Computers in Biology and Medicine 92 (2018) 110–117

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/compbiomed

Iso-risk air no decompression limits after scoring marginal decompression sickness cases as non-events

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ARTICLE INFO

Keywords:
Hyperbaric
Deep sea diving
Marginal
Decompression sickness
DCS
Gas content
Inert gas

ABSTRACT

Decompression sickness (DCS) in humans is associated with reductions in ambient pressure that occur during diving, aviation, or certain manned spaceflight operations. Its signs and symptoms can include, but are not limited to, joint pain, radiating abdominal pain, paresthesia, dyspnea, general malaise, cognitive dysfunction, cardiopulmonary dysfunction, and death. Probabilistic models of DCS allow the probability of DCS incidence and time of occurrence during or after a given hyperbaric or hypobaric exposure to be predicted based on how the gas contents or gas bubble volumes vary in hypothetical tissue compartments during the exposure. These models are calibrated using data containing the pressure and respired gas histories of actual exposures, some of which resulted in DCS, some of which did not, and others in which the diagnosis of DCS was not clear. The latter are referred to as marginal DCS cases. In earlier works, a marginal DCS event was typically weighted as 0.1, with a full DCS event being weighted as 1.0, and a non-event being weighted as 0.0. Recent work has shown that marginal DCS events should be weighted as 0.0 when calibrating gas content models. We confirm this indication in the present work by showing that such models have improved performance when calibrated to data with marginal DCS events coded as non-events. Further, we investigate the ramifications of derating marginal events on model-prescribed air diving no-stop limits.

1. Introduction

The signs and symptoms of decompression sickness (DCS) in humans, which is associated with reductions in ambient pressure during diving, aviation, or certain manned spaceflight operations, can include, but are not limited to joint pain, radiating abdominal pain, paresthesia, dyspnea, general malaise, cognitive dysfunction, cardiopulmonary dysfunction, and death [1,2]. DCS is typically categorized as either type 1 pain only, or type 2 neurological [3,4]. Our focus here is on the problem of DCS caused by decompressions from hyperbaric exposures, not decompressions to hypobaric pressures, such as those experienced by pilots on ascent to high altitudes and astronauts during extravehicular activities. Haldane et al. [5] are commonly credited with developing the first effective strategy for preventing DCS in man. The latter entailed tracking gas content in a series of independent compartments. Within each compartment, the gas content was used to calculate the level of supersaturation that was not allowed to exceed a maximum value by the algorithm. A decompression was considered unsafe with the inevitability of DCS if the critical supersaturation was exceeded in any compartment, or safe with no possibility of DCS if the critical supersaturation was not exceeded in any compartment. Although this approach has since been extensively refined [6–10], it retains the shortcoming of being unable to explicitly control the risk of DCS in the calculation of decompression schedules.

Recognizing that the occurrence of DCS has both deterministic and stochastic mechanisms, workers at the United States Navy (USN) Naval Medical Research Institute (NMRI) developed models to predict the probability of DCS occurrence during hyperbaric exposures and compute decompression schedules that incur user-specified risks of DCS [11–23]. These models feature calibration against data describing a collection of hyperbaric exposures and their binary outcomes: either DCS occurred or it did not. There is currently no definitive diagnostic test for DCS. In the absence of a definitive test, the outcomes of some dives are an ambiguous collection of signs and symptoms. These ambiguous outcomes are termed

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https://doi.org/10.1016/j.compbiomed.2017.11.012
Received 20 January 2017; Received in revised form 13 November 2017; Accepted 14 November 2017

Table 1
Summary of features in the models investigated. All models are composed of three parallel, uncoupled, well-stirred compartments. Exponential gas uptake and elimination prevailed in each compartment unless otherwise noted by an "X" in the Linear Kinetics column. For the models which allowed linear gas kinetics, they were only allowed in the second compartment. Oxygen only participated in the second compartment when present. The threshold term was only applied to the third compartment.

Model	Linear Kinetics	Oxygen	Threshold
PLBX3			
Model 1	X		
Model 2		X	
Model 3			X
LE1 (USN93)	X		X
Model 4	X	X	
Model 5		X	X
LEM (LEM-NMRI98)	X	X	X

marginal DCS events, do not require recompression therapy, and spontaneously resolve. Examples of marginal DCS events are aches or mild pain in a single joint lasting less than 60 min or pain in multiple joints lasting less than 30 min [24,25]. Pain with any other manifestation, such as visual disturbances, and difficulties with balance, speech, and/or comprehension, whether or not these other manifestations self-resolve, would not be classified as a marginal DCS event.

