Artificial Lung: A New Inspiration

Joseph B. Zwischenberger MD
Johnston-Wright Professor and Chairman: Department of Surgery

j.zwische@uky.edu

The University of Kentucky
Lexington, Kentucky
Presenter Disclosure Information

Joseph B. Zwischenberger, M.D.

Research supported in part through

• Competitive funding:
  National Institutes of Health (SBIR, STTR, T-32)

• Contracts:
  MC3, Ann Arbor Mi
  Medarray Inc. Ann Arbor Mi
  Avalon Laboratories, LLC, Grand rapids Mi

Patent: Avalon Elite™
Introduction

• Respiratory failure is now the 3rd leading cause of death in the USA

• Despite advances, death from acute respiratory failure remains ~ 40%

• ARDS NET Trial demonstrated decreased mortality with Low Tidal Volume Ventilation (6 ml/Kg vs. 12 ml/Kg)
Treatments for Severe Hypoxemic Respiratory Failure

- High PEEP vs. Low PEEP
- Recruitment Maneuvers
- Pressure Control Ventilation
- Airway Pressure Release Ventilation
- High Frequency Oscillatory Ventilation
- High Frequency Percussive Ventilation

All transiently improve oxygenation but NONE HAVE PRODUCED A MORTALITY BENEFIT!!

Esan et.al. CHEST 2010, 137(5):1203-1216
VENOARTERIAL ECMO: Bartlett 1979
VENOVENOUS ECMO
Single, Double Lumen Cannula
For total gas exchange alone

Zwischenberger/Drake 1989
<table>
<thead>
<tr>
<th></th>
<th>Total #</th>
<th>% Survived</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>24,770</td>
<td>85</td>
</tr>
<tr>
<td>Cardiac</td>
<td>4,375</td>
<td>61</td>
</tr>
<tr>
<td><strong>Pediatric</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>4,009</td>
<td>65</td>
</tr>
<tr>
<td>Cardiac</td>
<td>5,423</td>
<td>64</td>
</tr>
<tr>
<td><strong>Adult</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>2,620</td>
<td>63</td>
</tr>
<tr>
<td>Cardiac</td>
<td>1,680</td>
<td>53</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>46,509</td>
<td>74</td>
</tr>
</tbody>
</table>
Oxygen transfer
Carbon Dioxide Removal
CO₂ Removal

CO₂ removal and O₂ transfer are uncoupled:

– CO₂ is transferred across the membrane gas exchanger

– Low Frequency Ventilation: O₂ diffuses across the native lungs

Ted Kolobow 1977
AVCO$_2$R: Carbon Dioxide Removal (get the bad air out) with a low-resistance gas exchanger in a simple arterio-venous shunt

Zwischenberger 1996
AVCO$_2$R Outcome

- 5/5 completed 72 hr trial
- 3/5 Discharged
- 2 minor complications
- 8/8 completed 72 hr trial for ARDS with hypercapnia
- 5/8 Discharged
- No major complications
Arteriovenous CO$_2$ Removal NOVALUNG (Europe): Overall Survival 70%

percutaneous cannulation of femoral artery and vein
Impact of CO$_2$ Homeostasis

CO$_2$ flux is greatly reduced by AVCO$_2$R, and may be important in:

- organ tissue neutrophil apoptosis
- resolution of inflammation
- maintaining a normal alveolar milieu
Paracorporeal Artificial Lung: PA-PA Configuration

- 100% flow through device
- Full lung metabolic function
- No risk of stroke or $R\to L$ shunt
  - High right heart power requirement

Right Heart Failure!!

