EIT monitoring of the liquid-ventilated lung

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Liquid ventilation

- Total liquid ventilation (TLV) uses perflubron instead of air for gas exchange.
- Perflubron is a dense liquid with high solubility for respiratory gasses ($\text{O}_2$, $\text{CO}_2$).
- Density ($\rho \approx 2$) helps it keep open dependent lung regions which can be collapsed (atelectatic) or undergo cyclical opening.
- Proposed Application: Protective ventilation strategy for
  - extremely premature neonates,
  - ARDS patients

**TABLE 2—Reports of Clinical Trials of Humans Treated With LAV**

<table>
<thead>
<tr>
<th>Year</th>
<th>Reference #</th>
<th>Populations</th>
<th>N</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989–94</td>
<td>4, 158, 159</td>
<td>Preterm neonates</td>
<td>6</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td>1996</td>
<td>61</td>
<td>Preterm neonates</td>
<td>13</td>
<td>Severe RDS</td>
</tr>
<tr>
<td>1996</td>
<td>62, 160</td>
<td>Term neonates</td>
<td>4</td>
<td>CDH on ECLS</td>
</tr>
<tr>
<td>1996</td>
<td>164</td>
<td>8 weeks–5.5 years</td>
<td>6</td>
<td>Respiratory failure–ECLS</td>
</tr>
<tr>
<td>1996</td>
<td>165</td>
<td>1–17 years</td>
<td>10</td>
<td>ARDS</td>
</tr>
<tr>
<td>1996</td>
<td>54–56, 166, 167</td>
<td>19–55 years</td>
<td>10</td>
<td>ARDS on ECLS</td>
</tr>
<tr>
<td>1997</td>
<td>52, 59, 161</td>
<td>Term neonates</td>
<td>6</td>
<td>ARDS/CDH</td>
</tr>
<tr>
<td>1997</td>
<td>168</td>
<td>Adults</td>
<td>65</td>
<td>Respiratory failure</td>
</tr>
</tbody>
</table>

(Wolfson et al, Pediatric Pulmonology, 1998)


*Partial liquid ventilation leads to clinical improvement and survival in some infants with severe respiratory distress syndrome who are not predicted to survive.*
<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>Clinical Research phases II and III, 56 centres / 311 patients “PLV ... does not improve outcome compared with CMV.” (Kacmarek et al, Resp. Crit. Care, 2005)</td>
</tr>
<tr>
<td>2009</td>
<td>“Only full lung liquid ventilation with a dedicated liquid ventilator is the most logical approach to apply LAV efficiently and reliably in humans” (Costantino, Micheau et al, ASAIOJ 2009)</td>
</tr>
<tr>
<td>2015</td>
<td>Hypothermic TLV is protective after cardiac arrest (Kohlhauer et al, crit Care Med 2015)</td>
</tr>
</tbody>
</table>
Total- (TLV) vs Partial- (PLV) liquid ventilation

Air

Gas

TLV

PFC

PLV

Gas

PFC

Liquid-Gas interface (surfactant)

Liquid-Liquid interface (↓ tension)

Some PFC coat alveoli, others form droplets. Inhomogeneity across lungs
Why EIT?

Challenges of TLV

- Monitoring of quantity/location of PFOB
- Induction phase, during which a mixture of air and fluid is in the lung.

Hypothesis: EIT can help clarify the time courses of distributions of air and PFOB

Previous work: Wolf et al 2010\(^1\) studied EIT and liquid ventilation, but did not address the induction phase.
Experimental Protocol

- Supine lamb (term), tracheotomy, conventional ventilation
- Instrumentation: EIT electrodes (SigmaTôme II), Arterial & Venous lines
- Conventional (air) ventilation: Pressure controlled, PEEP=14 cm H₂O.
- PFOB filling
- TLV ventilation: volume controlled mode (60 minutes)
- PFOB emptying
- Conventional (air) ventilation: Pressure controlled, PEEP=14 cm H₂O.
- Euthanasia of animal

Inolivent-6
Liquid Ventilator
Guaranteed TV
Pressure Limited
2 volumetric pumps
4 valves
Results: Induction phase

A: Conventional, B: Disconnect, C: Filling, D, E: TLV
Results: Induction phase

A: Conventional, B: Disconnect, C: Filling, D, E: TLV

Global EIT (AU)

EIT monitoring of the liquid-ventilated lung, Adler et al, 2016/06/21
Results: Induction & Stabilization Phase

A: Air  C: +20s  D: +80s  E: +180s  E: +180s  F: +7min  G: +30min

EIT monitoring of the liquid-ventilated lung, Adler et al, 2016/06/21
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Distinguish Air / PFOB with forced oscillation?

Problem: PFOB and Air are both non-conductive; how to distinguish?

Protocol: 2 Hz Forced oscillation of Liquid should couple to liquid more strongly than air
Perfusion during Liquid Ventilation

Problem: What happens to lung perfusion during TLV?

EIT monitoring of the liquid-ventilated lung, Adler et al, 2016/06/21
Perfusion during Liquid Ventilation

Problem: What happens to lung perfusion during TLV?

EIT monitoring of the liquid-ventilated lung, Adler et al, 2016/06/21
• EIT can help understand the physiological during liquid ventilation.
  • Initially: PFC in dependent, gas more ventrally.
  • over time, redistribution of ventilation → more uniform.

• Next step: currently performing a larger (N = 10) study, which will include EIT and fluoroscopy

• How to separate air and PFC in images?
References


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Introduction: Total liquid ventilation uses liquid perflubron instead of air for gas exchange. It has several possible applications, especially for the immature lungs of extremely premature neonates, and in the damaged lungs of ARDS patients. Since perflubron is dense ($\rho \approx 2$) it helps keep open dependent lung regions which can be collapsed (atelectatic) or undergo cyclical opening with traditional positive-pressure ventilation. One clear challenge with liquid ventilation is the induction phase, during which a mixture of air and fluid is in the lung. We are hopeful that EIT can help clarify the time courses of distributions during this phase, and thus help improve strategies for induction. One previous report studied EIT and liquid ventilation [1], but did not address the induction phase.

Objective: To investigate whether EIT can help clarify the distribution of ventilation during the liquid-ventilation induction phase.

Methods: One healthy lamb (male, age 3 days, 4.2 kgs) was anesthetized and ventilated in a supine position using pressure control ventilation (PIP 14 cmH2O, PEEP 4 cm H2O). Sixteen EIT electrodes were attached in a tranverse plane and images acquired at 4.7 frames/s using the Sigmatome II EIT device. During the experimental phase of interest, the ventilator was disconnected and perflubron was introduced and liquid ventilation commenced.

Results: Images were reconstructed using a GN algorithm with electrode movement compensation. The figure shows the global EIT image (arbitrary units, non-conductive changes are positive) vs. time (seconds). At four instants (vertical lines) the EIT image is shown. Phases of A) air ventilation, D) disconnection, L) liquid ventilation are seen. Images show a movement of the ventilated region in the dependent direction. From L2 and L3 show a stable ventilated region in the dependent lungs. L1 appears to show both air and liquid in the lungs.

Discussion: EIT images appear to show useful information about the physiological changes during the induction of liquid ventilation. As understood, the perflubron ventilation occurs primarily in the dependent lobes of the lung, while gas ventilation occurs more ventrally. We see an initial phase where both air and fluid are seen in the lungs. In further monitoring over the next 30 minutes (not shown) there is a redistribution of ventilation to achieve a more uniform pattern. These results suggest EIT can help understand the physiological changes during liquid ventilation.

References: