**Navy Experimental Diving Unit 321 Bullfinch Road Panama City, FL 32407-7015**

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# **DECOMPRESSION FROM He-N2-O2 (TRIMIX) BOUNCE DIVES IS NOT MORE EFFICIENT THAN FROM He-O<sub>2</sub> (HELIOX) BOUNCE DIVES**



**DAVID J. DOOLETTE KEITH A. GAULT WAYNE A. GERTH**

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### **INTRODUCTION**

Nitrogen [a](#page-5-0)nd oxygen<sup>a</sup> (nitrox) breathing mixtures are impractical for deep diving because gas mixtures with a high partial pressure of nitrogen are narcotic and dense, which results in mental impairment and increased work of breathing, respectively. Instead, a mixture of helium and oxygen (heliox) is usually breathed for dives deeper than 150 feet sea water (fsw), because helium is not narcotic and is less dense than nitrogen. However, a longer decompression obligation is thought to accrue during a heliox bounce dive than during a nitrox bounce dive<sup>1</sup> (a bounce dive is one of insufficient duration for the body to completely equilibrate with inspired inert gas partial pressures). If this difference in decompression requirements for heliox and nitrox is real, breathing a helium-nitrogen-oxygen mixture (trimix) for moderately deep bounce dives may have the advantage of reducing nitrogen narcosis and work of breathing compared to breathing nitrox, but result in less decompression obligation than breathing heliox.

Decompression obligation accrues during the course of a dive as the partial pressures of gases in body tissues approach equilibrium with increased inspired gas partial pressures. With decompression, ambient pressure can drop below the sum of tissue gas partial pressures, in which case bubbles may form and can cause decompression sickness (DCS).<sup>2</sup> The probability of DCS ( $P_{DCS}$ ) is minimized by decompressing slowly, to limit bubble formation and growth while allowing gas washout from tissues. Helium and nitrogen have different diffusivities and solubilities, properties that influence tissue gas uptake and washout and bubble growth. Differences in gas uptake and washout and bubble growth can manifest in a difference in decompression obligation for dives conducted breathing heliox and nitrox. For instance, nitrogen washes out more slowly than helium from body tissues with slow gas exchange,<sup>3-5</sup> and this probably underlies the slower required rate of decompression from nitrox saturation dives than from heliox saturation dives $6,7$  (a saturation dive is one of sufficient duration for all the body tissues to completely equilibrate with inspired inert gas partial pressures). A related phenomenon manifests in decompression algorithms used to schedule bounce dives. In this case, slower uptake of nitrogen than helium into modelled compartments can result in less decompression obligation prescribed for a dive conducted breathing nitrox or trimix compared to a dive conducted breathing heliox.<sup>1</sup>

It is not clear whether there is a real difference in decompression requirements for nitrox and heliox bounce dives. The few human data comparing nitrox and heliox dives to the same depth are conflicting, and do not provide compelling evidence of a difference in decompression requirement.<sup>8-10</sup> In rats, no-stop bounce dives breathing heliox did result in a greater incidence of DCS than dives to the same depth and time breathing nitrox.<sup>11,12</sup> However, the results from trimix dives with rats did not demonstrate a clear relation between helium fraction and incidence of DCS.<sup>11,12</sup> Currently, a full set of trimix decompression tables are being developed and tested for the semi-closed circuit Canadian Underwater Mine-countermeasures Apparatus (CUMA) that are shorter than

<span id="page-5-0"></span> $\overline{a}$ <sup>a</sup> "Nitrogen" and "oxygen" are used throughout this report to mean the gases N<sub>2</sub> and O<sub>2</sub>, respectively. Standard chemical notations (e.g.  $N_2$ ,  $O_2$ , and He) will be used only where these are more readable than the corresponding words.

the corresponding (i.e., same depth and bottom time) CUMA heliox schedules.<sup>13,14</sup> In the past, a limited number of trimix decompression schedules have been tested by the Royal Navy for surface-supplied diving<sup>15-17</sup> and by the U.S. Navy for the MK 6 semiclosed circuit underwater breathing apparatus (UBA); $^{18,19}$  each of these programs tested trimix schedules that were shorter than the heliox schedules for the same mode of diving in use at those times. None of these studies were designed to demonstrate a real difference in decompression efficiency for trimix and heliox.<sup>13-19</sup>

The majority of U.S. Navy diving to depths where trimix might usefully replace heliox is conducted using the MK 16 MOD 1 closed-circuit UBA. For some modes of diving, there are some well-established disadvantages of helium compared to nitrogen that make trimix an attractive alternative to heliox: helium is expensive; helium has high thermal conductivity which makes thermoregulation in a heliox atmosphere difficult, and the high speed of sound in helium can render speech unintelligible. However, none of these disadvantages of helium are important for the MK 16 MOD 1 UBA because breathing gas is recycled, divers are not immersed in a heliox atmosphere, and voice communications are not typically used. On the other hand, replacing heliox with trimix for the MK 16 MOD 1 UBA would entail the logistical costs of more complex gas mixing and reduced operational depth because of nitrogen narcosis and increased work of breathing. The principal potential advantage of trimix over heliox for MK 16 MOD 1 diving would be if decompression were more efficient. This study evaluates whether decompression from trimix bounce dives is substantially more efficient than from heliox dives by comparing the incidences of DCS following dives with the identical depth/time schedule, but conducted breathing either trimix or heliox.

#### **METHODS**

### **DECOMPRESSION SCHEDULE SELECTION**

Multi-gas decompression algorithms that calculate uptake and washout for both helium and nitrogen often prescribe a longer decompression for bounce dives breathing heliox than for dives to the same depth and bottom time conducted breathing trimix with the same total inert gas content. Typically, the greater decompression obligation arises because of faster uptake of helium than of nitrogen into modelled compartments with relatively fast half-times. At the end of bottom time, a higher sum of inert gas partial pressures in these faster compartments results in deeper prescribed decompression stops for the heliox dive than for the trimix dive. During deep decompression stops, continued gas uptake into slow half-time compartments increases the prescribed duration of shallower stops, and therefore increases total decompression time. This behavior is marked in decompression algorithms in which nitrogen half-times are substantially longer than helium half-times in all compartments, for instance in the ZH-L16 algorithm, in which nitrogen half-times are set a priori at 2.65-fold longer than helium half-times in all compartments.<sup>10</sup> The prescribed decompression times for corresponding heliox and trimix dives are less markedly different using the Linear Exponential Multigas (LEM) probabilistic decompression model that underlies the U. S. Navy MK 16 MOD 1 He-O<sub>2</sub> decompression tables.<sup>20</sup> This version of LEM has three

compartments, and has parameters, including half-times for helium and nitrogen, found by fit to a database ("he8n25") of air, nitrox, heliox, and a few trimix dives. In the LEMhe8n25 compartment with intermediate rate of gas exchange, the half-time for nitrogen is 52% longer than for helium (33.0 vs. 21.8 minutes), and this compartment results in prescription of deeper decompression stops for heliox than for trimix dives in the manner described above. In the fastest compartment, the half-time for nitrogen is shorter than for helium (3.29 vs. 10.5 minutes), and slower washout of helium than of nitrogen from this compartment can result in prescription of deeper stops and longer times at these stops for heliox dives than for trimix dives of sufficient bottom time for near-complete equilibration of the compartment with helium (90% equilibration of this compartment with helium occurs in 35 minutes). Figure 1A shows the difference in total decompression stop times (TST) for LEM-he8n25 schedules for a range of MK 16 MOD 1 heliox and trimix decompression schedules calculated for a target  $P_{DCS}$  of 2.3%, the target  $P_{DCS}$  of the MK 16 MOD 1 He-O<sub>2</sub> decompression schedules in the U.S. Navy Diving Manual. If such difference in prescribed decompression times reflects a true difference in decompression requirements arising from helium and nitrogen, then dives following identical depth/time schedules would have higher  $P_{DCS}$  if breathing heliox than if breathing trimix (of the same total inert gas content), as illustrated in Figure 1B. The present experiment compared the incidences of DCS following heliox and trimix dives with the same depth/time schedule. This design avoids confounding by differences in TST or stop depth distribution.

The principal requirements for the test schedule<sup>[b](#page-7-0)</sup> were: 1) sufficient time on the bottom to allow time for substantive differences in helium and nitrogen uptake to occur; and 2) a  $P_{DCS}$  likely to result in a measurable incidence of DCS. In order to design a practicable and operationally relevant dive trial, there were additional desirable characteristics for a test schedule: a) a large estimated difference in  $P_{DCS}$  for trimix and heliox breathing gases so that a difference in DCS incidence might be detected in a reasonable number of man-dives; b)  $P_{DCS}$  not so high as to result in unacceptably frequent or severe DCS that would be a concern for safety of the subjects (arbitrarily, LEM-he8n25 estimated  $P_{DCS}$ <6%); c) the depth in a range where trimix diving would be useful; and d) maximum total dive time of four hours, as is typical for U. S. Navy MK 16 MOD 1 diving.

To meet these latter criteria, the test schedule was selected from a range of decompression schedules generated using the LEM-he8n25 probabilistic decompression model. Probabilistic decompression models can be used two ways: 1) to estimate the  $P_{DCS}$  of a decompression schedule and; 2) in conjunction with a search algorithm, to find the shortest decompression schedules at a target  $P_{DCS}$ .<sup>2</sup> Both these functions were used to generate candidate test schedules. First, LEM-he8n25 was used to generate MK 16 MOD 1 decompression schedules for trimix at target  $P_{DCS}$  of 2.3 % for dives to depths in the range 150–300 fsw (10 fsw increments) for bottom times in the range 5–60 minutes (5 minute increments). Trimix was nominally 1.3 atm constant  $PO<sub>2</sub>$ and equal parts helium and nitrogen (details are given in the legend for Figure 1).

<span id="page-7-0"></span> $\overline{a}$ <sup>b</sup> The terms 'depth/time schedule' or 'test schedule' indicate a schedule for which the breathing gas is not uniquely defined, as opposed to term 'decompression schedule', which has its customary meaning of a depth/time/breathing gas schedule.



Figure 1. Panel A shows the difference in total decompression stop times (TST) in minutes between trimix and heliox MK 16 MOD 1 decompression schedules calculated with LEM-he8n25 for a target  $P_{DCS}$  of 2.3%. Panel B shows the increase in LEM-he8n25-estimated  $P_{DCS}$  for MK 16 MOD 1 heliox dives conducted on trimix decompression schedules calculated for a target  $P_{DCS}$  of 2.3%. In Panel B, the schedules included a 30-minute period of breathing 0.70 atm PO<sub>2</sub> heliox or trimix on the surface before descent. In both Panels A and B, the decompression schedules were calculated for inspired gas in which the inert gas component was either all helium (heliox) or equal parts helium and nitrogen (trimix). The decompression schedules in Panels A and B were calculated with the following conventions used to calculate the MK 16 MOD 1 He- $O<sub>2</sub>$  decompression schedules in the U.S. Navy Diving Manual: a descent rate of 60 fsw/min; an ascent rate to and from stops of 30 fsw/min; a 20 fsw last stop depth; and an inspired gas with constant oxygen partial pressure (PO $_2$ ) of 0.70 atm from the surface until descent past 32 fsw, then a constant PO<sub>2</sub> of 1.3 atm, and a PO<sub>2</sub> of 0.70 atm on ascent shallower than 12 fsw.