ASAIO 2004 – Wang/Zwischenberger
Assisted RA-PA Artificial Lung

1. Right ventricular assist device (RA-PA) 100% of cardiac output through the Paracorporeal Artificial Lung to prevent right heart failure

2. Requires only one PA anastomosis

3. Insertion without CPB

4. Spares pulmonary hilum for subsequent transplant

ASAIO 2006 – Wang/Zwischenberger
Ambulatory, Compact, and Paracorporeal Successful to 4 weeks

Artificial Lung

Outlet Cannula

Inlet Cannula

MicroMed Pump

Pump Driver

Zwischenberger/Wang STSA 2006
Problem Alert!! RA access and PA anastomosis too delicate for ambulation

Goal: To develop a minimally invasive double lumen cannula for a Paracorporeal Artificial Lung to:

– Avoid Thoracotomy
– Avoid Major Vessel Central Access
– Avoid recirculation

Based on VV ECMO cannulation
Wang-Zwisch DLC ➔ Avalon Elite®

- Ultra-thin membrane reinfusion lumen
- Anti-kink stainless steel reinforced catheter with ultra-thin wall
- Reinforced reinfusion port
- Extended tip introducer
Avalon Elite® Catheter Placement: image guidance required
Newborn with Meconium Aspiration on Avalon Elite®
VVDL ECMO 6 days: No Recirculation
ECMO in 2006

- Complex
- Labor intensive
- Expensive
- Time Limited
- Thrombogenic
- System failures

(Why are they still BLUE??)
Safer ECMO Technology: 2011

- Low resistance gas exchangers
- Low pressure, low trauma pumps
- Self regulating circuit
- Image-guided vascular access
- Double lumen cannula
- Non-thrombogenic coatings
Goal: Ambulatory Paracorporeal Artificial Lung
56 yo idiopathic pulmonary fibrosis: uncomplicated bilateral lung tx 3/08
12/08 Trichosporon pneumonia, post-infectious obliterative bronchiolitis.
Listed for redo transplant Feb ’08.

Alert 3-3-09  Chuck Hoopes (UCSF ): the first Ambulatory Lung Assist patient using Avalon Cannula, Quadrox and Centrimag!!

Total gas exchange - no recirculation
Exercise at the bedside
ECMO as bridge to lung Transplant
Cleveland Clinic Clinic Experience n=7

2 - non intubated resp failure (ambulatory)
5 - intubated with inadequate ventilation

6/7 lung transplant , 1/7 died on wait list

1 single, 5 double lung transplant all weaned from ECMO within 24 hrs, 1 death day 26

5/7 survivors 1-16 mo

Yun et al ISHLT 2010
This is ECMO?

“walking bypass”…RA to Ao cannulation
(BiV failure, PHTN s/p PEA..to HLTx)

“walking ECMO”…dual lumen Avalon VV (hypoxia, hypercarbea secondary BOS.. to redo BLTx)

“ambulatory right heart bypass”…PA to LA cannulation
(RV failure, hypoxia, PHTN s/p PEA..to BLTx)
Pulmonary transplant and “orphan diseases” ... pulmonary veno-occlusive disease (PVOD)


(A) Small sized vein demonstrates marked intimal proliferation and narrowing of the lumen (B) Two adjacent veins contain organizing thrombi (200X magnification)
Failing Fontan: Percutaneous cannula based CP Assist Device (CPAD)

• AvalonElite™ DLC:
  – Insert from jugular vein to SVC-extracardiac conduit.
  – Blood drains through side openings in SVC and end openings in conduit-IVC.

Wang/Zwisch 2011
Percutaneous RVAD

Wang/Zwisch 2012

Blood Pump

Infusion Lumen

Drainage Lumen Openings

Pre-Curved Extension Infusion Cannula

Superelastic Shape-Memory Alloy

Drainage opening widely open to Left RA
Organ Block Support

Schematic drawing of lung assessment ex vivo
PAP = pulmonary-arterial pressure
LAP = left-arterial pressure
Artificial Lung: A New Inspiration

Joseph B. Zwischenberger MD

Johnston-Wright Professor and Chairman: Department of Surgery

j.zwische@uky.edu

The University of Kentucky
Lexington, Kentucky