

# Evaluation of the Danish Aerospace Corporation Portable Pulmonary Function System

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## ABSTRACT

A research project designed to investigate changes in maximal oxygen consumption ( $\text{VO}_2\text{max}$ ) during and following long duration flight on the International Space Station (ISS) has recently been completed. The device used to measure oxygen consumption ( $\text{VO}_2$ ) on board ISS, the Portable Pulmonary Function System (PPFS) manufactured by the Danish Aerospace Corporation (DAC), is based on previous-generation devices manufactured by DAC, but the PPFS has not been validated for analyzing metabolic gases or measuring cardiac output (Qc). The purpose of the present evaluation is to compare PPFS metabolic gas analysis measurements to measurements obtained using a clinically-validated system (ParvoMedics TrueOne© 2400 system; Parvo). In addition, Qc data collected with the PPFS were compared to Qc measurements from echocardiography. **METHODS:** Ten subjects completed three cycle exercise tests to maximal exertion. The first test was conducted to determine each subject's  $\text{VO}_2\text{max}$  and set the work rates for the second and third (comparison) tests. The protocol for the two comparison tests consisted of three five-minute stages designed to elicit 25%, 50%, and 75%  $\text{VO}_2\text{max}$  (based upon results from the initial test), followed by one-minute stages of increasing work rate (25 watts/minute) until the subject reached maximal effort. During one of the two comparison tests, metabolic gases and Qc were assessed with the PPFS; metabolic gases and Qc were assessed with the Parvo and by echocardiography, respectively, during the other test. The order of the comparison tests was counterbalanced.  $\text{VO}_2\text{max}$  and maximal work rate during the comparison tests were compared using *t* tests. Mixed-effects regression modeling was used to analyze submaximal data. **RESULTS:** All of the data were within normal physiological ranges. The PPFS-measured values for  $\text{VO}_2\text{max}$  were 6% lower than values obtained with the Parvo (PPFS:  $3.11 \pm 0.75$  L/min; Parvo:  $3.32 \pm 0.87$  L/min; mean  $\pm$  standard deviation;  $P = 0.02$ ); this difference is probably due to flow restriction imposed by the PPFS Qc accessories. Submaximal  $\text{VO}_2$  values were slightly lower when measured with the PPFS, although differences were not physiologically relevant. The PPFS-measured values of submaximal carbon dioxide production ( $\text{VCO}_2$ ) were lower than the data obtained from Parvo, which could be attributed to lower fractions of expired carbon dioxide measured by the PPFS. The PPFS Qc values tended to be lower than echocardiography-derived values. **CONCLUSIONS:** The results of the present study indicate a need to further examine the PPFS and to better quantify its reproducibility; however, none of the findings of the current evaluation indicate that the PPFS needs to be modified.

## INTRODUCTION

The National Aeronautics and Space Administration (NASA) Human Research Program (HRP) has developed an integrated research plan to address the health risks that might impede human exploration beyond Earth's orbit (Human Research Program Integrated Research Plan, NASA HRP 47065). One of the risks identified by NASA's Integrated Research Plan is the "Risk of reduced physical performance capabilities due to reduced aerobic capacity."

Maximal oxygen uptake ( $VO_{2max}$ ), also known as aerobic capacity, is the maximal rate at which a person can consume oxygen ( $O_2$ ) during exercise, and is directly related to the ability to perform prolonged and strenuous work (1, 2). There is clear evidence from bed rest studies (10) and short-duration spaceflight that  $VO_{2max}$  is reduced after exposure to both simulated and actual microgravity (12, 16), particularly when minimal or no exercise is performed during the exposure period. However, results from longer spaceflight missions, based upon submaximal exercise test results, have been less clear. During the Skylab missions, submaximal exercise testing was performed approximately every six days, and there appeared to be no overall trend (increase or decrease) in the heart rate (HR) response to standard exercise work rates (up 75% of pre-flight  $VO_{2max}$ ). These results were interpreted to indicate that  $VO_{2max}$  was unchanged during missions up to three months in duration (14, 15, 21). Similar submaximal exercise tests were performed each month during early ISS missions. In contrast to Skylab results, ISS crewmembers experienced an elevated HR response to exercise in the first weeks of the mission, which suggested that  $VO_{2max}$  may have been compromised, but there appeared to be some recovery over the course of a six-month mission (18). In the first week after landing, the HR responses to exercise of both the Skylab and ISS crew members were elevated, which is consistent with a decline in  $VO_{2max}$ . Multiple factors other than aerobic deconditioning can influence the HR response to exercise and given the error in estimating  $VO_{2max}$  from submaximal exercise data (11), it was unclear until recently (16) how much, or even if,  $VO_{2max}$  is affected by long-duration spaceflight.

Oxygen uptake during exercise ( $VO_2$ ) is influenced by both central (related to the heart) and peripheral (related to  $O_2$  extraction and distribution of blood flow in the muscle tissues) factors. The relationship between these factors is expressed in a relation commonly known as the Fick equation (20):

$$VO_2 = Q_c (a-v)O_2 \text{ difference}$$

in which cardiac output ( $Q_c$ ) is the amount of blood pumped from the heart's left ventricle per minute and is the product of HR and the volume of blood ejected from the left ventricle per beat (also known as stroke volume [SV]). Arterial to venous  $O_2$  difference "(a-v) $O_2$ " is the difference between  $O_2$  levels in the arterial and venous blood, i.e.  $O_2$  extraction of the tissues. Thus, any factor that influences HR, SV, or  $O_2$  extraction may influence  $VO_2$  or  $VO_{2max}$ .