Schedules included a 30-minute period of breathing 0.70 atm  $PO<sub>2</sub>$  on the surface before descent for operational reasons (see Diving subheading on page 10). Then, the  $P_{DCS}$ was estimated for these same depth/time schedules but conducted breathing heliox. Figure 1B shows the difference (heliox-trimix) in LEM-he8n25-estimated  $P_{DCS}$  between some of these decompression schedules. The reverse procedure, first calculating heliox decompression schedules at a relatively high  $P<sub>DCS</sub>$  and then evaluating these depth/time schedules for trimix breathing, resulted in differences in  $P_{DCS}$  too small to test in a practicable number of man dives.

The depth/time schedule that best met the desirable characteristics for a test schedule was to 200 fsw with a bottom time of 40 minutes and 119 minutes of decompression stops. The schedule is given in the bottom row of Table 1. Although the test schedule was calculated for a target  $P_{DCS}$  of 2.3% using a 60 fsw/min descent rate, the schedule was dived using a 40 fsw/minute descent to minimize the incidence of ear and sinus squeezes. The LEM-he8n25-estimated  $P_{DCS}$  of the test schedule with 40 fsw/min descent rate is 2.14% with trimix diluent and 5.56% with heliox diluent. For comparison, the corresponding heliox decompression schedule calculated for a target  $P_{DCS}$  of 2.3% using 60 fsw/min descent but dived using a 40 fsw/min descent rate is given also given in Table 1, but this schedule was not used in this protocol. More details about the test schedule are given in Appendix A.



Table 1. Comparison of trimix and heliox\* MK 16 MOD 1 decompression schedules

Divers breathe from MK 16 MOD 1 UBA for 30 minutes prior to starting compression. \*The heliox schedule (shaded) is given for comparison only, and was not used in this protocol †

<sup>T</sup>LEM-he8n25-estimated P<sub>DCS</sub> at descent rate of 40 fsw/min for indicated gas mixtures

### **EXPERIMENTAL DESIGN**

For U.S. Navy MK 16 MOD 1 diving there are practical reasons to retain heliox instead of changing to trimix if there is not an important difference in decompression efficiency. Therefore, it is desirable to test for non-inferiority of heliox as well as superiority of trimix. Such a design requires testing for practical equivalence in, as well as for a difference in, decompression efficiency of the two gas mixtures. Practical equivalence is not established by insufficient evidence to reject a conventional null hypothesis of no difference. Instead, the experimental design tested whether or not the decompression efficiencies of trimix and heliox differ by an amount that is of practical importance. A 20% difference in TST was considered of practical importance. For the range of depths and bottom times analyzed in the preceding section (illustrated in Figure 1), shortening TST by 20% increased the estimated  $P_{DCS}$  of heliox dives by approximately 1.5%.

Therefore, a difference in  $P_{DCS}$  between heliox and trimix dives of more than 1.5% was considered of practical importance for the present experiment. Non-inferiority of heliox would be established by failure to reject the null hypothesis  $(H_0)$ :  $P_{DCS. trimit} \ge P_{DCS. heliox}$ 1.5%. Superiority of trimix would be established by rejecting the null hypothesis. Formulating the null hypothesis in this way, as non-inferiority of heliox, recognizes that rejecting  $H_0$  if trimix decompression is not more efficient than heliox decompression would provide support for a change to present U. S. Navy diving procedures that would be costly and potentially dangerous.

A difference in  $P_{DCS}$  was assessed from any difference in observed incidence of DCS. The outcome of each man-dive was categorized according to the Weathersby et al. 1988 criteria for the U. S. Navy decompression database.<sup> $21$ </sup> The categories are A1) definite DCS requiring recompression; A2) "marginal DCS" or "niggles"; B) unknown outcome (data cannot be used); C) not DCS. These categories are described in more detail in Appendix B. The test statistic was the number of category A1 DCS on the trimix schedule minus the number of category A1 DCS on the heliox schedule  $(x_{\text{trimix}} - x_{\text{heliox}})$ . Up to 100 man-dives were planned for each breathing gas in a group-sequential design. Heliox and trimix dives were generally conducted on alternating weeks, and up to 16 man-dives were accrued each week. The data was evaluated each time 16 man-dives, excluding any category B outcomes, were completed on each of the heliox and trimix decompression schedules. The trial was to stop if any of the stopping rules in Table 2 was met.



Table 2. Stopping rules for determining difference in  $P_{DCS}$  between decompression schedules

If the trial stopped with a negative value of  $x_{\text{trimix}} - x_{\text{heliox}}$  (stop-low), this would be evidence to reject  $H_0$  and conclude that trimix has greater decompression efficiency than heliox. If the trial continued to 100 man dives on each profile or if the trial stopped with a positive value of  $x_{\text{trimix}}$ - $x_{\text{heliox}}$  (stop-high), this would be evidence to retain the H<sub>0</sub> and conclude that trimix does not afford an increase in decompression efficiency over heliox.

Figure 2 shows a Monte Carlo simulation of possible trial outcomes for different possible values of  $P_{DCS}$  for the trimix schedule and assuming  $P_{DCS}=5.56\%$  for the heliox schedule. Simulations of this sort were used to estimate the accuracy of the groupsequential trial design, using methods illustrated in Figure 3,<sup>22</sup> and described in greater detail in Appendix C. The measures of accuracy are the conditional probabilities of possible trial outcomes  $R_0$  (retain H<sub>0</sub>) or  $R_1$  (reject H<sub>0</sub>) under the conditions that either  $P_{\text{DCS.trimix}}$ ≥ $P_{\text{DCS.heliox}}$ -1.5% (H<sub>0</sub> is true) or  $P_{\text{DCS.trimix}}$ < $P_{\text{DCS.heliox}}$ -1.5% (H<sub>0</sub> is false),<sup>22</sup> and are given in Table 3.



Figure 2. Monte Carlo simulation of the proposed trial showing the probability of trial outcomes (y-axis) for different possible values of  $P_{DCS}$  of the trimix dive (x-axis) and assuming  $P_{DCS}=0.056$  for the heliox dive. Stop-low is the outcome of stopping with a negative value of  $x_{\text{trimix}} - x_{\text{heliox}}$  (reject H<sub>0</sub> in favor of lower P<sub>DCS</sub> for trimix). Stop-high is the reverse outcome. Indeterminate is continuing to 100 man-dives on each profile without a stop-high or stop-low.

Table 3. Accuracy of the group-sequential trial



The probability of incorrectly retaining the null hypothesis,  $P(R_0|H_0$  is false), has two components: 1) an 8.0% probability of an incorrect stop-high; and 2) an 18.8% probability of continuing to 100 man-dives on each schedule without meeting the stopping rules in Table 2.

As noted above, the accuracies in Table 3 were calculated assuming  $P_{DCS.heliox}=5.56\%$ . The sensitivity of these results to the assumed  $P_{DCS, helioX}$  was assessed by calculating the conditional probabilities of trial outcomes for different values of  $P_{DCS, heliox}$  in the range 2–10%. Most of the conditional probabilities of outcomes were relatively

insensitive to changes in  $P_{DCS, heliox}$ . The only sensitivities were for decreasing values of  $P_{DCS,heliox}$  in the range 2–5% with the condition that  $H_0$  is false ( $P_{DCS,trimix}$ < $P_{DCS,heliox}$ -1.5%). Under these conditions,  $P(R_1|H_0|)$  is false) was decreased, and the probability of continuing to 100 man-dives on each schedule without meeting the stopping rules (and therefore accepting  $H_0$ ) was increased, but the probability of a stop-high was relatively unchanged. However, the estimate  $P_{DCS,heliox}=0.0556$  is considered reliable because LEM-he8n25 was developed for, and validated with, MK 16 MOD 1 heliox dives.<sup>20</sup>



Figure 3. The heavy line shows the probability (y-axis) of accepting  $H_0(R_0)$  for different possible values of  $P_{DCS}$  for the trimix dive (x-axis) and assuming  $P_{DCS}=0.0556$  for the heliox dive. This curve is the sum of the stop-high and indeterminate curves (≡1−stop-low) of the trial simulation given in Figure 2. The area under this curve is the  $P(R_0)$  for all possible values of P<sub>DCS.trimix</sub>. The hatched area (to the right of the vertical line at 0.0406 and below 1) defines the domain where  $H_0$  is true: all trial outcomes for real P<sub>DCS.trimix</sub>≥P<sub>DCS.heliox</sub>-0.015. The un-hatched area (to the left of 0.0406 and below 1) defines the domain where  $H_0$  is false: all trial outcomes for real  $P_{DCS.trimix}$ < $P_{DCS.heliox}$ -0.015.  $P(R_0|H_0$  is true) is the fraction of the hatched area that is under the  $R_0$  curve and  $P(R_0|H_0|s)$  is false) is the fraction of the un-hatched area that is under the  $R_0$  curve. Similar calculations are made from the  $R_1$  (stop-low) curve. Illustration of the  $R_1$  curve calculations and details of the method are given in Appendix C.

### **EQUIPMENT AND INSTRUMENTATION**

All experimental dives were completed in the wet pot of the Ocean Simulation Facility (OSF) at the Navy Experimental Diving Unit (NEDU). The OSF was set up to accommodate four divers at a time. Wet pot water temperature was actively controlled to a target of 80±2 °F (27±1 °C). Custom-built, hysteresis-braked (model HB210, Magtrol; Buffalo, NY), underwater cycle ergometers were located in the wet pot so that when in use, the diver pedaled in a semi-prone position (approximately 15° head-up inclination) to mimic underwater fin swimming, and the diver's mid-chest was three feet below the water surface. Depth was measured in feet of sea water (fsw) as the gauge pressure above the wet pot plus the 3 fsw water column to diver mid-chest level. Depth, water temperature, pedaling cadence, and cycle ergometer hysteresis brake settings were digitized and recorded with a microcomputer-based data acquisition system every two seconds throughout each dive.

Divers' breathing gas (heliox or trimix) was supplied by MK 16 MOD 1 UBAs. This UBA has a breathing circuit in which the diver's expired gas passes through a counterlung and carbon dioxide absorbent canister and is rebreathed. Three oxygen sensors in the breathing circuit are monitored by onboard electronics which trigger the addition of oxygen via a piezo-electric valve if  $PO<sub>2</sub>$  drops below a set point. The MK 16 MOD 1  $PO<sub>2</sub>$ set point is 0.75 atm from the surface until the UBA descends to 32 fsw, at which point the PO<sub>2</sub> set point switches to 1.3 atm; the PO<sub>2</sub> set point returns to 0.75 atm when the UBA ascends to 13 fsw. $^{23}$  The volume of the breathing circuit is maintained by mechanical addition of diluent gas. In these experiments the diluent was either 88% He / 12%  $O_2$  (heliox) or 44% He /44% N<sub>2</sub> / 12%  $O_2$  (trimix).

