

Monitoring Tissue Oxygen Saturation in Microgravity on Parabolic Flights

Thomas G. Smith¹, Federico Formenti^{1,2}, Peter D. Hodkinson^{1,3}, Muska Khpal^{1,4}, Brian P. Mackenwells^{1,5}, and Nick P. Talbot^{1,6}

¹Aerospace Medicine Research Group, University of Oxford, Oxford, UK; ²Centre of Human and Aerospace Physiological Sciences, King's College London, London, UK; ³Royal Air Force Centre of Aviation Medicine, RAF Henlow, UK; ⁴Anaesthetics Department, University College Hospital, London, UK; ⁵Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK; ⁶Nuffield Department of Medicine, University of Oxford, Oxford, UK

ABSTRACT

Future spacecraft and crew habitats are anticipated to use a moderately hypobaric and hypoxic cabin atmosphere to reduce the risk of decompression sickness associated with extravehicular activity. This has raised concerns about potential hypoxia-mediated adverse effects on astronauts. Noninvasive technology for measuring tissue oxygen saturation (StO₂) has been developed for clinical use and may be helpful in monitoring oxygenation during spaceflight. We conducted a technical evaluation of a handheld StO₂ monitor during a series of parabolic flights, and then undertook a preliminary analysis of the data obtained during the flights from six individuals. The StO₂ monitor operated normally in all gravity conditions. There was considerable variability in StO₂ between and within individuals. Overall, transition to

microgravity was associated with a small decrease in StO₂ of 1.1±0.3%. This evaluation has established the basic function of this technology in microgravity and demonstrates the potential for exploring its use in space.

INTRODUCTION

Near-infrared spectroscopy provides a non-invasive means of measuring tissue oxygenation, exploiting the characteristic light absorption properties of oxygenated and deoxygenated hemoglobin in the near-infrared wavelength range to determine tissue oxygen saturation (StO₂). Monitors typically measure oxygen saturation across a muscle tissue field containing both arterial and venous blood, such as the thenar eminence of the hand. In clinical practice, StO₂ has mainly been developed as an indicator of peripheral tissue perfusion in critically ill patients, as StO₂ is lowered when perfusion is reduced in association with, for example, major hemorrhage or sepsis (Duret et al., 2015; Neto et al., 2014). A fall in StO₂ can also be caused by a reduction in oxygen delivery to the tissues when blood oxygen content is reduced, such as at high altitude or when gas exchange is impaired in the lungs (Martin et al., 2009; Sandfeld et al., 2013).

Due to the shape of the hemoglobin-oxygen dissociation curve, a moderate fall in arterial

Key words: StO₂; Hypoxia; Hypobaric Cabin; Weightlessness; Zero g; Suborbital Spaceflight

Correspondence to: Dr. Thomas G. Smith
Aerospace Medicine Research Group
Nuffield Division of Anaesthetics
University of Oxford
John Radcliffe Hospital
Oxford OX3 9DU, United Kingdom
Telephone: +44-1865-221590
E-mail: thomas.smith@ndcn.ox.ac.uk

partial pressure of oxygen from normal levels would be expected to cause a greater reduction in StO₂ than in arterial oxygen saturation measured by pulse oximetry (SpO₂), and may therefore provide a means of detecting more subtle changes in oxygenation. A handheld StO₂ monitor has recently been developed for portable use, introducing the potential to measure StO₂ noninvasively in challenging environments such as space. StO₂ monitoring could be investigated for its utility in various clinical scenarios in space, and could also be explored as a means of monitoring potential effects of the spaceflight environment on oxygenation.

In the future this could include the effects of moderately reduced cabin pressure with consequently reduced oxygen levels, which NASA and others have proposed for the design of future spacecraft and crew habitats (Bacal *et al.*, 2008; Norcross *et al.*, 2013; Scheuring *et al.*, 2008). Such an atmosphere would expose astronauts to a mildly hypoxic environment comparable to a commercial aircraft cabin, which is known to stimulate classic physiological responses, such as ventilatory acclimatisation (Fatemian *et al.*, 2001), erythropoietin secretion (Gunga *et al.*, 1996), and hypoxic pulmonary vasoconstriction (Smith *et al.*, 2013; Smith *et al.*, 2012; Turner *et al.*, 2015). This design approach would have the benefit of making extravehicular activity safer and easier with respect to the risk of decompression sickness and associated denitrogenation protocols, as well as other potential advantages including reduced risk of fire, decreased structural strength and weight requirements, reduced requirement for stored or generated oxygen, and even a speculative effect as a countermeasure against spaceflight anemia (Bacal *et al.*, 2008; Buckley, 2006; Scheuring *et al.*, 2008). However, the wider health and performance implications of this environment require careful consideration, including the scope for physiological interaction between hypoxia, hypobaria, and hypogravity, which has yet to be investigated (Norcross *et al.*, 2013). Measurements of StO₂ could be a useful adjunct in this setting, and we aimed to evaluate portable StO₂ monitoring technology with a view to future use in space using parabolic aircraft flights to assess its function in microgravity.

