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Reliability of the Danish Aerospace Corporation Portable Pulmonary Function System

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ABSTRACT

Metabolic gas analysis is a critical component of investigations that measure cardio-pulmonary exercise responses during and after long-duration spaceflight. The primary purpose of the current study was to determine the reliability and intra-subject repeatability of a metabolic gas analysis device, the Portable Pulmonary Function System (PPFS), designed for use on the International Space Station (ISS). The second objective of this study was to directly compare PPFS measurements of fractions of expired oxygen and carbon dioxide (FEO_2 and $FECO_2$) to values obtained from a well-validated clinical metabolic gas analysis system (ParvoMedics TrueOne© [PM]). **METHODS:** Eight subjects performed four peak cycle tests to maximal exertion. The first test was used to prescribe work rates for the subsequent test sessions. Metabolic gas analysis for this test was performed by the PM, but samples of FEO_2 and $FECO_2$ also were simultaneously collected for analysis by the PPFS. Subjects then performed three additional peak cycle tests, consisting of three 5-min stages designed to elicit 25%, 50%, and 75% maximal oxygen consumption (VO_2max) followed by stepwise increases of 25 W/min until subjects reached volitional exhaustion. Metabolic gas analysis was performed using the PPFS for these tests. Intraclass correlation coefficients (ICC), within-subject standard deviations (WS SD), and coefficients of variation (CV%) were calculated for the repeated exercise tests. Mixed model regression analysis was used to compare paired FEO_2 and $FECO_2$ values obtained from the PPFS and the PM during the initial test. **RESULTS**: The ICC values for oxygen consumption (VO_2), carbon dioxide production (VCO_2), and ventilation (V_E) indicate that the PPFS is highly reliable (0.79 to 0.99) for all exercise levels tested; however, ICCs for respiratory exchange ratio (RER) were low (0.11 – 0.51), indicating poor agreement between trials during submaximal and maximal exercise. Overall, CVs ranged from 1.6% to 6.7% for all measurements, a finding consistent with reported values that were obtained using other metabolic gas analysis techniques. The PPFS and PM produced comparable FEO_2 data; however, there was less agreement between measures of $FECO_2$ obtained from the two devices, particularly at lower CO_2 concentrations. **CONCLUSIONS:** The PPFS appears, in practically all respects, to yield highly reliable metabolic gas analysis data. Lower reliability of RER measurements reported in the literature and likely is not a function of the PPFS device. Further examination of PPFS CO_2 data is warranted to better understand the limitations of these PPFS measurements. Overall, the PPFS when used for repeated measures of cardio-pulmonary exercise should provide accurate and reliable data for studies of human adaptation to spaceflight.

INTRODUCTION

As specified in the National Aeronautics and Space Administration (NASA) Human Research Program's Integrated Research Plan (NASA HRP 47065, 2010), acquisition of data regarding maximal oxygen consumption (VO_2max) during and after spaceflight is a high priority to support future space exploration endeavors. A metabolic gas analysis system capable of being used in spacecraft is required to support this requirement. One such device, known as the Pulmonary Function System (PFS), was developed for International Space Station (ISS) use and was validated in the Exercise Physiology Laboratory at NASA Johnson Space Center (15). The PFS has been used to support studies of resting metabolism and cardiac function on board ISS, but this device is not portable and is confined to a relatively immobile rack location. The exercise equipment onboard ISS has changed locations since earlier expeditions, and the cycle ergometer used for exercise testing was moved to a different module than the one containing the PFS. Thus, the need for a portable metabolic gas analysis device for ISS use arose. The Portable Pulmonary Function System (PPFS) was developed by a contractor to the European Space Agency, Damec Research Aps (currently named Danish Aerospace Corporation, [DAC]). The PPFS is a smaller version of the PFS that can be used on board the ISS in any location that has power and data connections.

A NASA-sponsored validation study of the PPFS was conducted in 2009, before it was delivered to the ISS (17). The metabolic gas analysis values from the PPFS were comparable to values obtained from a well-validated reference system ParvoMedics TrueOne© (PM) (2, 6, 7), and any statistically significant differences that did occur were not clinically relevant. However, the reproducibility of the PPFS measurements were not examined in the 2009 study, and results suggested that PPFS measurements of expired carbon dioxide ($FECO_2$) may differ from $FECO_2$ values measured by the reference system. The hardware design precluded measuring expired oxygen (FEO_2) or $FECO_2$ from both devices simultaneously, and further investigation was warranted.

The primary purpose of the current study was to examine the reliability and intra-subject repeatability of metabolic gas analysis data obtained from the PPFS during exercise tests that included both steady-state submaximal stages and maximal exertion levels. The secondary purpose was to collect FEO_2 and $FECO_2$ data simultaneously in a manner that would allow direct comparison of the data obtained from the PPFS and the data from the PM.

METHODS

Subjects

Eight healthy subjects (**Table 1**) volunteered to participate in this study. Subjects passed a modified Air Force Class III physical exam before they participated and received written and verbal explanations of test protocols before providing written informed consent. The NASA Johnson Space Center Committee for the Protection of Human Subjects reviewed and approved the test protocols and procedures.

Table 1. Subject Characteristics (mean ± SD). Reported VO_2max values were measured in the initial peak cycle test.

