ALTITUDE DECOMPRESSION SICKNESS (DCS) RISK ASSESSMENT COMPUTER (ADRAC)

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1. INTRODUCTION

Decompression sickness (DCS) is caused by exposure to significant reductions in environmental pressure. These situations are encountered during diving, high altitude exposures or artificially induced pressure changes in hyperbaric or hypobaric chambers. For large and rapid pressure reductions, supersaturation occurs as a result of the inability of tissue gas exchange processes to expel excess nitrogen. These gases, which come out of solution when tissues are sufficiently supersaturated, collect as bubbles in the tissue. The size and location of these bubbles are thought to have a significant effect on the resulting DCS symptoms. The risks can be minimized or prevented with sufficient denitrogenation by prebreathing pure oxygen before such exposures.

The risk of DCS increases with extended exposure times, very high altitudes, and greater physical activity during the exposure. The assessment of DCS risk for both civilian and military personnel under specified flight protocols is a critical problem that the USAF deals with on a regular basis. To provide answers to these questions, and also to obtain a clearer understanding of the effects of denitrogenation, the High Altitude Protection Function of the Air Force Research Laboratory is developing an appropriate model to predict DCS risk using physical and physiological principles.

2. PRIOR MODELING ATTEMPTS

Most altitude DCS modeling has focused on mathematical models describing bubble growth. Van Liew et al. [1] developed a probabilistic model of altitude DCS. The mechanistic principles used in the model were based on the premise that the risk of DCS is related to the number of bubbles and the volume of gas that can be liberated from a unit of tissue. The authors developed equations that incorporated these premises, and used these equations in the risk function. They tested several models to determine the one that best fit the data. The covariates (risk factors) used in the model were duration of 100% oxygen at ground level (prebreathing), atmospheric pressure after ascent, and exposure duration. Gerth and Vann [2] developed an extensive model for bubble dynamics to provide an assessment of DCS. The bubble dynamic equations were similar to those used by Van Liew et al. In the report, the percentage of individuals with DCS was used as the response variable and maximum likelihood methods were used to estimate the model parameters. In an appendix, the authors discussed the need for including onset times of DCS to improve the predictions from the model.

Kumar et al. [3], [4], [5], [6] in a series of papers, recognized that survival analysis techniques are the most appropriate to model DCS risk. They developed logistic and loglinear models to predict DCS as a function of Tissue Ratio, which is a measure of tissue nitrogen decompression stress. Another covariant used was CMB (circulating microbubbles) status. The models used the logarithm of time to DCS and maximum likelihood techniques to estimate the model's parameters. The articles allude to the fact that censoring occurs for individuals who did not exhibit any symptoms of DCS. Conkin et al [7] in a recent paper discussed in some detail the use of survival times and censoring using the loglogistic model. They also discussed different forms of the risk functions using certain mechanistic assumptions similar to those of Van Liew and others

The survey of current literature in the area of altitude DCS shows the limitations of the models that are currently in use. The description of the bubble growth dynamics using approximate (quasi-steady state) models for example, is one of them. Such an approach, due to the

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equilibrium assumption inherent in it, cannot account for the influence of any initial conditions. Approximate models were selected in order to obtain a non-complicated numerical solution leading most of the times as showed in [8] to erroneous results. Moreover, most of them examine the effect of one or two factors on the DCS risk. In reality, the risk of DCS is affected by a number of competing factors like the preoxygenation time, exposure time, exercise status, symptom and VGE (Venus Gas Emboli) onset times, and altitude. In order to develop a model that adequately describes the phenomenon of DCS, all these factors should be included in a survival model. This would determine the relative importance of the different factors, and possibly provide a method of controlling the risk of DCS. There is clearly a need for a comprehensive model that includes all these factors and the proper utilization of the bubble data information.

3. METHODS

We have conducted experiments on human subjects in a hypobaric chamber for the past several years, creating a unique database of over 2000 altitude exposures with a variety of flight profiles. The subjects were exposed to different altitudes, varying preoxygenation times, and different prebreathing mixtures. The subjects were monitored continuously and were required to report any unusual pain or other symptoms. If the symptoms were indicative of DCS, the experiment was terminated with the subject being brought down to ground level. Several measurements were recorded during the experiment including onset time of DCS, physical activity and time spent in the chamber. During each exposure, venous gas emboli were recorded by precordial 2-D echocardiography. All of the data that were collected are now included in the AFRL Hypobaric Research Database.

Pressure levels in the database ranged from 141 mmHg (40,000 ft) to 380 mmHg (18,000 ft). The preoxygenation times ranged from 0 to 240 minutes, and the exposure time ranged from 120 minutes to 480 minutes. The subjects performed different types of exercise. They were classified as rest, mild exercise, and heavy according to the amount of oxygen consumption. When we analyzed the data we found that subjects who performed mild exercise in flights of moderate/long duration (240 minutes or longer) were more likely to have high bubble grades. For individuals at rest with low prebreathing times, high grades were also observed. If prebreathing times were moderate or high, the individuals almost always had very low bubble grades. The time at which the maximum grade is attained could be interpreted as a 'survival time' and modeled accordingly. We therefore used two separate models: one that did not include bubble data (prebreathe times larger than 30 minutes) and one that included them (0-30 minutes of preoxygenation time).

