Naval Aerospace Medical
Research Laboratory

A Forehead-Mounted Measure of O_2 Saturation: The Potential for in Cockpit Hypoxia Early Detection and Warning

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NAMRL Report Number 10-26

Reviewed and Approved
09-07-2010

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The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.

This work was funded by work unit number 70805.

The study protocol was approved by the Naval Aerospace Medical Research Laboratory Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects.

Executive Summary

While hypoxia is traditionally considered a problem specific to fixed-wing platforms, symptoms of hypoxia have been documented among rotary-wing pilots and aircrew flying at altitudes as low as 8,000 ft. Effective hypoxia-related mishap prevention relies upon rapid recognition of hypoxia symptoms and expeditious execution of emergency procedures. This is particularly challenging in rotary wing aircraft, where the lack of adequate training makes reliance on hypoxia self-detection an ineffective solution. An automated warning would be preferable, but currently no military aviation platform is outfitted with a physiological monitoring system to alert pilots and aircrew of impending hypoxic episodes.

The monitoring of hemoglobin saturation (SpO_2) with a pulse oximeter is the standard of care in clinical settings and Navy aircrew hypoxia training. Limitations exist, however, for peripherally placed pulse oximeters. In response to the limitations, the commercial market has introduced pulse oximeters that are placed on the forehead, providing a more central measure of blood hemoglobin oxygen saturation. Previous studies have reported that the forehead sensors are as accurate as finger-mounted oximeters with fewer technical disadvantages. These technological advancements should enable forehead-mounted monitors to detect hypoxia more rapidly, accurately, and reliably than finger-mounted oximeters, especially for military applications.

The objectives of this experiment were to compare the sensitivity of, and agreement between, a forehead-mounted pulse oximeter and finger-mounted pulse oximeter for application in a hypoxia early warning detection system, and to determine if the forehead reflectance sensor could be mounted within an aviation helmet.

Nineteen active duty military personnel voluntarily participated in the study. After appropriate medical screening, all subjects donned an aviation flight mask connected to the Reduced Oxygen Breathing Device (ROBD), and were then instrumented with a forehead reflectance pulse oximeter, a finger pulse oximeter, a blood pressure cuff, and a skin temperature sensor. Following instrumentation, subjects breathed ambient air for 10 min through the ROBD to allow for acclimation. This was followed with one of two counterbalanced ascent profiles used to model rapid exposures to altitude. Each profile consisted of 8,000 ft and 18,000 ft altitude plateaus for 12 min and 30 min, respectively, with a recovery period of 12 min between exposures. Data were collected at 1 Hz from both sensors for the duration of the protocol. In addition, the viability of mounting the reflectance sensor in the interior of a standard flight helmet was tested. The sensor was successfully integrated inside the helmet; however, after the subject donned the helmet, there was considerable motion artifact due to pressure fluctuations.

Results from the altitude exposure protocol indicate an exceptionally strong agreement between the Forehead and Finger sensors at all ranges of desaturation. The sensitivity analyses revealed that the Forehead sensor was significantly faster when responding to rapid changes in SpO_2 than the Finger, especially during the 18,000 ft exposure. While the data may seem to suggest that the Forehead sensor is accurate and sensitive to altitude induced changes in SpO_2, major drawbacks exist for the technology utilized in the current study. Motion artifacts significantly limited the ability to collect useful data and the in-helmet portion of the study had to be discontinued due to sensor incompatibility issues. Reflectance technology remains promising, but significant improvements aimed at diminishing noise, curbing motion artifact, and improving reliability with advancements such as read-through technology, are required to reduce errant measurements before it can be considered for aviation applications.

INTRODUCTION

Hypoxia represents an insidious and sometimes deadly occupational hazard among military aviators. According to U.S. Army Safety Center statistics, from 1980 to 2005 there were 6 hypoxia-related accidents, three of which were Class A, and two resulting in fatalities with 15 soldiers lost. The reported loss to the Army was nearly $40 M when accounting for equipment and personnel injuries (1). While traditionally considered a problem specific to fixed-wing platforms, researchers have found that "rotary-wing aircrew can be repeatedly exposed to moderately high altitude (up to 18,000 feet pressure altitude) making hypoxia, and its performance effects, a real hazard" (10; p. 1). Current operations in Afghanistan often require use of rotary wing aircraft for high altitude troop insertion, placing pilots and aircrew at risk. But the risk of hypoxia may extend beyond high-altitude operations. Symptoms of hypoxia have been documented among rotary-wing pilots and aircrew flying at altitudes as low as 8,000 ft (19).

Hypoxia-related mishap prevention relies on the ability of pilots and aircrew to recognize the early symptoms of hypoxia and to initiate emergency procedures (14). This is particularly challenging in rotary wing aircraft as annual and quadrennial physiology training does not typically require hypoxia exposure and procedures training. This is due in part to traditional rotary wing mission profiles, performance ceilings of aircraft, and lack of emergency equipment, such as supplemental oxygen, which is designed to facilitate aircrew recovery during, and after, a hypoxic incident. The lack of adequate training makes reliance on hypoxia self-detection an ineffective solution. An automated warning would be preferable, but currently no military aviation platform is outfitted with a physiological monitoring system to alert pilots and aircrew of impending hypoxic episodes.

The monitoring of hemoglobin saturation (SpO_2) with a pulse oximeter is the standard of care in clinical settings and is currently used for safety monitoring during U.S. Navy aircrew hypoxia training (16, 22). Pulse oximeters are most commonly placed on the finger, but under conditions such as high altitude exposure where vasoconstriction would likely occur, a peripherally placed pulse oximeter would result in delayed hypoxia detection and inaccurate readings. Furthermore, aviation mission tasks require extensive use of the hands, precluding placement of an oximeter probe on the finger. To counter the limitations involved with peripheral oximeter placement, the commercial market has introduced pulse oximeters that are placed on the forehead, providing a more central measure of blood hemoglobin oxygen saturation. Studies have reported that forehead oximeters are at least as accurate as finger-mounted oximeters under normal testing conditions, and due to their central placement, are affected less by vasoconstriction, motion artifact, and are able to respond more quickly to desaturation events (12,20) (9, 15, 24). Also, during conditions which lead to poor peripheral perfusion, forehead sensors have demonstrated greater accuracy than finger sensors (6, 15, 17). While the forehead location does not completely circumvent motion and positional challenges to data acquisition, recent investigations indicate that new artifact rejection technology programmed into forehead-mounted reflectance oximeters may be less susceptible to errant readings and noise (12, 16, 25). The advantages, along with continued technological advancements, should enable forehead-mounted monitors to detect hypoxia more rapidly, accurately, and reliably than finger- mounted oximeters, especially in aviation operational environments. The deployment of a reliable hypoxia early detection and warning system would allow aircrew to initiate countermeasures before their performance is significantly degraded, potentially saving lives and assets.

The objectives of this experiment were two-fold: 1) to compare the sensitivity of, and agreement between, a forehead-mounted pulse oximeter and finger-mounted pulse oximeter for application in a

hypoxia early warning detection system, and 2) to determine if the forehead-mounted sensor could be mounted within an aviation helmet and accurately and reliably detect hypoxia. We hypothesized that the forehead sensor would provide greater sensitivity in detecting oxygen saturation changes during hypoxia exposure when compared to the finger pulse oximeter. The second hypothesis was that the forehead reflectance oximeter would provide comparably accurate oxygen hemoglobin saturation readings when compared to the finger pulse oximeter at low-moderate altitude exposure and greater accuracy at higher altitudes.

METHOD

Subjects. Nineteen active duty military personnel (17 males and 2 females) between the ages of 21-28 (mean = 23.1 yrs, S.D. = 1.4) voluntarily participated in the study. All had a current flight physical and were medically screened according to inclusion and exclusion criteria (Appendix A). In addition, subjects were non-smoking, had lived at < 5,000 ft for the previous 3 months, and were asked to refrain from prescription medications, over-the-counter medications, supplements, and alcohol for 48 hours prior to testing. Females with a positive urine pregnancy test were excluded. The study protocol was approved by the Naval Aerospace Medical Research Laboratory Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects.

Equipment and Physiological Measures

Reduced Oxygen Breathing Device 2 (ROBD). The ROBD (Environics®) is a computerized gas-blending instrument that manipulates blood oxygenation levels by simulating transitions to altitude in a normobaric environment. The system uses thermal mass flow controllers to combine nitrogen and oxygen to produce air mixtures equivalent to altitudes from sea level to 34,000 ft (10,363 m). The gas was delivered to the subject through a corrugated aviator hose (2.1 m long; 1.9 cm diameter) and a MBU-12/P aviation oxygen breathing mask (Gentex Corp, Simpson, PA). The mask incorporates two, one-way valves that permit one-way movement of inhaled and expired gases. A correctly-sized mask was chosen for each subject to ensure a snug fit over the subject's mouth and nose according to instructions as provided in NAVAIR 13-1-6.7-3.

Datex Ohmeda 3900 P pulse oximeter. The Datex Ohmeda 3900 P is an FDA-approved two-wavelength pulsatile system that meets ISO standards. This oximeter was used to measure SpO_2 at the finger tip of the non-dominant index finger. Averaging of SpO_2 and pulse rate values was set to 3 sec. This device has been used extensively within research and medical communities.

Nonin 8000R reflectance pulse oximeter. The Nonin 8000R is a commercially available reflectance sensor from the Nonin PureLight® line which is used to measure SpO_2 at the forehead. This device was interfaced with a data collection platform via the Nonin OEM III module. Averaging of SpO_2 and pulse rate values was set to 3 sec.

FiO_2. Fraction of inspired oxygen was measured via a port in the mask hose approximately 2.54 cm from the mask/hose connection with a ML206 Gas Analyzer (ADInstruments Pty Ltd, Bella Vista, Australia). FiO_2 data were collected to verify ROBD manipulation of altitude.

Heart rate. Heart rate was measured continuously throughout the experiment via the pulse oximeters as described above for subject safety.

Blood pressure. Arterial pressure was determined non-invasively by automated brachial auscultation via the Propaq Encore 206EL (Welch Allyn, Inc., Skaneateles Falls, NY) every 3 min for the entire experiment to ensure subject safety.

Temperature. Skin temperature was measured continuously using a ML309 Thermistor Pod (ADInstruments Pty Ltd, Bella Vista, Australia). A disposable YSI Tempheart adhesive pad was used to insulate the probe from ambient room temperature. These data were collected as a crosscheck for potential peripheral vasoconstriction.

Data collection platform. All sensor-related and physiological variables were recorded on a Shuttle XPC computer (Model SA76G2) at 1 s intervals using LabVIEW v 8.2 (National Instruments Corp., Austin, TX), except blood pressure which was collected separately at 3 min intervals during rest periods between blocks of a cognitive task.