	Male (n=5)	**Female (n=3)**
Age (yr)	37.4 ± 11.5	29.7 ± 2.5
Weight (kg)	86.9 ± 11.2	54.4 ± 2.9
Height (cm)	179.8 ± 7.0	161.7 ± 5.3
VO_2max (ml/kg/min)	39.6 ± 4.6	40.8 ± 9.7

The cycle ergometer used for all testing was a LODE Excalibur Sport (Groningen, NL). The subjects fasted overnight before the testing sessions and consumed a standardized dietary supplement

(Ensure®, Abbott Laboratories) about 2 hours before testing. Dietary extremes affect metabolic gas analysis results (24), so the dietary control ensured that none of the subjects consumed either an extremely high-fat or high-carbohydrate meal before their tests. Tests were performed between 08:30 a.m. and 10:00 a.m., with one exception; scheduling constraints compelled one subject to perform a trial in the afternoon, 2 hours after consuming Ensure®. The subject ate a light breakfast early that morning but otherwise followed the constraints of the study. None of the subjects performed heavy exercise during the 24 hours before the testing sessions. Subjects also refrained from caffeine consumption for 12 hours prior to testing.

Peak Cycle Tests

Subjects performed an initial peak cycle test using the same protocol that astronauts performed to measure VO_2max before an ISS mission (20, 21). Subjects with a body mass of > 65 kg cycled for three minutes at 50, 100, and 150 watts (W) followed by stepwise increases of 25 W/min until peak exertion was reached. Subjects with body mass < 65 kg cycled for three minutes at 50, 75, and 100 W, followed by stepwise increases of 25 W/min until peak exertion was attained. The test was terminated by the subject at volitional exhaustion (i.e., the subject indicated that they could no longer continue) or the subject could not maintain a pedal cadence at or near 75 revolutions per minute. During this initial test, the PM system was used to analyze expired metabolic gases. VO_2 and work rate data from the first test was used to prescribe the protocol for PPFS reliability tests.

Each subject performed three additional peak cycle tests to obtain data from the PPFS to assess its reproducibility. This cycle exercise testing protocol, identical to that used for an ISS exercise study (16), consisted of three 5-minute stages designed to elicit 25%, 50%, and 75% of the individual's previously determined VO_2max (from the initial peak cycle test). These stages were followed by stepwise increases of 25 W/min work rate until subjects reached volitional exhaustion. The first of these repeatability trials was conducted within a month of the initial test, with subsequent trials separated from each other by at least a week to minimize the potential effects of residual soreness or fatigue. No more than three weeks elapsed between any two trials. Subjects were instructed to not substantially vary their physical activities between trials.

For all repeatability trials, prior to the start of exercise subjects rested quietly for five minutes in the seated position on the ergometer while resting heart rate (HR) and blood pressure (BP) were measured. HR and heart rhythm were measured electrocardiographically using the PPFS, which has an internal electrocardiogram (ECG) recording system. Volumes of expired gases along with HR were measured continuously throughout the exercise test protocol.

Metabolic Gas Analysis Systems

The PM system uses a paramagnetic oxygen analyzer (operating range 0%-25% O_2) and an infrared single-beam, single-wavelength carbon dioxide analyzer (operating range 0%-15% CO_2) to measure the composition of expired gases. The subject inspires through a two-way non-rebreathing valve (Hans Rudolph Model 2700, Kansas City, MO), and expired air composition is analyzed in a 4-liter mixing chamber. The inspired gas composition was assumed to be standard atmospheric values (i.e., 20.93% O_2 and 0.03% CO_2). Expired ventilation is measured using a Hans Rudolph Model 3813 linear pneumotach (operating flow range 0-800 L/min). Computational software is provided with the system. In the initial test, data were collected continuously by the PM system and were averaged in 30-second intervals to the nearest whole breath. For purposes of this study, the accepted value of VO_2max was taken as the highest VO_2 attained for a 60-second period (average of two consecutive 30-second values), which for all tests corresponded to the final minute of exercise.

The PPFS uses two types of technology for gas analysis. A photoacoustic method of gas analysis is used to measure CO_2 concentration. In this technique, the gas sample is exposed to intermittent infrared light. The gas sample absorbs the light, and the heat from the absorbed energy results in an increase in pressure in the sample chamber. The intermittent infrared light is divided into different pulsation frequencies and is filtered optically. Each optical filter allows only specific wavelengths of light to pass through. The wavelengths correspond to the infrared absorption spectra of the sample gases. When the light source is removed the gas cools down, resulting in a pressure fluctuation. Because the pulsation frequency is in the audible range, the pressure fluctuation becomes an acoustic signal that is detected by a microphone. The sounds recorded by the microphone are analyzed and the amplitude of each signal is used to calculate the gas concentration. The PPFS operating range for CO_2 concentration is from 0% to12%. An Oxigraf™ sensor in the PPFS is used for O_2 analysis. The Oxigraf™ uses a spectroscopy technique for laser diode absorption in which the sample gas is exposed to a laser with a wavelength of 760 nm (the peak of oxygen absorption). The laser signal is attenuated in proportion to the concentration of O_2 present in the sample. The PPFS operating range for O_2 concentration is from 0% to 100%. When using the PPFS during exercise testing, the subject inspires through a DAC custom-designed two-way non-rebreathing valve and the expired gases are sampled in a 15-liter anesthesia bag that serves as a mixing reservoir. Ventilation is measured on the inspired side of the non-rebreathing valve using a DAC custom-designed pneumotach (operating flow range 0-900 L/min). The technologies used for PPFS metabolic gas analysis are further described by Clemensen and colleagues (6). A proprietary software package developed by DAC, named ADAM, was used to compute metabolic gas analysis variables.