A contractor to the European Space Agency, Damec Research ApS (currently named Danish Aerospace Corporation [DAC]), developed a metabolic gas analysis system capable of measuring  $VO_2$  on board ISS. This device, named the Portable Pulmonary Function System (PPFS), was used to measure astronauts'  $VO_{2max}$  during long-duration space flight (16). The current report describes our efforts to validate measurements obtained from the PPFS by comparing PPFS measurements of metabolic gas analysis obtained during exercise tests with equivalent measurements obtained using the ParvoMedics TrueOne© 2400 system (ParvoMedics, Sandy, UT). The ParvoMedics system has been validated (8) for accurate measurement of  $VO_2$  and has been used in the Exercise Physiology Laboratory at NASA Johnson Space Center since 2004 but was not designed for use on ISS. The second purpose of the present study was to compare the non-invasive measurements of  $Q_c$  obtained by the PPFS to measurements obtained using echocardiography.

## METHODS

### *Subjects*

Ten healthy volunteers participated in the ground-based study described here (**Table 1**). Subjects passed a modified Air Force Class III physical exam before they participated in the study 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  $\pm$  SD) BY SEX.

	Male	Female
<b>n</b>	6	4
<b>Age (yr)</b>	37.5 $\pm$ 9.5	36.0 $\pm$ 9.2
<b>Weight (kg)</b>	80.1 $\pm$ 10.6	55.6 $\pm$ 2.6
<b>Height (cm)</b>	180.8 $\pm$ 4.3	162.6 $\pm$ 4.1
<b>VO<sub>2</sub>max (ml/kg/min)</b>	48.7 $\pm$ 9.3	46.2 $\pm$ 5.0

### *Overall Protocol*

Subjects performed three peak cycle tests to measure VO<sub>2</sub>max. The LODE Excalibur Sport (Groningen, NL) cycle ergometer was used for all testing.

The initial peak cycle test used the same protocol used to measure the pre-flight VO<sub>2</sub>max in astronauts before early ISS missions (18). During the initial test, subjects with a body mass of > 65 kg cycled for three minutes each at 50, 100, and 150 watts (W), after which work rate was increase 25 W/minute until maximal exertion. If the subject's body mass was < 65 kg, the subjects cycled for three minutes each at 50, 75, and 100 W, after which work rate increased 25 W/minute until maximal exertion. If an individual who was <65 kg reported that they regularly participated in cycle exercise, the first protocol described above was used for this initial test. For either protocol, the work rate was increased until subjects indicated that they could no longer continue or until they could no longer maintain a pedal cadence of 75 revolutions per minute. During this initial test, the ParvoMedics TrueOne© (ParvoMedics, Salt Lake City, UT) system was used to perform metabolic gas analysis. The VO<sub>2</sub> and work rate data from the initial test were used to design the protocol for the second and third (comparison) tests.

The second and third tests were designed to compare the metabolic gas analysis and Qc measurements from the two different devices. The testing protocol for these comparison tests was based on the submaximal cycle test used by Skylab astronauts (14, 15, 21) and for the ISS Periodic Fitness Evaluation during early ISS mission (18), but the protocol was extended to achieve VO<sub>2</sub>max. Specifically, the protocol for the comparison tests consisted of three five-minute stages designed to elicit 25%, 50%, and 75% of the individual's VO<sub>2</sub>max that was previously determined from the initial peak cycle test. The three initial stages were followed by work rate increases of 25 W/minute until subjects reached their maximal effort. This is the same exercise protocol that was used in a study of ISS astronauts (16). Comparison tests were performed in a counterbalanced order; one test was performed using the ParvoMedics TrueOne© system paired with echocardiography to measure Qc, and one test was performed using the PPFS to obtain metabolic gas analysis data and Qc measurements using a rebreathing technique. These tests were repeated within one month of the initial test, and the two tests were separated by at least one week to minimize the potential effects of residual soreness or fatigue.

Before starting the exercise, the subjects rested quietly for five minutes in supine and seated positions while measurements of HR, heart rhythm, and blood pressure (BP) were taken. HR and rhythm were measured electrocardiographically (Q-Stress, Quinton Instruments, Seattle, WA), and BP



was measured using a mercurial sphygmomanometer and stethoscope. HR, heart rhythm, and metabolic expired gas were measured continuously throughout the test. BP was measured once during each submaximal exercise stage, and ratings of perceived exertion (5) were reported during the last 30 seconds of each stage. BP was recorded during the recovery period after the test, and the subject was monitored for any adverse effects caused by maximal physical exertion.

### ***Metabolic Gas Analysis Systems***

The dependent variables for comparisons between the two systems were  $\text{VO}_2$ , carbon dioxide production ( $\text{VCO}_2$ ), expired ventilation ( $\text{V}_E$ ), and fractions of expired oxygen and carbon dioxide ( $\text{FEO}_2$  and  $\text{FECO}_2$ ).