Experimental Procedures

Equipment and testing. To ensure normal hemoglobin and hematocrit levels before initiation of the protocol, a blood draw was conducted using a 21-gauge needle and a 4-ml BD Vacutainer® (Becton–Dickinson, Rutherford, NJ) blood collection tube. Three to four drops of blood were tested by the conductivity method using an i-Stat blood analyzer with E3+ cartridges (Abbot Point of Care, Inc., East Windsor, NJ). Women were excluded if pregnant as determined by QuickVue One–Step hCG (human Chorionic Gonadotropin Urine) urinalysis (Quidel Corp., San Diego, CA). All subjects completed a compliance questionnaire to limit potential confounds (Appendix B). Subjects moved to a thermoneutral room, assumed an upright position in a chair, and donned the aviation flight mask connected to the ROBD. Subjects were then instrumented with the following equipment: Nonin 8000R reflectance pulse oximeter on the forehead, Datex-Ohmeda pulse oximeter placed on the non-dominant hand index finger, an Encore blood pressure cuff placed on the opposite side of the oximeter, and a skin temperature sensor placed on the non-dominant hand. All sensor attachment sites were swabbed with 70% isopropyl alcohol pads. Excess moisture/degreaser residue was removed with a clean, dry gauze pad. The application site for the Nonin 8000R was the middle of the forehead approximately 2.54 cm above the supraorbital ridge; it was attached with the adhesive plastic housing provided by the manufacturer. If sufficient adherence could not be attained (typically due to perspiration), additional medical tape was used per manufacturer's instructions. Participants were instructed to refrain from movement as much as possible in order to minimize oximeter measurement errors. Following instrumentation, subjects breathed ambient air for 10 min through the ROBD to allow for acclimation to the system and the laboratory setting.

Hypoxia exposure. Two counterbalanced ascent profiles were used to model rapid (2-3 sec) exposures to altitude. Each profile consisted of two altitude plateaus, 8,000 ft for 12 min and 18,000 ft for 30 min.[1] Subjects were randomly assigned to one of the two altitude profiles. Profile A (Figure 1) presented the ascent to 18,000 ft first and Profile B (Figure 2) presented the ascent to 8,000 ft first. A 12 min period to record baseline physiological data preceded the first altitude exposure in both profiles.

[1] All altitude exposures are listed in feet. For the reader accustomed to meters: 8,000 ft ≈ 2348 m, 18,000 ft ≈ 5486 m.

Each plateau was followed by 12 min of recovery at sea level. The altitudes were sustained until one of the following conditions was met: 1) elapse of the planned time at altitude, 2) a finger measured SpO_2 < 50%, or 3) symptoms limitation as determined by the participant or investigator. Oxyhemoglobin saturation was collected on a 1 sec time scale (1 Hz). Successful altitude manipulation was validated using the FiO_2 data. During exposure to hypoxia, participants completed several successive 3 min blocks of SynWin, a computerized cognitive task. The cognitive task served as a distracter to ensure subjects were not focusing on the potential discomfort of being hypoxic. The cognitive component is not discussed in this report, but will be published separately.

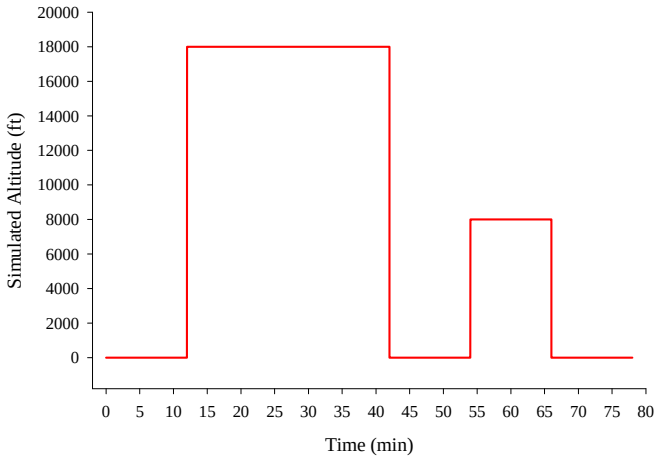

Figure 1. Flight Profile A

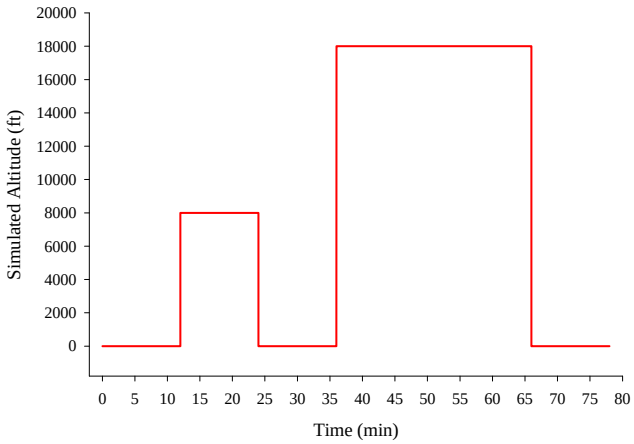

Figure 2. Flight Profile B

In Helmet Use Feasibility Testing. The viability of mounting the reflectance sensor internal to a standard HGU 68/P flight helmet was tested using a set of practical head movements and other pre-determined evaluation criteria. The most basic test was designed to determine if the sensor could be mounted into the padded section of the helmet rim while maintaining appropriate contact with the subject's forehead. The sensor was successfully integrated inside the helmet; however, after the subject donned the helmet, the sensor light emitting diode was positioned too far above the optimal application site range. To mitigate this problem, an external mounting system was constructed. The sensor was affixed to the end of a flexible metal mount, the proximal end of which was attached to the front, exterior portion of the helmet, approximately 2.5 cm above the helmet brow line. The sensor was placed on the distal end of the metal mount which curved downward placing the sensor in the correct anatomical location. The metal mount possessed sufficient pressure to ensure proper contact without allowing excessive movement of the sensor. This premise held true as long as subjects sat quietly during sensor readings. However, when subjects were allowed normal movements, unacceptable artifact due to pressure fluctuations was keenly evident. Given these results, further applied testing, which would unnecessarily expose subjects to hypoxia, was deemed inappropriate.

ANALYTIC APPROACH

As previously discussed, the in-helmet-mounted sensor portion of the study did not yield coherent, readable data, and therefore these data were not included in the analysis section. Reflectance sensor data from the hypoxia exposure portion of the study were examined for accuracy, agreement with the more widely studied finger oximeter, and sensitivity, or speed with which the forehead sensor could detect a

true desaturation event. A number of standard sensor performance criteria definitions had to be modified or omitted due to protocol limitations. The results presented in subsequent sections are described and presented within these limitations. The definitions below provide the framework for data analyses and results.

Terminology and Working Definitions

Determination of SpO_2 plateaus. SpO_2 variance due to the hypoxic ventilatory response, as well as inherent random noise of the oximeters, prevented computer automated determination of stable saturation plateaus. Severinghaus et al. (18) have discussed this problem, stating that, "…this variability defeated an attempt to mathematically define a plateau portion of the response" (p. 80). Therefore, ranges for minimum plateaus (SAT_{min}) and maximum plateaus (SAT_{max}) were determined by graphical inspection in an analogous manner to that employed by the aforementioned authors. The range of SAT_{min} was considered to start as soon as saturation readings began fluctuating around a minimum value and to end at the onset of a subsequent sustained increase in saturation readings. In other words, the range of SAT_{min} was the most stable portion of a minimum plateau during altitude exposures. SAT_{min} itself was calculated as the average O_2 saturation readings over the specified time range. SAT_{max} was calculated in a similar manner. The range of SAT_{max} was taken to be the most stable portion of a maximum plateau during recovery from altitude exposure.

Accuracy. When testing the accuracy of pulse oximeters, arterial blood gas analysis (ABG) is typically considered the "gold standard" for determination of hemoglobin oxygen saturation. Bias (offset of the data from the true value) and precision (size of the data cloud) can then be calculated and combined into one measure, A_{rms} (accuracy root mean square) giving an overall indication of accuracy. However, it is unclear how, in a rapid hypoxia exposure study, one would "match" the radial artery sample to forehead SpO_2. As discussed by previous researchers (5), "during a rapid desaturation study, not only are low saturation levels required but stable plateaus must also be induced. In effect, the body is constantly at odds with the goals of a desaturation study" (p. S86). The authors provide some of the test conditions that must be controlled to limit error including: delay time in the systemic arterial blood supply, creation of saturation plateaus, reduction of interfering substances, and physiological conditions that increase the noise to signal ratio.

In light of the risks/discomfort posed to subjects, the near impossibility of simultaneously controlling the above mentioned variables and, doubts concerning the accepted methodology of comparing SpO_2 values to ABG reference values at single points in time, a clinically acceptable measure of oxygen saturation was employed using relatively stable saturation plateaus. Therefore, the Forehead sensor was compared to the Finger sensor to determine accuracy during saturation minimums and maximums ($SAT_{min/max}$). Accuracy was then calculated as accuracy root mean square (A_{rms}), given by $A_{rms} = \sqrt{bias^2 + SD^2}$, where bias = SpO_2 – SaO_2 and SD is the standard deviation of the bias. Finger SpO_2 was substituted for SaO_2 in the equation for bias, and finger/forehead SpO_2 values were given by $SAT_{min/max}$ values, hence the expressions for bias used here were SAT_{max} (Forehead) – SAT_{max} (Finger) and SAT_{min}(Forehead) - SAT_{min}(Finger). SD was the standard deviation of these differences. Although the word *accuracy* has been used to describe the A_{rms} results, it is used here as a way of summarizing sensor performance in more readily understandable terms than the more in depth analysis of agreement discussed in the next section.

Agreement. In the current study, agreement was defined as the degree to which the Forehead concurred with the clinically accepted standard of the Finger during dynamic changes in blood oxygen saturation. Three analytic approaches were utilized to cross-validate the agreement between Finger and Forehead sensors. To quantify agreement and sensitivity, a 2 (altitude: 8,000 and 18,000 ft, within subjects) × 2 (sensor: Forehead, Finger, within subjects) × 2 (Profile: A,B, between subjects) mixed model was constructed. Using this model, a series of Repeated Measures Analysis of Variance (ANOVAs) was conducted for each dependent variable. Significant omnibus effects were followed by post-hoc analyses using Fisher's Least Significant Difference (LSD) method. The alpha level was set at .05. All ANOVAs were carried out in a similar manner; therefore, subsequent descriptions will be abbreviated. Statistical analyses were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL).

Specific to agreement, ANOVAs were performed to test for significant differences between sensor mean readings during baseline/recovery stages (i.e., SAT_{max}) and altitude exposures (i.e., SAT_{min}). Linear regressions were carried out to assess correlation of sensor readings across the 8,000 and 18,000 ft altitude exposures to provide a visual representation of sensor relations. Because the correlation coefficient ($\mathbf{r}^2$) does not provide information regarding bias and spread of bias values (SD), correlational analyses were followed up by Bland-Altmann analyses of sensor SAT_{min} values.

Sensitivity. The rate at which a sensor detects a true desaturation event (3). The particular outcome measures used to determine sensitivity within the 2 X 2 X 2 mixed model are defined below.

Time to Change from Baseline (TΔBL). This measure consisted of determining the time required after the beginning of hypoxia exposure for oximeters to fall substantially from baseline readings. A substantial fall, or change from baseline (ΔBL), was defined as: ΔBL = baseline – (3 × SD of baseline). The term *baseline* here refers to average sensor readings across stable maximum plateaus (SAT_{max}) as well as true baseline – the 12 minute period prior to altitude exposures common to both profiles. An upper limit value of 3×SD was chosen to ensure ΔBL fell outside the noise range of the sensors but close to the onset of desaturation events. Time to change from baseline (TΔBL) was calculated with a computer algorithm that identified the time at which ΔBL occurred and then subtracted the start time (as determined by FiO_2 readings) of the hypoxia exposure. This portion of the analysis was performed in Excel 2003. In the rare event that SpO_2 spikes made algorithmic calculation impractical, determination of ΔBL was accomplished through graphical inspection.