In addition to the four primary MK 16 MOD 1 UBAs worn by the divers, one additional MK 16 MOD 1 charged with the same diluent as the primary UBAs accompanied the divers for use as an emergency breathing system in the event of a primary UBA failure. Each primary MK 16 MOD 1 UBA was instrumented with a gas sampling block placed in line with the inhalation hose at its junction with the carbon dioxide absorbent canister. The emergency MK 16 MOD 1 was not fitted with a sampling block. Each sampling block housed a thermistor and a micro-fuel cell oxygen sensor (K-1D, Teledyne Electronics Technologies) with the sensing surfaces in contact with but not obstructing the gas flow path. Prior to the dive trial, the K-1D oxygen sensors were tested for a linear response to  $PO<sub>2</sub>$  from 0.21 to 2.1 atm. The oxygen sensor mV output was recorded over at least one minute at air pressures from 0 to 297 fsw in steps of 33 fsw (1 atm) and at an air temperature of  $25\pm0.5$  °C. These data were fit by a straight line with  $r^2$ >0.9998 for all fuel cells. Before each dive, the oxygen sensors were calibrated with 100% nitrogen and 100% oxygen at one atm abs. PO $_2$  calculated from the daily two-point calibration and temperature of the gas in the sampling block were recorded every two seconds throughout each dive.

A port in each sampling block was connected to 80 feet (24.4 m) of 0.079 inch (2 mm) internal diameter nylon tubing which penetrated the OSF hull and through which gas could flow to a quadrupole mass spectrometer (Extrel MS; Pittsburg, PA) tuned to detect helium, nitrogen, oxygen, and carbon dioxide. Gas flow from one sampling tube at a time was directed to the mass spectrometer with an automatic gas switching valve. Gas flows from the tubes not directed to the mass spectrometer were vented through individual rotameters. Gas flow was driven by the pressure differential between the wet pot and outside the OSF. After each change of OSF depth, flows from each of the four sampling tubes were adjusted to 150 mL/min with manual flow metering valves between the sample tube and automatic gas switching valve, and flows through the rotameters were confirmed with a bubble flow meter.

Before each dive, the mass spectrometer was calibrated with gas fractions over the range of 0–100% oxygen, nitrogen, and helium, and 0–8.9% for carbon dioxide. During the dive, the gas switching block sequentially directed gas flow from each of the four UBA sample tubes to the mass spectrometer. Gas from each UBA flowed to the mass spectrometer for 20 s and the signal for the last 10 s was averaged and recorded with the data acquisition system. In this manner, the gas fractions from each UBA were recorded at approximately 80 s intervals.

Prior to the dive trial, the gas transit time from inside the OSF to the mass spectrometer and the mass spectrometer 0–90% response time were characterized using the method detailed in NEDU TR 02-10 (Appendix G).<sup>20</sup> Briefly, each sample line was connected via a solenoid valve to two gas-filled bags inside the OSF. The solenoid valve opened the sample line to one or other bag. One bag was inflated with pure helium and the other bag was inflated with either 88% He / 12%  $O_2$  or 44% He /44% N<sub>2</sub> / 12%  $O_2$ . The OSF was pressurized and flow of helium through each gas sample line was set to 150 mL/min. The solenoid valve was energized to open the gas sample line to the high oxygen bag and the time from this event to 90% of full-scale mass spectrometer oxygen signal 'on' response characterized. The corresponding 'off' response after de-energizing of the solenoid to open the gas sample line to the helium bag was also characterized. The effective latency was the mean of these on and off responses. These measurements were made in triplicate at each of 200, 70, 40, 30 and 20 fsw and for each of heliox and trimix sample gases. Second-order polynomials were fit to the effective latency versus depth data for each gas mixture and for each UBA sample line. The resulting curves were used in post-processing to correct the recorded data acquisition file for the gas transit time and mass spectrometer response time.

### **DIVING**

Thirty-seven qualified U. S. Navy divers gave informed consent under NEDU Institutional Review Board approved protocol 13-24/40056. Three divers did not participate in diving and two divers participated only in dives that were aborted during descent. At the time of their first dive in this study, the 32 divers who completed experimental dives had mean (S.D.) age of 33 (6) years, body weight of 197 (26) pounds or 89.4 (11.9) kg, height of 71 (3) inches or 1.81 (0.06) m, BMI of 27 (3), body fat estimated from body dimensions<sup>24</sup> of 19 (5) %. All 32 divers were male. Individual diver details are given in Appendix D. A Diving Medical Officer judged all divers to be physically qualified for diving on the basis of review of medical records and a physical examination. Immediately before each experimental dive, divers reported any current injury or illness and their amounts of exercise and sleep, any alcohol consumed, and any medications used in the previous 24 hours. On the bases of this self-report and a brief interview, a Diving Medical Officer either cleared or disqualified divers for participating in each experimental dive.

Prior to entering the OSF, divers dressed in full neoprene wet suits (including hoods, booties, and gloves), emergency safety harnesses, and MK 16 MOD 1 UBAs. Each primary MK 16 MOD 1 was equipped with a MK 24 full face mask. The MK 24 included a switchover assembly allowing gas to be breathed from the MK 16 MOD 1 or from an

open-circuit emergency gas supply. Divers simultaneously performed the following procedure to purge excess nitrogen from the lungs and UBA. Divers fitted the MK 24 full face mask with the switchover handle in the open-circuit mode. Divers exhaled fully through the open-circuit exhaust then turned the switchover handle to the closed-circuit mode and inhaled a full breath from the MK 16 MOD 1. Divers repeated this procedure for the next two consecutive breaths. After the third consecutive inhalation, divers remained in closed-circuit mode breathing from the MK 16 MOD 1. Divers then completed checks of the MK 16 MOD 1. One at a time, divers entered the OSF trunk where the gas sampling tube and thermistor cable were connected to the gas sampling block on the MK 16 MOD 1, then entered the wet pot. In the wet pot divers assumed a semi-prone position on their cycle ergometer, fully submerged with mid-chest approximately three feet below the wet pot water surface.

Thirty minutes after divers began breathing from the MK 16 MOD 1 UBA, the wet pot air space, trunk, and C chamber were compressed by the introduction of compressed air, at a target descent rate of 40 fsw/min, until the pressure at diver mid chest level (chamber air pressure plus three fsw hydrostatic pressure) was equivalent to 200 fsw. Delays in descent were accommodated by adjusting the time at bottom as detailed in Appendix A. Approximately one minute after reaching bottom, the divers began exercising on the cycle ergometers. Divers pedaled at a target cadence of 60 rpm with the ergometer hysteresis brake controller (W.E. Collins; Braintree, MA) set at 50 watts so that divers' work rate (incorporating the extra power required due to submersion in this diving dress) was approximately 125 watts.<sup>25</sup> Divers exercised intermittently (six minutes on / six minutes off) for an estimated average diver oxygen consumption of 1.3 L/min.<sup>26,27</sup> Divers exercised until approximately five minutes before ascent and then rested in a seated position with mid chest level three feet below the wet pot water surface until the end of bottom time and throughout decompression. The wet pot, trunk, and C chamber were decompressed at 30 fsw/min to and between decompression stops. Decompression stops were taken as given in Table 4. Periodically throughout the dive, divers provided a self-assessment of their own thermal status on a scale of zero (comfortable) to 10 (unbearable).



Table 4. Test schedule as used in the experiment

Divers breathe from MK 16 MOD 1 for 30 minutes immediately prior to compression. Descent rate 40 fsw/min. Ascent rate 30 fsw/min.

\* Time at Bottom in minutes does not include the targeted five-minute descent time. <sup>†</sup>Stop time does not include travel to stops.

After surfacing, divers were observed for two hours during which time they remained seated and at rest. A Diving Medical Officer interviewed all divers at 10 minutes and two hours after surfacing, and again the following day (19–21 hours after surfacing). The principal purpose of these interviews was to establish standard times at which divers were definitely free of signs and symptoms of DCS; this information is required for

incorporating these data into the U. S. Navy decompression database. Divers were instructed to immediately report any unusual signs and symptoms that occurred outside of these interview times.

Diving took place in two phases: a five-week period and a two-week period separated by seven weeks. One dive per day was conducted, Monday through Thursday, at approximately the same time each day (the time of day of completing decompression ranged from 12:05 to 13:55). Three or four divers participated each day. Divers participated in one to eight experimental dives (median = 3). The schedule of each diver's participation in experimental dives is given in Appendix E. Divers were required to avoid any hyperbaric or hypobaric exposure for a minimum of 48 hours before and following any experimental dive. These restrictions were to avoid alterations in tissue inert gas partial pressures, gas supersaturation, and bubble growth that could influence  $P_{DCS}$  of the experimental dive. These restrictions also effectively imposed a minimum surface interval between experimental dives of about 68 hours. A 60-hour surface interval is considered to minimize acclimatization.<sup>28</sup> Acclimatization refers to the apparent decrease in susceptibility to DCS, by unknown mechanisms, over successive (or nearly successive) days of hyperbaric exposures.<sup>29-31</sup> In order to minimize confounding by any acclimatization effect persisting longer than 60 hours, all divers participated in a decompression dive 3–10 days prior to each experimental dive. This preceding 'work-up' dive was either a previous experimental dive on this protocol or a dry chamber air decompression dive specified to be 130 fsw for 15 minutes bottom time with a 30 fsw/min ascent rate and a decompression stop at 20 fsw for four minutes.

### **RESULTS**

### **SCHEDULES AND DECOMPRESSION SICKNESS**

Fifty man-dives were completed on the heliox schedule with no diagnosed incidents of DCS. Forty-six man dives were conducted on the trimix schedule and two divers were diagnosed with DCS by the duty Diving Medical Officer. Details of the DCS incidents are given in Appendix F. These two cases met the criteria for research outcome classification A1 (definite DCS requiring recompression). This difference in DCS incidences between trimix and heliox met a stop-high interim stopping criterion (Table 2), and diving stopped with the null hypothesis retained.

The two divers with DCS following the trimix schedule had both previously completed two dives on the heliox schedule. One of these divers had previously completed an additional trimix dive without incident. In all, 22 divers completed dives on both the heliox and trimix schedules. Four divers completed only heliox dives and six divers completed only trimix dives. The schedule of divers' participation on each test schedule is given in Appendix E. The numbers of completed man-dives on the two schedules are not multiples of the planned group size (16) because three or four man-dives were completed at a time.

