Newer techniques for extracorporeal lung support

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Conflict Of Interest

• Grants from Maquet, Drager

• Consultant for Maquet, Novalung Gambro

• Patents in CO2 removal technology

• Patent in respiratory monitoring
Extracorporeal CO$_2$ removal (ECCO$_2$R)

• **Role** of ECCO$_2$R?
• **Why** improving ECCO$_2$R
• **How** to improve ECCO$_2$R?
Extracorporeal CO2 removal (ECCO2R)

- Role of ECCO2R?
- Why improving ECCO2R?
- How to improve ECCO2R?
- Clinical cases
### Why

#### Future

<table>
<thead>
<tr>
<th>Renal support (CVVH)</th>
<th>Partial extracorporeal support (ECCO₂R)</th>
<th>Total extracorporeal support (ECMO)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood flow (l/min)</strong></td>
<td><strong>V-V</strong> 0.3-0.5, <strong>A-V</strong> 1.0-2.5, <strong>V-V</strong> 0.5-2</td>
<td><strong>V-V</strong> 2.0-5.0, <strong>A-V</strong> 5.0</td>
</tr>
<tr>
<td><strong>Vascular access</strong></td>
<td><strong>V-V</strong> shunt, <strong>A-V</strong> shunt, femoral shunt</td>
<td><strong>V-V</strong> shunt, <strong>A-V</strong> shunt</td>
</tr>
<tr>
<td><strong>Catheter’s diameter (F)</strong></td>
<td>12 F, 14 F, A: 13, &gt;15 F</td>
<td>Inlet 19-24, A: 19-24</td>
</tr>
<tr>
<td><strong>Priming volume (ml)</strong></td>
<td>140-160, 300, 350</td>
<td>Outlet 15-21, V: 16</td>
</tr>
<tr>
<td><strong>Needs for heparin (IU/min)</strong></td>
<td>4-12, 4-18, 3.5-10</td>
<td>10-20, 10-20</td>
</tr>
<tr>
<td><strong>Membrane surface (m²)</strong></td>
<td>1.3, 1.3</td>
<td>1.8, 1.8</td>
</tr>
<tr>
<td><strong>CO₂ extraction (% of baseline)</strong></td>
<td>–, 25, 50, &gt;50</td>
<td>&gt;50, &gt;50</td>
</tr>
<tr>
<td><strong>O₂ transfer (ml/min)</strong></td>
<td>–, 10, 20-60</td>
<td>140-340, 340</td>
</tr>
</tbody>
</table>

*Future:* >40


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*Note:* The table above does not include all possible permutations of support types and modalities, but highlights some key differences and considerations between V-V, A-V, and total extracorporeal support. Future advancements aim to improve efficiency and efficacy, particularly in CO₂ extraction and O₂ transfer parameters.
Improving extracorporeal CO2 removal

- Constraints
  - Normal blood contains 25 mMol/l CO2
  - Normal VCO2 10 mMol/min
  - 0.5 l of blood carries total VCO2
  - Changing CO2 contents changes pH
Improving extracorporeal CO2 removal

• Targets:
  – Safety
  – Easy to apply
  – Simple operation
  – Performance (CO2 removed/ Blood flow)
Improving extracorporeal CO2 removal

- Minimizing blood flow:
  - Minimizes cannulation problems
  - Minimizes extracorporeal circulation risks
  - Regional anticoagulation?
Improving extracorporeal CO2 removal

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Extracorporeal CO2 removal (ECCO2R)

- Role of ECCO2R?
- Why improving ECCO2R
- How to improve ECCO2R?
Extracorporeal CO2 removal (ECCO2R)

- Role of ECCO2R?
- Why improving ECCO2R
- How to improve ECCO2R?
  - HOW TO GET A LOT OF CO2 OUT FROM A SMALL AMOUNT OF BLOOD
How to improve CO2 removal?