T94 (8,000 ft). Because subjects' SpO_2 rarely fell below 90% during the 8,000 ft exposure, the time required for the sensors to reach 94% SpO_2 (T94) was compared. This is a commonly used clinical alarm threshold for low SpO_2.

T90 (18,000 ft). For the 18,000 ft exposure, a comparison of the time required for the sensors to reach 90% SpO_2 (T90) was made. This value represents a common testing limit employed in sensor studies to establish sensitivity.

Maximum Desaturation Rate (MDR) and Time to Maximum Desaturation Rate (TMDR). A method of characterizing sensor responsiveness was developed in which responsiveness was defined as the time required to reach the maximum rate of change of sensor readings during desaturation events. During previous work in our lab it was observed that sudden exposures to low oxygen concentration gas

mixtures (8.0 – 15.4%) produce asymmetric sigmoidal hemoglobin saturation curves. A five-parameter sigmoid (5PS) function with the ability to accommodate the resulting asymmetry was used to model oximeter readings versus time. In addition to providing another means of characterizing desaturation response curves (i.e., sensor sensitivity), this was undertaken to obtain information regarding the feasibility of slope detection during real-time SpO_2 monitoring as a method for early detection of hypoxic events. Plotting and curve fitting were performed with SigmaPlot 10 (Systat Software, Inc., 2006). The 5PS equation is:

$$f(t) = y_0 + a / (1 + \exp(-(t-t_0)/b))^{\wedge}c ,$$

(t = independent variable, t_0 = inflection point, y_0 = bottom asymptote,
a = range of dependent variable, b = slope factor, and c = asymmetry factor)

Maximum desaturation rate (MDR) was the maximum slope attained by the 5PS curve fitted to the data. MDR was calculated to qualify the rate at which the sensors are able to detect a true desaturation event. Time to maximum desaturation rate (TMDR) was the time at which this maximum slope occurred minus the start time of the altitude stage (as determined by FiO_2), calculated to quantify the sensitivity of each sensor to the beginning of a true desaturation event. In order to attain the best fit for the initial part of the desaturation curve, the 5PS model was fitted to data from stable baseline/recovery to approximately the beginning of significant ventilatory compensation, as evidenced by transient spikes or plateaus in O_2 saturation readings. Model parameters calculated in SigmaPlot were used in MathCad 14.0 (PTC, 2007) to determine MDR and TMDR. TMDR was found by solving $f''(t,t_0,a,b,c,y_0) = 0$ for time (t). MDR was calculated by using TMDR in the equation for the first derivative, i.e., $f'(TMDR,t_0,a,b,c,y_0) = MDR$.

RESULTS AND DISCUSSION

The primary purpose of this study was to assess and characterize the accuracy and sensitivity of a forehead-mounted reflectance oximeter compared to a finger pulse oximeter during exposure to, and recovery from, varying levels of hypoxia. The ultimate goal was to determine if reflectance technology would be well-suited for use as an in-cockpit hypoxia early warning detection system. Analytic results and corresponding discussion is provided by benchmark measure in the following sub-sections.

Accuracy

Table I summarizes the accuracy of the Forehead sensor with the Finger taken as the accepted standard. A_{rms} values fell within the manufacturer stated limits of accuracy (± 3% in the 70-100% saturation range) during all flight profile stages, except for the 18,000 ft exposure during which average SpO_2 fell below 70%. The A_{rms} value of 3.09% during the 18,000 ft exposure was just outside the accepted 3% cutoff, but within conventional measurement error tolerances. Skin temperature data were analyzed to determine any potential impact of vasoconstriction on sensor performance. Results indicated no significant changes in skin temperature across time; therefore, these data were not included in subsequent analyses. Inferring accuracy from pulse oximetry data poses several challenges, the largest, and most applicable for aeromedical settings, is the lack of experimentally derived reference values for low oxygen concentration levels. Manufacturers currently use values obtained from studies utilizing

healthy, generally young subjects breathing hypoxic gas mixtures in a controlled laboratory setting. Because subject safety was a concern in these experiments, the lowest measured SaO_2 values were around 75% (18). Oximeter manufacturers and research data corroborate a ± 2% accuracy of pulse oximeter measurements compared to actual hemoglobin saturation measures, if the desaturation range is limited to 70-100%. When values fall below approximately 70%, finger pulse oximeters generally use a programmed extrapolation technique based on known values to measure hemoglobin saturation in the lower ranges. Even with these inherent technological limitations, useful statements can be made regarding the accuracy of the forehead reflectance oximeter, because any existing measurement bias at lower saturations would be systematic, and statistically controllable. The Forehead sensor proved to be as accurate as the Finger, with a small deviation at the lowest saturation reading. This is consistent with the pulse oximeter literature which describes increasing measurement error at low saturations, with some reports indicating that values below 80% are subject to significant error (24). One might expect to find a significant or fairly large bias between the two sensors with increasing desaturation. Peripheral measures have been reported as more susceptible to vasoconstriction, and therefore, subject to greater measurement error; although this was not evident in the current study. Moreover, peripherally placed sensors are prone to motion artifact which often results in falsely low pulse oximeter readings. The accuracy data in the current study did not reveal a large bias between sensor readings at any saturation level, and no sustained false low readings were observed. Movement during testing was limited to the greatest extent possible, but some movement naturally occurred. This level of movement did not negatively influence the Finger or Forehead data.

Table I
Forehead: Bias and Precision

	Bias	Precision	A_{rms}
Baseline	-0.08	1.77	1.77
8K	-1.19	2.14	2.44
8K REC	-0.01	1.49	1.49
18K	0.61	3.03	3.09
18K REC	0.07	1.63	1.64

A_{rms} = accuracy root mean square; Bias = mean; Precision = SD.
$A_{rms} \leq \pm 3\%$ (manufacturer's accuracy for 70-100% SpO_2 range).

Agreement

SAT_{max}. The omnibus test between sensors at SAT_{max} was not significant (Table II). However, a closer examination of sensor standard deviations during baseline readings indicated that the Forehead sensor was prone to larger variance during conditions of normal hemoglobin saturation. Though not statistically significant, the implication of greater variance at baseline, or "noisy" baseline readings, (those with a larger standard deviation) could make it difficult to discern a true desaturation trend. If baseline readings are unstable, the exact point of departure from the actual baseline reading would be obscured by random reading error. Results indicating larger standard deviations when compared to the finger are in contrast with the literature suggesting that reflectance oximeters, especially when the sensor

is centrally placed, are less prone to physiological and external noise and motion artifact. The inherent stability of the forehead sensor also appears to hold true in more robust motion environments. Yamaya et al., (25) reported that a forehead-mounted reflectance oximeter was more accurate than a finger-mounted pulse oximeter during bouts of intense exercise. The potential influence of differential variance at baseline requires further exploration and is not limited to the agreement analysis, but may negatively affect the ability to discern sensor sensitivity as discussed in the following sub-section.

Table II
SAT_{max} ANOVA Results

	Mean %	SD
Baseline		
F	98.06	0.98
FH	97.98	1.78
8K REC		
F	97.74	1.20
FH	97.73	1.34
18K REC		
F	97.24	1.15
FH	97.31	1.61

Note. F = finger; FH = forehead; REC = recovery; Omnibus *f* test was ns, F (1,15) = .007, p = .935; therefore post-hoc comparisons were not made. (n = 17)

SAT_{min}. An initial ANOVA for SAT_{min} at 8,000 ft revealed a statistically significant difference between the Forehead and Finger sensors (Table III). Specifically, the Forehead sensor was negatively biased in reference to the Finger sensor, with a lower mean SpO_2 percentage. However, visual examination of the data suggested that the difference was attributable to 3 subjects with extremely low Forehead sensor readings at baseline. After a review of the subject files the cause of the low values was deemed to be sensor placement. The readings were outside of a three standard deviation range of the mean, thus they were classified as outliers, excluded, and the data were re-analyzed. When the outliers were excluded from the analysis, there were no significant differences between Forehead and Finger sensors at 8,000 ft [F (1, 13) = 1.85, p = .197]. An ANOVA for SAT_{min} at 18,000 ft was also not significant (Table III), suggesting strong agreement between sensors across altitudes. Agreement at *SAT_{min}* is vitally important to ensure operational validity of the Forehead sensor. If utilized in a hypoxia early warning system, a large negative bias could result in false alarms and a large positive bias would reflect insensitivity to changes in blood oxygen saturation and translate into missed or delayed alarms. Minimally, strong agreement with a clinical standard, such as the Finger, is necessary before the technology could be considered for use as an aircrew hypoxia detection device.

Correlation during altitude exposures. Forehead and Finger readings were highly correlated during altitude exposures (8,000 ft: R_{adj}^2 = .93, p < .001; 18,000 ft: R_{adj}^2 = .98, p < .001). Figure 3 displays Forehead versus Finger SpO_2 readings along with the regression line and line of agreement for the 18,000 ft exposure. Figure 3, in conjunction with Figure 4 which displays average sensor readings for Profile A, clearly depicts sensor responses during an acute hypoxic event. Starting from baseline readings in the top-right quadrant, the observed data points fall sharply from the line of agreement to the regression line, an effect which can be attributed to a faster response of the Forehead sensor to changes in saturation. As the altitude exposure proceeds, a tight fit to the regression line from approximately 96-

80% saturation reflects the similarity of sensor response during the initial phase of rapid desaturation. The regression line and the majority of the data points lie beneath the line of identity from approximately 96% to 75% saturation. This indicates that the centrally placed Forehead sensor is faster than the Finger sensor through this phase of hypoxic exposure. Scatter about the regression line increases with increasing levels of hypoxia due to the combined effects of lag between sensor responses to SpO_2 spikes, significant reading oscillations caused by hyperventilation, and random noise including possible measurement error due to lower perfusion. Visual inspection of the left-bottom quadrant of Figure 3 reveals a data cluster that corresponds to the saturation range at the end of the exposure around which SAT_{min} was centered. This dense clustering (circled for emphasis) provides visual confirmation of the strong agreement between Finger and Forehead sensors at SAT_{min} previously demonstrated by the ANOVAs.

Table III
SAT_{min} ANOVA Results

	Mean %	SD	*F*	*p*
8K (All Ss)				
F	92.23	2.07	5.41	0.03
FH	91.05*	3.31		
8K (No Outliers)				
F	92.21	2.19	1.85	0.20
FH	91.50	3.41		
18K (All Ss)				
F	66.62	4.94	1.59	0.23
FH	67.23	4.63		

Note. *Forehead sig. different from Finger, p<.05; F = finger; FH = forehead; 8K All Ss (n = 18); 8K No Outliers (n = 15) 18K All Ss (n = 17)

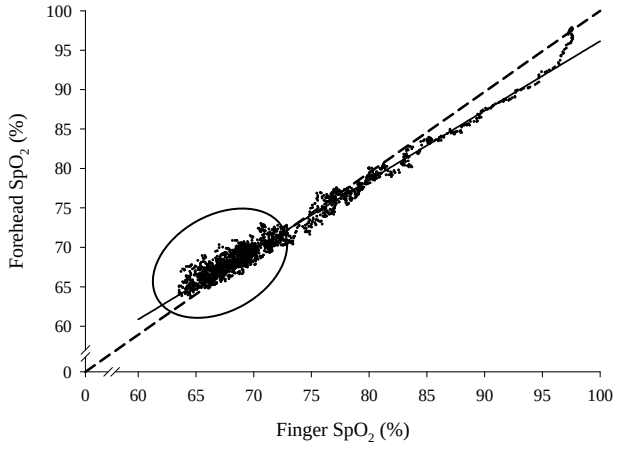

Figure 3. Forehead SpO_2 plotted against Finger SpO_2 with linear regression line (solid) and line of agreement (dashed) for the 30 minute exposure at 18,000 ft. Strong agreement between Finger and Forehead sensors at SAT_{min} is evident in the circled portion of the lower left quadrant.

