Title: Miniaturization of extracorporeal heart/lung assist

by: Dr. Rüdger Kopp – University Hospital RWTH Aachen
What means Extracorporeal Heart/Lung Assist?

**Extracorporeal Lung Assist (ECLA) Extracorporeal CO₂ Removal (ECCO₂R)**
- Veno-venous perfusion
- High flow or low flow
- Indication: Respiratory Failure

**Extracorporeal Life Support (ECLS)**
- Combined heart and lung support
- Veno-arterial perfusion
- High flow
- Indication: Acute heart failure
  Combined heart/lung failure

**Extracorporeal Membrane Oxygenation (ECMO)**
ECMO: History

First successful ECMO (72h), Santa Barbara 1971

Veno-venous ECMO for ARDS, Aachen 1998

State of the art – ECMO 2000

- No certified commercially available systems
- Oxygenator and blood-pump certified for a lifespan of 6 hours.
- Effective runtime about 3-6 days

Rescue-therapy for
- Severe Acute Respiratory Distress Syndrome with hypoxemia
- Severe post-cardiotomy cardiac failure
Miniaturization with optimized components
PMP-Oxygenator and Diagonal-Blood-Pump

6 pigs with salvage induced lung injury

ECMO: Not only for hypoxemia?

Gas exchange

Dissociation in his components
T. Kolobow/L. Gattinoni

Oxygen uptake
via native lung
with lung protective ventilation
or spontaneous ventilation

CO₂-Elimination
via ECCO₂R / pECLA
With low extracorporeal blood flow

Adapted from Gattinoni L et al. Int J Artif Organs 1979
Pumpless arterio-venous ECLA

- Pumpless arterio-venous perfusion
- First miniaturized system

- Low resistance oxygenator
- Priming volume: 240 ml
- Heparin coated surface
- No membrane leakage
ECMO versus pECLA: Gas transfer
Experimental data

O₂-transfer

\[ \text{O}_2\text{-transfer} \]

% of total transfer

CO₂-elimination

\[ \text{CO}_2\text{-elimination} \]

67±27 ml/min

16±6 ml/min

115±39 ml/min

71±35 ml/min

## ECMO versus pECLA: Haemodynamics

### Experimental data

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Pre-lung lavage</th>
<th>ALI before ECC</th>
<th>1</th>
<th>4</th>
<th>8</th>
<th>16</th>
<th>24</th>
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<tbody>
<tr>
<td></td>
<td>Stroke volume (ml)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>mECMO</td>
<td>62 (10)</td>
<td>65 (14)</td>
<td>72 (11)</td>
<td>69 (12)*</td>
<td>55 (13)</td>
<td>49 (12)*</td>
<td>53 (8)*</td>
</tr>
<tr>
<td>pECLA</td>
<td>62 (12)</td>
<td>64 (17)</td>
<td>63 (19)</td>
<td>57 (14)</td>
<td>55 (12)</td>
<td>54 (14)</td>
<td>54 (12)</td>
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<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>mECMO</td>
<td>101 (11)</td>
<td>91 (12)*</td>
<td>94 (15)</td>
<td>87 (6)*</td>
<td>86 (8)</td>
<td>80 (15)</td>
<td>83 (12)</td>
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<tr>
<td>pECLA</td>
<td>111 (11)</td>
<td>108 (13)</td>
<td>99 (11)</td>
<td>99 (16)</td>
<td>94 (16)*</td>
<td>92 (19)*</td>
<td>92 (17)*</td>
</tr>
<tr>
<td>Left cardiac work (kg m)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>mECMO</td>
<td>7.6 (2.0)</td>
<td>6.9 (1.6)</td>
<td>7.4 (1.2)</td>
<td>5.2 (0.8)*</td>
<td>4.5 (1.0)*</td>
<td>4.4 (1.5)*</td>
<td>5.0 (1.4)*</td>
</tr>
<tr>
<td>pECLA</td>
<td>8.2 (2.0)</td>
<td>8.4 (5.2)</td>
<td>7.7 (4.8)</td>
<td>6.6 (3.2)</td>
<td>6.2 (2.6)</td>
<td>6.3 (2.4)</td>
<td>6.8 (2.0)</td>
</tr>
<tr>
<td>Right cardiac work (kg m)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mECMO</td>
<td>0.7 (0.4)*</td>
<td>1.3 (0.6)</td>
<td>1.1 (0.3)</td>
<td>1.4 (0.3)</td>
<td>1.1 (0.4)</td>
<td>1.2 (0.5)</td>
<td>1.2 (0.4)*</td>
</tr>
<tr>
<td>pECLA</td>
<td>0.9 (0.2)</td>
<td>1.4 (0.9)</td>
<td>1.2 (0.6)</td>
<td>1.5 (0.4)</td>
<td>1.4 (0.4)</td>
<td>1.5 (0.4)</td>
<td>1.6 (0.5)</td>
</tr>
<tr>
<td>Total organ perfusion (litre min⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mECMO</td>
<td>5.5 (1.3)</td>
<td>5.7 (1.1)</td>
<td>6.1 (0.9)</td>
<td>4.6 (0.5)*</td>
<td>4.0 (0.7)*</td>
<td>4.4 (1.3)*</td>
<td>4.7 (1.4)</td>
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<tr>
<td>pECLA</td>
<td>5.7 (1.6)</td>
<td>5.8 (3.0)</td>
<td>4.5 (2.7)</td>
<td>3.6 (1.5)*</td>
<td>3.6 (1.2)*</td>
<td>3.9 (1.1)*</td>
<td>4.4 (0.8)</td>
</tr>
<tr>
<td>Total oxygen delivery to organs (ml min⁻¹)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mECMO</td>
<td>577 (125)*</td>
<td>469 (121)</td>
<td>438 (129)</td>
<td>368 (92)</td>
<td>368 (108)</td>
<td>343 (103)*</td>
<td>394 (130)</td>
</tr>
<tr>
<td>pECLA</td>
<td>605 (151)*</td>
<td>432 (80)</td>
<td>421 (95)</td>
<td>396 (83)</td>
<td>371 (70)</td>
<td>380 (73)</td>
<td>348 (49)</td>
</tr>
</tbody>
</table>
Pumpless arteriovenous ECLA
How can it help the intensivist?