The models used to fit the data were based on the loglogistic distribution, with survival function given by:

$$S(t) = \frac{1}{1+(\lambda * t)^{\gamma}} \quad (1)$$

The cumulative distribution function (Cdf) is defined as F(t) = 1-S(t), i.e. the probability of developing symptoms by time t. The risk function for the loglogistic curve is given by:

$$r(t) = \frac{\lambda\gamma(\lambda * t)^{(\gamma-1)}}{1+(\lambda * t)^{\gamma}} \quad (2)$$

The parameter $\gamma = 1/\sigma$, where σ is a scale parameter. If $\sigma < 1$, the risk function of the loglogistic curve increases to a peak, and then decreases towards zero. This is the shape, which accurately describes the risk of DCS over time. The parameter λ depends on the vector of risk factors $\vec{x}$ through the following equation:

$$\lambda = \exp(-\beta' \vec{x}) \quad (3)$$

where beta is a vector of unknown parameters which will be estimated from the data. Using the functions defined above, we can write the likelihood function:

$$L(\beta,\gamma) = \prod_{i=1}^{M} f(t_i) \prod_{j=1}^{N-M} S(t_j) \quad (4)$$

where M is the number of uncensored observations and N is the total number of observations in the data set. Here f (t)=F'(t) is the probability density function. We used the statistical software package SAS to maximize the likelihood and obtain estimates of the unknown parameters. The results are provided in Tables 1-2. The tables provide the estimates of the parameters, the standard error of the estimates,

and a chi-square value used to assess the relative importance of the different risk factors.

The weights for the various groups are displayed in the two tables below (PRES = pressure, BRTALT = ratio of prebreathing time/time at maximum altitude, EX = exercise code, MAXT = onset time of maximum venus gas emboli).

The first table does not include bubble data, meanwhile the second one does. It is clear that in Table 2 the MAXT covariant dampens the effect of all the other covariates. The EX covariate, in table 2, was found to be nonsignificant in this model. However, exercise is still a part of the predictions because it has an effect on MAXT.

Variable	DF	Estimate	Std. Err.	Chi-sq.	p-value
INT	1	-8.00	2.45	10.63	0.0011
PRES	1	2.53	0.44	32.57	0.0001
BRTALT	1	1.29	0.39	11.26	0.0008
EX	1	-0.53	0.14	13.68	0.0002
SCALE	1	0.60	0.03		

Table 1. Parameter estimates for the weighted model

Variable	DF	Estimate	Std. Err.	Chi-sq.	p-value
INT	1	-3.66	1.80	4.12	0.0424
PRES	1	1.34	0.31	17.37	0.0001
BRTALT	1	0.96	0.30	10.21	0.0014
MAXT	1	0.01	0.00	183.58	0.0001
SCALE	1	0.37	0.02		

Table 2. Parameter estimates for the weighted model including bubble data

The risk vector has five inputs. Four of them must be entered manually by the user and the fifth one is being calculated automatically by calling a subroutine. The four risk parameters are the altitude, the exposure time at that altitude, the exercise level, and the preoxygenation time. Once those parameters are known the program calls subroutine "bubgrow". Its function is to calculate the onset time of the maximum bubble radius (MAXT) in order to provide the main program with the fifth and final risk factor. This is a very complicated process and is described in detailed in the next section. If the preoxygenation time is more than 30 minutes it skips subroutine "bubgrow" and continues to calculate the probability from the cumulative distribution function.

4. BUBBLE GROWTH MODEL

Subroutine "bubgrow" is a program that solves numerically a system of equations describing bubble growth due to a hypobaric decompression. It returns a single value, and that is the onset time of the maximum bubble radius. The equations used are described in detail in [8] but we will also present them here in brief. The model consists of an advection-diffusion equation coupled with two ordinary differential equations named: the conservation of mass and momentum equations. The system is in spherical coordinates and it describes the growth of a single bubble surrounded by a limited amount of tissue. Since blood leaving the capillaries removes nitrogen gas from the system, a sink term in the diffusion equation (Equation 5) was added to account for this tissue nitrogen loss (due to capillary-tissue gas exchanges that take place in a uniformly perfused region of the body).