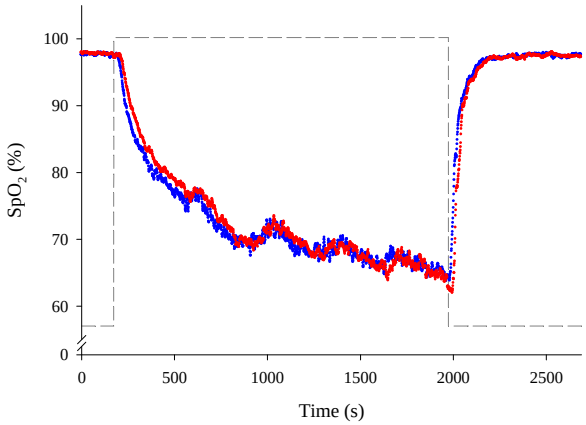

Figure 4. Average SpO_2 for the 18,000 ft exposure and recovery for the Forehead (blue) and Finger (red) across time. The lines are nearly identical, reinforcing the strength of agreement between the two sensors. Close inspection of the Forehead (blue) line reveals an advantage over the Finger in terms of speed to detect changes in SpO_2, an effect further explored in the Sensitivity section of the results. The gray dotted line represents the altitude up to 18,000 ft.

Finally, a Bland-Altmann analysis was conducted to determine precision and bias of the Forehead sensor in direct relation to the finger at SAT_{min}. In Figures 5 and 6, the mean line of the two sensors is presented with an upper and lower bound of ± 2 SD. Observed values for the Forehead are plotted in each figure. For the 8,000 ft exposure (Figure 5), a narrow range of scatter of +.86 and -3.4% respectively, was observed. For 18,000 ft, a wider range was observed (Figure 6), with an upper and lower limit of +6.7 and -5.4%. The small standard deviation and relative balance of scatter above and below the mean suggests that the Forehead is precise and unbiased at the 8,000 ft exposure. These findings corroborate the agreement findings from the ANOVA and correlational analyses. Visual inspection of Figure 6 may lead one to infer a significant positive bias or lack of precision in Forehead sensor readings at 18,000 ft. Analysis uncovered only a slight, statistically insignificant, positive bias for the Forehead. The wide range in point scatter may still raise concerns about the level of agreement of the Forehead sensor when compared to the clinical standard. There are several practical explanations that may account for the variation, most of which have been previously elucidated. The two factors accounting for the majority of the variability, and most germane to this investigation, are distinct differences in the nature and impact of motion artifact between sensor types and lack of sensor calibration outside of 70-100% SpO_2 range. For the former, normal activity elicits greater use of the hands compared to the head resulting in more error variance in finger readings. These results were anticipated even with methodological controls. The latter is not an issue in clinical settings where intervention often occurs if saturations fall below 90%, but the lack of calibration at lower saturations poses a distinct problem for operational use. For instance, in aviation where SaO_2 values can drop precipitously and where intervention is self-administered, use of a technology with unknown parameters can be deadly. In sum, the forehead reflectance sensor proved precise and unbiased in regard to the finger sensor, but additional validation at less than 70% SpO_2 is required.

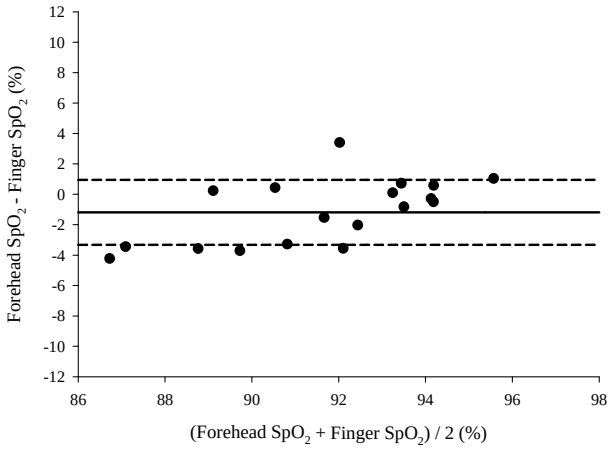

Figure 5. Bland-Altmann analysis for the 8,000 ft exposure comparing Forehead and Finger sensors, with observed values (dots) plotted around the mean (solid horizontal line) and upper and lower lines of agreement (dashed lines, M +/- 2 SD). A narrow range of scatter over a clincally acceptable range with upper and lower limits of agreement of +.86 and -3.4% respectively, was observed, suggesting excellent agreement between sensors.

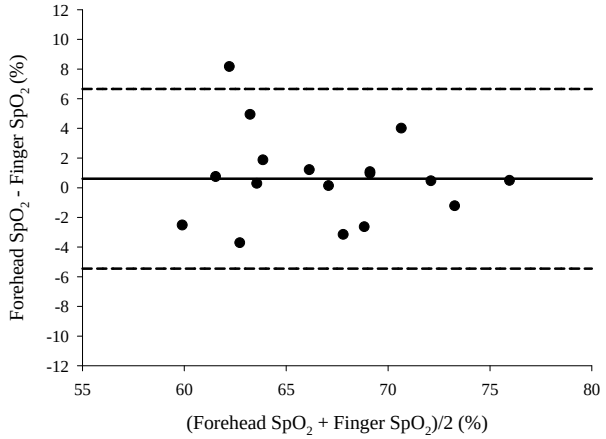

Figure 6. Bland-Altmann analysis for the 18,000 ft exposure comparing Forehead and Finger sensors, with observed values (dots) plotted around the mean (solid horizontal line) and upper and lower lines of agreement (dashed lines, M +/- 2 SD). Though a wider range of scatter was observed compared to the 8,000 ft exposure, readings remained within acceptable limits of agreement,with upper and lower limits of agreement of approximately +6.7 and -5.4%.

Agreement Summary. There was virtually no difference between sensors at SAT_{max}, indicating excellent agreement between sensors during periods of high saturation (baseline and recovery). The comparison of readings at SAT_{min} produced a similar result with strong agreement between sensors at both altitudes. The nature of this agreement was supported by a strong correlation between sensor readings, coupled with precision and lack of significant bias at the nadirs of saturation. Figure 7 provides a graphical summary of sensor mean values for SAT_{min} and SAT_{max} at all altitude stages, indicating robust agreement.

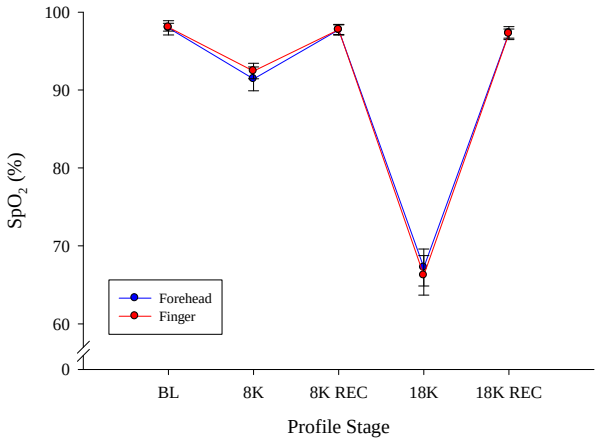

Figure 7. Visual summary of agreement between Forehead (blue) and Finger (Red) for average $SpO_{2\ readings}$ across all altitude stages. The lines track nearly identically in all five scenarios. Note: BL = baseline; 8K = 8,000 ft exposure; 8K REC = Recovery from 8,000 ft exposure; 18K = 18,000 ft exposure; 18K REC = Recovery from 18,000 ft exposure.

Sensitivity

8,000 ft Exposure. There were no significant differences observed at 8,000 ft for either TΔBL or T94 (Table IV). Because low signal-to-noise ratio prevented curve fitting, TMDR was calculated using averaged subject data; therefore significance was not established. These results are presented graphically in Figure 8.

18,000 ft Exposure. No significant difference was observed for MDR at 18,000 ft. between Finger (M=-.210, SD = .07) and Forehead (M=-.218, SD = .084). Results for the three time-dependent sensitivity measures indicate that the Forehead sensor detected a true desaturation event significantly faster than the Finger sensor during the 18,000 ft exposure (Table IV and Figure 9). The true magnitude of this increased detection speed is illustrated by the medium to large effect sizes for each analysis (η_p^2: TΔBL = .52, TMDR = .58, T90 = .69), suggesting that the sensitivity differences between the Forehead and Finger sensors at 18,000 ft are both statistically and operationally significant.

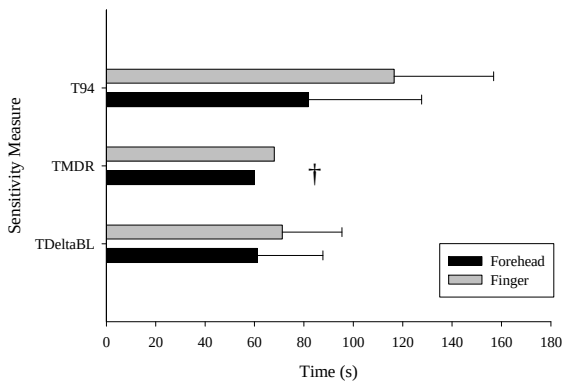

Figure 8. ANOVA results for the three time-dependent sensitivity outcome variables during the 8,000 ft exposure. No significant differences were seen. Bars represent Standard Deviation (SD). Note: T94 = time required for sensors to reach 94% SpO_2; TMDR = Time to Maximum Desaturation rate; TΔBL = Time to Change from Baseline. † = No SD calculated, see Table IV TMDR.

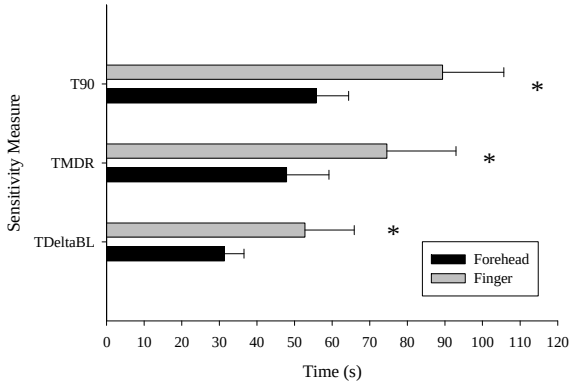

Figure 9. ANOVA results for the three time-dependent sensitivity outcome variables during the 18,000 ft exposure. Bars represent Standard Deviation (SD). Significant differences (*) were present for all three comparisons such that the Forehead sensor was faster in responding to an acute desaturation rate. Note: T90 = time required for sensors to reach 90% SpO_2; TMDR = Time to Maximum Desaturation rate; TΔBL = Time to Change from Baseline.