Expired Gas Sampling Comparisons

During the initial peak cycle test, fractions of expired oxygen (FEO_2) and expired carbon dioxide ($FECO_2$) were sampled concurrently by PPFS and the PM. The distal end of the PPFS gas sampling capillary tube was affixed adjacent to the gas sampling port of the PM (internal to the PM mixing chamber). Data collection from both devices was started at the same time under room-air conditions. Subjects breathed into the mixing chamber at seated rest for two minutes prior to the start of exercise. Following the exercise test, both the PM and the PPFS gas sample capillary tubes were extracted from the mixing chamber simultaneously. This produced a step function in the FEO_2 and $FECO_2$ data from each device, allowing precise synchronization of the two data streams. For statistical comparisons, data from each device were expressed as 30-second averages. A total of 217 paired FEO_2 and $FECO_2$ observations were obtained using this method.

STATISTICAL METHODS

The repeatability of maximal and sub-maximal gas-exchange data was assessed from the results of the three duplicate trials with the PPFS. Maximal values were derived for each outcome by averaging the final 60 seconds of exercise test data. These values were then analyzed using one-way ANOVA to estimate the within-subject standard deviation (WS SD) and the intra-class correlation coefficients (ICC). The within-subjects coefficients of variation (CV %) was calculated as the ratio of the WS SD to the mean value over all subjects expressed as a percentage. Outcome measures evaluated were: VO_2max (both L/min and ml/kg/min), maximum volume of carbon dioxide produced (VCO_2max, L/min), maximal respiratory exchange ratio (RERmax), maximal ventilation (V_E, L/min), maximal heart rate (HRmax, beats/min), oxygen pulse (ml/beat) and maximal watts obtained. Maximal watts were estimated by linear interpolation between the highest work rates in the last two 30-second intervals, and values were calculated based on time spent at the highest workload as a fraction of one minute. For example, if a subject terminated a test at 24 sec between 300W and 325W, the maximal watt value was recorded as 310W = 300W + (24/60) x 325W. A similar ANOVA model was used to assess repeatability in terms of WS SD, ICC, and CV% for the same outcome measures at each of the 25%, 50%, and 75% VO_2max sub-maximal exercise stages.

Paired values of FEO_2 and $FECO_2$ obtained from the PM and PPFS during the initial peak cycle test were compared with a mixed-model regression analysis that modeled each PPFS measurement as $\beta_0 + \beta_1$ times the corresponding PF measurement + random error. The random error component of the model allowed for differences between subjects in both slope (β_1) and intercept (β_0). After fitting the model, 95% confidence limits for β_0 and β_1 were obtained, and we also tested the joint null hypothesis that $\beta_1 = 1$ and $\beta_0 = 0$ (a perfect match).

RESULTS

Maximal Exercise

Table 2 contains the ICC, WS SD, and mean CV% values of the PPFS measurements at maximal exercise. Of these, the ICC values demonstrated very strong intra-subject reliability, with the notable exception of RER (ICC = 0.51). The CV for all variables were less than 6%. The individual and the mean values obtained at maximum exercise are shown in **Figure 1**. As shown in panel D, the RER values for two subjects were not stable, varying by as much as 0.16 from trial to trial. One of these subjects was the individual who performed the afternoon trial.

Table 2. Intraclass Correlation Coefficients (ICC), Within-Subject Standard Deviations (WS SD), and Coefficients of Variation (CV%) at Maximal Exertion.

Variable	ICC	WS SD	CV(%)
VO_2max (L/min)	0.98	0.11	3.6
VO_2max (ml/kg/min)	0.92	1.91	4.6
VCO_2max (L/min)	0.94	0.18	5.4
RERmax	0.51	0.05	4.0
$V_E$max (L/min)	0.94	6.34	5.6
HRmax	0.96	2.96	1.6
Oxygen Pulse (ml/beat)	0.98	0.53	3.1
Watts max	0.96	10.32	3.7

For this report the following convention was used when interpreting the ICC data: 0-0.2 indicates *poor* reliability, 0.3-0.4 indicates *fair* reliability, 0.5-0.6 indicates *moderate* reliability, 0.7-0.8 indicates *strong* reliability, and >0.8 indicates *very strong* reliability. (Adapted from: http://www.stattools.net/ICC_Exp.php#Interpretation%20of%20results)