ParvoMedics TrueOne© system uses a paramagnetic  $\text{O}_2$  analyzer (operating range 0-25%  $\text{O}_2$ ) and an infrared single-beam, single-wavelength, carbon dioxide ( $\text{CO}_2$ ) analyzer (operating range 0-15%  $\text{CO}_2$ ) to measure the composition of expired gases. The subjects inspired through a two-way non-rebreathing valve (Hans Rudolph Model 2700, Kansas City, MO) and expired air composition was sampled from a four-liter mixing chamber. The inspired gas composition was assumed to be standard atmospheric values (i.e., 20.93%  $\text{O}_2$  and 0.03%  $\text{CO}_2$ ).  $\text{V}_E$  was measured using a Hans Rudolph Model 3813 linear pneumotachometer (operating flow range 0-800 L/min). Computational software was provided with the system. Data were collected continuously by the ParvoMedics system and were averaged in 30-second intervals to the nearest whole breath.  $\text{VO}_{2\text{max}}$  was accepted as the highest  $\text{VO}_2$  attained for a single 30-second period.

The PPFS uses two types of technology for gas analysis. A photoacoustic method of gas analysis is used to measure  $\text{CO}_2$  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  $\text{CO}_2$  concentration is from 0% to 12%. An Oxigraf™ sensor in the PPFS is used for  $\text{O}_2$  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  $\text{O}_2$  absorption). The laser signal is attenuated in proportion to the concentration of  $\text{O}_2$  present in the sample. The PPFS operating range for  $\text{O}_2$  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. Similar to the Parvomedics data reduction, the data were averaged in 30-second intervals to the nearest whole breath.

### ***Cardiac Output Measurements***

To obtain  $\text{Q}_c$  measurements from echocardiography, two-dimensional imaging was used to obtain the aortic annulus diameter (d) from the parasternal long axis during supine rest before the exercise tests. Continuous-wave Doppler from the apical window (2- to 4-MHz phase array probe, iE33, Phillips Ultrasound, Andover, MA) was used to obtain aortic blood velocity time integral in three to five heartbeats during the last minute of rest and each five-minute exercise stage. Images were stored digitally for offline analysis and independently analyzed by two experienced, registered sonographers.

Aortic annulus area ( $\pi \cdot d^2/4$ ), stroke volume (annulus diameter x velocity time integral), and Qc (stroke volume x heart rate) were calculated.

Qc measurements using the PPFS involved subjects rebreathing into and out of a bag containing 2.5-3.5 liters of a gas composed of 1% Freon R-22, 1% sulfur hexafluoride (SF<sub>6</sub>), 40% O<sub>2</sub>, and 58% N<sub>2</sub>. The subjects started the rebreathing procedure after an exhalation at a self-selected time point during seated rest and within the last minute of each five-minute stage of exercise. The rebreathing protocol consisted of eight breaths (approximately 30 seconds during rest and 20 to 25 seconds during exercise). The ADAM software calculated Qc using formulas that are described elsewhere (4). Briefly, Qc was calculated using the rate of disappearance of Freon R-22 (a blood-soluble gas) from the rebreathed air as measured from the end-tidal expiratory gas fractions. Adequate gas mixing in the lungs, required for accurate Qc measurements, was determined by measuring the end-tidal expiratory gas fractions of SF<sub>6</sub> (a blood-insoluble gas). Freon R-22 and SF<sub>6</sub> were sampled through a Nafion<sup>®</sup> catheter connected to a port adjacent to the mouthpiece of the PPFS.

### ***Statistical Methods***

The PPFS measures were compared to those obtained with the Parvomedics device using expected and actual responses to a range of workloads experienced by the subjects during submaximal exercise. To achieve this comparison, we used mixed-effects regression models (7) to estimate the mean output of gas measurements (VO<sub>2</sub>, VCO<sub>2</sub>, V<sub>E</sub>, FEO<sub>2</sub> and FECO<sub>2</sub>) obtained on the Parvomedics device as either a linear or a quadratic function of work rate (depending on the type of output), allowing for random subject differences and within-subject measurement errors. We then used another mixed-effects regression model to estimate the bias (mean difference between the two devices: PPFS – Parvomedics) as a function of the mean. From this second regression model, we also calculated 95% confidence limits for the bias, which are displayed for each of the measurements. The plots are similar to Bland-Altman plots (3), except that in our case, by modeling the physiological responses as functions of workload, we make allowance for repeated measures on subjects as well as reduce sensitivity to the effect of measurement errors in the standard device (in this case, the Parvomedics). The mean VO<sub>2</sub>max and maximal work rate attained during the tests with each device were also compared using paired *t* tests.

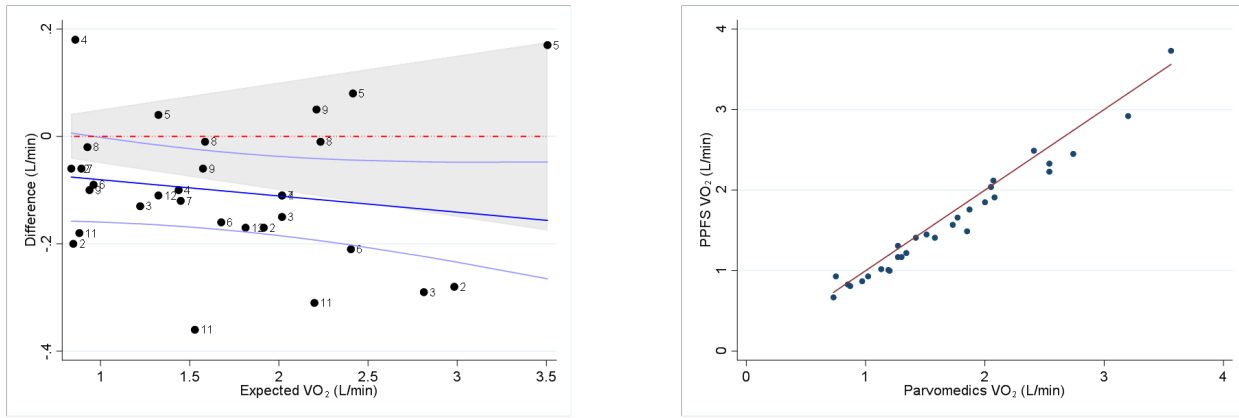
The analysis of the PPFS and echocardiographic Qc and SV data followed a strategy similar to that used for the metabolic gas analysis comparisons, with one important difference: because there is no compelling evidence in the literature to suggest that either of the methods should serve as a standard (17), the data collected from each device was modeled as a function of cycle ergometer work rate.