• Two main approaches:
  – Carbonic anhydrase
  – Acidification
CO₂ blood content

5% dissolved CO₂ (pCO₂ x 0.03)

90% HCO₃⁻ + H⁺ ↔ H₂CO₃ ↔ CO₂ + H₂O

5% carbamino compounds

Membrane lung works on ΔPCO₂

Venous blood
~650 ml CO₂/l blood
CO₂ blood content

5% dissolved CO₂ (pCO2 x 0.03)

90% HCO₃⁻ + H⁺ ↔ H₂CO₃ ↔ CO₂ + H₂O

CA accelerates the equilibrium (both directions)

5% carbamino compounds

Venous blood

~650 ml CO₂/l blood
ACID Changes the equilibrium and increases PCO2

90% $\text{HCO}_3^-$ + $\text{H}^+$ ↔ $\text{H}_2\text{CO}_3$ ↔ $\text{CO}_2$ + $\text{H}_2\text{O}$
pH = 7.39
PCO2 = 40 mmHg
HCO3- = 24 mMol/l
BE = 0

pH = 6.57
PCO2 = 208 mmHg
HCO3- = 18.7 mMol/l
BE = -10

VCO2 increases
Which ACID?

Non-metabolizable
- Hydrochloric acid

Metabolizable
- Lactic acid
- Citric acid

Equally effective on extracorporeal VCO2
Which ACID?

Metabolizable
- Lactic acid

> Quickly metabolized
> Not harmful
> Easy to measure at the bedside
Exp. n°1 How much acidification?

6 pigs
37±2 Kg

L-lactic acid
4,5%
(0.5 N)

1 mEq/min
2 mEq/min
5 mEq/min

Gas Flow
FiO2 100%
10 l/min

Blood Flow
500 ml/min

35: 1484-1487

Quadrox D
Exp. n°1 >> How much acidification?

CO₂ removal (ml/min)

Adult CO₂ production

+ 16%  + 30%  + 64%

Blood flow = 500 ml/min

Acid Infusion (mEq/min)

0 1 2 5

104ml 121ml 131ml 171ml

Exp. n°2 >> Long term safety and efficacy

Maximum pH drop 0.04

No complications, No hemolysis

Zanella, Anesthesiology 2014: 120: 416
Extracorporeal carbon dioxide removal through ventilation of acidified dialysate: An experimental study
Exp. N°4 >> ML on dialysate circuit

Evaluating efficacy and safety of enhanced extracorporeal CO₂ removal through acidification and ventilation of dialysate.

- Blood Flow: 250 ml/min
- Gas flow: 10 l/min, 100% O₂
- Lactic Acid: 2.5 mEq/min

8 randomized 1-h steps repeated 3 times:
4 dialysate flows (200/400/600/800 ml/min) ± lactic acid infusion

Zanella, et J Heart Lung Transplant 2014, 33: 536
Which ACID?

Non-metabolizable
- Hydrochloric acid

Metabolizable
- Lactic acid
- Citric acid

- Cannot be metabolized
- Progressive accumulation
- A removal system is required
How to acidify blood without infusion of exogenous compounds?

Electrodialysis

Image from: http://glossary.periodni.com/
Respiratory Electrodialysis
A Novel, Highly Efficient Extracorporeal CO₂ Removal Technique

Alberto Zanella¹, Luigi Castagna¹, Domenico Salerno¹, Vittorio Scaravilli¹, Salua Abd El Aziz El Sayed Deab¹, Federico Magni¹, Marco Giani¹, Silvia Mazzola², Mariangela Albertini², Nicolò Patroniti¹,³, Francesco Mantegazza¹, and Antonio Pesenti¹,³

Am J Respir Crit Care Med 2015
Respiratory electrodialysis
Minute Volume

First Baseline  ECCO$_2$R  Respiratory Electrolysis  Final Baseline

Minute Volume L/min

0  1  2  3  4  5  6  7  8  9
Respiratory electrodialysis CO₂ removal

First Baseline

ECCO₂R

Respiratory Electrodialysis

Final Baseline

VCO₂ ml/min

 NL VCO₂

 ML VCO₂

*%

*$%$
Respiratory electrodialysis

Arterial pH

First Baseline  ECCO$_2$R  Respiratory Electrodialysis  Final Baseline

Arterial pCO$_2$ mmHg

First Baseline  ECCO$_2$R  Respiratory Electrodialysis  Final Baseline
Extracorporeal Blood flow l/min

- Respiratory electrodialysis
- Standard ECCO$_2$R

VCO$_2$ ML (ml/min)

Extracorporeal Blood flow l/min