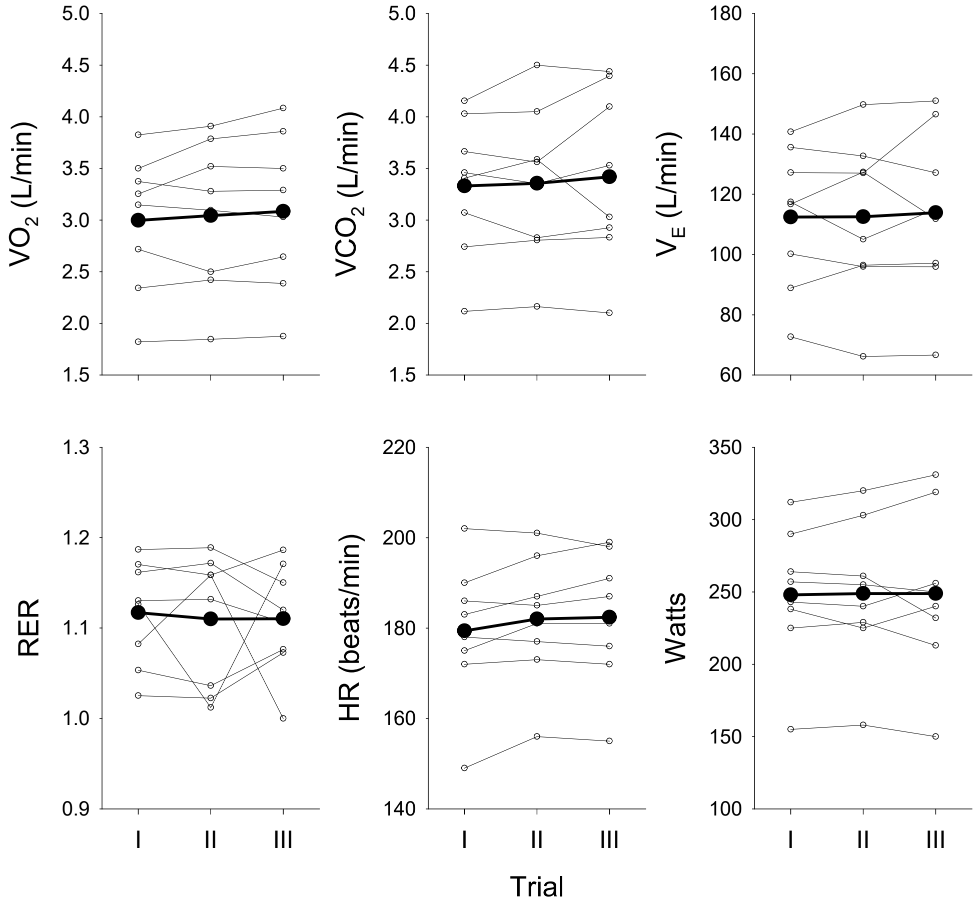

Figure 1. Metabolic gas analysis, HR, and work rate (watts) data measured at maximal exertion during three trials (I, II, III). The mean values are shown as dark circles connected by heavy, solid lines. Smaller, open symbols connected by thin lines represent the data from individual subjects.

Submaximal Exercise

Table 3 displays the ICC, WS SD, and mean CV% values of the dependent variables measured during the 25%, 50%, and 75% of VO_2max levels of exercise. As was the case for the maximal exercise values, the ICC data indicated strong to very strong intra-subject reliability for the variables studied with the exception of RER (ICC range 0.11 – 0.31). The mean CV did not exceed 7% for any combination of variables and in most cases was much lower than 7%. The individual and mean values for each level of exercise (**Figures 2-4**) appeared to be very reproducible, with the notable exception of the RER values (**Figure 3**).

Table 3. Intra-class Correlation Coefficients (ICC), Within-Subject Standard Deviations (WS SD), and Coefficients of Variation (CV%) during Submaximal Exercise

	25% VO_2max			50% VO_2max			75% VO_2max		
Variable	**ICC**	**WS SD**	**CV (%)**	**ICC**	**WS SD**	**CV (%)**	**ICC**	**WS SD**	**CV (%)**
VO_2 (L/min)	0.90	0.05	4.9	0.95	0.07	4.4	0.99	0.06	2.6
VCO_2 (L/min)	0.79	0.06	6.7	0.90	0.09	5.6	0.97	0.11	4.4
RER	0.31	0.04	4.4	0.11	0.04	4.0	0.24	0.03	3.2
V_E (L/min)	0.83	1.71	5.7	0.84	3.13	6.6	0.96	3.42	4.5
HR (beats/min)	0.93	5.07	5.2	0.87	5.92	4.7	0.93	4.16	2.7
Oxygen Pulse (ml/beat)	0.93	0.69	6.5	0.97	0.544	4.1	0.98	0.48	3.2

For this report the following convention was used when interpreting the ICC Data: 0-0.2 indicates *poor* reliability, 0.3-0.4 indicates *fair* reliability, 0.5-0.6 indicates *moderate* reliability, 0.7-0.8 indicates *strong* reliability, and >0.8 indicates *very strong* reliability. (Adapted from: http://www.stattools.net/ICC_Exp.php#Interpretation%20of%20results)