Initially, the gas concentration is assumed to be uniformly distributed throughout the tissue with magnitude equal to C_o depending on the duration of prebreathe prior to ascent to altitude. At altitude, the bubble expansion (due to Boyle's law) reduces the bubble pressure and induces a concentration gradient in the tissue (since the bubble pressure is related to the concentration, in the tissue layer adjacent to the bubble, through Henry's law). In turn, this initiates the bubble growth process that is governed by the following equations (dots denote differentiation with respect to time):

Bubble growth model equations

$$\frac{\partial C}{\partial t}+u_r\frac{\partial C}{\partial r}=\frac{D}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right)-kC \quad ; R(t)<r<\delta(t) \qquad (5)$$

$$\frac{d}{dt}\left(\frac{P_g R^3 M}{R_g T}\right)=3\rho D R^2\left(\frac{\partial C}{\partial r}\right)_{r=R} \qquad (6)$$

$$\rho\left(\frac{1}{2}(\xi^{4/3}-1)R\dot{R}^2-(\xi^{1/3}-1)(R^2\ddot{R}+2R\dot{R}^2)\right)=(P_g-P_{f_a})R-2\sigma+4\eta(\xi-1)\dot{R} \qquad (7)$$

where r=R(t) is the location of the bubble surface, r=δ(t) is the radius of the outer shell that encloses the bubble, $\xi=R^3/(V+R^3)$ (ξ is nondimensional), P_{fa} is the equilibrated (at ambient level) pressure of dissolved N_2 outside the tissue shell, $V=\delta^3-R^3$ is $3/4\pi$ times the tissue volume surrounding the bubble, D is the diffusion constant, u_r is the velocity of the radial flow field induced by the bubble surface motion, k is the perfusion rate constant, R_g is the gas-law constant, T is the temperature, M is the molecular weight of the gas, ρ is the density associated with the concentration measured in moles of dissolved gas per unit volume of tissue, P_g is the partial pressure of the diffusing gas inside the bubble, σ is the surface tension, η is the viscosity of the tissue surrounding the bubble and C is the gas concentration (which is a function of time and space). The initial condition for the concentration is:

$$C(r,0)=C_o \quad (8)$$

Since there are other bubbles growing in close proximity, the amount of dissolved gas in the tissue available for each bubble is finite. The concentration gradient at the outer boundary of the tissue shell is assumed zero at all times (no flux through the outer boundary of the shell). Nevertheless, the amount of gas in the tissue and the bubble is not constant, due to the sink term in the diffusion equation, which accounts for the perfusion effect on bubble growth. Hence the boundary conditions for Equation 5 are as follows:

$$C(R,t)=K_h P_g \quad (9)$$

$$\frac{\partial C(\delta,t)}{\partial r}=0 \quad (10)$$

where K_h is the Henry's law constant.

5. RESULTS

Here we test the model over a wide spectrum of altitude profiles and the results are compared with the equivalent research exposures taken from the database (see Table 3).

The first profile describes a 35,000-ft flight with 75 minutes of preoxygenation time and 180 minutes exposure time. The exercise level conducted by the subjects is considered heavy and all of them breathe 100% oxygen throughout the entire flight profile. The ascent rate is 5000 ft/min. The predicted DCS risk from ADRAC was 91.7 %. For the exact same profile but with mild exercise, ADRAC predicted a 58.8% risk. The observed risks, taken directly from the database, were 96.6% and 56.6% respectively. As one can see the predicted and observed values are very close and well within a reasonable error range.

Next we will test the model's capability of predicting risk for two different preoxygenation

schedules. Both exposures are at 30,000-ft, breathing 100% oxygen. The ascent rate is again 5000 ft/min and the preoxygenation times are 90 and 240 minutes respectively. The predicted risks computed by ADRAC were 60.7% for the 90 minutes of preoxygenation time, and 43.8% for the 240-minute one. During both of the exposures the subjects were performing mild exercises. Once again, the observed risks, from the database, were 56.0% and 45.3%.

Altitude is one of the most important risk parameters. The next two flight scenarios examine how altitude affects the risk of DCS and how ADRAC performs when altitudes are altered. The first profile represents an exposure to 25,000-ft with zero preoxygenation time, 5000 ft/min ascent rate, mild exercise breathing 100% oxygen throughout the entire exposure. The second profile is an exposure to 21,200-ft under the same conditions described above. The exposure times were 4 and 6 hours respectively. The calculated risks for those two flights were 80.8% and 16.9%. The equivalent observed values were 81.3% and 17.5%.

In Table 3 we summarize the results and a straight comparison with the observed values can conclude that all of the tested profiles were within +/- 5% error.

Altitude Profiles	% of DCS Risk taken from the Armstrong Laboratory Hypobaric DCS Research Database	% of DCS Risk calculated from ADRAC
35,000 ft altitude, 75 minutes of preoxygenation time, 180 minutes of exposure time, heavy exercise	96.6%	91.7%
35,000 ft altitude, 75 minutes of preoxygenation time, 180 minutes of exposure time, rest	56.6%	58.8%
30,000 ft altitude, 90 minutes of preoxygenation time, 240 minutes of exposure time, mild exercise	56.0%	60.7%
30,000 ft altitude, 240 minutes of preoxygenation time, 240 minutes of exposure time, mild exercise	45.3%	43.8%
25,000 ft altitude, 0 minutes of preoxygenation time, 240 minutes of exposure time, mild exercise	81.3%	80.8%
21,200 ft altitude, 0 minutes of preoxygenation time, 360 minutes of exposure time, mild exercise	17.5%	16.9%

Table 3

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