

A Prototype Miniaturized Metabolic Gas Analysis System

Tammy Anderson, Joseph Orr Ph.D.

Abstract

Microgravity adversely affects several physiological systems. As space exploration moves to extended flights, understanding which mechanisms microgravity influences may contribute to the health and safety of astronauts aboard. Maximum oxygen consumption (VO_2 max) testing is used to monitor changes to cardiorespiratory function. Currently the equipment used to such testing aboard the International Space Station (ISS) is large and requires a significant amount of power. We propose the use of a modified metabolic management system, currently approved for clinical use, for exercise stress testing.

I. INTRODUCTION

The absence of gravity in space adversely affects several physiological systems of the body including calcium absorption resulting in bone density loss, cardiovascular deconditioning, muscular atrophy, and neurovestibular function. Upon returning to the Earth's gravitation field some of these conditions are only partially reversible.¹⁻⁵ Previous missions have demonstrated that the hazards associated with such an unforgiving environment often require maximum cognitive performance and physical fitness for survival. As space exploration progresses from short-duration flights to long term residency, minimizing the effects of weightlessness on the body will be of increasing importance for the safety of crew members for both inflight well-being and postflight recovery.⁶

A combination of aerobic and resistance exercise regimen protocols have been suggested as a possible countermeasure against detrimental physical deconditioning due to microgravity.^{7,8} Since the Skylab missions, periodic stress tests, which have the advantage of being noninvasive, were administered to

crew members as a way of assessing the health status of multiple major body systems.⁹⁻¹² The most commonly measured parameter during exercise stress tests is maximum oxygen uptake (VO_2 max).¹³ During exercise the cardiovascular system must function optimally to provide systemic oxygen transport and utilization. At some point during maximal exercise the linear relationship between O_2 consumption and mechanical power plateaus. This point, known as VO_2 max, is considered the best indicator of cardiorespiratory endurance and aerobic fitness. Consequently it can be used to quantify and track cardiovascular deconditioning.

To determine the VO_2 max, respiratory gas flow and the concentration of inspired and expired oxygen and carbon dioxide must be recorded simultaneously while the subject is performing a specific exercise protocol. Aboard the space station, the standard protocol, which consisted of regular increases in the speed and intensity of exercise, is performed via bicycle ergometer (**Figure 1**).¹⁴ Since the rate of oxygen uptake directly correlates with the rate of metabolic energy expenditure, this metabolic gas analysis system can also be used to determine nutritional requirements for crew members. This process is known as indirect calorimetry and is the primary clinical method for assessing metabolic rate.



Figure 1 Officer Jeff Williams assists Flight Engineer Thomas Reiter perform a VO_2 max test during ISS Expedition 13

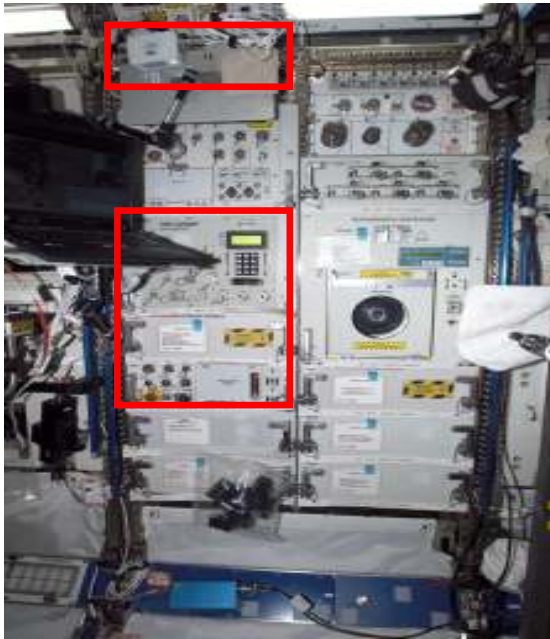


Figure 2 GASMAP metabolic analyzer (highlighted by red boxes) as integrated in the HRF on the ISS

The metabolic gas analyzer, GASMAP, integrated into the human research facility (HRF) aboard the International Space Station (ISS) system is large (one 1 x 8 panel unit drawer and two 1x4 panel unit drawers, 51 Kg total) and requires a significant amount of power (205 watts), **Figure 2**. The prototype metabolic measurement system was developed as research project at the University of Utah. It was refined and delivered to Johnson Space Center in 1988.¹⁵ The system was self-calibrating and offered many advantages over earlier metabolic measurement systems.

During the past 3 years, our group at the University of Utah has worked in collaboration with a division of Philips Electronics and others to develop a metabolic measurement system for use in anesthesia and intensive care. This system, shown in **Figure 3**, is much smaller than the GASMAP device (less than 5 in³) weighs less than 0.5 Kg and requires less than 2 watts. We have demonstrated the accuracy and robustness of this device in a patient simulator, in human volunteers and in the intensive care unit (ICU).