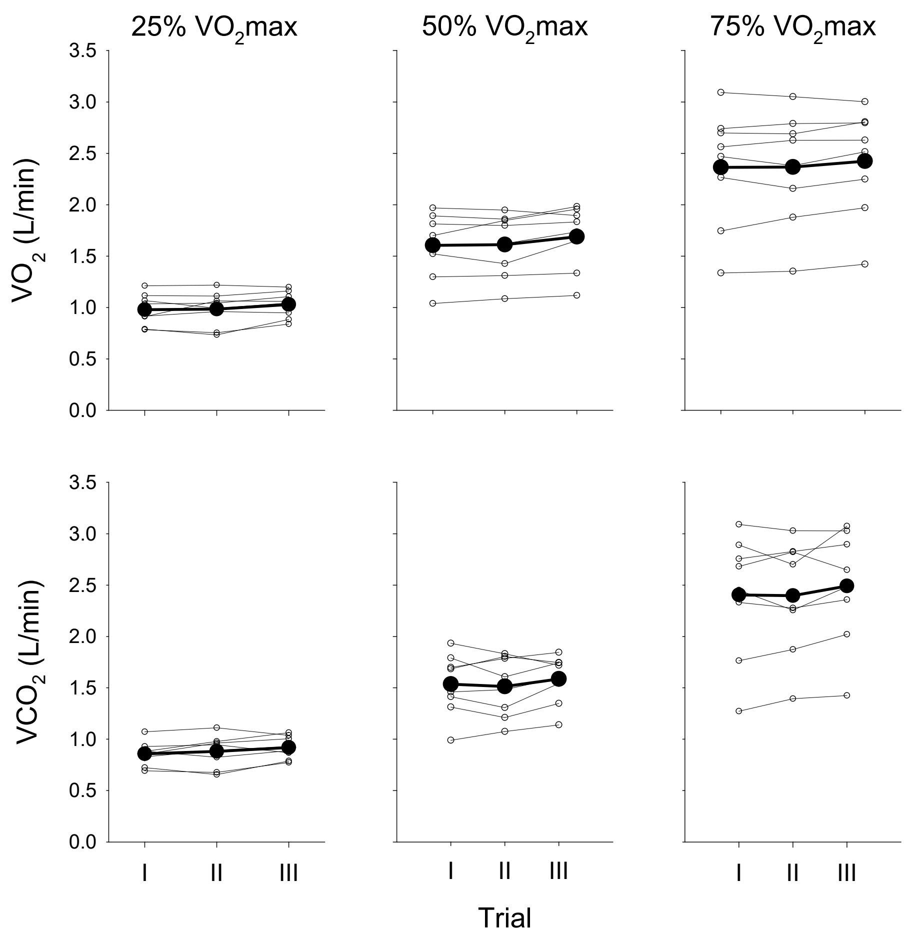

Figure 2. VO_2 and VCO_2 during submaximal exercise across the three trials (I, II, III). The mean values are shown as dark circles connected by heavy, solid lines. Smaller, open symbols connected by thin lines represent the data from individual subjects.

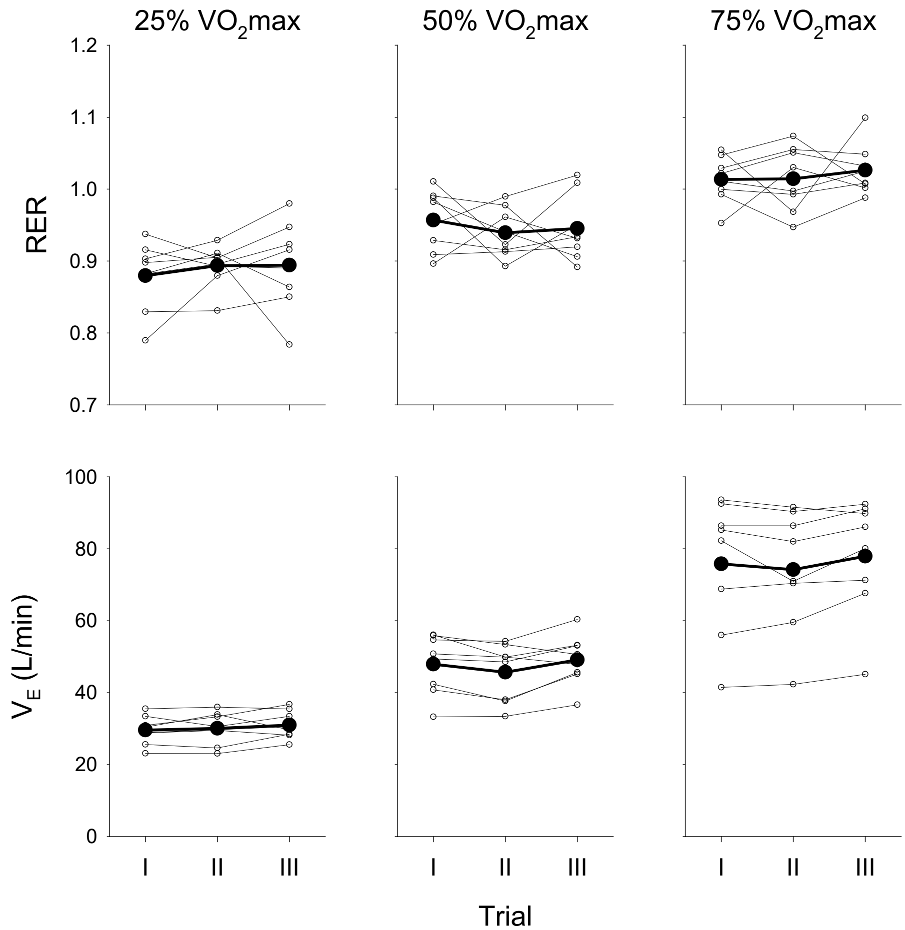

Figure 3. RER and V_E submaximal exercise data across the three trials (I, II, III). The mean values are shown as dark circles connected by heavy, solid lines. Smaller, open symbols connected by thin lines represent the data from individual subjects.