## **RESULTS**

### ***Submaximal Exercise***

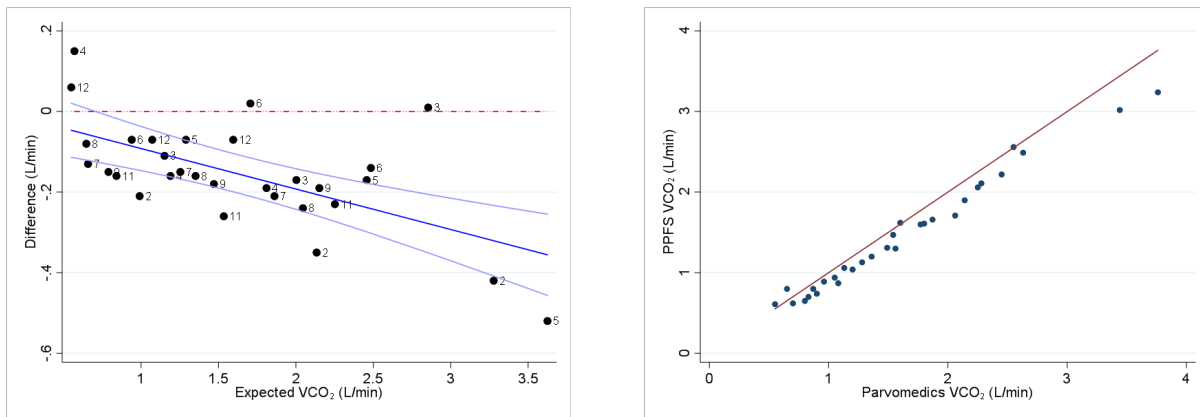
All of the metabolic gas analysis data, irrespective of the device used for measurement, were within normal physiological ranges. Thus, there were no gross errors in output from either the PPFS or the Parvomedics system.

Comparisons of the absolute VO<sub>2</sub> values measured by the two devices are shown in **Figure 1**. In general, the PPFS-measured values were lower than those measured by the Parvomedics system.



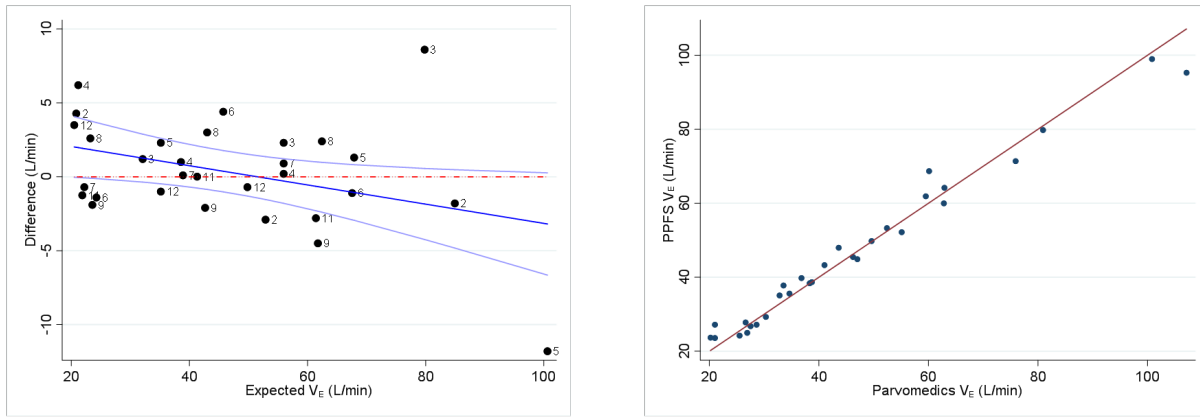
**Figure 1.**  $VO_2$  values observed during the submaximal stages of testing. The left panel displays the observed differences (PPFS-Parvomedics) between the two devices. Expected  $VO_2$  (x-axis) for each exercise level is predicted from the relationship between  $VO_2$  and work rate for these subjects, as measured by the Parvomedics (the “clinical standard” device). The numbers displayed next to the data points are subject identifiers (three data points for each subject). The gray shaded area indicates  $\pm 5\%$  of the expected  $VO_2$ . The solid straight line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the  $VO_2$  values of the two devices evaluated. The solid line is the line of identity.

The  $VCO_2$  data are displayed in **Figure 2**. As was the case for  $VO_2$ , the PPFS values were lower than the data measured by the Parvomedics system. The disparity between the two devices increased as the values of  $VCO_2$  rose.