Table IV
TΔBL, TMDR, T94, and T90 ANOVA Results

		Mean (s)	SD (s)	*F*	*p*
TΔBL					
	F-8K	71.22	51.53	1.34	0.26
	FH-8K	61.22	52.22		
	F-18K	52.78	25.92	18.71	0.0005
	FH-18K	31.39	12.65		
TMDR					
	F-8K	68.00	n/a		
	FH-8K	60.00	n/a		
	F-18K	74.56	36.12	21.86	0.0003
	FH-18K	47.89	22.42		
T94					
	F-8K	116.50	61.98	2.72	0.12
	FH-8K	81.88	76.07		
T90					
	F-18K	89.39	31.09	36.96	0.00001
	FH-18K	55.78	17.17		

Note. F = finger; FH = forehead; TΔBL = Time to Change from Baseline; TMDR = Time to Maximum Desaturation Rate; T94 = time required for sensors to reach 94% SpO_2 ; T90 = time required for sensors to reach 90% SpO_2 ; (n = 17).

The strong agreement for MDR (Mean Difference = -.008), along with inspection of individual and subject average data plots, provide a clear indication of the similarity between sensor desaturation response curves but with a significant time lag in the Finger response as indicated by the time-dependent

measures. The 5PS calculation and examination of MDR underscores and elaborates upon the point made by MacLeod and colleagues (14), who noted "When compared to [forehead] oximeters, the desaturation response curves of the finger oximeters were similar both in duration and the minimum displayed SpO_2 value but demonstrated a temporal 'right shift' of the curve" (p. 60). The similarity of sensor responses and temporal lag of the Finger sensor is represented by plots of SpO_2 readings for two typical subjects in Figures 10 and 11. Similar findings were reported by Sugino et al., (20) when comparing time to lowest reading, time of recovery, and lag time between a forehead probe and finger oximeter. Under conditions of simulated reduced peripheral perfusion, the forehead sensor detected decreasing levels of SpO_2 significantly faster than the Finger and the time to full recovery was significantly longer for the Finger. Sugino and colleagues concluded that forehead placement of the sensor improved patient monitoring and supplied more timely information compared to conventional finger pulse oximetry. In high-risk settings such as the emergency room and surgical suite, the ability to obtain and act on accurate and relevant information is important. The cockpit of an aircraft is no exception. A physiological monitoring system must possess the ability to quickly sense a change in aircrew status and provide appropriate feedback for pilot decision-making. The sensitivity of a particular sensor technology must be considered for future testing in operational contexts. Sensitivity will be a key factor in establishing the lowest SpO_2 cutoff value for warning alarms and avoidance of repeated false alarms. Too many false alarms would eventually train the aircrew to ignore the warning, rendering the system all but useless. Conversely, insufficient sensitivity may cost the military valuable lives and assets. Future development in sensor sensitivity should aim to decrease lag between real-time SpO_2 values and detection, and increase oxygen sensing capability.

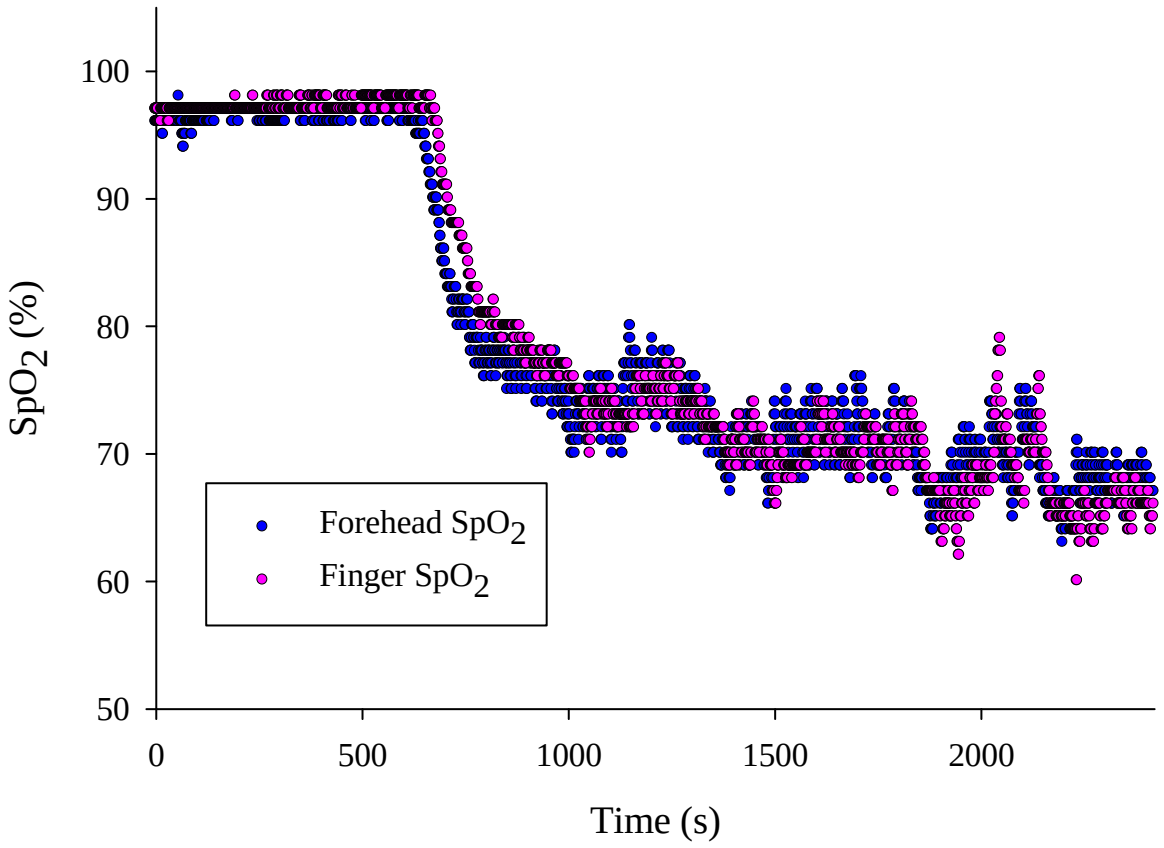

Figure 10. Average SpO_2 for the 18,000 ft exposure for the Forehead (blue) and Finger (red) across time for Subject 18. Temporal lag of the Finger sensor compared to the Forehead sensor is evident during acute desaturation from approximately 500 to 1000 seconds – note that the Forehead line is visibly farther left than the Finger line.

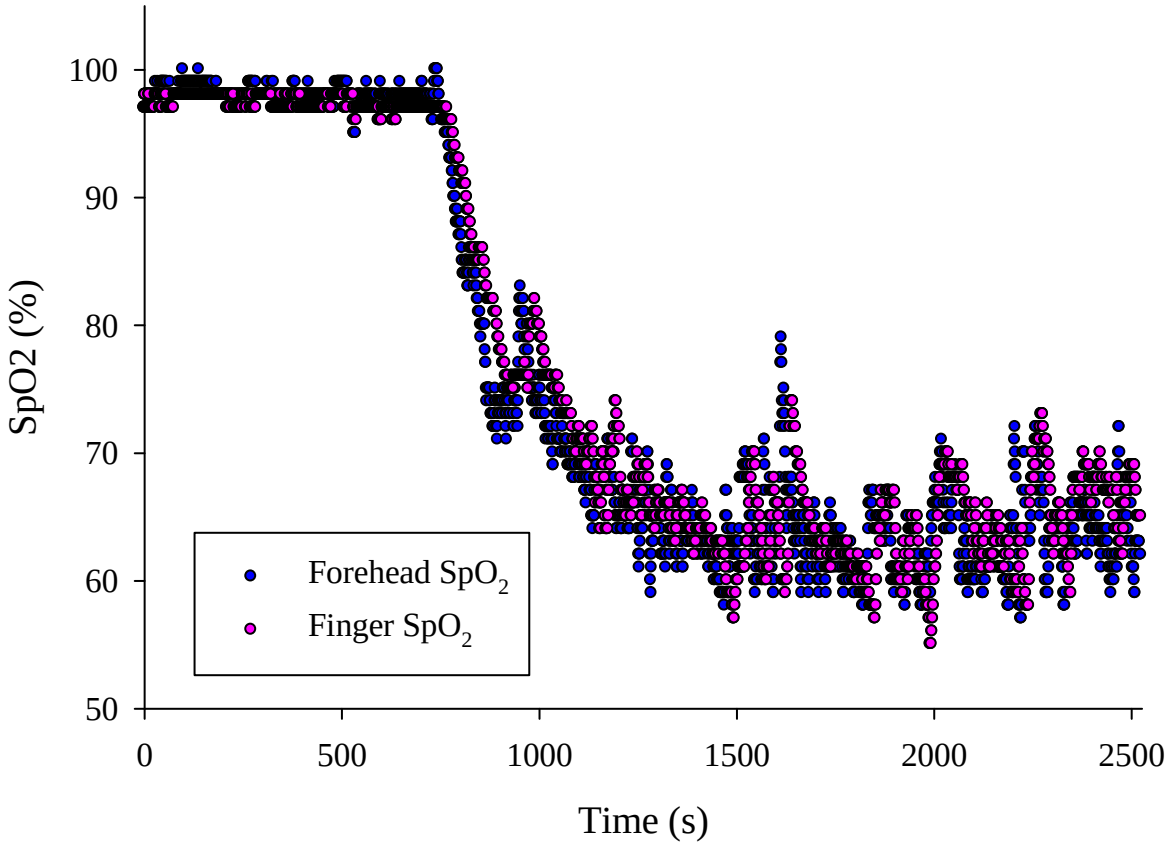

Figure 11. Average SpO_2 for the 18,000 ft exposure for the Forehead (blue) and Finger (red) across time for Subject 12. Temporal lag of the Finger sensor compared to the Forehead sensor is evident during acute desaturation from approximately 500 to 1000 seconds – note that the Forehead line is visibly farther left than the Finger line.

Sensitivity Summary. There is virtually no difference between sensors at 8,000 ft where both sensors displayed a similar ability to successfully detect the more subtle initiation of desaturation. Results for the more severe O_2 desaturation at 18,000 ft indicate that the Forehead sensor detected true desaturation significantly faster than the Finger. These findings are in agreement with the literature comparing forehead and finger oximetry. Severinghaus et al. (18) noted response times of 10–20 s for the ear and 24–35 s for finger oximeters. Similarly, Trivedi et al. (21) reported that the ear and forehead sensors performed consistently faster than the finger sensors with mean desaturation times of 38 s, 42 s and 57 s, respectively. Authors reporting on sensitivity under conditions of vasoconstriction also found that the forehead sensor was significantly faster than the finger, detecting hypoxia 1-2 min sooner (6, 15). Data from the current study suggests that forehead reflectance technology is more sensitive to sudden drops in SpO_2 than traditional pulse oximetry, a potential advantage in operational applications.

Limitations

Several limitations were encountered during the execution of this study. The most significant limitation was the considerable motion artifact resulting from subject head movements. Sudden head movement or furrowing of the forehead resulted in dropped measurements; therefore extreme restriction of subject movement during the data collection phase was required. This type of safeguard made

possible the examination of the sensor technology and provided useful information toward recommendations for future work and operational integration. Similarly, the extreme sensitivity to pressure changes with the reflectance sensor caused a significant number of dropped values and made meaningful data collection almost impossible. These results made apparent the incompatibility of this generation of sensor with the aviation helmet. Lastly, the complexity of the non-linear physiologic data collected under more severe hypoxic conditions required a unique analytic approach. Traditional clinical instrumentation analyses, such as Bland-Altmann, had to be supplemented with adaptive non-linear modeling to allow for identification and quantification of meaningful outcomes. This multi-faceted approach was highly successful, but creating customized statistical solutions requires highly specialized skill and a significant investment of time.