The experimental protocol accommodated delays in descent of up to five minutes and some delays required modification of the time at bottom (see Appendix A). There were occasional inconsequential delays in descent to accommodate divers who were slow to equalize ear or sinus air spaces. The longest delay involved a hold for ear squeeze occurring at 21 fsw. The OSF was decompressed to the surface and the afflicted diver removed. Five minutes after the start of the first compression, the remaining three divers were again compressed, at 40 fsw/min, and completed the dive with the full 35 minutes time at bottom. On another occasion, the primary display on a diver's MK 16 MOD 1 failed during compression. There was a 4 minute 36 s delay at 148 fsw while the affected diver switched to the emergency MK 16 MOD 1. Compression was then resumed and the four divers completed the dive with the time at bottom reduced by three minutes to adjust for the hold. These seven man-dives with delays at or near the five-minute maximum were all using trimix diluent, none resulted in DCS, and are included in the 96 completed man-dives.

Fifteen man-dives were aborted, none of which are included in the 96 man-dives completed. On three occasions, compression of the OSF was aborted and all divers were returned to the surface because a diver was unable to equalize ear or sinus air spaces rapidly enough to accommodate the target compression time. On one occasion, all divers were returned to the surface soon after reaching the bottom because of an apparent failure of the emergency MK 16 MOD 1. In fact, the emergency MK 16 MOD 1 had not failed and the event is noteworthy because it involved previously undocumented behavior of the MK 16 MOD 1 UBA secondary display: the secondary display indicates "1.- -" if the maximum display value of 1.99 atm  $PO_2$  is ex[c](#page-17-0)eeded.<sup>c</sup> The  $PO_2$  in the emergency MK 16 MOD 1 exceeded 1.99 atm during compression to 200 fsw, and the resulting, unrecognized display was interpreted as a failure of the secondary display. The PO<sub>2</sub> in the breathing circuit of a closed-circuit UBA can increase above the PO<sub>2</sub> set point during descent, and whereas it is well documented that such  $PO<sub>2</sub>$  overshoot in the MK 16 MOD 1 can exceed 1.99 atm, this was not expected with a 40 fsw/min descent to 200 fsw, even in the emergency MK 16 MOD 1 that was not being breathed.<sup>20,23,32</sup> Several factors could cause a higher than expected PO<sub>2</sub> overshoot in a MK 16 MOD 1 from which oxygen is not been consumed and gas is not being circulated: the  $P_2$  may be above the 0.75 atm set point before leaving surface; less diluent may be added during descent than expected; and added diluent may not mix completely with gas in the vicinity of the oxygen sensors.

Divers were generally thermally comfortable throughout the dives. Divers were generally warm during the work at bottom and the median thermal status score at the end of bottom time was 1 (very slight discomfort). The median thermal status score at the end of decompression was 0 (no discomfort). The highest thermal status score recorded was 3 (occasional shivering), occurring during decompression.

<span id="page-17-0"></span> $\overline{a}$  $\textdegree$  As a result of this event, this behavior has since been documented in: SEA 06-EXM (PMS-408(EOD)), *Technical Manual, Underwater Breathing Apparatus MK 16 MOD 1, Description, Operation and Maintenance, Revision 2*, NAVSEA SS600-AQ-MMO-010/0910-LP-028-5850 (Washington (DC): Naval Sea Systems Command, 2014)

### **UBA GAS COMPOSITION**

UBA gas composition was analyzed for all but the one dive in which the emergency MK 16 MOD 1 was used. UBA gas compositions from typical trimix and heliox dives are illustrated in Figure 4. There was no practical difference in UBA oxygen control between heliox and trimix dives. The mean  $(S.D.)$  of the time-weighted average P $O<sub>2</sub>$  for the trimix dives was 1.37 (S.D.=0.04, n=45) atm and for the heliox dives was 1.36 (S.D.=0.04, n=50) atm (unpaired t-test, t=1.2867, p=0.2014). The nitrogen content of the breathing gas is expressed as fraction of the inert gas:  $FN_2$ / $(FN_2 + FHe)$ . For the trimix dives, the mean of the time-weighted average of  $FN<sub>2</sub>$  ( $FN<sub>2</sub>+FHe$ ) was 0.519 (S.D.=0.008, range 0.505–0.538, n=45). These figures indicate that the trimix the divers breathed was, as planned, composed of approximately equal fractions of nitrogen and helium. A small amount of nitrogen contaminated the UBA gas on all heliox dives, for these heliox dives the time-weighted average of  $F_{N2}/(F_{N2}+F_{He})$  was 0.021 (S.D.=0.008, range 0.007– 0.043, n=50). The maximum carbon dioxide fraction measured during each dive ranged from zero to 0.0003 and was not different between trimix and heliox dives (unpaired ttest, t=0.5632, p=0.5758). Time-weighted average PO<sub>2</sub> and  $FN_2$ /(FN<sub>2</sub>+FHe) for all dives are given in Appendix G.

#### **DISCUSSION**

The present results indicate that decompression from trimix bounce dives is not more efficient than from heliox dives. This null hypothesis was retained with high power because the trial met a stop-high criterion (more DCS on the trimix than on the heliox schedule). To our knowledge, this is the first prospective comparison of trimix and heliox dives with enough man-dives on each decompression schedule for a statistically reliable comparison, and in which the same depth/time schedule was used for both trimix and heliox dives. This latter design feature avoids confounding of the results by differences in depth/time schedules. Previous programs to develop trimix decompression schedules have been premised on a greater decompression efficiency of trimix compared to heliox, and have been interpreted in that light. However, careful examination of such studies reveals that they are not in conflict with the present results.

The U. S. Navy developed and tested trimix decompression schedules for the MK 6 semi-closed circuit UBA as early as 1962, but no decompression tables and no comprehensive report of the testing were published. In two conference proceedings, Workman presented a few MK 6 trimix decompression schedules which had shorter TST than the corresponding heliox decompression schedules.<sup>18,19</sup> The latter schedules were promulgated in the "Helium-Oxygen Decompression Table for Mixed-Gas Scuba Using 68-32% Helium-Oxygen Supply Mixture" in NEDU TR 1-65.<sup>33</sup> That report documents testing of 48 single-dive heliox decompression schedules (i.e., not including no-stop dives and repetitive dive series), many with shorter TST than the schedules that appear in the final tables. These schedules were typically tested with four man-dives each, and resulted in six treated cases of DCS in 166 man-dives.<sup>33</sup> A search of the archived NEDU diving log books located tests of 15 decompression schedules using the MK 6 semi-closed circuit UBA supplied with trimix  $(34\%$  He  $/$  34% N<sub>2</sub>  $/$  32 % O<sub>2</sub>) that

were comparable to the heliox [d](#page-19-0)ives reported in NEDU TR 1-65. $d$  These trimix dives had on average 19 minutes less TST than (or approximately half the TST of) the corresponding heliox dives documented in NEDU TR 1-65. However, typically only two man-dives (maximum of six) were conducted per trimix schedule, for a total of 46 man dives resulting in two treated cases of DCS. These are insufficient data to assess the relative decompression efficiency of trimix versus heliox in these dives.

The Royal Navy reported sea trials of two trimix decompression schedules in the early 1980s.15,16 These schedules were for 15-minute bottom times at 70 and 80 msw using surface-supplied trimix with oxygen decompression. Eighty-five man-dives were completed resulting in two cases of DCS. Apparently these schedules were developed on the premise of greater decompression efficiency than corresponding heliox schedules.<sup>17</sup> In the Royal Navy Diving manual of that era, there is a decompression table for surface-supplied heliox diving comprising schedules for 15-minute bottom times at 60, 75, and 90 msw. $^{34}$  The 75 msw heliox schedule tabulated in that manual has slightly longer TST than the 80 msw trimix schedule tested in the sea trials. However, full reports of the development and laboratory trials of the trimix schedules are not availabl[e](#page-19-1), $e^e$  and there is no report of a prospective comparison of trimix and heliox decompression schedules.

Trimix decompression tables using in-water oxygen decompression have recently been developed for the Canadian Underwater Mine-countermeasures Apparatus (CUMA), a semi-closed circuit UBA.<sup>13,14</sup> These trimix tables are an alternative to, and were calculated to have shorter decompression times than, the CUMA heliox tables.<sup>35</sup> Notably, both the CUMA heliox and trimix schedules are longer than the corresponding schedules in the U. S. Navy MK 16 MOD 1 He-O<sub>2</sub> decompression tables.<sup>20</sup> The success of the shorter CUMA trimix schedules is not in itself a demonstration of greater

<span id="page-19-1"></span><span id="page-19-0"></span> $\overline{\phantom{a}}$ <sup>d</sup> These 46 trimix dives appear in NEDU diving log books numbers 57 and 62 and occurred between September 1962 and September 1964. A further 191 trimix bounce dives, occurring over the period 1963 to 1966, are recorded in NEDU diving log books 58, 59, 62, 63, and 65. There are 22 trimix dives (1 DCS and 1 marginal DCS) to depths from 30 to 200 fsw also using MK 6 semi-closed circuit UBA, but with supply gas flows and oxygen fractions that are different from those used in NEDU TR 1-65. There are 46 trimix dives (5 DCS and 2 marginal DCS) to depths from 200 to 550 fsw using umbilical supplied MK 6 semi-closed circuit UBA with switching to 100% oxygen for decompression stops at 50 fsw and shallower. There are 25 trimix dives (6 DCS and 1 marginal DCS) to depths from 300 to 500 fsw mostly using the "Deep Sea He-O<sub>2</sub> rig" (a few dives used band masks) with switching to 100% oxygen for decompression stops at 50 fsw and shallower. There are 98 constant  $PO<sub>2</sub>$  trimix no-decompression or minimaldecompression (15 minutes TST) dives (1 DCS) to depths from 70 to 200 fsw, some of which Workman presented in a conference proceedings.<sup>19</sup> These dives appear in NEDU log book number 63 and include 54 dives using 1.3 atm  $PO<sub>2</sub>$  trimix and 44 dives using 1.6 atm  $PO<sub>2</sub>$  trimix. In all these log books, trimix is referred to as "multimix", and with few exceptions comprised equal fractions of helium and nitrogen. e The Admiralty Marine Technology Establishment (AMTE) reports of sea trials of the trimix schedules<sup>15,16</sup> cite earlier reports of laboratory trials, but whereas the reports of the sea trials are listed in the U.K. National Archives, the reports of the laboratory trials are not. Inquiries at different times to the successors to ATME Physiological Laboratory (Defence Evaluation and Research Agency and QinetiQ) have also not located these reports. The original chamber logs for these dives do exist, and these trimix dives form a subset of the calibration data for LEM-he8n25.<sup>20</sup> That subset comprises 192 man-dives resulting in 11 cases of DCS. Sixty-eight of these dives follow similar schedules to those tested in the sea trials, and none of these 68 chamber dives resulted in DCS.