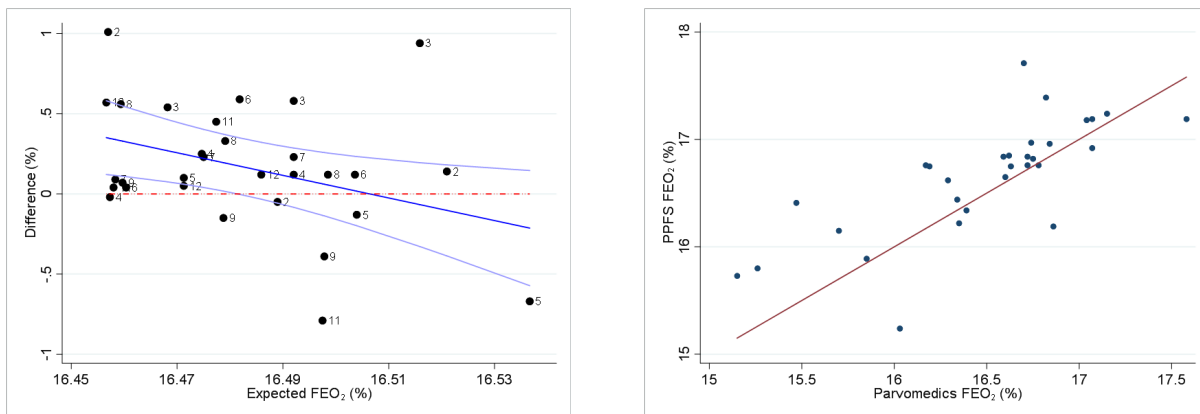
**Figure 2.**  $VCO_2$  values observed during the submaximal stages of testing. The left panel displays the observed differences (PPFS-Parvomedics) between the two devices. Expected  $VCO_2$  (x-axis) for each exercise level was predicted from the relationship between  $VCO_2$  and work rate for these subjects, as measured by the Parvomedics device. The numbers displayed next to the data points are subject identifiers (three data points for each subject). The solid straight line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the  $VCO_2$  values of the two devices evaluated. The solid line is the line of identity.

**Figure 3** illustrates the ventilation data. The values from the PPFS and the Parvomedics were quite close; the 95% confidence intervals of the difference between the two devices contained zero (no difference) throughout the range of data observed in the evaluation.



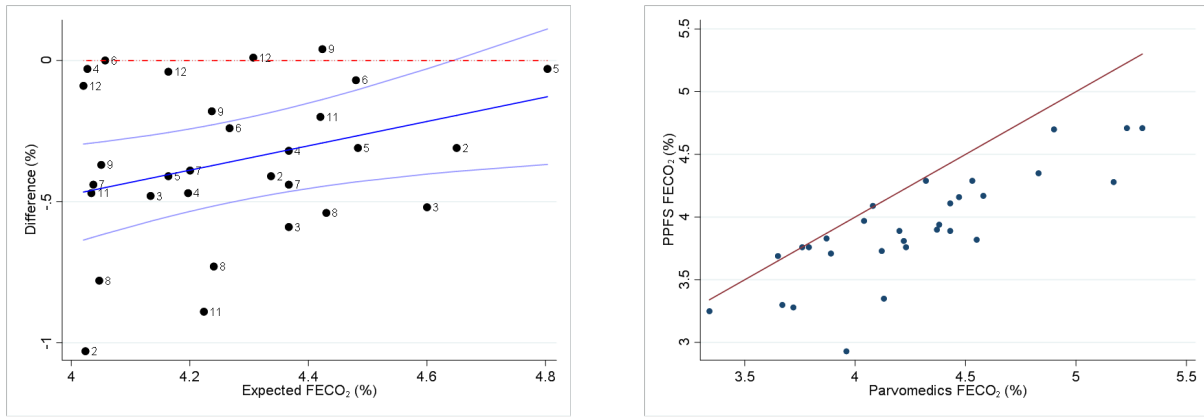
**Figure 3.**  $V_E$  values observed during the submaximal stages of testing. The left panel displays the observed differences (PPFS-Parvomedics) between the two devices. Expected  $V_E$  (x-axis) for each exercise level is predicted from the relationship between  $V_E$  and work rate for these subjects, as measured by the Parvomedics. The numbers displayed next to the data points are subject identifiers (three data points for each subject). The solid straight line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the  $V_E$  values of the two devices evaluated. The solid line is the line of identity.

The  $FEO_2$  measured by each device was fairly comparable (**Figure 4**). At the very lowest levels, the 95% confidence interval was slightly above a difference of zero, which indicates that the PPFS values were slightly higher than the Parvomedics values. This would cause computed  $VO_2$  values from the PPFS to be lower.



**Figure 4.**  $FEO_2$  values observed during the submaximal stages of testing. The left panel displays the observed differences (PPFS-Parvomedics) between the two devices. Expected  $FEO_2$  (x-axis) for each exercise level is predicted from the relationship between  $FEO_2$  and work rate for these subjects, as measured by the Parvomedics. The numbers displayed next to the data points are subject identifiers (three data points are present for each subject). The solid straight line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the  $FEO_2$  values of the two devices evaluated. The solid line is the line of identity.

