Utilization of Hypobaric Oxygenation for Gaseous Microemboli Removal in a Hollow Fiber Diffusion Membrane Oxygenator

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Stephen Francis¹ BS  
Jeffrey Riley MHPE, CCT, CCP

Second Year Perfusion Students at Midwestern University
No Disclosures

- I have no affiliations with manufacturers, competing interests, nor any relationships financial or otherwise that may affect this presentation
- Quadrox iD oxygenator is being utilized outside of the manufacturers recommendations
Numerous Arterial Gas Emboli Occur during Closed-Circuit Extracorporeal Membrane Oxygenation

York Jiao, M.D., Robert B. Schonberger, M.D., Jeffrey B. Gross, M.D., Keith E. Gipson, M.D., Ph.D.
University of Connecticut School of Medicine, Farmington, Connecticut, United States

• Numerous Arterial Gas Emboli Occur during Closed-Circuit Extracorporeal Membrane Oxygenation
• “Suggest a role for arterial filtration or other GME removal methodology”
# Background

**“Oxygen” Mechanism**

<table>
<thead>
<tr>
<th>Gas content</th>
<th>FiO2 = 21%</th>
<th>FiO2 = 40%</th>
<th>FiO2 = 100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>N2</td>
<td>70%</td>
<td>54%</td>
<td>0%</td>
</tr>
<tr>
<td>O2</td>
<td>19%</td>
<td>35%</td>
<td>89%</td>
</tr>
<tr>
<td>CO2</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>H2O</td>
<td>6%</td>
<td>6%</td>
<td>6%</td>
</tr>
</tbody>
</table>

### Background

**“Pressure” mechanism**

<table>
<thead>
<tr>
<th>Absolute Atmospheres</th>
<th>Suction Required</th>
<th>Max $pO_2$ Achievable</th>
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<tbody>
<tr>
<td>1 ata</td>
<td>0 mmHg</td>
<td>713 mmHg</td>
</tr>
<tr>
<td>0.66 ata</td>
<td>-250 mmHg</td>
<td>455 mmHg</td>
</tr>
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<td>0.33 ata</td>
<td>-500 mmHg</td>
<td>203 mmHg</td>
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#### Polymethylpentene Diffusion Hollow Fibers

- **Diffusion of Oxygen**
- **Reduced Diffusion of Oxygen**
- **Greatly Reduced Diffusion of Oxygen**
- **Diffusion of Nitrogen**
- **Diffusion of Nitrogen**
Background

“Pressure” mechanism

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Polymethylpentene Diffusion Hollow Fibers
**Background**

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“Pressure” mechanism

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**Polymethylpentene Diffusion Hollow Fibers**

- **Diffusion of Oxygen**
- **Reduction of Oxygen**
- **Diffusion of Nitrogen**
- **Greatly Reduced Diffusion of Oxygen**
Undersaturation Mechanism

**Background**

“Undersaturation” Mechanism

Pa\(O_2\) < P\(\text{bubbleO}_2\)

Purpose

• Minimize GME using hypobaric oxygenation for ECMO
  – Manipulation of Dalton’s Law of Partial Pressures
  – Manipulation of Partial Pressure “Diffusion” or “undersaturation” Gradients
  – Keep the circuit simple
    • Utilizing existing ECMO blood path technology to reduce GME during ECMO
Materials

• Quadrox iD oxygenator
  – Normal (control)
  – Vent port sealed (hypobaric)

• EDAC (Emboli detection and classification) QUANTIFIER x 3
  – Pre-oxygenator
  – Post-oxygenator
  – Arterial Cannula

• Air/ GME infusion simulates constant air down venous line
  – 50ml/min of air introduced into venous inlet

• “Patient”
  – Hardshell VR (RX15)
  – Hoffman clamps = SVR (control and hypobaric)

