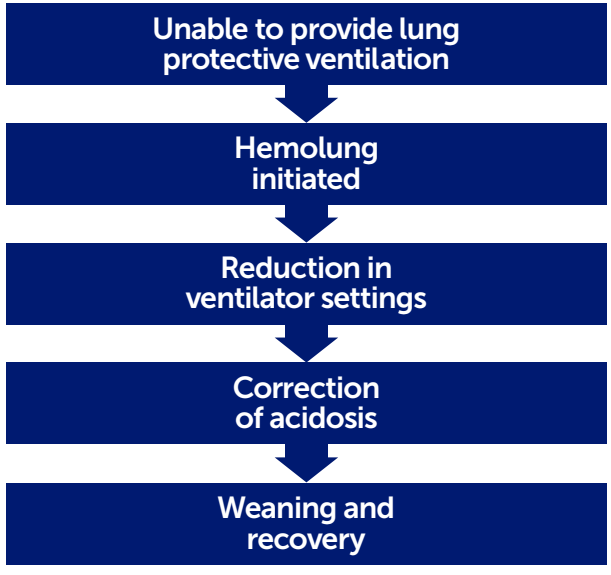
> "Of all the available forms of extracorporeal gas exchange, partial lung support, also known as $ECCO_2R$ or respiratory dialysis, is the most promising, because it offers unique advantages while carrying a low potential for complications"

Morimont, et al. Critical Care (2015) 19:117

Case study:
Hemolung RAS during ARDS

- 41 year old male admitted to the ICU with severe bilateral traumatic leg injuries, ARDS, and metabolic acidosis from sepsis.
- The patient became difficult to ventilate, high inspiratory pressures (46-50 cmH_20) were necessary in an effort to minimize worsening concomitant respiratory acidosis.
- Hemolung therapy was initiated to reduce peak inspiratory pressure and correct respiratory acidosis.
- Within 4 hours of Hemolung therapy, inspiratory pressure rapidly decreased while acidosis simultaneously improved (Table 2).
- Normocapnia was restored and consistently maintained at low inspiratory pressures over the next 7 days, leading to weaning from the Hemolung, extubation and recovery.

Read the entire case report at ALung.com



	Pre-Hemolung	Hour 4	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Peak Inspiratory Pressure (cmH_2O)	39	25	28	30	15	15	24	24	24
pH	7.29	7.37	7.47	7.42	7.42	7.36	7.41	7.43	7.46
$PaCO_2$ (mmHg)	43.8	43.0	34.3	40.9	39.7	46.9	42.2	38.3	44.0
Bicarbonate (mmol/L)	20.8	24.8	24.6	26.1	25.5	26.1	26.1	25.0	30.7
CO_2 Removal (mL/min)	-	83	65	61	64	69	59	56	30*

* weaning

Table 2. Changes in inspiratory pressure, pH, $PaCO_2$, bicarbonate, and CO_2 removal over the 7 day course of Hemolung RAS therapy.

Goals achieved:

- Implemented lung protective ventilation (reduced inspiratory pressures)
- Corrected respiratory acidosis and hypercapnia
- Lung recovery facilitated

> "The implementation of $ECCO_2R$ devices can represent the missing link between the prevention of ventilator-induced lung injury and pH control"

Terragni, et al. Curr Opin Crit Care (2012) 18:93

Clinical Support

Our support team includes clinical specialists and engineers who are committed to ensuring safe and reliable use of ALung's products to achieve optimal clinical outcomes.

ALung's support begins with a comprehensive training program delivered by our skilled clinical specialists. We ensure your staff is fully prepared to safely and effectively deliver extracorporeal CO_2 removal with the Hemolung RAS.

When the time comes for your first patient treatment, we're happy to help. On-Site Case Assistance is offered to every customer and provided at your request.

Our clinical specialists are also available 24/7 to immediately address any questions or issues which you may have. Call us, anytime.

Our technical service team offers comprehensive calibration and preventive maintenance programs to ensure your device is always ready for use.

For immediate support, please call us:

France (toll free): 0800-918846
Germany (toll free): 0800-181-6344
United Kingdom: 0-808-189-1190
All others: +1-724-506-5149

References

1) Burki NK, Mani RK, Herth FJF, et al. A novel extracorporeal CO2 removal system: Results of a pilot study of hypercapnic respiratory failure in patients with COPD. CHEST 2013;143:678-86.

2) Chandra D, Stamm JA, Taylor B, et al. Outcomes of non-invasive ventilation for acute exacerbations of COPD in the United States, 1998-2008. Am J Respir Crit Care Med 2011;185:152-9.

3) Stefan MS, Nathanson BH, Higgins TL, et al. Comparative effectiveness of noninvasive and invasive ventilation in critically ill patients with acute exacerbation of chronic obstructive pulmonary disease. Crit Care Med 2015;43:1386-94.

4) Kluge S, Braune S, Engel M, et al. Avoiding invasive mechanical ventilation by extracorporeal carbon dioxide removal in patients failing noninvasive ventilation. Intensive Care Medicine 2012;38:1632-9.

5) Mani RK, Schmidt W, Lund LW, et al. Respiratory dialysis for avoidance of intubation in acute exacerbation of COPD. ASAIO 2013;59:675-8.

6) Del Sorbo L, Pisani L, Filippini C, et al. Extracorporeal CO2 removal in hypercapnic patients at risk of noninvasive ventilation failure: A matched cohort study with historical controls. Crit Care Med 2015;43:120-7.

7) Cole S, Barrett N, Glover G, et al. Extracorporeal carbon dioxide removal as an alternative to endotracheal intubation for non-invasive ventilation failure in acute exacerbation of COPD. JICS 2014;15:344-6.

8) Bein T, Weber-Carstens S, Goldmann A, et al. Lower tidal volume strategy (≈ 3 ml/kg) combined with extracorporeal CO2 removal versus 'conventional' protective ventilation (6 ml/kg) in severe ARDS: the prospective randomized Xtravent-study. Intensive Care Med 2013;39:847-56.

9) Terragni PP, Del Sorbo L, Mascia L, et al. Tidal volume lower than 6 ml/kg enhances lung protection: role of extracorporeal carbon dioxide removal. Anesthesiology 2009;111:826-35.

10) The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342:1301-8.

11) Needham DM, Yang T, Dinglas VD, et al. Timing of low tidal volume ventilation and intensive care unit mortality in acute respiratory distress syndrome. A prospective cohort study. Am J Respir Crit Care Med 2014;191:177-85.

Disclaimer

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Always refer to the Instructions for Use for complete indications and clinical instructions.

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Please consult the Hemolung RAS Instructions for Use for the complete set of warnings, cautions, and potential complications related to providing $ECCO_2R$ therapy with the Hemolung RAS.

Caution: Federal law (USA) restricts this device for sale by or on the order of a physician. Not for sale in the USA.