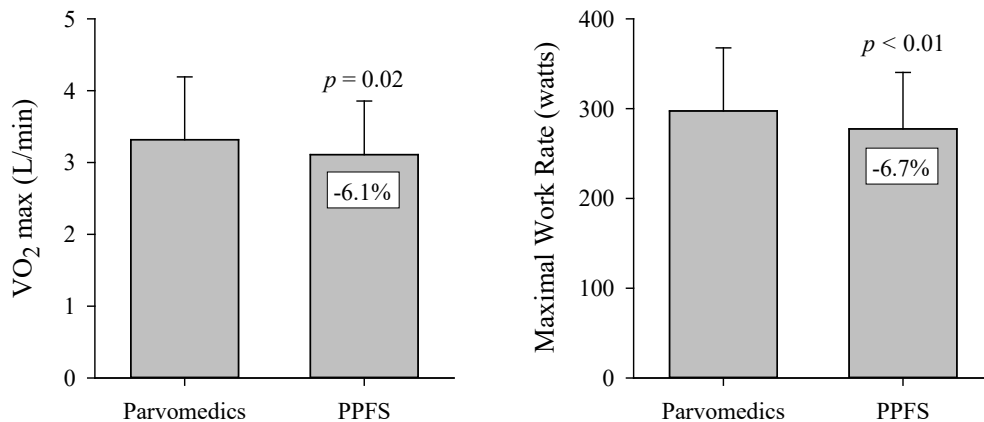
$FECO_2$  values are illustrated in **Figure 5**. The PPFS values were clearly lower than the Parvomedics values across the range of data produced by our subjects.



**Figure 5.** FE<sub>CO</sub>2 values observed during the submaximal stages of testing. The left panel displays the observed differences (PPFS-Parvomedics) between the two devices. Expected FE<sub>CO</sub>2 (x-axis) for each exercise level is predicted from the relationship between FE<sub>CO</sub>2 and work rate for these subjects, as measured by the Parvomedics. The numbers displayed next to the data points are subject identifiers (three data points for each subject). The solid line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the FE<sub>CO</sub>2 values of the two devices evaluated. The solid line is the line of identity.

### Maximal Exercise

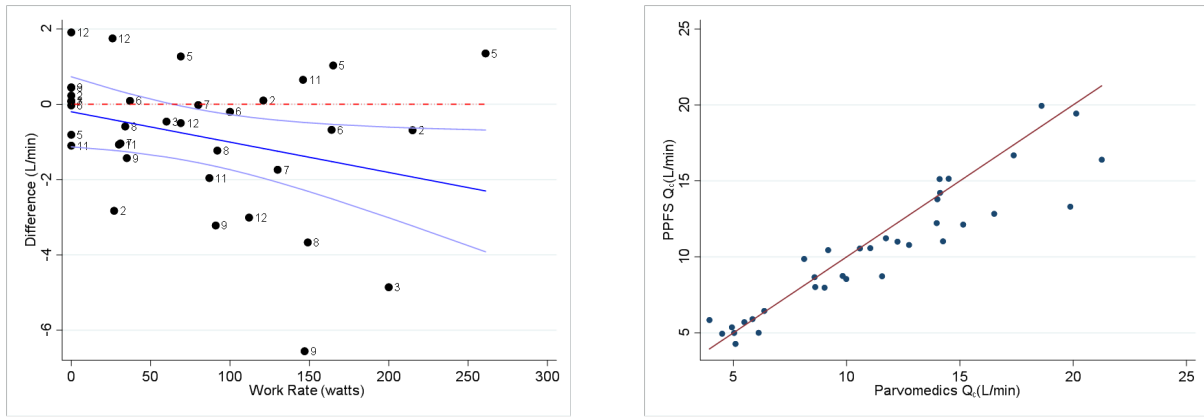
The average VO<sub>2</sub>max attained by the subjects was higher when measurements were obtained with the Parvomedics device (**Figure 6**). The higher Parvomedics VO<sub>2</sub>max also was associated with a higher peak work rate attained during testing.



**Figure 6.** Mean VO<sub>2</sub>max (left panel) and maximal cycle work rate (right panel) attained during the tests using the Parvomedics and PPFS devices. Note that the PPFS trial produced a lower VO<sub>2</sub>max in almost direct proportion to the lower work rate attained.

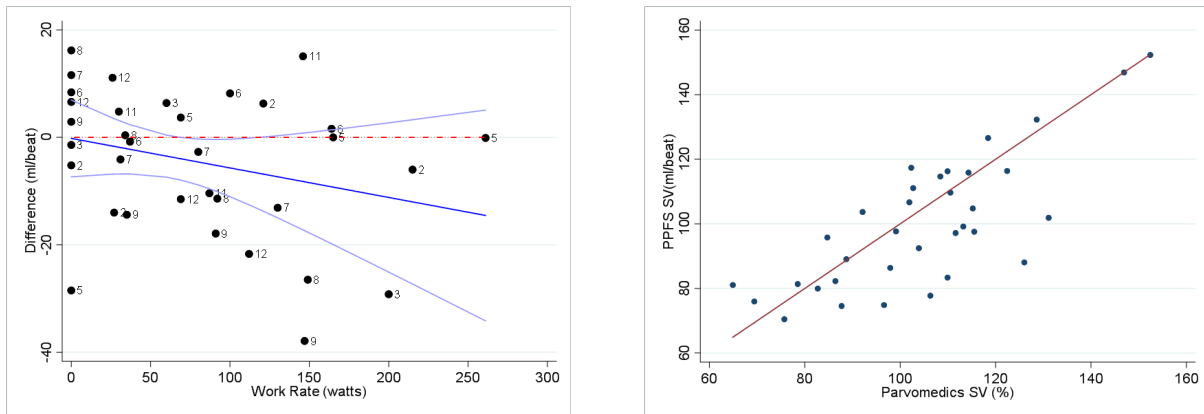
### Cardiac Output

The Q<sub>c</sub> values obtained from the PPFS and echocardiographically are displayed in **Figure 7**. At resting levels the two methods provided comparable data; however, with increasing exercise work rate the echocardiographic data were lower than the associated PPFS data.