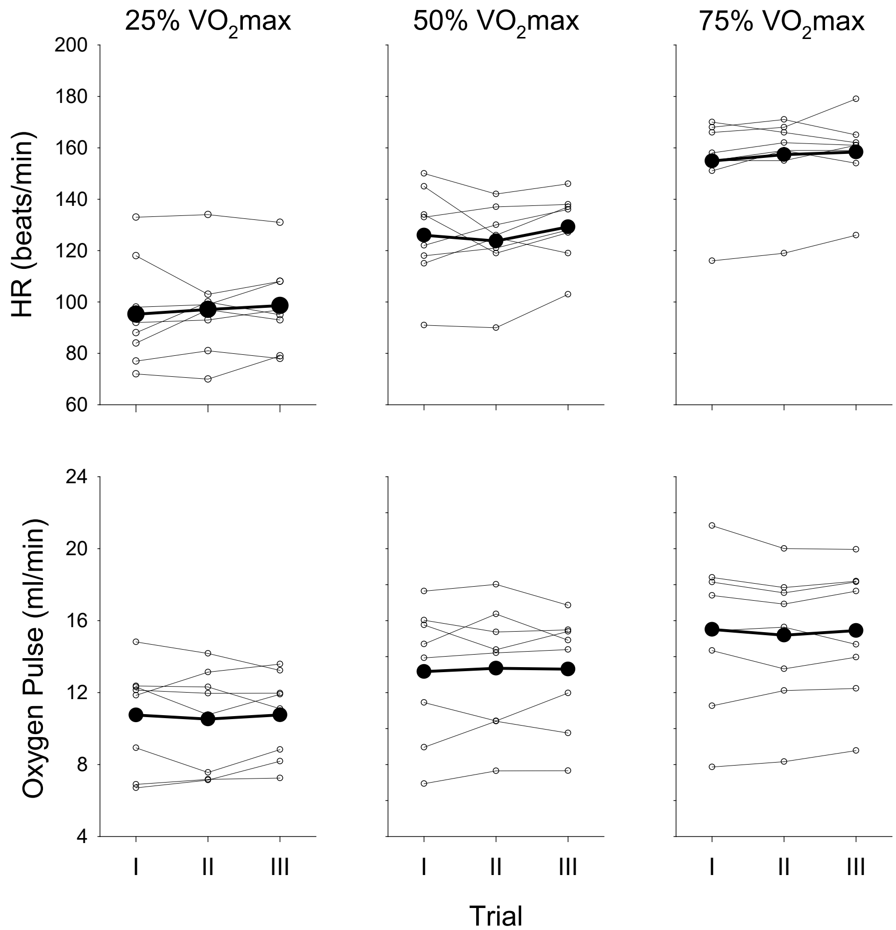

Figure 4. HR and oxygen pulse submaximal exercise data across the three trials (I, II, III). The mean values are shown as dark circles connected by heavy, solid lines. Smaller, open symbols connected by thin lines represent the data from individual subjects.

FEO_2 and $FECO_2$

Figure 5 shows the FEO_2 and $FECO_2$ values that were measured simultaneously using the PPFS and the PM systems. The FEO_2 data from the two devices were comparable. The estimated linear equation expressing the relationship between the devices was PPFS FEO_2= (0.982*PM FEO_2) + 0.265 ($\hat{\beta}_1 = 0.982$, $\hat{\beta}_0 = 0.265$). The values β̂1 and β̂2 were not significantly different from 1.0 and 0, respectively ($P = 0.55$, joint test). The $FECO_2$ data collected from each of the devices also matched fairly well, but not as closely as the FEO_2 data; the estimated relationship was PPFS $FECO_2$= (0.921*PM FEO_2) + 0.390 ($\hat{\beta}_1 = 0.923$, $\hat{\beta}_0 = 0.390$). While there was not enough evidence ($p = 0.11$, joint test) to show a significant departure from the optimal values $\beta_1 = 1$ and $\beta_0 = 0$, the 95% confidence interval for β_1 (0.84, 1.00) indicated a probable reduced gain ($\beta_1 < 1$) in PPFS output relative to changes in PF measurements (**Fig. 5B**).

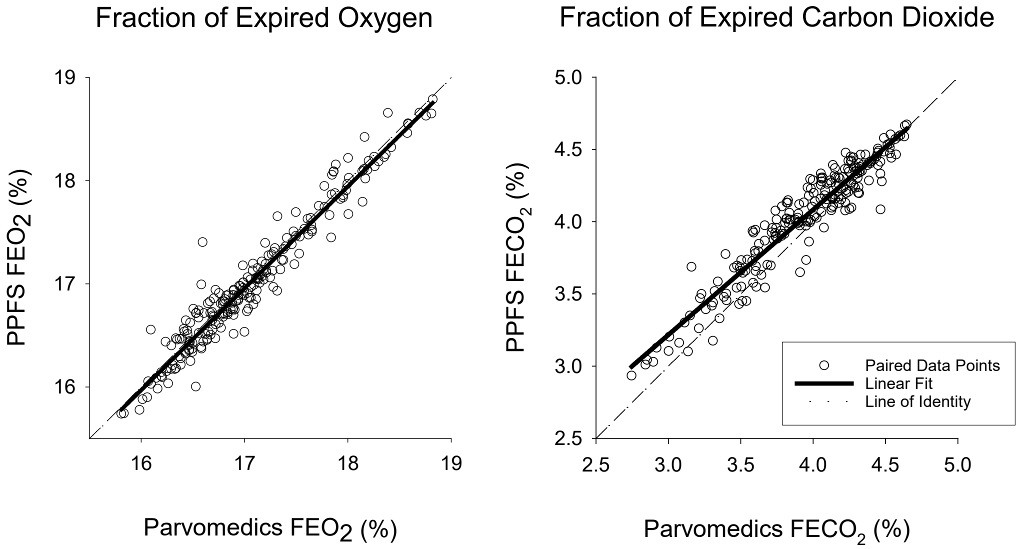

Figure 5. The FEO_2 (left panel) measured by the two devices were comparable; the slope of the line describing their relationship did not differ from 1.0 and its intercept did not differ from 0. The $FECO_2$ (right panel) measured by two devices also were highly related. However, for $FECO_2$, the slope of the line describing the relation between the measurements from the two devices was slightly less than 1.0. Future investigators may consider using a calibration factor when using the PPFS $FECO_2$ values for metabolic calculations.

DISCUSSION

The primary finding of this study is that gas analysis measurements obtained with the PPFS were very repeatable, with the exception of the RER (see below). The secondary finding of this study was that while FEO_2 values from the PPFS and PM were strongly correlated, values of $FECO_2$ obtained with the PPFS tended to be lower than corresponding values observed with the PM.