MATERIALS AND METHODS

Personnel

Six members of the research team participated in the study, five men and one woman (mean [\pm SD] age 33 \pm 4 yr). All personnel were in good health and provided written informed consent. The study was approved by the Oxford Tropical Research Ethics Committee and by the NASA Institutional Review Board, and was conducted in accordance with the Declaration of Helsinki.

Equipment

The technology under evaluation was the InSpectra StO₂ Spot Check (model 300) (Hutchinson Technology Inc., Hutchinson, MN, USA). This is a commercial off-the-shelf monitor that weighs 400 g and is powered by a rechargeable battery. The reusable sensor is designed to be clipped to the thenar eminence of the hand, and thenar StO₂ was the main measure of interest in this study. The sensor has also been used on the medial plantar surface of the foot, although this may be less reliable (Van Haren *et al.*, 2013). Real-time StO₂ is measured continuously and the display value is updated every two seconds.

Protocol

This work was undertaken at Ellington Field, Houston, Texas, as part of a parabolic flight campaign through the NASA Flight Opportunities Program. There were four 0 g parabolic flights on a modified Boeing 727 aircraft, with three personnel on each flight, and all flights followed the same profile. There were 40 parabolic trajectories per flight, with a short period of level flight in between each bracket of 10 parabolas. Each parabola provided approximately 17 seconds of microgravity during freefall, when the gravito-inertial acceleration was 0 g, in between periods of modest hypergravity of up to approximately 1.8 g (Karmali and Shelhamer, 2008). The cabin pressure altitude was maintained constant at 5,600 ft (1,700 m) throughout the parabolas. On a small number of parabolas the g profile or cabin pressure altitude varied from these values, such as with early pullout from the final parabola of a bracket, and these were excluded from the evaluation.

Measurements

Study personnel formally evaluated the monitor technology and performed StO_2 measurements on each other, and pulse oximetry was used to measure SpO_2 and heart rate (WristOx₂ 3150, Nonin Medical Inc., Plymouth, MN, USA). On each flight, three 10-parabola brackets were dedicated to recording measurements from each of the three study personnel in turn, with one individual as the test subject and the other two recording measurements during each bracket. Measurements were made in this way on 120 parabolas across the four flights. The fourth 10-parabola bracket on each flight was used for technical evaluation of other aspects of the monitor's function, including powering on/off, self-test function, and ease of use while free-floating. When performing measurements, StO_2 monitors and pulse oximeters were attached continuously at the hand and foot over the 10-parabola bracket, and each variable was recorded simultaneously at the end of each microgravity and hypergravity phase. Hands and feet were kept warm to avoid possible effects of peripheral vasoconstriction. Parabolic measurements were made in the supine position, which during microgravity meant floating horizontally above the aircraft floor, and were compared with supine measurements at 1 g performed pre-flight and in-flight (during level flight prior to the parabolas).

Statistical Analysis

Although primarily a technical evaluation, unique StO_2 data were obtained in the course of this evaluation, and in order to take full advantage of this opportunity we conducted a preliminary analysis of the effect of dynamic transition from $\sim 1.8 g$ to $0 g$ using Student's two-tailed t -test for paired samples. Measurements from all four flights were used in the analysis. Values of $P < 0.05$ were considered statistically significant, and data are reported as mean \pm SEM.

RESULTS

The StO_2 monitor technology functioned normally in all gravity conditions, including powering on/off and performing its self-test function. The monitor was generally easy to use in microgravity, and this was aided by tethering it to the body. The 1-meter cable length was

appropriate for use in weightless conditions and the visual display was easy to read. The monitor provided thenar StO_2 measurements appropriately during parabolas, which are shown in Figure 1. For each person, StO_2 is reported from an average of 17 parabolas, and there was considerable variability between and within individuals (Figure 1).