**Figure 7.**  $Q_c$  values observed during the submaximal stages of testing. The left panel displays the differences (PPFS-Echocardiograph) observed between the two devices across exercise work rates (0 W = seated rest). The numbers displayed next to the data points are subject identifiers (three data points for each subject). The solid straight line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the  $Q_c$  values of the two methods evaluated. The solid line is the line of identity.

**Figure 8** contains the SV data from the echocardiograph and the PPFS. Stroke volume tended to be higher when measured by echocardiography, with the margin of the upper 95% confidence interval falling close to no difference across the range of values measured.



**Figure 8.** SV values observed during the submaximal stages of testing. The left panel displays the differences (PPFS-Echocardiograph) observed between the two devices across exercise work rates (0 W = seated rest). The numbers displayed next to the data points are subject identifiers (three data points for each subject). The solid straight line is the mean relationship, and the curves are 95% confidence intervals for the mean difference. The right panel displays the relationship between the SV values of the two methods evaluated. The solid line is the line of identity.

## DISCUSSION

The primary purpose of this study was to determine whether consistent differences existed between two metabolic gas analysis systems, PPFS and Parvomedics, with respect to measuring  $\text{VO}_2$  during submaximal and maximal exercise. We also assessed differences between  $\text{Qc}$  measurements obtained with the PPFS and by echocardiography.

Our data show statistically significant differences between the PPFS and Parvomedics values of  $\text{VO}_2$  during submaximal exercise at loads up to 75%  $\text{VO}_{2\text{max}}$  (**Figure 1**), but this difference is not of sufficient magnitude to be physiologically important. The average differences observed in submaximal  $\text{VO}_2$  were just outside the 4%-6% intra-individual day-to-day variation in  $\text{VO}_2$  commonly reported in the literature (19). The upper 95% confidence interval computed from the differences between the two devices was not outside of the 4%-6% range. However, when measurements are repeated across the duration of a longitudinal study, it is important that all measurements (e.g., before, during, and after space flight) be conducted using the same device to avoid potential sources of error associated with different metabolic gas analysis systems.

It appears that the difference in submaximal  $\text{VO}_2$  values was not caused by different measures of  $V_E$  obtained by the two devices (**Figure 3**). This suggests that  $\text{FEO}_2$  measurements might explain the  $\text{VO}_2$  differences; conceptually  $\text{VO}_2$  is simply the product of  $V_E$  and the difference in  $\text{O}_2$  concentration between ambient air and expired air. However, it is difficult to pinpoint this as the precise cause of the discrepancy in  $\text{VO}_2$  values because the preponderance of the  $\text{FEO}_2$  data is clustered within a narrow range between 16 and 16.5%  $\text{O}_2$  (**Figure 4**).  $\text{FECO}_2$  also contributes to the calculation of  $\text{VO}_2$ , but its influence is negligible compared to  $\text{FEO}_2$  or  $V_E$ . To illustrate, at a  $\text{VO}_2$  of 4.68 L/min (a level representative of maximal exercise of our fittest subjects) if  $\text{FECO}_2$  was reduced by 0.4% (which is the average difference observed in  $\text{FECO}_2$  between the two devices in our tests; **Figure 5**), the calculated  $\text{VO}_2$  would be reduced only to 4.66 L/min.

Mean  $\text{VO}_{2\text{max}}$  obtained from the two devices was significantly different (**Figure 6**). However, this is not likely due to any measurement problems within the devices *per se*, in light of the fact that the 6.1% lower  $\text{VO}_{2\text{max}}$  measured with the PPFS was observed in combination with a 6.7% reduction in the peak work rate attained during the PPFS tests. The reduction in work rate achieved by the subjects during the PPFS comparison test might be due to a ventilatory flow restriction imposed by the PPFS. When using the PPFS, the subjects breathe through a valve and a mouth port tube that is lengthened to accommodate the  $\text{Qc}$  rebreathing bag adapter and the pneumatic valve, which controls flow into and out of the bag. The extended length of the port tube causes more flow limitation and resistance to breathing than the standard Hans Rudolph 2700 valve that is part of the Parvomedics device. Pressures in the respiratory valve up to 13.5  $\text{cmH}_2\text{O}$  were measured by the PPFS during peak exercise, and the pressure during submaximal exercise ranged from 2 to 5  $\text{cmH}_2\text{O}$ . A peak pressure of about 8  $\text{cmH}_2\text{O}$  is expected at peak exercise ventilation values when using the Hans Rudolph 2700 valve (<http://www.rudolphkc.com/pdf/691017%201008%20L.pdf>). The pressures measured by the PPFS do not seem to be in the range that would cause marked limitation to submaximal exercise, although ventilation at maximal exercise levels may be impaired (9), thus limiting performance.

The differences in  $\text{VCO}_2$  values obtained from the two devices (**Figure 2**) are likely to be directly attributable to the different  $\text{FECO}_2$  data (**Figure 5**). The primary contributing variables used in the calculation of  $\text{VCO}_2$  are  $V_E$  and  $\text{FECO}_2$ . As noted above,  $V_E$  measurements did not differ significantly between the two devices. The disparity between  $\text{FECO}_2$  values measured by the Parvomedics device and the PPFS are not easily explainable because both systems use infrared measuring techniques for detecting  $\text{CO}_2$  concentrations.

