TOWARDS A PROBABILISTIC ASSESSMENT OF HYPOBARIC DECOMPRESSION SICKNESS TREATMENT


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Human Research Program Investigators’ Workshop

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DCS treatment in space

Matching needs to resources.
probabilistic nature of symptoms and symptom resolution

- DCS symptom during EVA is probabilistic;
  no guarantee of a symptom, just a probability.
- Symptom resolution during treatment is also probabilistic;
  no guarantee of symptom resolution, just a probability.
- You maximize the $P(\text{symptom resolution})$ with additional pressure, oxygen, and time.
- Also adjunctive therapy to support tissue recovery.
symptom resolution = bubble dissolution

- Boyle’s Law compression (closed, isothermal, ideal gas system):
  \[ P_2 - P_1 = \frac{V_1}{V_2} \times P_1 - P_1 \]
  \[ P_2 - P_1 \text{ is } \Delta P, \text{ as psid.} \]

- Bubble-to-tissue N\textsubscript{2} diffusion gradient and the O\textsubscript{2} window:
  \[ P_{\text{bub N}_2} = P_B + \frac{2\gamma}{r} + M - P_{\text{bub O}_2} - P_{\text{bub CO}_2} - P_{\text{bub H}_2O} \]

- Tissue Bubble Dynamics Model integrates both through time as \( \frac{dr}{dt} \):
  \[
  \frac{dr}{dt} = -\frac{\alpha D}{h} \left( P_B - vt + \frac{2\gamma}{r} + \frac{4}{3} \pi r^3 M - P_t - P_{\text{met}} \right) + \frac{rv}{3} \frac{P_B - vt + \frac{4\gamma}{3}r + \frac{8}{3} \pi r^3 M}{P_B - vt + \frac{4\gamma}{3}r + \frac{8}{3} \pi r^3 M}
  \]
Tissue Bubble Dynamics Model (TBDM)

- An open, isothermal system where mass enters or leaves.

\[ \Delta P = P_1 \times \frac{V_1}{V_2} - P_1 \]

- Note that “time” to achieve a \( \Delta P \) is available from the TBDM.

NASA 1982 - 2009 symptom data

- The JSC Hypobaric DCS Database documents 969 exposures from 47 different altitude tests.
- Symptoms are from 119 subjects diagnosed with DCS.

<table>
<thead>
<tr>
<th>symptom category</th>
<th>symptom resolution details</th>
<th>count</th>
<th>% of 220 symptoms</th>
<th>resolution pressure data available</th>
<th>% of 195 pressure data available</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>resolved at altitude</td>
<td>37</td>
<td>16.8</td>
<td>37</td>
<td>19.0</td>
</tr>
<tr>
<td>B</td>
<td>resolved on repressurization</td>
<td>137</td>
<td>62.2</td>
<td>121</td>
<td>62.0</td>
</tr>
<tr>
<td>C</td>
<td>resolved at site pressure</td>
<td>17</td>
<td>7.7</td>
<td>17</td>
<td>8.7</td>
</tr>
<tr>
<td>D</td>
<td>resolved after HBO for a persistent symptom at site pressure</td>
<td>20</td>
<td>9.1</td>
<td>20</td>
<td>10.2</td>
</tr>
<tr>
<td>E</td>
<td>no treatment pressure information exits</td>
<td>9</td>
<td>4.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F</td>
<td>resolved but then reoccurred or was new and treated with HBO</td>
<td>13</td>
<td>-</td>
<td>195</td>
<td>100</td>
</tr>
<tr>
<td>total</td>
<td></td>
<td>220</td>
<td>100.0</td>
<td>195</td>
<td>100</td>
</tr>
</tbody>
</table>
• P(symptom resolution) modeled as a log-logistic function of observed $\Delta P$ and two other explanatory variables.
• We used 154 symptoms from 119 subjects diagnosed with DCS.
symptoms linked to TBDM through $\Delta P$

DATA STATS

P(symptom resolution)

computed $\Delta P$

TBDM simulations
- pressure
- oxygen
- time
### Regression Results (n=154 Symptoms)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate ± 95% CI</th>
<th>Standard Error*</th>
<th>z-score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B_1$</td>
<td>0.633 (0.50 to 0.80)</td>
<td>0.077</td>
<td>-3.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$B_2$</td>
<td>1.682 (1.00 to 2.35)</td>
<td>0.344</td>
<td>4.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AMB</td>
<td>-1.089 (-1.96 to -0.22)</td>
<td>0.444</td>
<td>-2.45</td>
<td>0.014</td>
</tr>
<tr>
<td>$T_s$ (min)</td>
<td>0.00395 (0.001 to 0.007)</td>
<td>0.0015</td>
<td>2.61</td>
<td>0.009</td>
</tr>
</tbody>
</table>