• PPRV (positive pressure relief valve)
Materials

- Safety
Methods

• Hypobaric oxygenation
  – Sub-atmospheric pressures created by placing suction on the gas outlet of oxygenator.
    • Emergency vent port blocked with a silicone sealant
    • -250mmHg of vacuum (0.67ata) applied
      – 760mmHg = 1ata
    – 100% Oxygen “sweep” gas connected to inlet of oxygenator.
Methods

• $[\text{pO}_2]$ – controlled by vacuum

• $[\text{pCO}_2]$ – controlled by “sweep” gas flow

<table>
<thead>
<tr>
<th>$\text{pO}_2$</th>
<th>$\text{pCO}_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\uparrow$ Vacuum = $\downarrow \text{pO}_2$</td>
<td>$\uparrow \text{O}_2 \text{ Sweep} = \downarrow \text{pCO}_2$</td>
</tr>
<tr>
<td>$\downarrow$ Vacuum = $\uparrow \text{pO}_2$</td>
<td>$\downarrow \text{O}_2 \text{ Sweep} = \uparrow \text{pCO}_2$</td>
</tr>
</tbody>
</table>

Methods

AMESIAN SOCIETY OF EXTRACORPOREAL TECHNOLOGY

RX15R
Sorin Revolution
Centrifugal Pump
EDAC
RX15R
EDAC
FX15
Hoffman Clamp
Hoffman Clamp
Room Air
Vacuum Regulator
Sorin 3T
Pr
P
R
V
Analog Pressure
Sorin S5
Digital Pressure
Quadrox-iD
Flow Regulator
100% Oxygen
Vacuum Regulator
Sorin Revolution Centrifugal Pump

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Methods

Control Trials

• 2 min each; done at 37°C, 28°C, and 18°C:
  – 100% oxygen and no vacuum
  – 3.5 L/min @150mmHg line pressure
  – 5.0 L/min @ 200mmHg line pressure
  – 10 trials done at each temperature and flow/line pressure combination (n=60)

Hypobaric Trials

• 2 min each; done at 37°C, 28°C, and 18°C:
  – 100% oxygen and -250mmHg vacuum
  – 3.5 L/min @ 150mmHg line pressure
  – 5.0 L/min @ 200mmHg line pressure
  – 10 trials done at each temperature and flow/line pressure combination (n=60)
Results

- JMP Statistical Analysis
- Multiple Linear Regression
  - Temperature
  - Vacuum
  - Flow
  - Line Pressure

\[ \text{Pcnt Oxy Removal Predicted} \]
\[ P < 0.0001 \quad \text{RSq} = 0.91 \quad \text{RMSE} = 0.007 \]
Results

- Significant variables affecting % GME removal
  - Temperature
  - Vacuum
  - Flow

\[
\begin{align*}
0.9585242729 \\
+ \text{Match}[\text{Flow (L/min)}] \\
\begin{cases}
3.5 \Rightarrow 0.0149108649 \\
5 \Rightarrow -0.0149108649 \\
\text{else} \Rightarrow . \\
18 \Rightarrow -0.020580664575 \\
28 \Rightarrow -0.000270855275 \\
37 \Rightarrow 0.02085151985 \\
\text{else} \Rightarrow . \\
\end{cases} \\
+ \text{Match}[\text{Temp (°C)}] \\
\begin{cases}
150 \Rightarrow 0 \\
200 \Rightarrow 0 \\
\text{else} \Rightarrow . \\
\end{cases} \\
+ \text{Match}[\text{Line Pressure (mmHg)}] \\
\begin{cases}
-250 \Rightarrow 0.00839610441667 \\
0 \Rightarrow -0.00839610441667 \\
\text{else} \Rightarrow . \\
\end{cases} \\
\end{align*}
\]
Results: Pre-oxygenator