The main limitation of the present system is that it is not capable of measuring

oxygen uptake during exercise conditions with larger gas flows. We propose that by modifying the breathing apparatus and increasing the lumen diameter we could build a prototype version of the critical care metabolic gas analyzer that would be suitable for exercise testing.



Figure 3 The prototype critical care system circuitry and sensors. The proposed study would modify the gas flow sensor and algorithms to facilitate exercise testing

II. SENSOR DESIGN CONSIDERATIONS

Because our system uses a differential pressure type flow sensor, it requires a compromise between the resistance to flow experienced by the user, and the magnitude of the differential pressure signal from which flow is measured. On one hand, a large differential pressure in response to gas flow gives a stronger signal relative to noise; on the other hand, a resistive sensor restricts gas flow inhibiting the subjects breathing leading to a possible falsely low VO_2 max readings. It is critical that the flow sensor design offers the minimal amount of flow restriction needed while still producing enough signal to meet the measurement accuracy goals.

The breathing apparatus must not restrict intake airflow. In an ICU setting the flow is relatively small (± 180 liters/min maximum) and only requires a small lumen (<15 mm diameter) to support gas flow. During

exercise gas flows are in the range of ± 400 liters/min. We calculate a lumen between 23-27 mm will be required to support high flow volumes and minimize resistance felt by the subject.

To build the prototype breathing apparatus we customized a flow sensor utilized in a commercial system that is currently used to determine VO_2 max during exercise. Pressure ports, already included on the housing, determine differential pressure and could be connected via tubing to a pressure transducer. As the atmosphere on the space station is a controlled environment it is only necessary to measure the concentration of expired carbon dioxide. An on air-way non-dispersive infrared (NDIR) CO_2 gas analysis sensor was placed at a 45° angle into the lumen of the tube. A portion of the sensor extruded into the lumen to divert airflow to the sensor. To prevent ambient air diffusion across the sensor that may produce inaccurate readings, resistance was added to the end of the sensor in the form of additional length, **Figure 4**.

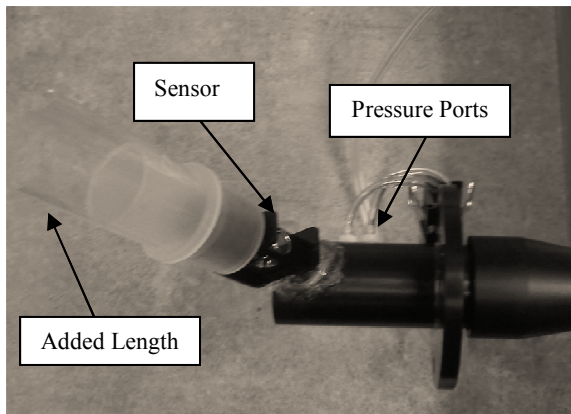


Figure 4 Breathing apparatus with the sensor at a 45° angle with added length to prevent diffusion back across the sensor.

III. CHARACTERIZATION OF SENSOR

Changes in sensor geometry have been shown to cause significant changes in the reported measured flow; therefore, it was necessary to verify that flow rates were not being compromised. To do this the mixed end-tidal CO_2 (ETCO_2) measurements of a reference sensor and the test sensor were compared.

A test lung was powered by an ESPRIT ventilator with the settings shown in **Table 1**. Carbon dioxide levels were set so that the partial pressure of ETCO_2 was between 34-36 mmHg, within an acceptable range for human ETCO_2 . The mechanical lung provided a tidal volume for each breath of 1 liter.

Table 1. ESPRIT Ventilator Parameters

TV	1037 mL	Rate	10 BPM
TR	10 BPM	TV	1139 ml
Total VE	10.4 L	O₂	21%
PIP	44.3 cm H ₂ O		

Flow Host software was used to record the flow parameters. After a one minute stabilization period the flow was recorded for 5 breaths on the reference sensor. The capnostat was moved to the test sensor and flow was again allowed to stabilize for 1 minute. After collecting the flow over a period of 5 breaths on the test sensor, the reference flow was recorded once more. The average partial pressure of ETCO_2 for 5 breaths at the reference site, test site, and reference site was 35.8 ± 0.08 , 35.7 ± 0.08 , and 35.8 ± 0.08 mmHg, respectively. These findings were repeated 3 times and the ETCO_2 was consistently found to be within an acceptable range, **Figure 5**.