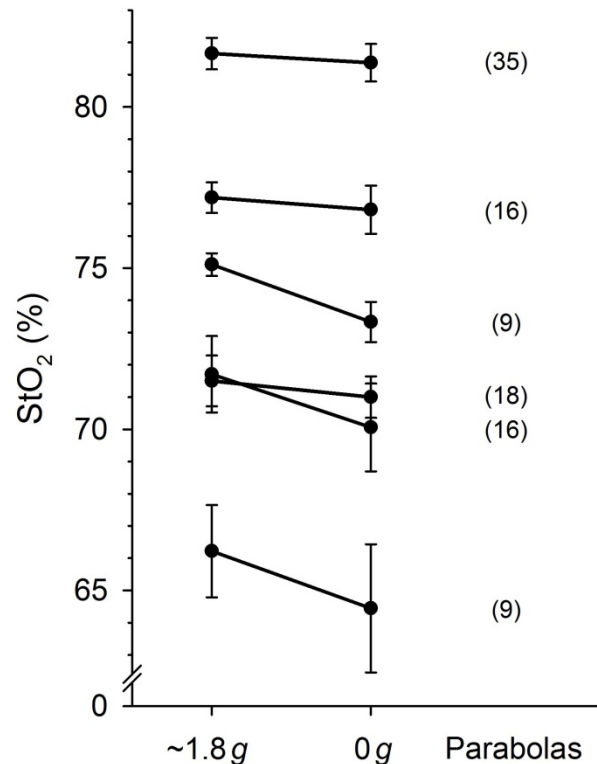


Figure 1. Tissue oxygen saturation (StO_2) in individuals during parabolas. Thenar StO_2 is shown for each of the six members of the research team. The number of parabolas on which each individual's measurements were obtained is also shown. Data are mean \pm SEM.

Baseline arterial oxygen saturation measured pre-flight was normal (SpO_2 $97 \pm 0.5\%$). Baseline StO_2 ($80 \pm 2\%$) was also within the wide normal range of approximately 70-85% that has been reported in the literature. Due to the mildly hypoxic cabin pressure altitude, arterial oxygenation was lowered in-flight (SpO_2 $93 \pm 0.7\%$; unchanged with microgravity [$P=0.3$]), and thenar StO_2 was likewise affected by cabin pressure in-flight ($74 \pm 3\%$) and is depicted in Figure 2. Transition to microgravity was associated with a small decrease in StO_2 of

1.1±0.3% (P=0.017), as shown in Figure 2. The StO₂ monitor is designed to be used on the hand and is not intended for use on the foot, and we found that StO₂ values at the foot were well below the physiological range both in 1 g (55±5% pre-flight) and in flight (50±3% during both ~1.8 g and 0 g). Heart rate did not change significantly during the parabolas (63±7 bpm; P=0.14).

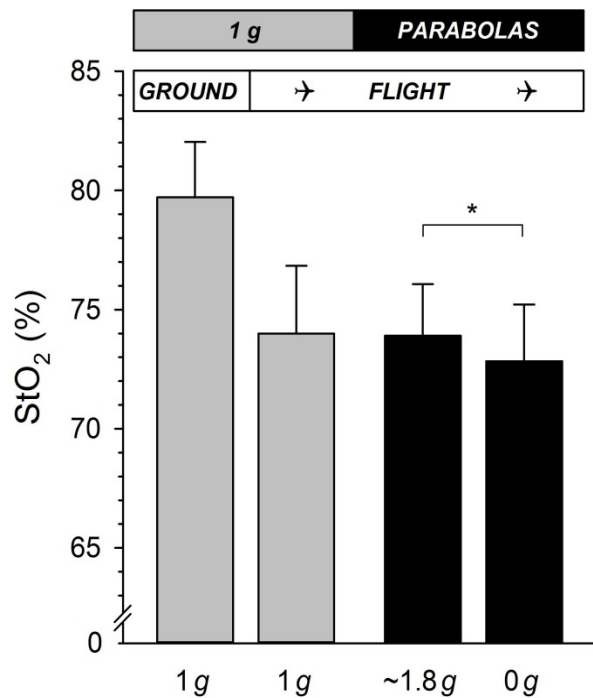


Figure 2. Tissue oxygen saturation (StO₂) during parabolic flights. Thenar StO₂ is shown (mean ± SEM). In-flight measurements were made at a constant cabin pressure altitude of 5,600 ft (1,700 m). Pre-flight and in-flight data recorded at 1 g are shown in grey, and microgravity/hypergravity data during parabolas are shown in black. The asterisk denotes a statistically significant change in StO₂ upon transition from hypergravity to microgravity.