- Easy management
- High CO₂-Elimination (up to ~150 ml/min)
- Good hemocompatibility
- Certified for 30 days

- Low O₂-Transfer (~40 ml/min)
- Risk of ischemia due to arterial cannula
- Increased cardiac work
- Limited mobilization of patient
Management of Extracorporeal Lung Support

Traditional concept

- Invasive Mechanical Ventilation
- ECMO
- Weaning

New concepts

- Invasive Mechanical Ventilation
- ECMO
- Weaning
- Invasive Mechanical Ventilation
- ECMO
- Weaning
- Non-invasive Ventilation/Spontaneous Breathing
- ECMO
- Weaning
What about mobilization with ECMO?
Double lumen cannulas for ECMO

Classical double lumen cannula
- 18 to 24 French
- 0.6 to 2.0 l/min

Double lumen cannula with back flow
- 20 to 31 French
- up to 5 l/min blood flow
- X-ray or echocardiography necessary

- No femoral cannula
- Shorter tubing
- Optimized mobilisation of patients
# iLA ACTIVE

A pump-driven miniaturized ECMO

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Cause of Lung Failure</th>
<th>PaO$_2$/FiO$_2$ Ratio</th>
<th>PaCO$_2$ (mm Hg)</th>
<th>Awake on FiO$_2$-R</th>
<th>Hospital Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>67</td>
<td>AECOPD</td>
<td>187</td>
<td>71</td>
<td>0.35 Yes</td>
<td>Yes</td>
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<tr>
<td>2</td>
<td>F</td>
<td>61</td>
<td>Graft failure—bridge to Re-LuTX</td>
<td>142</td>
<td>117</td>
<td>0.50 Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>25</td>
<td>Graft failure—bridge to Re-LuTX</td>
<td>351</td>
<td>82</td>
<td>0.30 Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>46</td>
<td>Emphysema—bridge to LuTX</td>
<td>138</td>
<td>70</td>
<td>0.50 No</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>25</td>
<td>Status asthmaticus</td>
<td>107</td>
<td>137</td>
<td>0.60 Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>38</td>
<td>Lung fibrosis</td>
<td>169</td>
<td>124</td>
<td>0.65 Yes</td>
<td>Yes</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Primarily hypoxic lung failure</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>41</td>
<td>Pneumonia</td>
<td>71</td>
<td>52</td>
<td>0.85 No</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>69</td>
<td>Pneumonia</td>
<td>76</td>
<td>81</td>
<td>0.85 No</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>64</td>
<td>ARDS</td>
<td>156</td>
<td>95</td>
<td>0.55 No</td>
<td>Yes</td>
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<tr>
<td>10</td>
<td>F</td>
<td>31</td>
<td>Graft failure after LuTX, pneumonia</td>
<td>100</td>
<td>62</td>
<td>0.60 No</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>51</td>
<td>Pneumonia, COPD</td>
<td>94</td>
<td>71</td>
<td>0.70 No</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>42</td>
<td>Pneumonia</td>
<td>85</td>
<td>105</td>
<td>0.85 No</td>
<td>No</td>
</tr>
</tbody>
</table>
# Modifications of iLA ACTIVE