16 Figure 4. UBA gas composition during a trimix dive (top) and heliox dive (bottom). The depth in fsw gauge is indicated on the left axis and gas partial pressures in atmospheres are indicated on the right axis. The traces with symbols indicate oxygen, nitrogen and helium partial pressures calculated from the ambient pressure in the wet pot and the fractions of these gases analyzed with mass spectrometer. The solid black trace (Fuel cell) is oxygen partial pressure calculated from the output of the K-1D micro-fuel cell oxygen sensor.

decompression efficiency of trimix compared to heliox. Unlike the MK 16 MOD 1, the CUMA does not maintain a constant  $PQ_2$ , and both the CUMA heliox and trimix decompression schedules are calculated with the conservative assumption of 1.0 atm PO2. During testing of the CUMA decompression schedules, the time-weighted average  $PQ<sub>2</sub>$  was substantially higher than 1.0 atm, $13,14,35$  and therefore these dives do not test the limits of the underlying algorithm that prescribed shorter decompression times for trimix than for heliox. Testing of the CUMA heliox with in-water oxygen decompression schedules resulted in a low incidence of DCS: only one case of DCS in 352 mandives.<sup>35</sup> The first series of CUMA trimix testing comprised 44 man-dives on four trimix schedules that had 17–55 minutes less TST (approximately 40% less TST) than the corresponding heliox schedules. No DCS occurred on three schedules, but the longest schedule, which had the greatest saving in TST compared to heliox, resulted in three definite and two possible cases of DCS in eight man-dives.<sup>13</sup> A revised set of 14 trimix schedules were tested which had 9–40 minutes less TST (average 23% less TST) than the corresponding heliox schedules, and these resulted in no DCS in 196 man-dives.<sup>14</sup> However, CUMA trimix decompression schedules with 44 minutes TST or more, which had the greatest saving in TST compared to the corresponding heliox schedules, resulted in a higher percentage of divers with high grades (≥ grade 3) of venous gas emboli than the corresponding heliox schedules.<sup>14</sup> The percentage of divers with high grades of venous gas emboli is used by Defence R&D Canada – Toronto as an indicator of high 'decompression stress'. Decompression stress is presumed to be positively associated with  $\mathsf{P}_\mathsf{DCS}$ .<sup>36</sup> This result suggests that although no DCS was observed on these trimix decompression schedules, they have a higher  $P_{DCS}$  than the corresponding heliox schedules.

The prescription of longer decompression times for heliox bounce dives than for trimix bounce dives for the same depth and bottom time arises as a result of prescription of deeper initial decompression stops for heliox than for trimix dives. The notion that heliox bounce dives require deeper initial decompression stops than trimix or nitrox dives is relatively entrenched in diving folklore, but does not appear to be based on direct, prospective comparison. The earliest U. S. Navy report on heliox diving (Momsen 1939), which promulgated the surface-supplied heliox "partial pressure" decompression table, [f](#page-21-0) states that longer times were required at deeper decompression stops for heliox diving than for nitrogen-based diving.<sup>39</sup> The report provides no experimental evidence to support this statement; although the executive summary states that nearly 700 mandives at depths up to 500 fsw were conducted, none of these dives are documented. NEDU TR 1-65 which promulgated the MK 6 heliox decompression tables, states that deeper decompression stops are required for heliox than for air dives, but the report does not describe any comparison of heliox and air dives to support this statement.  $33$ 

The idea that heliox dives require a deeper initial decompression stop than corresponding dives conducted breathing a nitrogen-based breathing mixture appears to have arisen from theoretical consideration of how the physicochemical differences between helium and nitrogen might result in faster uptake of helium than of nitrogen

<span id="page-21-0"></span><sup>————————————————————&</sup>lt;br><sup>f</sup> The decompression tables promulgated in this report still appear, in revised form,<sup>37,38</sup> as the Surface Supplied Helium-Oxygen Decompression Table in the current U. S. Navy Diving Manual.

from blood into the tissues during bottom time or faster flux of helium than of nitrogen from tissue into bubbles during decompression.<sup>39</sup> These processes are represented by latent (unobserved) variables in decompression algorithms, in part because the exact sites of bubble-tissue interactions that result in DCS are unknown. It is possible that helium uptake into tissues and into bubbles is faster than that of nitrogen at these unknown DCS-sites, but recent in vivo experiments do not support such differences for sites with gas exchange rates relevant to bounce diving.

Faster half-times for helium than for nitrogen in some decompression algorithms cause these algorithms to prescribe deeper decompression stops for heliox dives than for trimix or nitrox bounce dives.<sup>1</sup> These differences in half-times represent faster tissue:blood equilibration of helium than of nitrogen. Faster tissue:blood equilibration of helium than of nitrogen will occur in tissues where the tissue solubility of helium is lower than that of nitrogen, and will also occur, owing to the higher diffusivity of helium than of nitrogen, in regions where tissue:blood equilibration is diffusion-limited. There is data to support faster washout of helium than of nitrogen in very slowly exchanging compartments.3,4 However, direct measurement of helium and nitrogen exchange in tissues with faster gas exchange (of the same magnitudes that control decompression from bounce dives) indicate no difference in the exchange rates for nitrogen and helium.<sup>40</sup> These observations do not support faster half-times for helium than for nitrogen in the compartments that control the initial decompression stops from bounce dives.

Faster flux of helium than of nitrogen into bubbles could impose the requirement for deeper initial decompression stops, in order to limit bubble growth, for heliox dives than for nitrox or trimix dives. The flux of gas across the surface of a bubble is determined by the partial pressure difference of the gas across the bubble surface and the permeability (product of gas diffusivity and solubility) of that gas in the tissue at the bubble surface. Since helium has higher diffusivity than nitrogen, the permeability for helium may be higher than for nitrogen in many body tissues. Greater flux of helium than of nitrogen into bubbles is supported by experiments in gelatin, in which the permeability of helium exceeds that of nitrogen, and where the transport of gas to the bubble surface depends entirely on diffusion. In these experiments, nitrogen bubbles in gelatin saturated with nitrogen resume growth when the dissolved nitrogen is replaced by helium, and in complimentary experiments, helium bubbles shrink when the dissolved helium is replaced by nitrogen.<sup>41</sup> However, opposite results arise from observation of bubbles in vivo in rat tissues with intact blood supply, 42-44 and in which the diffusion region surrounding the bubble may be supplied with blood. In these experiments, following decompression from an air dive, air bubbles shrink if the animal breathes heliox, and following a heliox dive, heliox bubbles grow if the animal breathes air. Qualitatively similar results are observed in adipose tissue, where nitrogen permeability might exceed that of helium, and in aqueous tissues, where helium permeability might exceed that of nitrogen. These observations do not support faster growth of bubbles during decompression from heliox dives than during decompression from nitrox or trimix dives.

The LEM-he8n25 probabilistic decompression model behaves comparably with many deterministic decompression algorithms by prescribing deeper initial decompression

stops and longer TST for heliox than for trimix dives (see Table 1 and Figure 1). Similarly, LEM-he8n25 incorrectly predicted a higher  $P_{DCS}$  for heliox dives than for trimix dives conducted using the same depth/time schedule. A better prediction may be possible with an LEM model re-parameterized with the present data. Nevertheless, the LEM-he8n25-estimated  $P_{DCS}$  of the tested trimix decompression schedule (2.14%) falls within the 95% confidence limits of the observed DCS incidence on the trimix dives  $(0.52\%$ , 14.5%) and the LEM-he8n25-estimated  $P_{DCS}$  of the schedule conducted breathing heliox (5.56% ) falls within the 95% confidence limits of the observed DCS incidence on the heliox dives (0%, 5.82%). That the LEM-he8n25-estimate  $P_{DCS}$  for the heliox schedule was near the upper 95% confidence limit of the observed incidence is noteworthy, because LEM-he8n25-estimated  $P<sub>DCS</sub>$  are near the upper 95% confidence limit of observed incidence for a variety of heliox dives: single and repetitive MK 16 MOD 1 dives, CUMA dives with in-water or surface decompression with oxygen, and open-circuit in-water heliox dives with nitrox and oxygen decompression in the dry.20,45 Collectively, these data indicate a trend for LEM-he8n25 to slightly over-estimate  $P_{DCS}$ for heliox dives, but provide no concern for the applicability of LEM-he8n25 for MK 16 MOD 1 heliox diving.

The present experimental dives, which found no decompression advantage of trimix over heliox, were conducted using a depth and bottom time selected from the domain covered by the U. S. Navy MK 16 MOD 1 He-O<sub>2</sub> decompression table – relatively short duration bounce dives, in which decompression is initially governed by relatively fast exchanging tissues. It is possible that there is a domain of depth and bottom time for which heliox dives require a deeper initial decompression stop and longer total decompression time than trimix dives. This might occur for exceptionally long, subsaturation dives for which the deepest decompression stop is governed by tissues with slow gas exchange in which the uptake of nitrogen is slower than that of helium. Such dives, if they exist, would not be in a depth and bottom time domain where MK 16 MOD 1 or other closed-circuit self-contained trimix diving would be useful.

The present experimental trimix dives used a breathing gas mixture with approximately equal fractions of helium and nitrogen. This present mixture was chosen to have a large nitrogen fraction, so that any difference with respect to heliox could manifest. It is unlikely that a larger nitrogen fraction relative to helium would have yielded a different result, and larger nitrogen fractions are of increasingly limited practical application for deep diving. Increasing nitrogen fractions impose increasing limits on the maximum operating depths. For instance, in the MK 16 MOD 1  $N_2$ -O<sub>2</sub> decompression tables in the U.S. Navy Dive Manual, all dives deeper than 150 fsw are exceptional exposure. At 150 fsw, the nitrogen partial pressure in a MK 16 MOD 1 using air diluent is 4.24 atm, and this will be used, as an example, as a maximum practical inspired nitrogen partial pressure. For a MK 16 MOD 1 using a diluent with equal fractions of helium and nitrogen, the depth at which the nitrogen partial pressure is 4.24 atm, and therefore the maximum operating depth, is 290 fsw. The maximum operating depth for the MK 16 MOD 1 He- $O<sub>2</sub>$  decompression tables is 300 fsw. We are therefore confident there is not a practical trimix breathing gas that would provide a decompression advantage compared to heliox.

### **CONCLUSIONS AND RECOMMENDATIONS**

Decompression from trimix bounce dives is not more efficient than decompression from heliox bounce dives.

Potential disadvantages of heliox with respect to cost, thermal balance, and voice communications are of limited relevance to MK 16 MOD 1 diving.

The U. S. Navy should not pursue a trimix capability for MK 16 MOD 1 or other closedcircuit self-contained diving.