Besides the limitations listed above, the results from the current study confirm the importance of precision when placing the reflectance probe on the site. Several studies have reported a significant decrease in accuracy and an increase in erroneous readings when probes are located over areas where a disproportionately high volume of venous blood exists, or where "contamination" can occur such as skin areas with differential pigmentation or where less arterial vasculature is located (8, 12, 13). In addition, changes in the level of tension applied to the probe can have a direct affect on reading accuracy and agreement. When the probe is placed on the skin, only light pressure is applied through the adhesive properties of the sensor pad. Agashe, Coakley, and Mannheimer (2) and Dassel et al., (11) found a significant reduction in reading errors and increases in accuracy when applying external pressures ranging from 20-120 mmHg. The increased pressure appears to decrease venous pooling, which would in turn decrease venous pulsations at the site. Under pressure, the sensor readings are a more direct reflection of arterial blood saturation not corrupted by the less oxygenated venous blood, and the sensor is able to read the pulsatile signal more clearly. The attempt to place a sensor in the rim of an aviation helmet validates the difficulty in assuring accurate and consistent placement and pressure. Subject movement while wearing the helmet caused the signal to be dropped or fluctuate wildly. Helmet fit and movement of the helmet during subject motion tended to change the resulting pressure on the probe. Incorporating seamless solutions to these technical challenges into the design and operation of the reflectance sensor would be critically important before conducting further testing for applied aviation settings.

Future Studies

Early generation reflectance oximeter signal extraction methods and associated algorithms do not possess artifact rejection capability and therefore may not produce reliable data outside a controlled laboratory setting. Future studies should include new technology possessing advances such as, improved signal processing, motion-tolerant algorithms, data averaging and data holding techniques, and read-through motion capability designed to factor out extraneous signals not directly associated with SpO_2 readings. Current reflectance oximetry has proven to have advantages over pulse oximetry under controlled conditions. Incorporation of the aforementioned enhancements should improve the validity and reliability of data and allow the technology to be tested under more active, rigorous settings. Although still in the research and developmental stage, smart fabrics and interactive textiles are purported to be capable of sensing, actuating, storing, and communicating an individual's physiological state. If industry is successful in fielding this type of fibrous structure, it could represent a new avenue for noninvasive hypoxia monitoring.

Conclusion

The data suggest that the agreement between Forehead and Finger sensors is strong and that the Forehead sensor is dramatically more sensitive to altitude induced changes in SpO_2. Although the Forehead oximeter is both sensitive to a decline in O_2 hemoglobin saturation and accurate when compared to the clinical standard, significant modification is required to eliminate dropped measurements due to motion before it can be considered for aviation applications. Next generation reflectance sensors may provide motion-resistant technology to offset the aforementioned limitations.

Acknowledgements: The authors would like to express their sincere gratitude to Jeffrey B. Phillips, Ph.D., Fredrick Patterson, Ph.D., and Renee A. Lojewski, M.A. for their technical advice and assistance during the preparation of this report.
Sponsor: U.S. Army Aeromedical Research Laboratory, FT Rucker

References

1. Army Safety Center (2010). Risk Management Information System. Retrieved from https://safety.army.mil/statisticsdata/RMIS/tabid/374/Default.aspx
2. Agashe GS, Coakley J, Mannheimer, PD. Forehead pulse oximetry: Headband use helps alleviate false low readings likely related to venous pulsation artifact. Anesthes 2006, 105(6):1111-1116.
3. Barker, SJ. Standardization of the testing of pulse oximeter performance. Anesthesiology 2002; 94(S1):S17-S20.
4. Berkenbosch JW, Tobias JD. Comparison of a new forehead pulse oximeter sensor with a conventional digit sensor in pediatric patients. Respir Care. 2006, 51(7):726-731.
5. Batchelder PB, Raley DM. Maximizing the laboratory setting for testing devices and understanding statistical output in pulse oximetry. Anesth Analg 2007; 105(6):S85-S94.
6. Branson RD, Mannheimer PD. Forehead oximetry in critically ill patients: the case for a new monitoring site. Respir Care Clin N Am. 2004 Sep; 10(3):359-67, vi-vii.
7. Casati A, Squicciarini G, Baciarello M, Putzu M, Salvadori A, Fanelli G. Forehead reflectance oximetry: A Clinical comparison with conventional digit sensors during laparotomic and laparoscopic abdominal surgery. Journal of Clinical Monitoring and Computing. 2007 Oct; 21(5):271-6.
8. Cheng EY, Hopwood MB, Kay J. Forehead pulse oximetry compared with finger pulse oximetry and arterial blood gas measurement. J Clin Monit. 1988 Jul; 4(3):223-6.
9. Choi SJ, Ahn HJ, Yang MK, Kim CS, Sim WS, Kim JA, Kand JG, Kim JK, Kang JY. Comparison of desaturation and resaturation response times between transmission and reflectance pulse oximeters. Acta Anaesthesiol Scan. 2010 Feb; 54(2):212-7.
10. Curry I., Roller R.A. A physiological and human factors evaluation of a novel personal helicopter oxygen delivery system. Fort Rucker, AL: U.S. Army Aeromedical Research Laboratory 2007. USAARL Report No. 2007-14.
11. Dassel ACM, Graaff R, Sikkema M, Meijer A, Zijlstra WG, Aarnoudse JG. Reflectance pulse oximetry at the forehead improves by pressure on the probe. J of Clin Mon and Comput. 1995; 11(4):237-244.
12. Dresher R. Wearable forehead pulse oximetry: Minimization of motion and pressure artifacts. Unpublished manuscript 2006. Worcester Polytechnic Institute, MA.
13. Feiner JR, Severinghaus JW, Bickler PE. Dark skin decreases the accuracy of pulse oximeters at low oxygen saturation: The Effects of oximeter probe type and gender. Anesthes & Anal. 2007; 105(65):S18-23.
14. Fitzpatrick M. What is he doing? Approach: The Naval Safety Center's Aviation Magazine 2005; 50:20-21.
15. MacLeod DB, Cortinez LI, Cameron D, Wright DR, White WD, Moretti EW, Radulescu LR, Somma J. The desaturation response time of finger pulse oximeters during mild hypothermia. Anaesthsia. 2005; 60(1):65-71.
16. Nuhr M, Hoerauf K, Joldzo A, Frickey N, Barker R, Gorove L, et al. Forehead SpO_2 monitoring compared to finger SpO_2 recording in emergency transport. Anesthesia 2004, 59:390-93.
17. Schallom L, Sona C, McSweeney M, Mazuski J. Comparison of forehead and digit oximetry in surgical/trauma patients at risk for decreased peripheral perfusion. Heart Lung. 2007 May-Jun; 36(3):188-94.
18. Severinghaus JW, Naifeh KH, Koh SO. Errors in 14 pulse oximeters during profound hypoxia. J of Clin Mon 1989; 5:72 – 81.

19. Smith, A. (2005). Hypoxia symptoms reported during helicopter operations below 10,000 ft: A retrospective study. Aviat Space Environ Med 2005; 76:794-798.
20. Sugino S, Kanaya N, Mizuuchi M, Nakayama M, Namiki A. Forehead is as sensitive as finger pulse oximetry during general anesthesia. Can J Anaesth 2004; 51:432-6.
21. Trivedi NS, Ghouri AF, Lai E, Shah NK, Barker SJ. Pulse oximeter performance during desaturation and resaturation: a comparison of seven models. J Clin Anesth, 1997; 9:184-188.
22. Van Oostrom JH, Melker RJ. Comparative testing of pulse oximeter probes. Anesth & Anal 2004; 98, 1354-8.
23. Wagner JL, Ruskin KJ. Pulse oximetry: Basic principles and applications in aerospace medicine. Aviat Space Environ Med 2007; 78:973-978.
24. Webb RK, Ralston AC, Runciman WB. Potential errors in pulse oximetry. II. Effects of changes in saturation and signal quality. Anaesthesia. 1991 Mar; 46(3):207-12.
25. Yamaya Y, Bogaard HJ, Wagner PD, Niizeki K, Hopkins SR. Validity of pulse oximetry during maximal exercise in normoxia, hypoxia, and hyperoxia. J Appl Physiol. 2002 Jan; 92(1):162-8.

Appendix A. Confidential Medical Questionnaire

Screening Number:_____ Participant Number: ___(for office use only) Date: _____

Gender (check one): Male ☐ Female ☐

Age: _____ Height: _____ Weight: _____

Part 1- Directions: **Circle "Yes"** if you currently suffer from or have ever been diagnosed with the condition **AND** explain below the question.

Circle "No" if they don't apply.

These questions are being asked to ensure your safety in this study.

ALL ANSWERS WILL BE KEPT CONFIDENTIAL

1.	Do you currently or have you ever been diagnosed with asthma?	Yes	No
2.	Have you ever been diagnosed with heart/circulatory disease?	Yes	No
3.	Do you currently suffer from high blood pressure?	Yes	No
4.	Have you ever been diagnosed with emphysema?	Yes	No
5.	Have you ever suffered from pneumonia?	Yes	No
6.	Have you ever been diagnosed with epilepsy or seizure disorder?	Yes	No
7.	Have you used any tobacco products in the last 6 months?	Yes	No
a.	If yes, please list quantity, frequency and type of product: _____		
8.	Have you donated blood or plasma in the past 30 days?	Yes	No

9.	Do you take any prescribed medication on a regular basis?	Yes	No
a.	If yes, please list : _____		
10.	Have you taken a prescribed medication within the past 7 days?	Yes	No
a.	If yes, please list: _____		
11.	Do you take any herbal, protein, or power enhancing supplements on a regular basis?	Yes	No
a.	If yes, please list : _____		
12.	Have you taken any supplements within the past 7 days?	Yes	No
a.	If yes, please list: _____		
13.	Do you have a recent history of living at altitude? (>5,000 ft)	Yes	No
14.	Have you, in the past or at present, experience discomfort in confined spaces?	Yes	No
15.	Have you consumed any caffeine within the past 48 hours?	Yes	No
a.	If yes, how much? _____		
b.	Is this your normal amount? _____		
16.	Have you consumed any alcohol within the past 48 hours?	Yes	No
	Females:		
17.	Are you currently pregnant or lactating?	Yes	No

Part II- Directions: Answer the following questions to the best of your ability.

1.	Are you in your usual state of fitness?	Yes	No
a.	If not, please indicate the reason: _____		

1. Do you participate in resistance training exercises? Yes No

a. If yes, how many sessions per week?
_____

b. How long do your sessions last?
_____

c. At what intensity do you work during resistance training?
_____

2. Do you participate in aerobic (endurance) exercise? Yes No

a. If yes, how many times a week?
_____

b. What is the duration of your average aerobic exercise session?
_____

c. At what intensity do you work during aerobic exercise?
_____

3. Please identify any other exercise activities in which you participate on a regular basis.
_____

4. Have you been ill in the past week Yes No

a. If yes, please indicate the nature of the illness (e.g., flu, cold, etc.) _____

b. The severity of the illness (*Circle one*):

Very mild----------1----------2----------3----------4----------5----------**Very Severe**

c. Length of the illness Hours:_____ Days:_____

d. Major Symptoms: _____

e. Are you fully recovered? Yes No

5. Indicate all medication you have used in the past 24 hours.
(circle all that apply)

a. None
b. Sedatives/Tranquilizers
c. Aspirin/Tylenol/any analgesic
d. Antihistamines
e. Decongestants
f. Other (please specify)

_____

6. Do you take any over the counter medications (e.g., antacids, Benadryl, Tylenol, etc.) two (2) or more times a month? Yes No

7. How many hours did you sleep last night? _____

Was this amount sufficient? Yes No

List any other comments regarding your present physical state which might affect your performance.