* Symptom dependency considered.

\[
P(\text{symptom resolution}) = \frac{1}{1 + \exp(-\ln(\Delta P) - 1.682 + 1.089 \times \text{AMB} - 0.00395 \times T_s / 0.633)},
\]

where \( \text{AMB} = 1 \) if ambulation was as part of the exposure, otherwise \( \text{AMB} = 0 \); and where \( T_s \) is time (min) to onset of a DCS symptom.
Hypobaric DCS Treatment Model Example 1

Ts = 120 min

154 symptoms with 20 HBO
100 ambulation with 3 HBO
54 no ambulation with 17 HBO

P(symptom resolution)

ambulation
no ambulation

ΔP = 14.7 – 4.3 psia

Ts = 120 min
ΔP = P₁ × V₁/V₂ – P₁

9.37 = 4.3×1176964μm³ / 370255μm³ – 4.3 after 15 min

27.5 = 4.3×1176964μm³ / 159167μm³ – 4.3 after 75 min

120 min PB, 6-min ascent to 4.3 psia, DCS 60 min into an ambulatory EVA, 30 min delay, 15 min repress to 14.7 psia, and 60 min GLO.

<table>
<thead>
<tr>
<th>simulation</th>
<th>symptom onset</th>
<th>BGI</th>
<th>BGI @ repress</th>
<th>BGI @ Rx</th>
<th>computed ΔP</th>
<th>P(symptom resolution) ± 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-hr PB @ 14.7 psia</td>
<td>60</td>
<td>15.0</td>
<td>21.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>repress to 14.7</td>
<td>14.8</td>
<td>9.37</td>
<td>0.90</td>
<td>0.78 – 0.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-hr 100% GLO @ 14.7</td>
<td>11.2</td>
<td>27.5</td>
<td>0.98</td>
<td>0.93 – 0.99</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
discussion / forward work

- Approaches to validate the model:
  - Our results agree with 12-times more data: 89.0% (121/136) for NASA compared to 92.8% (1,516/1,633) for USAF symptoms that resolved during repressurization (Muehlberger et al. 2004).
  - Results from Duke University micronuclei research.
  - Some data do exist on symptom resolution with GLO (Krause et al. 2000).
  - No data exists on time to symptom resolution with or without GLO.

- The treatment model applies to symptoms detected early with a prompt treatment response.

- Time to symptom resolution is not explicit in the treatment model; it was not available for our symptom data.
  - However, an estimate of resolution time is available from the TBDM.

- Management ultimately concurs on an acceptable P(symptom resolution).
  - The hard work is to balance limited treatment resources with the likelihood of effective treatment.

thank you
Observed $\Delta P$ to resolve 138 symptoms compared to the computed ideal gas $\Delta P$ from TBDM. Linear regression for $\Delta P$ computed $= 1.0016 \times \Delta P$ observed $- 0.324$, $r^2 = 0.977$. 
Hypobaric DCS Treatment Model Results

154 symptoms

100 ambulation (historical data)

54 no ambulation (ARGO + PRP data)

\( a = 60 \text{ min DCS} \)
\( b = 120 \text{ min DCS} \)
\( c = 180 \text{ min DCS} \)
\( d = 240 \text{ min DCS} \)
## Muehlberger’s $\Delta P$ data

<table>
<thead>
<tr>
<th>symptom category</th>
<th>symptom resolution details</th>
<th>treatment pressure data</th>
<th>fraction of total 1,669</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>resolved at altitude</td>
<td>66</td>
<td>3.8</td>
</tr>
<tr>
<td>B</td>
<td>resolved on repressurization</td>
<td>1,433</td>
<td>84.3</td>
</tr>
<tr>
<td>C</td>
<td>resolved on repressurization but without documented resolution pressure</td>
<td>83</td>
<td>4.9</td>
</tr>
<tr>
<td>D</td>
<td>resolved at site pressure</td>
<td>117</td>
<td>6.9</td>
</tr>
<tr>
<td><strong>total symptoms resolved</strong></td>
<td></td>
<td>1,699</td>
<td>100.0</td>
</tr>
</tbody>
</table>

- Of 117 symptoms that resolved at site pressure, 112 were referred to HBO Rx.
- Of 1,433 symptoms that resolved during repress, 52 were referred to HBO Rx.
- For 93% of 1,433 symptoms that resolved during repress the subjects continued with 2-hr of GLO.