<table>
<thead>
<tr>
<th>Therapy:</th>
<th>iLA® membrane ventilator</th>
<th>iLA® active®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main function:</td>
<td>CO₂ removal + lung protection</td>
<td>CO₂ removal + lung protection + oxygenation support</td>
</tr>
<tr>
<td>Vascular access:</td>
<td>arteriovenous</td>
<td>venovenous</td>
</tr>
<tr>
<td>Membrane ventilator:</td>
<td>iLA®</td>
<td>MiniLung® petite</td>
</tr>
<tr>
<td>Cannulation:</td>
<td>NovaPort® one</td>
<td>NovaPort® twin</td>
</tr>
<tr>
<td>Pump driven:</td>
<td>no</td>
<td>yes</td>
</tr>
</tbody>
</table>

Blood flow: 0.5-1.5, -0.8, -2.4, 0.5-4.5, 1-7
ILAactive
Is it the better device?

- Veno-venous CO₂-elimination and additional O₂-transfer
- Jugular or femoral double lumen cannula

+ Compact design
+ Modular
+ Mobilization possible

? No heat exchanger
? No ultracompact design
Development of ECMO-Devices with coupled console, oxygenator and blood pump

ECMO for cardiogenic shock (n=21)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Before Mini-ECMO</th>
<th>2 h on Mini-ECMO</th>
<th>24 h on Mini-ECMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>aMAP [mmHg]</td>
<td>62.90 ± 12.37</td>
<td>74 (53–88)</td>
<td>78 (55–92)</td>
</tr>
<tr>
<td>bNorepinephrine [mg h⁻¹]</td>
<td>4.35 (0.0–30.0)</td>
<td>1.0 (0.0–3.2)</td>
<td>0.7 (0.0–2.6)</td>
</tr>
<tr>
<td>pH</td>
<td>7.25 (6.89–7.51)</td>
<td>7.40 (7.14–7.58)</td>
<td>7.43 (7.35–7.59)</td>
</tr>
<tr>
<td>bOR [mmHg]</td>
<td>87 (39–420)</td>
<td>224 (47–760)</td>
<td>207 (90–743)</td>
</tr>
<tr>
<td>bPaCO₂ [mmHg]</td>
<td>45 (26–75)</td>
<td>33 (29–39)</td>
<td>32 (23–48)</td>
</tr>
<tr>
<td>bLactate [mmol l⁻¹]</td>
<td>70 (10–222)</td>
<td>60 (10–304)</td>
<td>40 (10–223)</td>
</tr>
<tr>
<td>aECMO-flow [l min⁻¹]</td>
<td>3.2 ± 0.8</td>
<td>3.0 ± 0.9</td>
<td></td>
</tr>
</tbody>
</table>

ECMO for acute respiratory failure (n=22)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>pre ECMO (n = 22)</th>
<th>2 hours (n = 22)</th>
<th>Day 1 (n = 22)</th>
<th>Day 2 (n = 22)</th>
<th>End of ECMO (n = 16)</th>
<th>Day 1 after ECMO (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂/FiO₂ (mmHg)</td>
<td>60 (46 to 75)</td>
<td>123 (94 to 156)</td>
<td>153 (102 to 220)</td>
<td>158 (126 to 195)</td>
<td>265 (215 to 318)</td>
<td>230 (160 to 274)</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>67 (57 to 100)</td>
<td>34 (31 to 39)</td>
<td>37 (35 to 43)</td>
<td>43 (39 to 45)</td>
<td>42 (37 to 42)</td>
<td>41 (37 to 50)</td>
</tr>
<tr>
<td>pH</td>
<td>7.23 (7.17 to 7.32)</td>
<td>7.49 (7.41 to 7.54)</td>
<td>7.48 (7.43 to 7.49)</td>
<td>7.44 (7.43 to 7.45)</td>
<td>7.42 (7.39 to 7.49)</td>
<td>7.43 (7.35 to 7.44)</td>
</tr>
<tr>
<td>ECMO flow (L/min)</td>
<td>–</td>
<td>3.1 (2.7 to 3.4)</td>
<td>2.7 (2.5 to 3.1)</td>
<td>2.6 (2.4 to 2.9)</td>
<td>1.5 (1.4 to 1.6)</td>
<td>–</td>
</tr>
<tr>
<td>Lactic acid (mg/dL)</td>
<td>23 (15 to 36)</td>
<td>30 (16 to 49)</td>
<td>20 (16 to 30)</td>
<td>16 (12 to 24)</td>
<td>11 (9 to 17)</td>
<td>11 (7 to 12)</td>
</tr>
</tbody>
</table>

