The Case for ECCO₂R
Extracorporeal CO₂ Removal in Acute Respiratory Failure
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Please consult the Hemolung RAS Instructions for Use for the complete set of warnings and cautions related to providing ECCO\textsubscript{2}R therapy with the Hemolung RAS.
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1. What is Respiratory Dialysis?
2. ECCO$_2$R in acute exacerbation of COPD
3. ECCO$_2$R for lung protection in ARDS
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WHAT IS RESPIRATORY DIALYSIS?
Rest and Heal the Lungs

CO₂ removal, rather than O₂ delivery, is often a primary obstacle in the treatment of acute respiratory failure.

“Lung Rest,” with or without mechanical ventilation, is facilitated by extracorporeal carbon dioxide removal.
Extracorporeal CO\textsubscript{2} Removal

• Membrane lung removes CO\textsubscript{2} independently of the lungs
• Low blood flow rates (< 1 LPM)
• Clinically significant CO\textsubscript{2} removal
• Minimal O\textsubscript{2} delivery

Clinical Benefits

• Avoid intubation when NIV fails
• Facilitate protective ventilation
A simple, minimally invasive approach to ECCO$_2$R.

- Small catheter
- Low blood flow
- Simple circuit
- Efficient CO$_2$ removal
# The Range of ECLS Techniques

<table>
<thead>
<tr>
<th>Type</th>
<th>Extracorporeal CO$_2$ Removal</th>
<th>Full ECMO</th>
</tr>
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<tbody>
<tr>
<td><strong>Vascular Access</strong></td>
<td>Veno-Venous Single catheter 15 Fr Double-lumen</td>
<td>Veno-Venous 21-32 Fr Double-lumen, or Two single lumen 15-24 Fr</td>
</tr>
<tr>
<td><strong>Blood Flow</strong></td>
<td>~ 250 – 550 mL/min</td>
<td>2.0 – 5.0 L/min</td>
</tr>
<tr>
<td><strong>CO$_2$ Removal</strong></td>
<td>Up to 40%</td>
<td>Up to 100%</td>
</tr>
<tr>
<td><strong>O$_2$ Delivery</strong></td>
<td>~ 10%</td>
<td>Up to 100%</td>
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The Range of ECLS Techniques

The Case for ECCO2R (MKTG-2000-v1.1)
ECCO$_2$R first described in 1977

THE CARBON DIOXIDE MEMBRANE LUNG (CDML):
A NEW CONCEPT

T. Kolobow, L. Gattinoni, T. Tomlinson,
D. White, J. Pierce, and G. Iapichino

While oxygen is emphasized during cardiopulmonary bypass, awake subjects are highly sensitive to minor changes in arterial blood pCO$_2$. Breathing is affected significantly when a small fraction of CO$_2$ is removed by an extracorporeal artificial lung$^1$. The resting CO$_2$ production in an adult man (200 ml/min) is equivalent to CO$_2$ contained in 400 ml of blood; this is a unique characteristic of CO$_2$. This amount of CO$_2$ can be readily eliminated by partial clearance from 1.0 L of blood through the artificial lung. As an example, if part of CO$_2$ is removed by extracorporeal means, through an arteriovenous fistula, breathing for CO$_2$ removal will be reduced proportionately. This observation can be utilized to benefit in the reducing of tidal volume, peak inspiratory pressure and respiratory rate in selected patients with pulmonary insufficiency.

Kolobow et al., The Carbon Dioxide Membrane Lung: A New Concept, ASAIO J. 23:17-20,1977
ECCO₂R Technology Advances

Recent technological advances permit safer, simpler and more routine ECCO₂R applications

- Durable, biocompatible membranes
- Pumps to permit veno-venous support
- Wire-reinforced dual-lumen catheters
- Highly efficient “low-flow” devices
Respiratory Dialysis is Recognized

“A scenario is depicted whereby an efficient carbon dioxide removal device can maintain blood gas homeostasis of the patient with invasiveness comparable to hemodialysis”

“We do not need mechanical ventilation any more

“the very early application of this technique in selected patients with … chronic obstructive pulmonary disease exacerbations may prevent the need for mechanical support.”
EXTRACORPoreal CO$_2$ REMOVAL IN ACUTE EXACERBATION OF COPD
COPD Burden

- 3rd leading cause of death in the US \(^1\)
- 5th leading cause of death worldwide \(^2\)
- Growing incidence:
  - aging population
  - tobacco use in emerging markets
Defining AE-COPD

An exacerbation of COPD is:

“an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.”