Transient or ambiguous symptoms indicate potential occurrence of the sickness. In order to incorporate marginal DCS events, these occurrences were originally treated as half of a DCS event (weighted as 0.5) when included in the calibration data [13], though no statistical justification was given for this decision. Later, the weight given to marginal events was reduced to one-tenth of a DCS event based upon communications with USN dive medical officers, who indicated they were much less concerned with marginal DCS than full DCS [19]. More rigorous methods for incorporating different degrees of severity of DCS have since been published [26]. Recent work has found the inclusion of marginal DCS events with fractional weights detrimental to the overall performance of probabilistic models [27]. Rigorous statistical evaluation of marginal events has found that they are not combinable with the rest of the data in the BIG292 calibration set used by the authors. This past study points to the fact that while saturation data makes up 14.4% of the BIG292 calibration data set (discussed in more detail below) and marginal DCS events account for 3.3% of BIG292, 55% of the marginal DCS events occurred during saturation dives. This indicates that including marginal DCS events, even with a small fractional weight, grants saturation exposures undue weight in the calibration data. In this work, we evaluate the impact of treating marginal DCS events as non-events in the calibration data. We first determine if linear kinetics, a threshold term, and oxygen as a participating gas are still beneficial to model performance; as determined previously [12,15,17,19]. After we establish which model features are statistically justified, we investigate how the modified calibration data affects model performance.

2. Methods

2.1. Data

All data used in this study were taken from the USN N_2-O_2 dive database which has been previously published [12,24,25,28] and does not require approval from an institutional review board for use. The data are composed of time-series records for the pressure and gas inspired by the diver throughout each recorded dive. Successive points or "nodes" are connected by straight lines in the time domain to describe a dive as a series of segments, each of which is either an isobaric, compression, or decompression segment that may include a breathing gas switch. The outcome of each exposure is recorded as either 1.0 if DCS occurred, 0.0 if DCS did not occur, or 0.1 if marginal DCS occurred. If the outcome was DCS or marginal DCS, the time the subject was last known to be symptom free and the time at which the presence of DCS signs or symptoms were first confirmed are also recorded. Two subsets of the USN N_2-O_2 dive database were used in this study. The first set, BIG292, consists of 3322 exposures in 1038 different time and depth profiles within which 190 DCS events and 110 marginal DCS events occurred. BIG292 was used as the calibration data set for the LE1-USN93 model parameters [29]. The second set, NMRI98, augments BIG292 with an additional 1013 exposures in 266 additional profiles. These additional exposures used gases with increased oxygen content during either or both the on-bottom and decompression (ascent) phases of the dives. The inclusion of more profiles using gases with increased oxygen content makes the NMRI98 data set a more versatile calibration set than BIG292. The NMRI98 data set has a total of 223 full DCS events and 127 marginal DCS events. NMR98 was used as the calibration data set for a study of models incorporating oxygen as a participating gas [12,17].

2.2. Models

The PLBX3 exponential-exponential model [30,31], the linear-exponential model (LE1) [29], and the linear exponential multigas model (LEM) [12,17,32] were chosen as the basis for this work. Features of these models are summarized in Table 1. Each is a survival model in which the body is considered to consist of three independent, well-stirred, perfusion-limited gas exchange compartments. These compartments are not intended to represent distinct anatomical tissues, but are mathematical abstractions with no direct relationship to the underlying physiology. In each model, the probability of DCS for a given exposure, PDCS, is given as a function of the instantaneous risk of DCS, r_i, in each of $n = 3$ compartments:

$$PDCS = 1 - e^{-\sum_i^n g_i \int r_i dt}, \tag{1}$$

where, $g_i$is a compartmental scaling term or gain. This equation does not include time of onset and is integrated from the start of the dive to the right-censored time, the time at which observation ceased. Time of symptom onset is incorporated by calculating a joint probability including the probability of being symptom free (PS) until the last known time at which the subject was symptom free, T_1, and the probability of DCS occurring between $T_1$and T_2, the time at which the presence of symptoms was first confirmed [33].

$$PDCS = PS_{T_1} PDCS_{T_1,T_2} = e^{-\sum_i^n g_i \int_0^{T_1} r_i dt} \left(1.0 - e^{-\sum_i^n g_i \int_{T_1}^{T_2} r_i dt}\right). \tag{2}$$

In the absence of gas bubbles, the rate of change of the compartmental inert gas tension is

$$\frac{dP_T}{dt} = k\left(P^0_{N_2} + R_{N_2} t\right) - kP_T, \tag{3}$$

where$k$is a rate constant for the compartment and $P_T$is the tissue tension of the dissolved inert gas (nitrogen for this document), $P^0_{N_2}$is the nitrogen pressure at the beginning of the segment,$R_{N_2}$is the rate of change of the arterial inert gas tension during the dive segment, and $t$is time. The arterial inert gas tension is assumed to be in equilibrium with the alveolar gas. The solution to the differential Eq. (3) for the duration of a dive segment is the familiar mono-exponential expression [11,13,27,34] given by

$$P_T = \alpha e^{-kt} + R_{N_2} + \beta, \tag{4}$$

where the constants for the dive segment are