### **REFERENCES**

- 1. H. Keller and A. A. Bühlmann, "Deep Diving and Short Decompression by Breathing Mixed Gases," *Journal of Applied Physiology*, Vol. 20 (1965), pp. 1267-1270.
- 2. P. Tikuisis and W. A. Gerth, "Decompression Theory," in *Bennett and Elliott's Physiology and Medicine and Diving*, *5 ed.*, A. O. Brubakk, T. S. Neuman, eds. (Saunders, Edinburgh, 2003), pp. 419-454.
- 3. A. R. Behnke and T. L. Willmon, "Gaseous Nitrogen and Helium Elimination From the Body During Rest and Exercise," *American Journal of Physiology*, Vol. 131 (1940), pp. 619-626.
- 4. G. J. Duffner and H. H. Snider, *Effects of Exposing Men to Compressed Air and Helium-Oxygen Mixtures for 12 Hours at Pressures of 2-2.6 Atmospheres,* NEDU TR 1-59, Navy Experimental Diving Unit, Sep 1958.
- 5. D. J. Doolette and S. J. Mitchell, "Hyperbaric Conditions," *Comprehensive Physiology*, Vol. 1 (2011), pp. 163-201.
- 6. A. A. Bühlmann and H. Keller, "Saturation and Desaturation With  $N_2$  and He at 4 Atm," *Journal of Applied Physiology*, Vol. 23 (1967), pp. 458-462.
- 7. R. G. Eckenhoff and R. D. Vann, "Air and Nitrox Saturation Decompression: a Report of 4 Schedules and 77 Subjects," *Undersea Biomedical Research*, Vol. 12 (1985), pp. 41-52.
- 8. E. D. Thalmann, S. S. Survanshi, and E. T. Flynn, "Direct Comparison of the Effects of He, N2, and Wet or Dry Conditions on the 60 Fsw No-Decompression Limit" [abstract], *Undersea Biomedical Research*, Vol. 16 (1989), p. 67.
- 9. R. W. Hamilton, E. D. Thalmann, E. T. Flynn, and D. J. Temple, *No-Stop 60 fsw Wet and Dry Dives Using Air, Heliox, and Oxygen-Nitrogen Mixtures. Data Report on Projects 88-06 and 88-06A,* Technical Report 2002-002, Naval Medical Research Center, Jul 2002.
- 10. A. A. Bühlmann, *Decompression Decompression Sickness*, G. P. Michel, translator (Springer-Verlag, Berlin, 1984). English translation of German title *Dekompression - Dekompressionkrankheit*, first published 1983.
- 11. T. E. Berghage, C. Donelson, and J. A. Gomez, "Decompression Advantages of Trimix," *Undersea Biomedical Research*, Vol. 5 (1978), pp. 233-242.
- 12. R. S. Lillo, "Effect of N<sub>2</sub>-He-O<sub>2</sub> on Decompression Outcome in Rats After Variable Time-at-Depth Dives," *Journal of Applied Physiology*, Vol. 64 (1988), pp. 2042- 2052.
- 13. F. Bouak, R. Y. Nishi, and J. Beavis, *Development of CUMA Trimix Decompression Tables. Series 1, In-Water Oxygen Decompression Profiles,* Technical Memorandum TM 2009-032, Defence R&D Canada - Toronto, Jun 2009.
- 14. F. Bouak, R. Y. Nishi, and N. Holden, *Development of CUMA Trimix Decompression Tables. Series 2 to 3, In-Water Oxygen Decompression Profiles,*  Technical Memorandum TM 2010-126, Defence R&D Canada - Toronto, Dec 2010.
- 15. T. G. Shields, *Sea Trial of 70 and 80 Metre 15-Minute Trimix Decompression Schedules,* Report AMTE(E) R82-407, Admiralty Marine Technology Establishment Physiological Laboratory, 1982.
- 16. T. G. Shields, *Re-Trial at Sea of 70 and 80 Metre 15 Minute Trimix Decompression Schedules,* Report AMTE(E) R82-409, Admiralty Marine Technology Establishment Physiological Laboratory, 1982.
- 17. T. G. Shields, K. M. Greene, T. R. Hennessy, and H. V. Hempleman, "Trimix Diving to 75 Metres" [abstract], *Undersea Biomedical Research*, Vol. 5 Suppl (1978), p. 24.
- 18. R. D. Workman, "Studies of Decompression and Inert Gas-Oxygen Mixtures in the U.S. Navy," *Underwater Physiology II, Proceedings of the Proceedings of the 2nd Symposium on Underwater Physiology,* C. J. Lambertsen, ed., (National Academy of Sciences, Washington DC, 1963), pp. 22-28.
- 19. R. D. Workman, "Underwater Research Interests of the U. S. Navy," *Underwater Physiology III, Proceedings of the Proceedings of the 3rd Symposium on Underwater Physiology,* C. J. Lambertsen, ed., 1966 Mar 25-26, Washington DC, (William & Willkins, Baltimore, 1967), pp. 4-15.
- 20. W. A. Gerth and T. M. Johnson, *Development and Validation of 1.3 ATA PO<sub>2</sub>-in He Decompression Tables for the MK 16 MOD 1 UBA,* NEDU TR 02-10, Navy Experimental Diving Unit, Aug 2002.
- 21. D. J. Temple, R. Ball, P. K. Weathersby, E. C. Parker, and S. S. Survanshi, *The Dive Profiles and Manifestations of Decompression Sickness Cases After Air and Nitrogen-Oxygen Dives,* Technical Report 99-02, Naval Medical Research Center, 1999.
- 22. D. J. Doolette and W. A. Gerth, "Significance and Power of Sequential Bernoulli Trials" [abstract], *Undersea and Hyperbaric Medicine*, Vol. 36, No. 4 (2009), p. 257.
- 23. R. P. Layton, *Unmanned Evaluation of the Modernized MK 16 MOD 1 Partial Pressure of Oxygen (PO2) Control Performance,* NEDU TR 12-02, Navy Experimental Diving unit, Jul 2012.
- 24. J. A. Hodgdon, "Body Composition in the Military Services: Standards and Methods," in *Body Composition and Physical Performance: Applications for the Military Services*, B. M. Marriott, J. Grumstrup-Scott, eds. (National Academy Press, Washington DC, 1992), Ch. 4, pp. 57-70.
- 25. B. E. Shykoff, *Underwater Cycle Ergometry: Power Requirements With and Without Diver Thermal Dress,* NEDU TR 09-01, Navy Experimental Diving Unit, Jan 2009.
- 26. B. E. Shykoff, *Oxygen Consumption As a Function of Ergometer Setting in Different Diver's Dress: Regression Equations,* Technical Memorandum NEDU TM 09-06, Navy Experimental Diving Unit, Aug 2009.
- 27. D. J. Doolette, W. A. Gerth, and K. A. Gault, *Addition of Work Rate and Temperature Information to the Augmented NMRI Standard (ANS) Data Files in the "NMRI98" Subset of the USN N2-O2 Primary Data Set,* NEDU TR 11-02, Navy Experimental Diving Unit, Jan 2011.
- 28. E. D. Thalmann, "USN Experience in Decompression Table Validation," *Validation of Decompression Tables, Proceedings of the Proceedings of the 37th Undersea and Hyperbaric Medical Society Workshop,* H. R. Schreiner and R. W. Hamilton, eds., 1987 Feb 13-14, Bethesda, MD, USA, (Undersea and Hyperbaric Medical Society, Bethesda, MD, USA, 1989), pp. 33-44.
- 29. D. N. Walder, "Adaptation to Decompression Sickness in Caisson Work," *Biometeorology, Proceedings of the Proceedings of the Third International Biometeorological Congress,* S. W. Tromp and W. H. Weihe, eds., 1963 Sep 1-7, Pau, France, (Pergamon Press, Oxford, 1967), pp. 350-359.
- 30. D. H. Elliott, "Some Factors in the Evaluation of Oxy-Helium Decompression Schedules," *Aerospace Medicine*, Vol. 40 (1969), pp. 129-132.
- 31. E. D. Thalmann, *Development of a Decompression Algorithm for Constant 0.7 ATA Oxygen Partial Pressure in Helium Diving,* NEDU TR 1-85, Navy Experimental Diving Unit, Apr 1985.
- 32. W. A. Gerth, K. A. Gault, and S. J. Stanek, *Empirical Evaluation of the MK 16 MOD 1 UBA Breathe-Down Procedure,* NEDU TR 03-13, Navy Experimental Diving Unit, Jun 2003.
- 33. R. D. Workman and J. L. Reynolds, *Adaptation of Helium-Oxygen to Mixed-Gas Scuba,* NEDU TR 1-65, Navy Experimental Diving Unit, 1965.
- 34. Director of Naval Warfare, Procedures for Deep and Saturation Diving, BR 2806 (Suppl) (Ministry of Defence, 1985), Chapter 8, Table 3. 75m Diving – Decompression Schedules, p. 8-13.
- 35. R. Y. Nishi and M. R. N. Warlow, *Development of CUMA HeO2 Decompression Tables - Final Report,* Report 97-R-98, Defence and Civil Institute of Environmental Medicine, Sep 1997.
- 36. R. Y. Nishi, "Doppler and Ultrasonic Bubble Detection," in *The Physiology and Medicine of Diving*, *4 ed.*, P. B. Bennett, D. H. Elliott, eds. (W.B. Saunders, London, 1993), Ch. 15, pp. 433-453.
- 37. G. G. Molumphy, *Evaluation of Newly Computed Helium-Oxygen Decompression Tables at Depths Greater Than Provided for in the Published Tables, the Effectiveness of the Improved Recirculation System and the Feasibility of Accomplishing Useful Work by Highly Trained Divers at These Depths,* NEDU TR 9- 50, Navy Experimental Diving Unit, Oct 1950.
- 38. W. A. Gerth, "Decompression Sickness and Oxygen Toxicity in U. S. Navy Surface Supplied He-O<sub>2</sub> Diving," *Proceedings of the Advanced Scientific Diving Workshop,* M. A. Lang and N. E. Smith, eds., 2006 Feb 23-24, (Smithsonian Institution, Washington DC, 2006), pp. 17-26.
- 39. C. Momson, *Report on the Use of Helium Oxygen Mixtures for Diving,* NEDU Report 2, Navy Experimental Diving Unit, Apr 1939.
- 40. D. J. Doolette, R. N. Upton, and C. Grant, "Altering Blood Flow Does Not Reveal Difference Between Nitrogen and Helium Kinetics in Brain or in Skeletal Muscle in Sheep," *Journal of Applied Physiology*, Vol. 118 (2015), pp. 586-594.
- 41. R. H. Strauss and T. D. Kunkle, "Isobaric Bubble Growth: a Consequence of Altering Atmospheric Gas," *Science*, Vol. 186 (1974), pp. 443-444.
- 42. O. Hyldegaard and J. Madsen, "Influence of Heliox, Oxygen, and  $N_2O-O_2$  Breathing on N2 Bubbles in Adipose Tissue," *Undersea Biomedical Research*, Vol. 16 (1989), pp. 185-193.
- 43. O. Hyldegaard and J. Madsen, "Effect of Air, Heliox, and Oxygen Breathing on Air Bubbles in Aqueous Tissues in the Rat," *Undersea and Hyperbaric Medicine*, Vol. 21 (1994), pp. 413-424.
- 44. O. Hyldegaard and T. Jensen, "Effect of Heliox, Oxygen and Air Breathing on Helium Bubbles After Heliox Diving," *Undersea and Hyperbaric Medicine*, Vol. 34 (2007), pp. 107-122.
- 45. D. J. Doolette and W. A. Gerth, *Safe Inner Ear Gas Tensions for Switch to Air Breathing During Decompression,* NEDU TR 12-04, Navy Experimental Diving Unit, Mar 2013.