Maximal Exercise

The mean values for PPFS-measured VO_2, VCO_2, V_E, RER, HR, and watts at maximal exercise were consistent across the three repeatability trials (**Figure 1**). The intra-class correlation coefficients indicated very strong reliability (i.e., agreement between the trials for each subject) for all outcome variables studied, with the exception of RER, which only moderate repeatability (ICC = 0.51, **Table 2**). These findings are similar to ICC values reported from repeated exercise trials in other studies. For example, in a study reporting reliability of physiological measurements of walking economy, the ICCs of VO_2, V_E, HR and RER were 0.92, 0.92, 0.90, and 0.31, respectively (25). The vast majority of studies on the reliability of gas exchange measurements do not report ICC values of RER data. Because RER is a ratio derived from two other gas exchange measurements (RER = VCO_2/VO_2), it is likely that investigators consider reporting it to be redundant and unnecessary. However, as shown in the current study, the RER response to exercise can be quite variable even if the measurements of VO_2 and VCO_2 are highly reliable. The RER during exercise can be influenced by a number of factors, including pre-exercise diet, muscle fiber type, muscle glycogen content, lactate metabolism, and training volume (8). Although our subjects' diet was controlled before the tests and subjects refrained from heavy exercise the day before their tests, it is obvious that these restrictions did not completely remove variation in the RER response to exercise.

The CVs estimated from our subjects' maximal data agree with values reported in the literature for VO_2max (**Table 4**). For the outcome variables we studied, CV values ranged from 1.6% to 5.6% and in particular, the CV for VO_2 observed in this study (3.6%) agrees strongly with those reported from the multiple studies in **Table 4.** The implication is that a VO_2max variation of ± 3.6% with the PPFS is about as good as one could expect, even from ground-based hardware. If changes in VO_2max are greater than 3.6%, it is highly likely that VO_2max is being influenced by factors such as deconditioning, improvement in aerobic fitness, or motivation to perform the test. Mean VO_2max is reduced by approximately 20% compared to pre-flight after short-duration missions (~2 weeks) (14, 18), and VO_2max decreased by about 15% after long-duration missions (>90 days) (16). These changes in VO_2max that are well within the detection range for the PPFS.

Table 4. Summary of previous studies and their reported CV for VO_2. The higher values reported are from evaluations of metabolic gas analysis systems that produce less consistent results.

Citation	Measure	CV (%)
Armstrong and Costill (1)	Submaximal VO_2	4.4
Brawner et al. (3)	VO_2max	5.1
Carter and Jeukendrup (4)	VO_2 @ 100 and 150 watts	2.3 – 19.8*
Crouter et al. (7)	VO_2 (submax. to max. levels)	4.7 – 14.2*
Vilhena de Mendonça and Pereira (25)	VO_2max	8.6
Jensen and Johansen (10)	VO_2max	1.9
Katch et al. (11)	VO_2max	3.7-7.3
Kuipers (12)	VO_2max	7.6
Kuipers et al. (13)	VO_2max	7.9
Rosdahl et al. (22)	VO_2max	1.7-3.4
Wright et al. (26)	VO_2max	5.1-6.8

Submaximal Exercise

The mean values of VO_2 and VCO_2 (**Figure 2**), RER and V_E (**Figure 3**), and the HR and O_2pulse (**Figure 4**) collected during the 25%, 50%, and 75% levels of exercise were very stable from one session to the next. As was the case for the maximal exercise data, the RER value exhibited the greatest amount of variation, with the intra-class correlation coefficients ranging from 0.11 to 0.31 (**Table 3**). The other variables examined indicated strong to very strong reliability between test sessions. The CV values were within the 3%-7% range. For RER, even though the ICC values indicated poor reliability, the CV ranged from 3.2% to 4.4%, a value that is very consistent with published data (**Table 5**).

Table 5. A summary of previous studies and their reported CV for RER. The higher values reported are from evaluations of metabolic gas analysis systems that produce less consistent results.

Citation	Measure	CV (%)
Carter and Jeukendrup (4)	RER @ 100 and 150 W	3.2-11.7*
Vilhena de Mendonça and Pereira (25)	RER max	5.9
Goedecke et al. (8)	RER @ 25, 50, 75% W max	1.4–2.0
Rosdahl et al. (22)	RER max	1.2-8.0*

FEO_2 and $FECO_2$

FEO_2 values obtained from the PM and the PPFS ranged between 15.7 and 19.0% and were comparable (**Figure 5**). The coefficient of determination (R^2) of the relationship was >0.99 and the joint test of slope and intercept indicated no significant differences between 1.0 (95% conf. (0.92, 1.05)) and 0 (95% conf. (-0.81, +1.28)), respectively. These statistical results indicate that for practical purposes, the devices could be expected to yield similar results (19). Although the coefficient of determination also was quite high for the PPFS vs. PM relationship for $FECO_2$ ($R^2 > 0.99$), and the joint test of slope and intercept did not reject the hypothesized respective values of 1.0 and 0 (P = 0.11), the 95% confidence limits for the slope (0.84, 1.00) suggested a probable reduced gain. In this respect, the $FECO_2$ data from the two devices did not match as well as the FEO_2 values. We examined the expired gas fraction in the present study because the PPFS measurements of $FECO_2$ and VCO_2 were lower than the values from the PM in a previous study (17). This trend was verified in our current study. Therefore, it is possible that a calibration factor (equation) could be applied to the $FECO_2$ values obtained by the PPFS and adjusted values incorporated into the metabolic calculations performed by the PPFS. The ADAM software can do this with relative ease. Using the data from our study, we obtained the PPFs response model PPFS-$FECO_2$= 0.921*PM- $FECO_2$ + 0.390, based on the assumption that the PM is a "gold standard" device. The PM has been well validated for measurements of metabolic gas exchange at levels ranging from rest to peak exercise (2, 6, 7). We have been using the PM device in our laboratory since 2004 for routine pre- and post-flight testing of astronauts, and we performed an unpublished evaluation of the PM analyzer vs. mass spectrometer measurements of expired respiratory gases that showed excellent agreement of data. This PPFS response model could then be inverted to give the calibration equation:

$$FECO_2(\text{calibrated}) = (\text{PPFS-}FECO_2 - 0.390)/0.921.$$

Other Issues

Devices such as the PM, which assume normal room air concentrations of inspired air, cannot be used on the ISS because, under nominal circumstances ISS cabin O_2 concentrations are allowed to range from 19.2% to 23.5% at a pressure of 760 mmHg. CO_2 concentrations are typically in the 0.25%-0.5% range on the ISS, although 0.7% is the highest permissible level for long-term exposure and up to 1.0% is permissible for exposure of less than 24 hours (NASA ISS Generic Flight Rules, Volume B, 2011; online at http://mod.jsc.nasa.gov/da8/rules/vol_b/rules.htm).