DISCUSSION

This evaluation has established that the InSpectra StO₂ monitoring technology operates normally in microgravity. However we observed considerable inter-individual and intra-individual variability in StO₂ values, which is consistent with previous terrestrial studies and is one reason why StO₂ monitoring remains largely a research tool and has yet to be taken up widely in mainstream clinical practice (Lipsey et al., 2012; Van Haren et al., 2013). It has been suggested that, in

addition to possible limitations of the technology itself, various physiological factors could contribute to this variability, including tissue thickness and composition, fluid status, blood viscosity, and temperature-related changes in perfusion. Age did not vary greatly and is unlikely to have influenced our findings, although we note that long-duration astronauts are typically at least a decade older than this study's participants. Our findings do support using the device at the intended thenar site rather than the foot, where measurements were unreliable.

In the course of assessing this technology we obtained data on StO₂ during changing gravity conditions. This data is preliminary in nature and the usual limitations of parabolic flights apply, including a small sample size, short exposure times, and the potential for physiological effects of one phase (microgravity or hypergravity) to carry over into the subsequent alternate phase. Notwithstanding these limitations and the background variability, across multiple repeat measurements a small fall in StO₂ was observed in each individual on transition to microgravity. Such a small decrement has no physiological significance in itself, and an artifactual explanation cannot be excluded, but it is interesting to speculate whether this fall might represent the beginning of a larger effect of microgravity on tissue oxygenation that would have continued to develop had the weightless state been maintained beyond 17 seconds.

Although microgravity does not cause major impairment of gas exchange in the lungs (Prisk, 2014), limited evidence from a series of measurements on the Mir space station suggests that tissue oxygenation may nevertheless be somewhat decreased during spaceflight, perhaps due to slightly altered ventilation/perfusion matching in the lungs (Baranov, 2011; West, 2001). It is unfortunate that standard arterial blood gas analyses have not yet been performed in space, as these would be very helpful in interpreting isolated findings such as these, particularly in the light of the many 'hypoxia-mediated physiologic concerns' NASA has identified that could conceivably arise from or be worsened by a moderately hypoxic atmosphere in space (Norcross et al., 2013). These concerns include: visual impairment/intracranial pressure syndrome, sensorimotor performance deficits,

neurocognitive impairment, sleep disturbance, acute mountain sickness, diminished exercise capacity and cardiovascular performance, immunosuppression, oxidative stress and damage, nutritional deficiencies, and increased bone resorption with acceleration of bone loss and higher risk of renal stones (Norcross *et al.*, 2013). The true potential for any of these adverse factors to impact on future space missions is currently unknown, but would presumably be greater if the effects of a hypoxic cabin environment were superimposed on any underlying impairment of tissue oxygenation inherently associated with microgravity.

Although the use of a hypobaric exploration-class atmosphere of this kind is many years away, the acute combination of microgravity and mild hypoxia is likely to be experienced much sooner with the anticipated commencement of commercial suborbital spaceflights. For suborbital operators utilizing an airline-style cabin pressure, several minutes of microgravity will be superimposed on mild background hypoxia, and for spaceflight participants these factors will together interact with any influence of age, smoking, or pre-existing disease, and contribute to in-flight hypoxemia (as has been observed on a parabolic flight (Mackenzie *et al.*, 2007)). In addition to the period of weightlessness, suborbital spaceflights will also include significant high-g exposures which are in fact more likely to cause hypoxemia, and arterial oxygen desaturation has been demonstrated during normoxic centrifuge studies simulating anticipated suborbital acceleration profiles (Blue *et al.*, 2014; Blue *et al.*, 2012). Of course the true acceleration-weightlessness-acceleration profile of suborbital spaceflight cannot be simulated, and in-flight studies will be required to characterize the associated physiology when suborbital operations commence.

In summary, we have established that StO₂ monitoring is possible in microgravity and demonstrated the potential for exploring the use of this technology in space. In theory, astronauts could use this technology to detect a degree of tissue hypoxia that may not otherwise be apparent during future spaceflight operations, although the noise from background variability would need to be overcome, possibly with multiple repeat measurements. This evaluation has highlighted

our incomplete understanding of the physiological interaction between microgravity and hypoxia, and further research into the effects of changing gravity conditions on oxygenation is warranted.