46. R. Ball and E. C. Parker, "A Trial to Determine the Risk of Decompression Sickness After a 40 Feet of Sea Water for 200 Minute No-Stop Air Dive," *Aviation, Space, and Environmental Medicine*, Vol. 71 (2000), pp. 102-108.

### **APPENDIX A DECOMPRESSION SCHEDULES**

Table A-1. Test schedule as used.



Divers breathe from MK 16 MOD 1 for 30 minutes prior to starting compression. Descent rate 40 fsw/min. Ascent rate 30 fsw/min.

\* Time at Bottom in minutes does not include descent.

† Stop time does not include travel to stops.

### **CORRECTIONS FOR DELAYS IN DESCENT**

The test schedule was specified as 35 minutes time on bottom, which with a 40 fsw/min descent rate results in a bottom time of 40 minutes. In the event of a delay during decent, it is a simple calculation to adjust time on the bottom so that compartmental inert gas uptake is the same as for the planned schedule. Adjusted time at bottom ( $t_{\text{adj}}$ ) is calculated for descent delayed by short holds at constant depths (such as to prevent an ear squeeze) but otherwise at the specified decent rate. Under these conditions, gas uptake during travel can be ignored with only a small error, so that the target tension of a single inert gas (or equivalently the sum of multiple inert gases with the same compartmental time constant  $[TC]$ ) in any compartment  $(P_t)$  is approximated as:

$$
P_t = P_a + (P_{hold} - P_a) \times e^{-\frac{t_{adj}}{TC}},
$$

where  $P_a$  is the arterial inert gas tension on the bottom and  $P_{hold}$  is the compartmental inert gas pressure at the end of the hold.

Rearranging and inserting the solution for *Phold* for any particular depth and duration (*thold*) of a hold gives:

$$
t_{adj} = -\ln\left\{P_t - P_a\middle/\left\{\left[P_{a\_hold} + \left(P_0 - P_{a\_hold}\right) \times e^{-\frac{t_{hold}}{TC}}\right] - P_a\right\}\right\} \times TC,
$$

where  $P_{a\_hold}$  is the arterial inert gas tension at the hold depth and  $P_0$  is the compartmental inert gas pressure at the beginning of the dive (after the 30-minute prebreathe at the surface).

Table A-2 gives *tadj* subtracted from the planned 35-minute time on the bottom, for holds at 10 fsw increments and up to five minutes duration. In this range, values of *tadj*

calculated using the different compartmental time constants in the LEM-he8n25 model (range 4.7–327.7 minutes) differ by only a few seconds.



Table A-2. Decrease in time at 200 fsw to accommodate holds during descent

\*Hold depth in fsw includes water offset.

Compression to 200 fsw at target rate of 40 fsw/min  $(\pm 5 \text{ fsw/min})$ . The dive can be continued with delays in descent up to 5 minutes, otherwise the dive will be aborted.

If the hold occurs at 50 fsw or shallower, the dive continues with no adjustment to time at bottom. Otherwise the time at 200 fsw must be decreased by the amount shown below. Decompression will proceed according to the planned schedule.

### **APPENDIX B CRITERIA FOR DCS AS AN EXPERIMENTAL OUTCOME[g](#page-31-0)**

### A1: DCS requiring recompression

Joint pain persisting at least as long as tabulated below (whether recompressed or not)



Skin rash or mottling in combination with joint pain of any duration Dyspnea, unless clearly from barotrauma or anxiety hyperventilation syndrome Any spinal neurological symptoms supported by signs Any brain symptoms<sup>[h](#page-31-1)</sup>

Any [i](#page-31-2)nner ear symptoms,<sup>i</sup> unless clearly from barotrauma

Any suspicious symptom leading to and relieved by recompression

### A2: Marginal DCS (DCS not requiring recompression)<sup>1</sup>

Joint pain not persisting as long as tabulated above Moderate or severe fatigue Skin itch in water-immersed divers breathing air or  $N_2$ -O<sub>2</sub> Skin rash or mottling as only symptom Symptoms reported as "DCS not requiring recompression" not fitting other criteria

### B: Unknown outcome (data should not be used)

Headache, typical and common for this diver Vague abdominal or chest pain, not related to trauma or barotrauma Vague symptoms of any kind not responding to recompression or oxygen therapy attempted  $<$ 18 hours after dive<sup> $k$ </sup>

### C: Not DCS

No signs or symptoms reported Signs or symptoms reported 24 hours after surfacing Mild joint pain or fatique consistent with recent exercise Sharp pain consistent with joint sprain or impact injury Vague symptoms similar to Marginal DCS not responding to recompression therapy attempted >18 hours after dive<sup>1</sup>

<span id="page-31-0"></span><sup>&</sup>lt;u>。</u><br>Weathersby et al. 1988 criteria<sup>21</sup>; language reflects development for retrospective data review; not used for treatment decisions

<span id="page-31-1"></span><sup>&</sup>lt;sup>h</sup>e.g., visual blurring, "mental sluggishness"<br><sup>i</sup> e.g., uneteodinees, vertige, beering lees

<span id="page-31-2"></span>e.g., unsteadiness, vertigo, hearing loss

<span id="page-31-3"></span>Based on perception that lack of treatment will not result in morbidity

<span id="page-31-4"></span><sup>k</sup> Diver may have gone on to develop DCS if not treated

<span id="page-31-5"></span>At which time any DCS should have occurred

### **APPENDIX C ACCURACY OF A GROUP-SEQUENTIAL TRIAL**

In sequential trials, subjects are recruited sequentially and data are analyzed after each individual result or group of results become available. The trial stops as soon as the treatment effect first exceeds a pre-specified size. The outcome of the sequential trial is used as a test of an hypothesis in the sample collected at the point of stopping. For instance, a trial of a single decompression schedule, in which the outcome for each subject is decompression sickness (DCS) or no-DCS (Bernoulli trial), could be analyzed after each man-dive is completed (sequential trial) and stopped when the observed DCS incidence first exceeds some limiting value (stop-high) or drops below another limiting value (stop-low), and this taken as evidence that the decompression schedule has  $P_{DCS}$  greater or less than some value of interest. The trial described in this report was a comparison of two decompression schedules, and the trial was analyzed after each 16 man-dives were completed on each schedule (group-sequential) and was designed to stop if the absolute value of the difference in DCS incidences between the schedules exceeded a limiting value. This was to be taken as evidence against practical equivalence of the  $P_{DCS}$  of the two schedules.

A statistical hypothesis test in which the value of a statistic of some outcome measure in a sample from a population is classified as evidence to retain or reject a null hypothesis is an example of a binary classification test. Another example is a diagnostic test that classifies an individual as positive or negative for some disease. The fundamental measures of accuracy of a binary classification test are the sensitivity (true positive rate) and specificity (true negative rate). The sensitivity is the conditional probability of classifying an element as positive given that it truly is positive, and the specificity is the conditional probability of classifying an element as negative given that it truly is negative. The accuracy of a statistical hypothesis test is described in a complimentary way, typically by the conditional probability  $(α)$  of rejecting a null hypothesis given the null hypothesis is true (type I error, false positive) and the conditional probability (β) of retaining a null hypothesis given the null hypothesis is false (type II error, false negative). The relationship of these measures is tabulated in Table C-1.

Assessing the accuracy of hypothesis tests resulting from sequential trials is not straightforward, and we have developed a Monte Carlo simulation method for such assessments<sup>22</sup> that extends and corrects an earlier method.<sup>46</sup> Monte Carlo experiments analyze outcomes in multiple computer-generated random samples. For instance, the probability of an outcome is estimated by the proportion of samples in which the outcome occurs. Monte Carlo experiments can be used to assess the accuracy of statistical hypothesis tests by performing the test on repeated random samples from a statistical distribution that simulates the experiment, and computing the proportion of test results that equate to the conditional probabilities given in Table C-1.



Real Condition

Table C-1. Definition and nomenclature of measures of accuracy of binary classification tests

TN: True Negatives; FN: False Negatives; TP: True Positives; FP: False Positives

The trial described in this report tested the null hypothesis  $(H_0)$ :  $P_{DCS, trimit} \ge P_{DCS, heliox}$ 1.5%. The trial used the stopping rules given in Table 2 and replicated here in Table C-2. If the trial continued to 100 man dives on each profile or if the trial stopped with a positive value of  $x_{\text{trimix}} - x_{\text{heliox}}$  (stop-high), this would be evidence to retain  $H_0$  and conclude that trimix does not afford an increase in decompression efficiency over heliox. If the trial stopped with a negative value of  $x_{\text{trimix}} - x_{\text{heliox}}$  (stop-low), this would be evidence to reject  $H_0$  and conclude that trimix has greater decompression efficiency than heliox.





The stopping rules could be selected arbitrarily, but those in Table C-2 are integer values of  $|X_{\text{trimix}}-X_{\text{heliox}}|$  and the corresponding largest number of man-dives (# mandives) for which the proportion  $|x_{\text{trimix}}-x_{\text{heliox}}|/(# \text{ man-dives})$  has a lower 80% confidence limit>1.5%. It may seem counterintuitive that the specificity of the group-sequential trial is not simply equal to  $1-\alpha=80\%$ , as used to generate the stopping rules, but note that the data was analyzed each time 16 man-dives were collected on each schedule, and may stop at values which represent greater differences in DCS incidence than the stopping rules (e.g. 2/16, 2/32, 2/48, 3/64, 3/80, 3/96).

Figure C-1 shows a Monte Carlo simulation of possible trial outcomes for different possible values of  $P_{DCS}$  for the trimix schedule and assuming  $P_{DCS}=5.56\%$  for the heliox schedule. Each point on each of these curves is the fraction of 10,000 trial simulations with the indicated outcome. Each simulation consisted of subtracting a vector of 100 random samples from the Bernoulli distribution (possible values 0 and 1, representing no-DCS and DCS respectively), B(1,*p*) with *p*=0.0556, representing heliox dives, from a vector of 100 random samples from the Bernoulli distribution with *p* being the corresponding value of  $P_{DCS.trimix}$  on the x-axis. The running, cumulative sum along the resulting vector was calculated, and each 16<sup>th</sup> value compared to the stopping rules in Table C-2.