Global Initiative for Chronic Obstructive Lung Disease
Pathophysiology of AE-COPD

- AE-COPD often triggered by an infection
- NIV used to improve gas exchange and unload the respiratory muscles
- 15-25% NIV failure rate in AE-COPD

O'Donnell D E, and Parker C M Thorax 2006;61:354-361
Complications of MV in AE-COPD

- Intubation complications
- Dynamic hyperinflation
- Ventilator-associated pneumonia
- Sedation
- Immobility
- Deconditioning
- Reduced oral intake
- Patient discomfort
- Ventilator dependency

30% in-hospital mortality rate for AE-COPD on MV
Goals of ECCO$_2$R in AE-COPD

- Avoid injurious effects of MV
- Provide time for recovery from underlying cause of acute exacerbation
- Breath spontaneously, communicate, eat and drink
- Mobilize and rehabilitate
- Avoid ventilator dependency
Evidence for ECCO$_2$R in COPD
A Novel Extracorporeal CO₂ Removal System

Results of a Pilot Study of Hypercapnic Respiratory Failure in Patients With COPD

- All patients with NIV failure avoided intubation
- Device well tolerated
- Mean CO₂ removal 82 mL/min (33% production)
- Mean blood flow 430 mL/min w/ 15.5 Fr catheter

Device: Hemolung RAS

Rapid correction of pCO₂ / pH
Avoidance of intubation during acute exacerbation of chronic obstructive pulmonary disease for a lung transplant candidate using extracorporeal carbon dioxide removal with the Hemolung

“Compared with ECMO systems used for full respiratory or cardiopulmonary support, the Hemolung was substantially simpler to operate.”
Avoiding invasive mechanical ventilation by extracorporeal carbon dioxide removal in patients failing noninvasive ventilation

- Rapid correction of acidosis
- 19/21 patients avoided intubation
- Trend toward shorter hospital stay

“...preemptive application of ECCO$_2$R is a feasible therapeutic option to prevent intubation and invasive mechanical ventilation in selected patients with episodes of acute hypercapnic respiratory failure.”

Device: Novalung iLA
Pilot Study of Extracorporeal Carbon Dioxide Removal to Facilitate Extubation and Ambulation in Exacerbations of Chronic Obstructive Pulmonary Disease

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1Division of Pulmonary, Allergy, and Critical Care, Department of Medicine; and 2Division of Thoracic Surgery, Department of Surgery, Columbia University College of Physicians and Surgeons/New York-Presbyterian Hospital, New York, New York

Protocol:

- Demonstrated feasibility of ECCO$_2$R to facilitate early extubation in AE-COPD
- Patients ambulated without complication

Device: Maquet ECMO circuit


Rapid improvement of dyspnea and pH
Algorithm for use of low-flow \( \text{ECCO}_2 \text{R} \) in acute exacerbation of COPD failing NIV
EXTRACORPOREAL CO$_2$ REMOVAL TO FACILITATE PROTECTIVE VENTILATION IN ARDS
What is ARDS?

**Acute Respiratory Distress Syndrome**

- Acute onset of hypoxemic respiratory failure
- Increased capillary permeability results in accumulation of fluid inside the alveoli resulting in poor gas exchange

- Develops as a result of: Sepsis, toxic inhalation, aspiration, pneumonia, trauma, transfusion reaction, etc.
The Burden of ARDS

• 400,000 cases of ARDS worldwide annually
• High mortality (27 – 45%) \(^7\)
• Significant disability even in survivors
• Affects even those without chronic conditions
# Berlin Definition of ARDS

<table>
<thead>
<tr>
<th>Germany Definition of ARDS</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>PaO₂/FiO₂ (mmHg)</td>
<td>200 &lt; P/F ≤ 300 (or CPAP) ≥ 5</td>
<td>100 &lt; P/F ≤ 200 ≥ 5</td>
<td>P/F ≤ 100 ≥ 5</td>
</tr>
<tr>
<td>PEEP (cm H₂O)</td>
<td>≥ 5</td>
<td>≥ 5</td>
<td></td>
</tr>
<tr>
<td>Mortality [95% CI]</td>
<td>27% [24-30]</td>
<td>32% [29-34]</td>
<td>45% [42-48]</td>
</tr>
<tr>
<td>Duration of MV [IQR]</td>
<td>5 days [2-11]</td>
<td>7 days [4-14]</td>
<td>9 days [5-17]</td>
</tr>
<tr>
<td>Progression in 7 days (from baseline at diagnosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From Mild</td>
<td>29% [26-32]</td>
<td>4% [3-6]</td>
<td></td>
</tr>
<tr>
<td>From Moderate</td>
<td>13% [11-14]</td>
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</tbody>
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MV: A necessary evil in ARDS

“If correctly performed, mechanical ventilation “buys time” to allow other therapies to take effect; if performed incorrectly, it may kill the patient.”

Dr. Luciano Gattinoni
CMAJ 2008;178:1174-1176
Ventilator Induced Lung Injury (VILI)

Mechanical injury from ventilation (barotrauma, volutrauma, atelectrauma)

Systemic inflammatory response (biotrauma)

Multi organ failure $\rightarrow$ death

Death rarely from severe hypoxemia in ARDS!