Control Trial

Hypobaric Trial

CT 5.0 18
CT 3.5 18
CT 5.0 28
CT 3.5 28
CT 5.0 37
CT 3.5 37

EXP 5.0 18
EXP 3.5 18
EXP 5.0 28
EXP 3.5 28
EXP 5.0 37
EXP 3.5 37

Count in >40
Count in 20 - 40
Count in 0 - 20

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Results: post-oxygenator

Control Trial

<table>
<thead>
<tr>
<th>Trial</th>
<th>Count in &gt;40</th>
<th>Count in 20 - 40</th>
<th>Count in 0 - 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT 5.0 18</td>
<td>376</td>
<td>189</td>
<td>846</td>
</tr>
<tr>
<td>CT 3.5 18</td>
<td>239</td>
<td>139</td>
<td>846</td>
</tr>
<tr>
<td>CT 5.0 28</td>
<td>335</td>
<td>189</td>
<td>818</td>
</tr>
<tr>
<td>CT 3.5 28</td>
<td>189</td>
<td>139</td>
<td>818</td>
</tr>
<tr>
<td>CT 5.0 37</td>
<td>139</td>
<td>139</td>
<td>818</td>
</tr>
<tr>
<td>CT 3.5 37</td>
<td>50</td>
<td>240</td>
<td>239</td>
</tr>
</tbody>
</table>

Hypobaric Trial

<table>
<thead>
<tr>
<th>Trial</th>
<th>Count in &gt;40</th>
<th>Count in 20 - 40</th>
<th>Count in 0 - 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXP 5.0 18</td>
<td>150</td>
<td>37</td>
<td>672</td>
</tr>
<tr>
<td>EXP 3.5 18</td>
<td>37</td>
<td>123</td>
<td>418</td>
</tr>
<tr>
<td>EXP 5.0 28</td>
<td>123</td>
<td>19</td>
<td>491</td>
</tr>
<tr>
<td>EXP 3.5 28</td>
<td>19</td>
<td>146</td>
<td>491</td>
</tr>
<tr>
<td>EXP 5.0 37</td>
<td>120</td>
<td>9</td>
<td>328</td>
</tr>
<tr>
<td>EXP 3.5 37</td>
<td>9</td>
<td>52</td>
<td>123</td>
</tr>
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</table>
Results: Patient

Control Trial

Hypobaric Trial

<table>
<thead>
<tr>
<th></th>
<th>CT 5.0 18</th>
<th>CT 3.5 18</th>
<th>CT 5.0 28</th>
<th>CT 3.5 28</th>
<th>CT 5.0 37</th>
<th>CT 3.5 37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count in &gt;40</td>
<td>336</td>
<td>51</td>
<td>247</td>
<td>35</td>
<td>50</td>
<td>5</td>
</tr>
<tr>
<td>Count in 20 - 40</td>
<td>938</td>
<td>247</td>
<td>640</td>
<td>131</td>
<td>146</td>
<td>22</td>
</tr>
<tr>
<td>Count in 0 - 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<th>EXP 5.0 37</th>
<th>EXP 3.5 37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count in &gt;40</td>
<td>25</td>
<td>5</td>
<td>14</td>
<td>1</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Count in 20 - 40</td>
<td>157</td>
<td>68</td>
<td>48</td>
<td>7</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>Count in 0 - 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P<0.0001

Legend:
- Green: Count in >40
- Red: Count in 20 - 40
- Blue: Count in 0 - 20
Conclusion

• The strength of evidence presented within this study, along with the previous in-vitro and in-vivo study by Gipson et al. in Hartford, CT demonstrate the need for further research and development of hypobaric oxygenation.

• Hypobaric oxygenation be further explored as a “standard method care” for GME elimination.
Acknowledgements

• American Society of Extracorporeal Technology
• Midwestern University Faculty
• Mayo Clinic Rochester, MN
• Keith Gipson, MD, et al.
References

3. Willcox TW. Vacuum-assisted venous drainage; to air or not to air, that is the question. Has the bubble burst? JECT. 2002;34:24-28.