Figure C-1. Monte Carlo simulation of the proposed trial showing the probability of trial outcomes (y-axis) for different possible values of  $P_{DCS}$  of the trimix dive (x-axis) and assuming  $P_{DCS}=0.056$  for the heliox dive. Stop-low is the outcome of stopping with a negative value of  $x_{\text{trimix}}-x_{\text{heliox}}$  (reject H<sub>0</sub> in favor of lower  $P_{DCS}$  for trimix). Stop-high is the reverse outcome. Indeterminate is continuing to 100 man-dives on each profile without a stop-high or stop-low.

Figures C-2 and C-3 illustrate how the accuracy of the group-sequential is estimated. In Figure C-2, the heavy line shows probability of result  $R_1$  (rejecting H<sub>0</sub>) for different possible  $P_{DCS}$  of the trimix dive (x-axis). This curve is the stop-low curve given in Figure C-1. The area under this curve is the  $P(R_1)$  for all possible values of  $P_{DCS.trimix}$ . The hatched area (to the right of the vertical line at 0.0556-0.015=0.0406 and below 1) defines the domain where H<sub>0</sub> is true: all trial outcomes for real P<sub>DCS.trimix</sub>≥P<sub>DCS.heliox</sub>-0.015. The un-hatched area (to the left of 0.0406 and below 1) defines the domain where  $H_0$  is false: all trial outcomes for real  $P_{DCS.trimix}$ < $P_{DCS.heliox}$ -0.015. Figure C-3 shows the corresponding information for result  $R_0$  (retaining  $H_0$ ): the heavy line is the sum of

the stop-high and indeterminate curves (≡1−stop-low) of the trial simulation given in Figure C-1. The area under this curve is the  $P(R_0)$  for all possible values of  $P_{DCS-trimix}$ . The hatched area in Figure C-3 defines the same domains as do the hatched areas in Figure C-2.



Figure C-2. The heavy line shows the probability (y-axis) of rejecting  $H_0 (R_1)$  for different possible values of P<sub>DCS</sub> of the trimix dive (x-axis) and assuming P<sub>DCS</sub>=0.0556 for the heliox dive. This curve is the stop-low curve of the trial simulation given in Figure C-1. The area under this curve is  $P(R_1)$  for all possible values of P<sub>DCS.trimix</sub>. The hatched area (to the right of the vertical line at 0.0406 and below 1) defines the domain where H<sub>0</sub> is true: all trial outcomes for real P<sub>DCS.trimix</sub>≥P<sub>DCS.heliox</sub>-0.015. The un-hatched area (to the left of 0.0406 and below 1) defines the domain where H<sub>0</sub> is false: all trial outcomes for real P<sub>DCS.trimix</sub><P<sub>DCS.heliox</sub>-0.015.

The accuracy of the group-sequential trial is estimated from areas defined by the curves in Figure C-2 and Figure C-3. For instance, the probability of  $R_1$  given  $H_0$  is true is the conditional probability, defined by Bayes theorem,

 $P(R_1|H_0$  is true)= $P(R_1 \cap H_0$  is true)/ $P(H_0$  is true).  $P(R_1 \cap H_0$  is true) is the probability of R<sub>1</sub> for  $P_{DCS.trimix} \ge P_{DCS.heliox}$ -0.015, and is the hatched area under the  $R_1$  curve in Figure C-2. Since the only two possible outcomes are  $R_0$  or  $R_1$  (accept or reject  $H_0$ ),  $R_0$  and  $R_1$ partition the sample space  $(R_0+R_1=1)$ . Therefore, it follows from the law of total probability that  $P(H_0 \text{ is true})=P(R_0 \cap H_0 \text{ is true})+P(R_1 \cap H_0 \text{ is true}).$   $P(R_0 \cap H_0 \text{ is true})$  is the hatched area below the  $R_0$  curve in Figure C-3. For ease of calculation, note that since  $R_0 + R_1 = 1$ ,  $P(R_0 \cap H_0$  is true) is also the hatched area above the  $R_1$  curve shown in Figure C-2, and therefore,  $P(H_0 \text{ is true}) = P(R_0 \cap H_0 \text{ is true}) + P(R_1 \cap H_0 \text{ is true})$  is the area defined by the hatched rectangle in Figure C-2 (and also in Figure C-3). As a result,  $P(R_1|H_0)$  is true) is the fraction of the hatched area that is under the  $R_1$  curve in Figure

C-2. Similarly,  $P(R_1|H_0)$  is false) is the fraction of the un-hatched area below the  $R_1$ curve.  $P(R_0|H_0$  is true) and  $P(R_0|H_0$  is false) are similarly calculated from the fractions of the hatched and un-hatched areas below the  $R_0$  curve (Figure C-3). The conditional probabilities are given in Table 3 which is replicated below as Table C-3.



Figure C-3. The heavy line shows probability (y-axis) of retaining  $H_0 (R_0)$  for different possible values of  $P_{DCS}$  of the trimix dive (x-axis) and assuming  $P_{DCS}=0.0556$  for the heliox dive. This curve is the sum of the stop-high and indeterminate curves (≡1−stop-low) of the trial simulation given in Figure C-1.The area under this curve is the  $P(R_0)$  for all possible values of  $P_{DCS,trimix}$ . The hatched and un-hatched areas have the same meanings as in Figure C-2.

Table C-3. Accuracy of the group-sequential trial



This simulation method has previously been used to estimate the posterior probability of the hypothesis given a particular trial outcome has been obtained.<sup>46</sup> For instance, the hatched area under the  $R_0$  curve divided by the total area under the  $R_0$  curve, *P*(H<sub>0</sub> is true|R<sub>0</sub>)=*P*(H<sub>0</sub> is true∩R<sub>0</sub>)/*P*(R<sub>0</sub>)=98.8%.



### **APPENDIX D DIVER CHARACTERISTICS**

\*only divers who completed the experimental profiles are shown; <sup>†</sup>age at first dive in this study;<br><sup>‡</sup>calculated from height, waist circumference, and neck circumference according to U.S. Navy method <sup>24</sup>

# **APPENDIX E DIVING SCHEDULE**



The following tables show the dates on which each diver participated in the dive trial. H: heliox dive. T: trimix dive. Work-up dives not shown. Shaded boxes indicate DCS cases.

### **APPENDIX F MEDICAL INCIDENTS**

The following are the case narratives as written by the attending Diving Medical Officer (DMO) for each medical incident. Some commonly used short-hand has been expanded.

### **DIVER ID 19, 17JUNE 2014**

A 40 year old male active duty who completed the Trimix Experimental Dive protocol at 12:58 on Tuesday, 17 JUNE 2014 reports first noting a dull, achy pain in his right (dominant) shoulder, approximately 3.5 hours after completing the dive. The individual completed the post-dive two-hour observation period without symptoms, did some work around his office, and rode his bike home about 16:00 that afternoon. Soon after getting home, he first noticed the shoulder pain and activated the bends team at NEDU. DMO arrived at NEDU at 17:20 (within 10 minutes of notification) and observed as HM1 [duty corpsman] conducted a complete neurological examination on the surface.

Signs and Symptoms: Diver complained of 7/10 shoulder pain "inside the joint" without any other symptoms. The HM1 reported finding 4/5 weakness in both the extensor and flexor muscles for the right arm, but I believe that this is guarding and not a true neurological sign. Recommended the initiation of a U.S. Navy Treatment Table 6 for Type I DCS. No problems on descent to 60 fsw over 3-minute period. Diver reported decrease in shoulder pain from 7/10 to 2/10 immediately upon reaching 60 fsw. Diver started oxygen period and reported complete relief within 12 minutes of the first oxygen period. A complete neurological examination was performed and failed to demonstrate any residual abnormality. The Treatment Table 6 was completed without extensions and without incident, and the diver was observed for an abbreviated post-dive period. Symptoms did not re-occur. The diver was sent home in the care of the Command Master Chief and the diver's wife. On examination the following morning, the diver continued in good health. Final Diagnosis: Type I DCS - pain only, one joint involved. Complete resolution with one Treatment Table 6 - no extensions.

### **DIVER ID 35, 17JUNE 2014**

Background: A 44 year old male active duty who completed the Trimix Experimental Dive protocol at 12:58 on Tuesday, 17 JUNE 2014 reported everything normal after dive except for being very fatigued. The individual completed the post-dive 2-hour observation period without symptom. He was late (08:35) getting to work this morning [on 18 JUNE 2014] because his wife had to try multiple times to arouse him, which is not the usual case. The diver called ahead and was met in Sickbay of 08:40 by DMO and HM1, who conducted a complete neurological exam. Midway through the exam at 08:50 the DMO activated the Bends Watch team.

Signs and Symptoms: In addition to the increased feeling of fatigue, the diver expressed 4/10 dull ache pain in his lower back. On neurologic exam, the diver was found to have decreased sensation over an area on his back from approximately T8 to S1 and

approximately 10 inches on either side of the spine. This area was very well defined and was marked by HM1 with ink prior to hyperbaric treatment. The remainder of the objective exam was normal except for a very clumsy hand-flip with the diver's right (dominant) hand. The DMO made a diagnosis of DCS Type II and requested that a U.S. Navy Treatment Table 6 be initiated.

Treatment: No problems on descent to 60 fsw over 3-minute period. Diver reported decrease in back pain from 4/10 to 1/10 immediately upon reaching 60 fsw. Diver started first oxygen period and was noted to have immediate recovery of his hand coordination and shrinkage of the anesthetic region on his back by 6 inches on each side. By the 10-minute on oxygen point, the anesthetic region had shrunk to the size of "an egg" and was completely resolved within 15 minutes of breathing oxygen at depth. A complete neurological examination was performed and failed to demonstrate any residual abnormality. Although the U.S. Navy Diving Manual requires a Treatment Table 6 with full extensions be conducted for neurological DCS incidents, the DMO on the scene determined that the rapid recovery from, and the nature of the DCS symptoms warranted an extension of only one oxygen period 60 fsw - a decision reached prior to the diver experiencing symptoms of neurological oxygen toxicity 17 minutes into this third and final oxygen period at 60 fsw. The diver developed a pulsing spasm of his left pectoralis major muscle, elevated agitation, and a narrowing peripheral visual field - he was immediately switched to chamber air and permitted five minutes to recover while tended. At the 5-minute post oxygen toxicity event mark, the diver was sufficiently recovered to begin travel, on oxygen to the 30-foot decompression stop. The remainder of the TT6 was completed without incident and the diver was observed for an abbreviated 1-hour post-dive period. No reoccurrence of symptoms occurred.

Post-Treatment: The diver was sent home in the care of the Command Master Chief and the diver's wife. On examination the following morning, the diver continued in good health without complaint.

Final Diagnosis: Type II DCS - neurologic. Complete resolution with one Treatment Table 6 with extension by one oxygen period at 60 fsw, complicated by neurological oxygen toxicity symptoms during final oxygen period at 60 fsw.

## **APPENDIX G UBA GAS COMPOSITIONS**

### **HELIOX**





## **TRIMIX**