Gattinoni L, and Protti A CMAJ 2008;178:1174-1176
“Indeed, the only strategy that has demonstrated improved survival in patients with ARDS is the use of low tidal volume (VT) (≤6 ml/kg predicted body weight (PBW) ventilation, along with adequate positive end-expiratory pressure (PEEP), and limiting plateau pressure to ≤30 cm H$_2$O. Although this strategy aims to minimize VILI due to volutrauma or atelectrauma, recent studies have revealed that tidal hyperinflation may occur despite the use of this strategy and there may be advantages to reductions below 6 ml/kg PBW, even if plateau pressures are <30 cm H$_2$O.”
ECCO$_2$R facilitates lung protection

ECCO$_2$R facilitates de-escalation of ventilatory support with less risk of hypercapnia by offloading the lungs.

- Tidal volume $\leq$ 6 ml/kg PBW
- Plateau pressure $\leq$ 30 cm H$_2$O
- Limit / reduce hypercapnia
Remember, $\text{ECCO}_2\text{R}$ is not ECMO!

**ECMO**
Indicated for treating refractory hypoxemia in the most severe cases of ARDS.

**ECCO$_2$R**
Indicated for facilitating lung protective ventilation in ALL stages of ARDS.
ECCO\textsubscript{2}R in ARDS

Increasing Intensity of Intervention

- Respiratory Dialysis
  - (< 500 mL/min, VV, 15 Fr single catheter)
  - Facilitation of ultra-low tidal volume lung-protective ventilation
- NIV
- Low-Moderate PEEP
- Low Tidal Volume Ventilation
- High PEEP
- Higher PEEP
- Prone Positioning
- Neuromuscular Blockade
- iNO
- HFOV
- ECMO
- Full ECCO\textsubscript{2}R

PaO\textsubscript{2} / FiO\textsubscript{2}

- Mild ARDS (22%)
- Moderate ARDS (50%)
- Severe ARDS (28%)

The Case for ECCO2R (MKTG-2000-v1.1)
Only a minority of ARDS patients need full ECMO. For everyone else, ECCO$_2$R can facilitate protective mechanical ventilation.

**ARDS Severity**
*Initial + Within 7 days*

- **Mild**: 29%
- **Moderate**: 50%
- **Severe**: 13%

**ARDS**
- 22%
- 28%
Evidence for ECCO$_2$R in ARDS

Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

Role of Extracorporeal Carbon Dioxide Removal

Pier Paolo Terragni, M.D.,* Lorenzo Del Sorbo, M.D.,* Luciana Mascia, M.D., Ph.D.,* Rosario Urbino, M.D.,* Erica L. Martin, Ph.D.,* Alberto Birocco, M.D.,† Chiara Faggiano, M.D.,‡ Michael Quintel, M.D.,§ Luciano Gattinoni, M.D.,¶ V. Marco Ranieri, M.D.,||

Research

Pumpless extracorporeal interventional lung assist in patients with acute respiratory distress syndrome: a prospective pilot study

Markus Zimmermann1, Thomas Bein1, Matthias Artl1, Alois Philipp2, Leopold Rupprecht2, Thomas Mueller2, Matthias Lubnow2, Bernhard M Graf1 and Hans J Schlitt4

Lower tidal volume strategy ($\approx 3$ ml/kg) combined with extracorporeal CO$_2$ removal versus ‘conventional’ protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study
• ↓ Vt: 6 → 4 mL/kg
• ↓ PPLAT: 29 → 25 cm H₂O
• PaCO₂/pH normalized
• ↓ markers of lung injury
• ↓ pulmonary cytokines
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

• 79 patients randomized
• Reduced time on MV in patients with PaO₂/FIO₂ ≤150
• Reduced needs for analgesics and sedatives
• Significantly reduced levels of pro-inflammatory cytokine IL-6

“The use of very low VT combined with extracorporeal CO₂ removal has the potential to further reduce VILI compared with a ‘normal’ lung protective management.”
HEMOLUNG® RAS
The First Fully – Integrated Respiratory Dialysis® System

Cartridge + Catheter + Controller = HEMOLUNG® RAS
HEMOLUNG® RAS
A simple and efficient system for Respiratory Dialysis

- Low blood flow
  350-550 ml/min
- Small Catheter
  15.5 Fr Veno-venous
- Efficient ECCO$_2$R
  30% - 50% of lung function
The Hemolung Cartridge
- Blood Pump
- Advanced gas exchange membrane
- 7-day Use

The Hemolung Catheter
- 15.5 Fr Diameter
- Kink Resistant
- Femoral or Jugular

The Hemolung Controller
- CO₂ Removal Measured
- Auto Gas Handling
- 1 hr Battery Backup
ActivMix™ Gas Exchange Technology

ActivMix technology increases CO₂ removal at low blood flow rates.
For more information:
Please visit alung.com
References


8. Hemolung RAS Instructions for Use (current version available from ALung Technologies on request)