Room or cabin air gas composition also affects PPFS output; however the PPFS software is designed to incorporate and adjust for environmental measurements before each data analysis. During the current investigation, we used the same computational approach in our ground study as used in ISS operations. The PPFS acquires samples of both inspired and expired gases on a breath-by-breath basis (although mixing bag values are used for obtaining mixed-expired gas samples). Prior to testing, while the subject is in the resting phase and is connected to and breathing through the respiratory valves, samples of inspired concentrations (end inspiratory tidal) levels of O_2 and CO_2 are measured. These values are used in the subsequent metabolic calculations. The mean (±SD) "room air" value for O_2 measured by the PPFS in our investigation was 21.04 ± 0.13 %, which is not significantly different from the "normal" atmospheric value of 20.93%. In contrast, the "room air" concentration of CO_2 measured by the PPFS was 0.16 ± 0.03 %, which is about five times normal atmospheric values (0.03%). Although we are unsure of the cause, this is not surprising given that PPFS $FECO_2$ values were higher than PM values at the lower exercise intensities. However, the elevated level of CO_2 in the testing room does add a source of error into the metabolic calculations. Elevated room air CO_2 within the range we observed has a negligible effect on VO_2 calculations (<0.5 % difference in VO_2). However, when 0.16% instead of 0.03% is used as the room air value for inspired CO_2, VCO_2 values at all levels of exercise are lower by about 3% (assuming that the measured $FECO_2$ value is correct). Whereas this does not explain the instability of the RER measurements in this study, the ~3% reduction in VCO_2 is partially responsible for the RER value not reaching 1.1 (a value consistent with true maximal effort) during some of our tests. Judging from their appearance, subjective comments, and reported ratings of perceived exertion, we believe all our subjects gave maximal efforts during the tests.

In a previous PPFS validation study (17), we reported a 6.1% higher mean VO_2max when it was measured using the PM than when using the PPFS (PM: 3.32 ± 0.87 L/min, PPFS: 3.11 ± 0.75 L/min). We hypothesized that the difference in VO_2max was likely due to inspiratory and expiratory flow restrictions imposed by the PPFS cardiac output valve. Although it was not an objective of our current study, thus not reported in the results, the mean (± SD) VO_2max value measured by the PM in our initial test was 2.91 ± 0.70 L/min vs. 3.00 ± 0.66 L/min measured by the PPFS in the first of the three reliability trials. A paired *t*-test shows that this is not a significant difference (P=0.12). Granted, the testing protocols used to measure VO_2max at maximum exertion were different for the two devices in the current study, but nevertheless the result indicates that the PM and PPFS yield similar values for VO_2max. It is possible that simple random interactions between our subjects and the devices contributed to the higher PM values in our first evaluation.

Throughout this report oxygen consumption measured at maximal exertion during the peak cycle tests has been referred to as "VO_2max." This is technically not the correct terminology for our measurement because we performed no specific verification of a plateau in oxygen consumption with increasing work rates, which is the criterion for "true" VO_2max (23). However, not all individuals can attain this plateau and previous comparisons have reported no statistical difference between VO_2max and peak oxygen consumption, which is the correct description for the variable reported here. Further, because the terms VO_2max and peak oxygen consumption have been used interchangeably in various spaceflight and bed rest publications, we have chosen to use only "VO_2max" in the description of test results contained in this report.

CONCLUSIONS

In practically all respects the PPFS yielded highly reliable metabolic gas analysis data. RER was the only output variable that exhibited poor to fair intra-subject agreement; however, RER has been reported to be a physiologic response that exhibits poor ICC, and the CV of RER measured in this study for matches those published by others. The elevated levels of CO_2 in the testing room and lower concentrations of CO_2 measured during exercise should have been be more thoroughly controlled and/or accounted for, as they might have resulted in slightly lower VCO_2 values calculated by the PPFS. However, these observations regarding CO_2 measures seem to be stable, and all data collected using the PPFS would contain a similar bias. To clarify this, we recommend collecting more data to better calibrate the PPFS CO_2 values.

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APPENDIX A – ACRONYM LIST

BP	Blood Pressure
CO_2	Carbon Dioxide
CV%	Coefficients of Variation
$FECO_2$	Fractions of Expired Carbon Dioxide
FEO_2	Fractions of Expired Oxygen
HRP	Human Research Program
ICC	Intraclass Correlation Coefficients
ISS	International Space Station
NASA	National Aeronautics and Space Administration
O_2	Oxygen
PM	ParvoMedics TrueOne
PFS	Pulmonary Function System
PPFS	Portable Pulmonary Function System
RER	Respiratory Exchange Ratio
RERmax	Maximal Respiratory Exchange Ratio
V_E	Expired Ventilation
VCO_2	Carbon Dioxide Production
VCO_2max	Maximal Carbon Dioxide Production
VO_2	Oxygen Consumption
VO_2max	Maximal Oxygen Consumption
W	Watt
WS SD	Within-Subject Standard Deviations