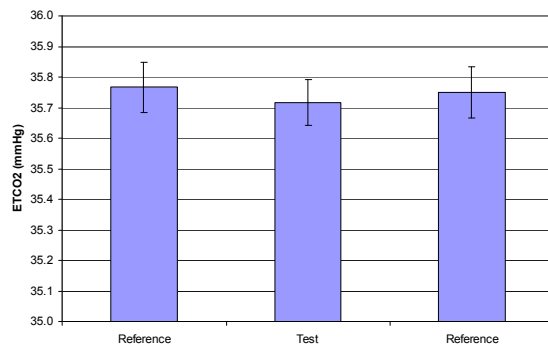


Figure 5 The average partial pressure of ETCO_2 for 5 breaths at the reference site, test site, and reference site was 35.8 ± 0.08 , 35.7 ± 0.08 , and 35.8 ± 0.08 mmHg, respectively

IV. DISCHARGE COEFFICIENT TABLE

The relationship between flow and differential pressure is derived using a modified version Bernoulli's equation, so that:

$$Flow = \frac{P_m T_{std}}{P_{std} T_m} K \sqrt{\frac{\Delta P T_m}{M_w P_m}} \quad (1)$$

where P_m , P_{std} , T_m , and T_{std} are the measured and standard pressures (mmHg) and temperatures (K), respectively; ΔP is the differential pressure (mmHg), and K is a correction factor that is flow dependent and includes gas composition, flow-discharge coefficients, and other factors.¹⁶

The correction factor, K , is used to adjust for errors resulting from assumptions made in the derivation process.

$$K = \frac{\text{Actual Flow Rate}}{\text{Theoretical Flow Rate}} \quad (2)$$

It is a dimensionless unit that is commonly referred to as the discharge coefficient. For our purposes, K is stored as an index dependent on barometric pressure, temperature, and humidity and will be stored in a lookup table.

In order to prove that our prototype sensor and algorithms could be used to predict flow, we tested the linearity of the flow versus differential pressure relationship. An ESPRIT ventilator was used to blow pure oxygen at a known flow. The flow of the ventilator was verified using a VT Plus GasFlow Analyzer. The VT Plus was calibrated using a 3 liter syringe and found to have a percent error of $\pm 0.83\%$. The differential pressure was measured using a NICO Cardiopulmonary Management System.

Figure 6 shows the relationship between the average flow and the square root of the differential pressure. At low flows the differential pressure was much more sensitive to noise, so it was necessary to gather data at 2 LPM increments. At higher flows the pressure was more stable and the relationship was very linear with an R-squared value of 0.996. The next step in building the coefficient table will be to incorporate the barometric pressure,

temperature, and molecular weights of the substance to develop equations that can be used to translate the data to different conditions, i.e. in space using air instead of pure oxygen.

Figure 7 shows the discharge coefficient correction factors. For the lookup table it will be necessary to interpolate between the known values. At higher levels of flow the differential pressure is more stable, and the K correction factor becomes almost constant.

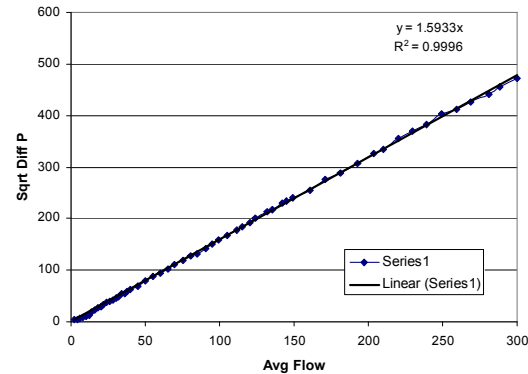


Figure 6 The linear relationship between the average flow and differential pressure. This relationship does not take into account the temperature, barometric pressure, or molecular weight of the substance.

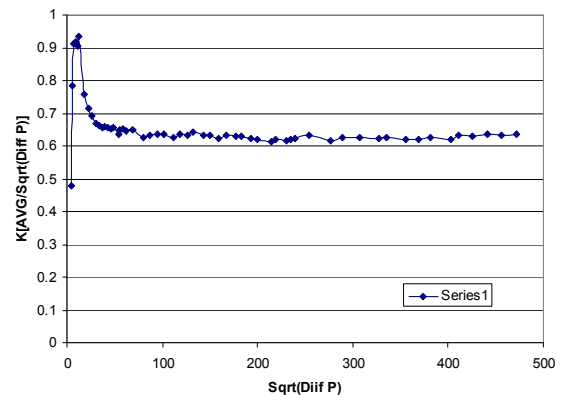


Figure 7 The discharge coefficient, K , over the differential flow.

V. FUTURE WORK

The discharge coefficients will be incorporated into the oxygen uptake system software and the flow measurement will be tested for accuracy over the range of interest

±400 L/min. We expect that the flow measurement will be accurate to within ±3%.