Appendix B. Compliance Questionnaire

Participant Number: _____ **Date:** _____ **Screening Number:** _____

Gender: *(please check one)* **Male** ☐ **Female** ☐ **Age:** _____

1. Have you donated blood or plasma in the past 30 days? Yes No

2. Have you used tobacco products in the last 30 days? Yes No

3. Have you consumed any caffeine within the past 48 hours? Yes No

a. If yes, how much? _____

b. Is this your normal amount? Yes No

4. Have you consumed any alcohol within the past 48 hours? Yes No

5. Have you spent time at altitudes in excess of 5,000 feet within the past month? Yes No

6. Have you taken any over-the-counter medications while enrolled in the study? Yes No

a. If yes, please list: _____

7. Have you taken any prescription medication while enrolled in in the study? Yes No

a. If yes, please list: _____

8. Have you taken any herbal, protein, or power enhancing supplements while enrolled in the study? Yes No

a. If yes, please list: _____

9. Have you participated in strenuous exercise in the last 7 days? Yes No

a. If yes, please list: _____

10. Please identify any other exercise activities in which you participated in the last 7 days.

_____

Thank you for your participation!

Appendix C. The 5-Parameter Sigmoid Model

The 5-Parameter Sigmoid Model

A five-parameter sigmoid (5PS) function was used to model SpO_2 versus time. Plotting and curve fitting were performed with SigmaPlot 10 (Systat Software, Inc.), which has built-in nonlinear regression capabilities (Levenberg-Marquardt algorithm). Closely related functions, such as the five-parameter logistic function (5PL), or variations thereof, have been used to model biological data that exhibit similar characteristics, such as baroreceptor reflex curves (28), quantitative real-time polymerase chain reactions (29), and bioassay dose-response curves (26, 27). The 5PS equation is repeated here for reference:

$$f(t) = y0 + \frac{a}{(1 + e^{-(t-t0)/b})^c}. \qquad \text{(Eq. 1)}$$

t = independent variable, t0 = inflection point, y0 = bottom asymptote,
a = range of dependent variable (y0 + a = top asymptote),
b and c = curvature parameters.

Previous authors (28) have pointed out the lack of parameter interpretability of the 5PS equation in the above form and have offered reformulations consistent with their specific research aims. We have used (Eq. 1) throughout our analysis because our purpose was not to ascribe theoretical or physical significance to the 5PS curve parameters.

It was necessary to choose a suitably restricted range of data from the overall altitude stage to ensure an appropriate curve fit for the initial phase of hemoglobin desaturation during which MDR and TMDR occur. Figures 12 and 13 illustrate the bi-phasic pattern of O_2 desaturation across the range of altitudes. The section labeled as Phase 1 is hypoxia onset and is characterized by an abrupt, fairly smooth downward curve. Phase 2 covers the lower O_2 desaturation range and depicts increased ventilation , and other compensatory mechanisms which serve to decrease the slope of the curve and eventually (if sufficient) cause SpO_2 to fluctuate around a quasi-stable minimum. Phase 2 was considered to start at the first sign of significant ventilatory compensation, as evidenced by transient spikes or plateaus in SpO_2 values. The five-parameter sigmoid curve was fitted to data from stable baseline/recovery to approximately the beginning of Phase 2 (Fig. 12 and 13). The process of curve fitting:

1) Plotted SpO_2 saturation versus time for stable baseline/recovery through the end of the altitude exposure as measured by the Forehead and Finger sensors.

2) Determined the demarcation time between Phase1 and Phase 2 by visual inspection.

3) Re-plotted the data from baseline/recovery to the demarcation time.

4) Ran 5PS regressions for each sensor. Confirmed curve fit by visual inspection and R^2 values. Note: Used $1/y^2$ for the weighting option and $c>0$ as the only parameter constraint.

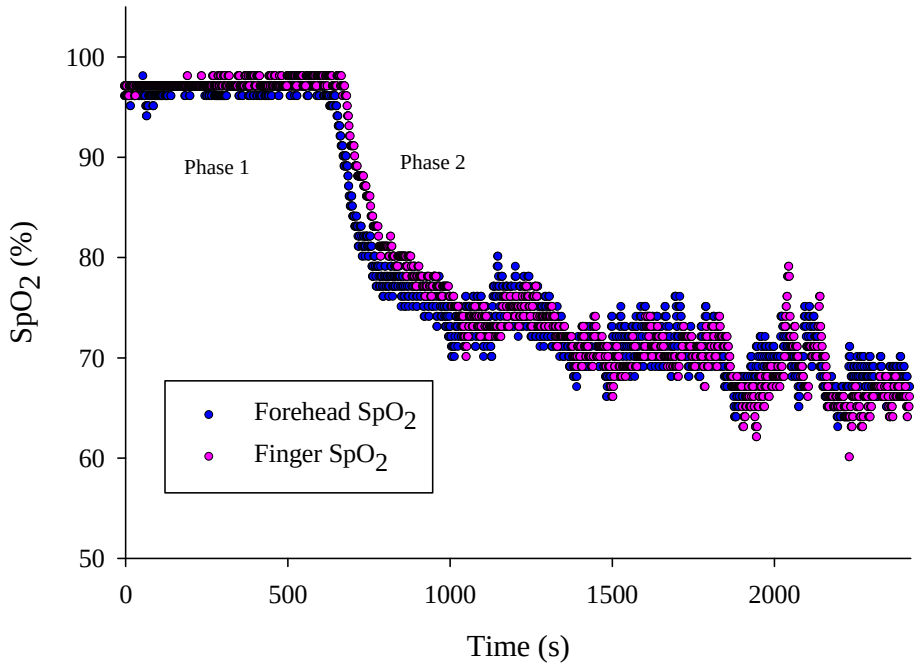

Figure 12. Subject 8: Entire 18,000 ft Exposure

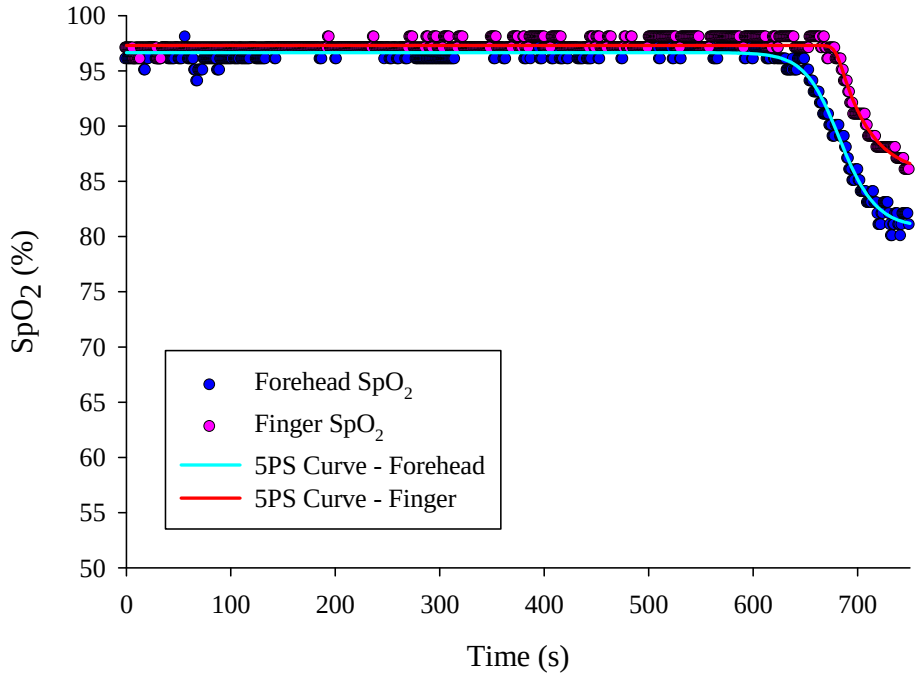

Figure 13. Subject 8. Truncated 18,000 ft Exposure

Parameter values calculated in SigmaPlot were used in MathCad 14.0 (PTC) to determine MDR and TMDR. The first step was calculating the first, second, and third derivatives of the 5PS function using MathCad's symbolic evaluation operators. The first and second derivative evaluations are excerpted from the MathCad worksheet and shown in Figure 14.

$$f(t,t0,a,b,c,y0) := y0 + \frac{a}{\left[1 + e^{\frac{-(t-t0)}{b}}\right]^{c}}$$

$$\frac{d}{dt}f(t,t0,a,b,c,y0) \rightarrow \frac{a\cdot c\cdot e^{-\frac{t-t0}{b}}}{b\cdot\left(e^{-\frac{t-t0}{b}} + 1\right)^{c+1}} \qquad \text{(Eq. 2)}$$

$$\frac{d^2}{dt^2}f(t,t0,a,b,c,y0) \rightarrow \frac{a\cdot c\cdot e^{-\frac{2\cdot(t-t0)}{b}}\cdot(c+1)}{b^2\cdot\left(e^{-\frac{t-t0}{b}} + 1\right)^{c+2}} - \frac{a\cdot c\cdot e^{-\frac{t-t0}{b}}}{b^2\cdot\left(e^{-\frac{t-t0}{b}} + 1\right)^{c+1}} \qquad \text{(Eq. 3)}$$

Figure 14. Derivative Equations. 5 Parameter Sigmoid Model

The first derivative (2) will attain its maximum value (MDR) when the second derivative (3) is equal to zero. Solutions to f ″(t,t0,a,b,c,y0) = 0 were obtained using the MathCad "root" function (Secant or Mueller method). For the initial root guess we were guided by graphical inspection and the inflection point output from SigmaPlot (t0). In some cases trial and error was required for the initial guess – however, poor initial value choices were easily identified as they resulted in either non-convergence or unreasonable root values. The time value obtained in this manner was TMDR. MDR was calculated by using TMDR in the expression for the first derivative. A representative example from a MathCad worksheet is shown in Figure 15.

Subject 01

Forehead

a: = 19.5995 b: = -.4567 c: = .0042 t0: = 625.8732 y0: = 76.1919

t: = 626 root [(f3(t, t0, a, b, c, y0)), t] = 625.86749

t: = 626

root [(f2(t, t0, a, b, c, y0)),t] = 628.37257 t: = 628.37257

fl (t, t0, a, b, c, y0) = - 0.17541

Finger

a: = 16.4961 b: = -.8537 c: = .0083 t0: = 657.9853 v0: = 81.835

t: = 657 root [(f3(t, t0, a, b, c, y0)), t] = 657.96436

t: = 658

root [(t, t0, a, b, c, y0)), t] = 662.0758 t: = 662.0758

f1 (t, t0, a, b, c, y0) = - .15285

Note: f1 = first derivative (given in Eq. 2, f2 = second derivative (given in Eq. 3), f3 = third derivative, (calculated for additional guidance in the root guess), Redefined variables in MathCad are automatically underlined.

