TOWARDS A PROBABILISTIC ASSESSMENT OF HYPOBARIC DECOMPRESSION SICKNESS TREATMENT


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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):
  \[ P_2 - P_1 = \frac{V_1}{V_2} \times P_1 - P_1 \]
  \( P_2 - P_1 \) is \( \Delta P \), as psid.

- Bubble-to-tissue \( N_2 \) diffusion gradient and the \( O_2 \) window:
  \[ P_{\text{bub} N_2} = P_B + 2\gamma/r + M - P_{\text{bub} O_2} - P_{\text{bub} CO_2} - P_{\text{bub} H_2O} \]

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

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

![Graph showing bubble growth index over time from ascent (min)]

- 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>total</td>
<td></td>
<td>220</td>
<td>100.0</td>
<td>195</td>
<td>100</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></td>
<td></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.

removed 37 that resolved before repress
symptoms linked to TBDM through $\Delta P$

DATA STATS

P(symptom resolution)

deltaP observed (psid)

% symptoms resolved

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>B₁</td>
<td>0.633</td>
<td>0.077</td>
<td>-3.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0.50 to 0.80</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B₂</td>
<td>1.682</td>
<td>0.344</td>
<td>4.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>1.00 to 2.35</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMB</td>
<td>-1.089</td>
<td>0.444</td>
<td>-2.45</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>-1.96 to -0.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tₛ (min)</td>
<td>0.00395</td>
<td>0.0015</td>
<td>2.61</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>0.001 to 0.007</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Symptom dependency considered.

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

where AMB = 1 if ambulation was as part of the exposure, otherwise 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

ΔP = 14.7 – 4.3 psia

P(symptom resolution) vs. deltaP (psid)

ambulation
no ambulation

T_s = 120 min
simulation example 2

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

9.37 = \(\frac{4.3 \times 1176964 \mu m^3}{370255 \mu m^3}\) – 4.3 after 15 min

27.5 = \(\frac{4.3 \times 1176964 \mu m^3}{159167 \mu m^3}\) – 4.3 after 75 min

<table>
<thead>
<tr>
<th>simulation</th>
<th>symptom onset</th>
<th>BGI</th>
<th>BGI @ repress</th>
<th>BGI @ Rx</th>
<th>computed (\Delta P)</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></td>
<td></td>
<td></td>
<td></td>
<td>14.8</td>
<td>9.37 0.90 0.78 – 0.96</td>
</tr>
<tr>
<td>1-hr 100% GLO @ 14.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11.2</td>
<td>27.5 0.98 0.93 – 0.99</td>
</tr>
</tbody>
</table>

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.
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 $- 0.324$, $r^2 = 0.977$. 

observed versus computed $\Delta P$
Hypobaric DCS Treatment Model Results

154 symptoms

100 ambulation (historical data)

54 no ambulation (ARGO + PRP data)

a = 60 min DCS
b = 120 min DCS
c = 180 min DCS
d = 240 min DCS
### Muehlberger’s ΔP 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></td>
<td>total symptoms resolved</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.