We will incorporate the modified flow sensor and flow measurement algorithms with the existing oxygen uptake measurement system. We will use our propane combustion patient lung simulator system to simulate an exercising subject. We will test the accuracy of the oxygen consumption measurement at 500, 1000, and 2000 ml/minute of oxygen consumption. Exercise ventilation will be simulated using a respiration rate of 20 breaths per minute and tidal volumes of 0.5, 1.0 and 2.0 liters/breath of air. We will compare the measured oxygen consumption against the known simulated oxygen consumption as calculated by the directly measured rate of propane flow into the flame. Algorithm adjustments will be made as needed until the desired accuracy of less than 5% error has been achieved

VI. REFERENCES

1. MACIAS BR, GROPPA ER, EASTLACK RK, *ET AL.* SPACE EXERCISE AND EARTH BENEFITS. *CURR PHARM BIOTECHNOL* 2005;6.
2. HAWKEY A. THE PHYSICAL PRICE OF A TICKET INTO SPACE. *JBIS-J BR INTERPLANET SOC* 2003;56.
3. LEVY MN TJ. CARDIOVASCULAR DECONDITIONING OF SPACE FLIGHT. *PHYSIOLOGIST* 1983;26.
4. LEBLANC A, ROWE R, SCHNEIDER V, EVANS H, HEDRICK T. REGIONAL MUSCLE LOSS AFTER SHORT DURATION SPACEFLIGHT. *AVIATION SPACE AND ENVIRONMENTAL MEDICINE* 1995;66.
5. NICGOSSIAN AE, CHARLES JB, BUNGO MW, LEACH-HUNTOON CS. CARDIOVASCULAR FUNCTION IN SPACE FLIGHT. *ACTA ASTRONAUTICA* 1991;24.
6. CONVERTINO VA. STATUS OF CARDIOVASCULAR ISSUES RELATED TO SPACE FLIGHT: IMPLICATIONS FOR FUTURE RESEARCH DIRECTIONS. *RESPIR PHYSIOL NEURO* 2009;169.
7. MOORE AD, LEE SMC, CHARLES JB, GREENISEN MC, SCHNEIDER SM. MAXIMAL EXERCISE AS A COUNTERMEASURE TO ORTHOSTATIC INTOLERANCE AFTER SPACEFLIGHT. *MEDICINE AND SCIENCE IN SPORTS AND EXERCISE* 2001;33.
8. SHACKELFORD LC, LEBLANC AD, DRISCOLL TB, *ET AL.* RESISTANCE EXERCISE AS A COUNTERMEASURE TO DISUSE-INDUCED BONE LOSS. *JOURNAL OF APPLIED PHYSIOLOGY* 2004;97.
9. GREENLEAF JE, BULBULIAN R, BERNAUER EM, HASKELL WL, MOORE T. EXERCISE-TRAINING PROTOCOLS FOR ASTRONAUTS IN MICROGRAVITY. *JOURNAL OF APPLIED PHYSIOLOGY* 1989;67.
10. LEVINE BD, LANE LD, GAFFNEY FA, BUCKEY JC, BLOMQUIST CG. MAXIMAL EXERCISE PERFORMANCE AFTER ADAPTATION TO MICROGRAVITY. *MEDICINE AND SCIENCE IN SPORTS AND EXERCISE* 1994;26.
11. CONVERTINO VA. PLANNING STRATEGIES FOR DEVELOPMENT OF EFFECTIVE EXERCISE AND NUTRITION COUNTERMEASURES FOR LONG-DURATION SPACE FLIGHT. *NUTRITION* 2002;18.
12. RUMMEL JA, MICHEL EL, SAWIN CF, BUDERER MC. MEDICAL EXPERIMENT M-171 RESULTS FROM THE 2ND MANNED SKYLAB MISSION. *AVIATION SPACE AND ENVIRONMENTAL MEDICINE* 1976;47.
13. FERRETTI G, CAPELLI C. MAXIMAL O-2 CONSUMPTION: EFFECTS OF GRAVITY WITHDRAWAL AND RESUMPTION. *RESPIR PHYSIOL NEURO* 2009;169.
14. LEE SMC, MOORE AD, BARROWS LH, FORTNEY SM, GREENISEN MC. PREDICTION SENSITIVITY OF MAXIMAL OXYGEN-CONSUMPTION ON THE CYCLE ERGOMETER. *FASEB JOURNAL* 1993;7.
15. ORR JA, WESTENSKOW DR, BAUER A. A PROTOTYPE GAS-EXCHANGE MONITOR FOR EXERCISE STRESS-TESTING ABOARD NASA SPACE STATION. *JOURNAL OF APPLIED PHYSIOLOGY* 1989;66.
16. JAFFE MBO, JOSEPH A. CONTINUOUS MONITORING OF RESPIRATORY FLOW. *IEEE ENGINEERING IN MEDICINE AND BIOLOGY MAGAZINE*, 2010:1-9.