ACKNOWLEDGEMENTS

This work was supported by the NASA Flight Opportunities Program and the Medical Research Fund of the University of Oxford. We thank Hutchinson Technology Inc. for loaning additional portable StO₂ monitors for use in this study. The funding sources had no role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

REFERENCES

- Bacal K, Beck G, Marratt MR (2008) Hypoxia, hypercarbia, and atmospheric control. In *Principles of Clinical Medicine for Spaceflight*, MR Barratt and SL Pool (eds). New York: Springer
- Baranov VM (2011) Physiological analysis of the possible causes of hypoxemia under conditions of weightlessness. *Human Physiology* **37**: 455-460
- Blue RS, Pattarini JM, Reyes DP, Mulcahy RA, Garbino A, Mathers CH, Vardiman JL, Castleberry TL, Vanderploeg JM (2014) Tolerance of centrifuge-simulated suborbital spaceflight by medical condition. *Aviation, Space, and Environmental Medicine* **85**: 721-729
- Blue RS, Riccitello JM, Tizard J, Hamilton RJ, Vanderploeg JM (2012) Commercial spaceflight participant G-force tolerance during centrifuge-simulated suborbital flight. *Aviation, Space, and Environmental Medicine* **83**: 929-934
- Buckey JC (2006) *Space Physiology*, New York: Oxford University Press
- Duret J, Pottecher J, Bouzat P, Brun J, Harrois A, Payen JF, Duranteau J (2015) Skeletal muscle oxygenation in severe trauma patients during haemorrhagic shock resuscitation. *Critical Care* **19**: 141
- Fatemian M, Kim DY, Poulin MJ, Robbins PA (2001) Very mild exposure to hypoxia for 8 h can induce ventilatory acclimatization in

- humans. *European Journal of Physiology* **441**: 840-843
- Gunga HC, Frommhold M, Hildebrandt W, Kirsch K, Röcker L (1996) Erythropoietin production during flights with pressurized aircrafts. *Lancet* **348**: 416
- Karmali F, Shelhamer M (2008) The dynamics of parabolic flight: flight characteristics and passenger percepts. *Acta Astronautica* **63**: 594-602
- Lipsey M, Woinarski NC, Bellomo R (2012) Near infrared spectroscopy (NIRS) of the thenar eminence in anesthesia and intensive care. *Annals of Intensive Care* **2**: 11
- Mackenzie I, Viirre E, Vanderploeg JM, Chilvers ER (2007) Zero G in a patient with advanced amyotrophic lateral sclerosis. *Lancet* **370**: 566
- Martin DS, Levett DZ, Mythen M, Grocott MP (2009) Changes in skeletal muscle oxygenation during exercise measured by near-infrared spectroscopy on ascent to altitude. *Critical Care* **13 Suppl 5**: S7
- Neto AS, Pereira VGM, Manetta JA, Espósito DC, Schultz MJ (2014) Association between static and dynamic thenar near-infrared spectroscopy and mortality in patients with sepsis: a systematic review and meta-analysis. *Journal of Trauma Acute Care Surgery* **76**: 226-233
- Norcross J, Norsk P, Law J, Arias D, Conkin J, Perchonok M, Menon A, Huff J, Fogarty J, Wessel JH, Whitmire S (2013) *Effects of the 8 psia/32% O₂ Atmosphere on the Human in the Spaceflight Environment*. NASA Technical Memorandum 2013-217377
- Prisk GK (2014) Microgravity and the respiratory system. *European Respiratory Journal* **43**: 1459-1471
- Sandfeld J, Larsen LH, Crenshaw AG, Jensen BR (2013) Muscle oxygenation, EMG, and cardiovascular responses for cabin attendants vs. controls. *Aviation, Space, and Environmental Medicine* **84**: 478-485
- Scheuring RA, Conkin J, Jones JA, Gernhardt ML (2008) Risk assessment of physiological effects of atmospheric composition and pressure in Constellation vehicles. *Acta Astronautica* **63**: 727-739
- Smith TG, Chang RW, Robbins PA, Dorrington KL (2013) Commercial air travel and in-flight pulmonary hypertension. *Aviation, Space, and Environmental Medicine* **84**: 65-67
- Smith TG, Talbot NP, Chang RW, Wilkinson E, Nickol AH, Newman DG, Robbins PA, Dorrington KL (2012) Pulmonary artery pressure increases during commercial air travel in healthy passengers. *Aviation, Space, and Environmental Medicine* **83**: 673-676
- Turner BE, Hodkinson PD, Timperley AC, Smith TG (2015) Pulmonary artery pressure response to simulated air travel in a hypobaric chamber. *Aerospace Medicine and Human Performance* **86**: 529-534
- Van Haren RM, Ryan ML, Thorson CM, Namias N, Livingstone AS, Proctor KG (2013) Bilateral near-infrared spectroscopy for detecting traumatic vascular injury. *Journal of Surgical Research* **184**: 526-532
- West JB (2001) Pulmonary gas exchange. In *Gravity and the Lung: Lessons from Microgravity*, GK Prisk, M Paiva, and JB West (eds). New York: Marcel Dekker, Inc.