Figure 15. Subject 01 Equations

In addition to calculating MDR and TMDR, the 5PS Method was used to calculate T90 and to estimate SAT_{min} for the 18,000 ft exposure. This provided a means of cross-checking the results obtained via computer algorithm, referred to in the following as Method 1.

5PS Threshold Calculations: Alternative T90 Calculation

The time at which O_2 saturation has reached an arbitrary percentage (p) can be found by solving Eq. 1 for t. Where y = p, the following results:

$$p = y0 + \frac{a}{(1 + e^{-(t-t0)/b})^c}. \qquad \text{(Eq. 4)}$$

Solving for t yields:

$$t = -b \ln\left[\left(\frac{a}{p - y0}\right)^{1/c} - 1\right] + t0. \qquad \text{(Eq. 5)}$$

The time to reach 90% saturation (T90) is equal to t (given by Eq. 5 with p = 90 and a,b,c,t0 substituted from the appropriate SigmaPlot output) minus the time at the start of the altitude exposure (t_{start}). Thus:

$$T90 = -b \ln\left[\left(\frac{a}{90 - y0}\right)^{1/c} - 1\right] + t0 - t_{start}. \qquad \text{(Eq. 6)}$$

We calculated T90 for the 18,000 ft exposure using Equation 6 and compared the results across sensors. The ANOVA was consistent with the results using Method 1; no significant difference was found between sensors [F (1,17) = 26.19, p = .00009).

Table V.
T90 According to 5PS Model

Sensor	Altitude (ft)	Mean (s)	SD (s)
Forehead	18,000	71.73*	21.77
Finger	18,000	101.24	33.63

Note. *Forehead significantly faster than Finger, $p < 0.001$

According to the 5PS model, it took both sensors somewhat longer to reach T90 (Forehead: $|MD|$ = 15.95, Finger: MD = $|11.85|$). This can be attributed to the fact that the real data is noisy, and therefore some points will dip below 90% saturation sooner than the smoothly changing 5PS curve. More importantly, the mean difference between sensors found using each method was in relatively good agreement (5PS Method: $|MD|$ = 29.51, Method 1: $|MD|$ = 33.61). According to both methods, the Forehead was about 30 seconds faster in reaching the T90 benchmark.

5PS Saturation Minimum: Alternative SAT_{min} Estimation

As previously noted, to obtain a good curve fit for the initial phase of desaturation, it was necessary to restrict the data range to Phase 1. When the 5PS model was fitted to data across the entire exposure, a good fit during Phase 1 was not attained; however, the model did provide another way of estimating SAT_{min}. Because the regression curves roughly bisect SpO_2 fluctuations at saturation nadirs, an estimation of SAT_{min} is given by the minimum value of the 5PS curve, which can be read directly from the SigmaPlot output (i.e., $SAT_{min} \approx y0$). One advantage of the 5PS method is that no observer bias enters the process of SAT_{min} determination. (Minimum plateaus had to be identified by graphical inspection in Method 1.) A comparison of y0 obtained via the 5PS Method and the values of SAT_{min} obtained by Method 1 was conducted with results indicating excellent agreement between the two methods. An ANOVA revealed no significant difference between methods for either sensor [Forehead: F (1,16) = .851, p = .37; Finger: F (1,16) = 4.08, p = .06; Table VI].

Table VI.
18,000 ft SAT_{min}: Method Comparison ANOVA Results

Sensor	Mean (Method 1)	Mean (5PS Method)	SD (Method 1)	SD (5PS Method)
Forehead	67.23	66.87	4.63	5.65
Finger	66.62	65.52	4.94	6.14

In addition, according to a follow-up ANOVA performed on the 5PS results, there was no difference between sensor means for SAT_{min}, F(1,16) = 2.49, p = .134.

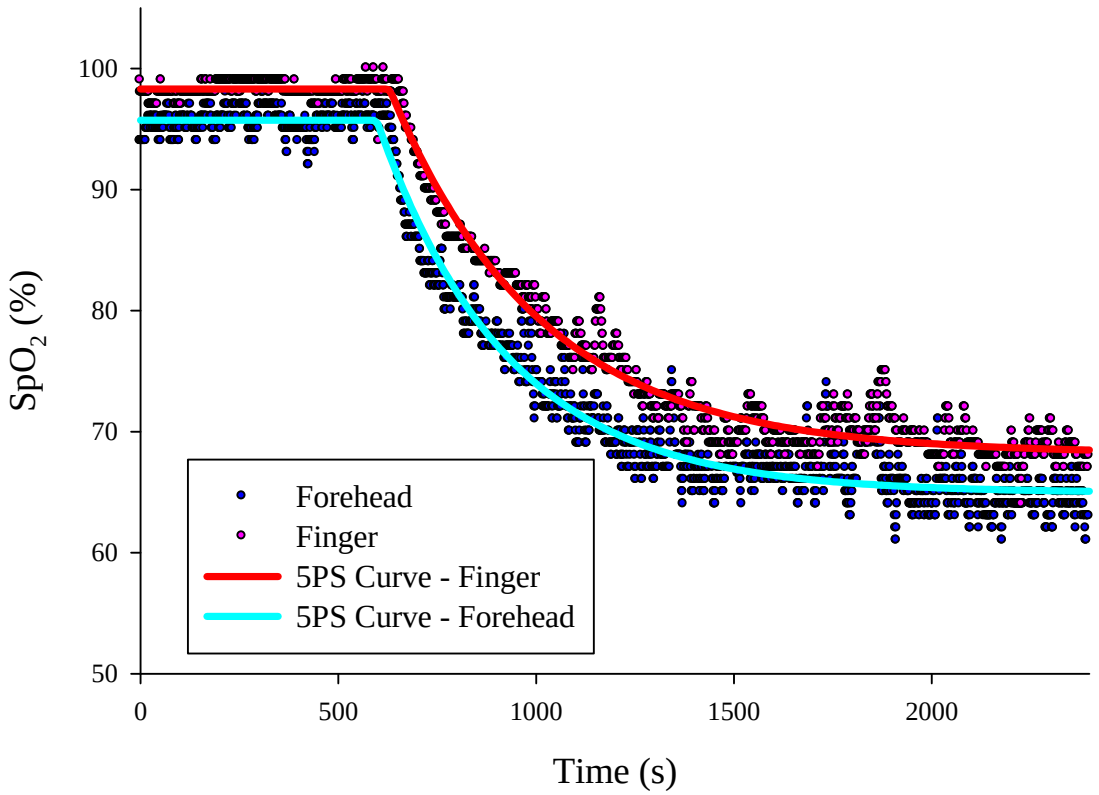

Figure 16. Entire 18,000 ft Exposure with the 5PS Regression for Subject 01

Appendix D. Pictures

Figure 17. Example of mask and sensor placement on forehead.

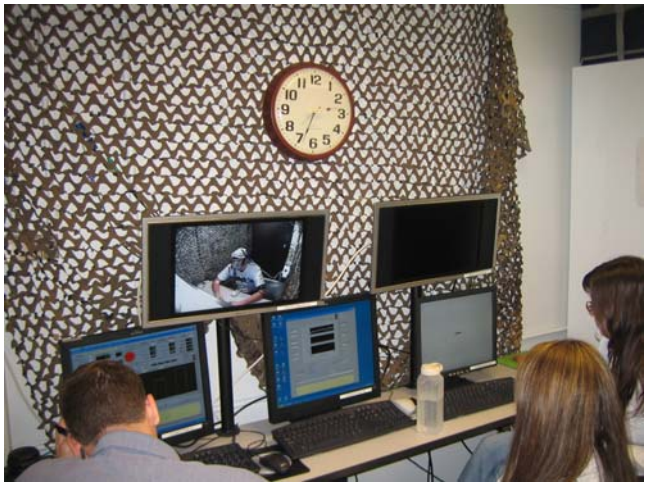

Figure 18. NAMRL Hypoxia Laboratory Subject Monitoring Center

Appendix References

26. Gottschalk PG, Dunn RD. The five-parameter logistic: A Characterization and comparison with the four-parameter logistic. Anal Biochem 2005; 343:54-65.
27. Liao JJZ, Liu R. Re-parameterization of five-parameter logistic function. J of Chemometrics 2009; 23:248-253.
28. Ricketts JH, Head GH. A five-parameter logistic equation for investigating asymmetry of curvature in baroreflex studies. Am J Physiol Regul Integr Comp Physiol 1999; 277:R441-R454.
29. Spiess A, Feig C, Ritz C. Highly accurate sigmoidal fitting of real-time PCR data by introducing a parameter for asymmetry. BMC Bioinformatics 2008; 9:221-232.

REPORT DOCUMENTATION PAGE

1. REPORT DATE (DD MM YY)
7 July 2010

2. REPORT TYPE
Technical Report

3. DATES COVERED (from – to)
January 2009-April 2009

4. TITLE
A Forehead-Mounted Measure of O_2 Saturation: The Potential for in Cockpit Hypoxia Early Detection and Warning

5a. Contract Number:
5b. Grant Number:
5c. Program Element Number:
5d. Project Number:
5e. Task Number:
5f. Work Unit Number: 70805

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Naval Aerospace Medical Reserach Laboratory
280 Fred Bauer Street Building 1811
Pensacola NAS, FL 32508

8. PERFORMING ORGANIZATION REPORT NUMBER
NAMRL 10-26

8. SPONSORING/MONITORING AGENCY NAMES(S) AND ADDRESS(ES)
United States Army Aeromedical Research Laboratory
Fort Rucker, AL 36362

10. SPONSOR/MONITOR'S ACRONYM(S)
USAARL

11. SPONSOR/MONITOR'S REPORT NUMBER(s)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT
Symptoms of hypoxia have been documented among rotary-wing pilots and aircrew. An automated hypoxia warning system would be the optimal warning system, but currently no military aviation platform is outfitted with a physiological monitoring system to alert pilots and aircrew of impending hypoxic episodes. The objectives of this experiment were to compare the sensitivity of, and agreement between, a forehead-mounted pulse oximeter (Forehead) and finger-mounted pulse oximeter (Finger) for application in an early warning detection system. Military personnel donned an aviation flight mask connected to the Reduced Oxygen Breathing Device (ROBD), and were instrumented with the Forehead and Finger oximeters. Following instrumentation, subjects breathed ambient air through the ROBD, followed with one of two counterbalanced ascent profiles used to model exposure to altitude, while data were collected from both sensors. Results indicate an exceptionally strong agreement between the Forehead and Finger sensors. The sensitivity analyses revealed that the Forehead sensor was significantly faster when responding to rapid changes in SpO_2 than the Finger. While the data may seem to suggest that the Forehead sensor is accurate and sensitive to altitude induced changes in SpO_2, major drawbacks exist for the technology utilized in the current study. Reflectance technology remains promising, but significant improvements aimed at diminishing noise, curbing motion artifact, and improving reliability are required to reduce errant measurements before it can be considered for aviation applications.

15. SUBJECT TERMS
Hypoxia, finger oximeter, forehead-mounted pulse oximeter

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	18a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Officer in Charge
UNCL	UNCL	UNCL	UNCL	35	18b. TELEPHONE NUMBER (INCLUDING AREA CODE) COMM/DSN: (850) 452-3486