Survival rate: 62–68%
Indications and disadvantages for integrated ECMO systems?

- **Maquet Cardiohelp:**
  - veno-venous ECMO for lung assist → ECLA
  - veno-arterial ECMO for heart/lung support → ECLS

- **Advantages:**
  - Compact design
  - Transportable
  - High performance (up to 7 l/min blood flow)
  - Certified for 30 days

- **Disadvantages:**
  - Components could not be changed, only complete system
  - No patient-side operation
New indications for ECLS and cardiac failure

- Post-cardiotomy cardiac failure
- Refractory cardiac arrest
- Pulmonary embolism
- Bridge to Lung/Heart transplant
- Cardiogenic shock
  - With high risk percutaneous coronary intervention
  - Before cardiovascular surgery
- Decompensated end-stage cardiac insufficiency with cardiogenic shock
Which different forms of extracorporeal heart/lung assist are possible?

**v-v/v-a ECMO**
- Veno-venous/arterial
- Pump driven
- Priming 500-1.000 ml
- High CO₂-elimination
- High O₂-transfer
- Bloodflow up to 5 l/min

**low-flow v-v ECLA**
- Veno-venous
- Pump driven
- Priming up to 500 ml
- Effective CO₂-elimination
- Moderate O₂-transfer
- Bloodflow up to 0.5 l/min

**a-v pECLA**
- Arterio-venous
- Pumpless
- Priming 250 ml
- Effective CO₂-elimination
- Low O₂-transfer
- Bloodflow 0.5-1.5 l/min
Miniaturization of ECMO
HEXMO

- Capillary membrane oxygenator: Membrane surface 0.9 m²
- Integrated blood pump
- Reduced filling volume about 90 ml
HEXMO
In-Vitro Study

- Animal study (n=6, t=4 hours)
What other innovative concepts are possible for extracorporeal gas exchange?
Respiratory Dialysis: Hemodec Decap

- Veno-venous CO$_2$-Elimination
- Bloodflow 0.2-0.4 l/min
- Jugular double lumen cannula

Pilot study: 7 sheep, runtime 3-12 h
Carbon dioxide Transfer of an oxygenator

**Diagram Description:**
- The graph on the left shows the CO\textsubscript{2} Removal (mL/min) as a function of Sweep Gas flow (L/min).
  - Lines represent different time points: 0 hour, 24 hour, 48 hour, and 72 hour.
  - Vertical bars indicate standard deviation.
- The graph on the right shows the relationship between CO\textsubscript{2} Removal (mL/min) and AVCO\textsubscript{2}R Blood Flow (L/min).
  - Arterial pCO\textsubscript{2} is indicated with a horizontal line.
ALung: An alternative concept

- Veno-venous flow: 0.35-0.55 l/min
- Jugular double lumen cannula
- Filling volume 260 ml
- Membrane surface 0.59 m²
- Active mixing of blood
- Vacuum driven gas flow
Alung: An alternative concept

20 patients with COPD and respiratory acidosis
Proof of concept study

Burki et al. CHEST 2013; 43:678–86
Conclusion

- In the last 10 years different concepts of miniaturized heart/lung support became commercially available.

- Today we have certified systems for the different indications with a runtime up to 30 days.

- Application of ECLA/ECLS/ECMO was simplified

- New indications were established for these devices:
  - Acute on chronic respiratory failure
  - Cardiac Assist for interventions/CPR/bridging
  - ...

Thank you for your attention!

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