$\text{Qc}$  and  $\text{SV}$  values obtained during exercise using the PPFS are lower than the measurements obtained by echocardiography (**Figures 7 and 8**). As noted in the statistical methods section of this report and in previous reports (17), there is no compelling evidence to suggest that one technique is more



accurate or valid than the other. However, in the present study, measurement of SV and Qc using echocardiography involved analysis of as few as three heart beats, whereas about 20 to 40 heart beats would occur during the rebreathing technique used for the PPFs. In addition, it becomes increasingly difficult to attain accurate ultrasound images with increasing cycle work rate because of subject movement. Thus, it is possible that the rebreathing technique was less prone to variation than echocardiography because beat-to-beat differences in SV are averaged over more heart beats and subject movement does not affect the measurement.

### ***Limitations***

An ideal comparison of metabolic gas analysis systems would entail the two systems being operated “in series” (i.e., measuring fractions and volumes of the same expired gases or from sensors in close proximity to one another) on the same subject. An “in series” evaluation eliminates day-to-day variation in the subjects’ response to exercise as a source of error. However, this type of setup often is not feasible because the two systems can interfere with each other and produce erroneous results. Discussions with the manufacturers of both the Parvomedics system and the PPFs led us to conclude that an evaluation with the two devices in series may lead to errors, particularly in gas sampling, and therefore our tests were performed using the devices on separate days. With this approach, valid comparisons of the  $\text{VO}_2$  and  $\text{VCO}_2$  data obtained from each device are still possible, although variables associated with the calculation of  $\text{VO}_2$  and  $\text{VCO}_2$  (i.e.,  $\text{FEO}_2$ ,  $\text{FECO}_2$  and  $\text{V}_E$ ) need to be assessed with caution. For example, an individual should have a similar  $\text{VO}_2$  response to a similar exercise load during two separate tests (an expected finding), but  $\text{V}_E$  could be higher in one trial and resulting in a higher  $\text{FEO}_2$  (13). Alternatively, we could have exchanged the PPFs and Parvomedics at the midpoint during a series of prolonged exercise stages. This approach would have eliminated day-to-day variation during submaximal data collections, but it would have introduced the distinct disadvantage of not being able to compare maximal responses; only one device could be used at a time to collect maximal exercise data. Therefore, the approach that we selected appeared to be the best compromise. However, although the data from our evaluation indicate that  $\text{FEO}_2$  values may differ, and the  $\text{FECO}_2$  values certainly differ, there is no way to conclusively prove this using the present data set.

The difference between  $\text{VO}_{2\text{max}}$  data obtained on the two devices is likely a limitation of the PPFs design. If Qc measurements are not desired, the PPFs can be used without the extended mouth-port adapter. This should reduce the flow limitation and allow subjects to exercise to higher loads. However, because one of the objectives of the ISS study (16) was to measure Qc, this is not viewed as an ideal solution.

It should be noted that throughout this report  $\text{VO}_2$  measured at maximal exertion during the peak cycle tests has been referred to as  $\text{VO}_{2\text{max}}$ . This is technically not the correct terminology for our measurement because we performed no specific verification of a plateau in  $\text{VO}_2$  with increasing work rates, which is the criterion for “true”  $\text{VO}_{2\text{max}}$  (22). However, not all individuals can attain this plateau, and previous comparisons have reported no statistically significant difference between  $\text{VO}_{2\text{max}}$  and peak  $\text{VO}_2$ , which is the correct description for the variable reported here. Further, because the terms “ $\text{VO}_{2\text{max}}$ ” and “peak  $\text{VO}_2$ ” have been used interchangeably in various spaceflight and bed rest publications, we have chosen to use only  $\text{VO}_{2\text{max}}$  in the description of test results contained in this report.

### **CONCLUSIONS**

There were no findings in this evaluation that preclude using the PPFs to obtain data before, during, or after ISS missions. In light of the differences observed in the  $\text{VO}_2$  and  $\text{VCO}_2$  measurements obtained by the PPFs and the Parvomedics devices, it is imperative that the same device be used for all pre-, in-, and post-flight testing if the data are to be compared across time points.

- The differences observed in submaximal  $\text{VO}_2$  were small and are probably not clinically relevant.



- The differences observed in submaximal  $\dot{V}CO_2$  are very likely due to differences in  $FECO_2$ . Although  $FECO_2$  has only a small effect on the computation of  $\dot{V}O_2$ , the effect could confound any research projects that examine  $\dot{V}CO_2$  as a variable of interest. We recommend that PPFS expired gas fraction measurements be further examined.
- The reduced  $\dot{V}O_{2max}$  and maximal work rate attained by the subjects during PPFS tests are likely due to a ventilatory flow limitation.
- The reproducibility of the PPFS measurements should be quantified.

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## APPENDIX A – ACRONYM LIST

BP	Blood Pressure
CO <sub>2</sub>	Carbon Dioxide
ECWG	Exploration Clinical Working Group
FECO <sub>2</sub>	Fractions of Expired Carbon Dioxide
FEO <sub>2</sub>	Fractions of Expired Oxygen
HRP	Human Research Program
ISS	International Space Station
MOG	Medical Operations Group
NASA	National Aeronautics and Space Administration
O <sub>2</sub>	Oxygen
PPFS	Portable Pulmonary Function System
Q <sub>c</sub>	Cardiac Output
SF <sub>6</sub>	Sulfur Hexafluoride
SV	Stroke Volume
V <sub>E</sub>	Expired Ventilation
VCO <sub>2</sub>	Submaximal Carbon Dioxide
VO <sub>2</sub>	Oxygen Consumption
VO <sub>2</sub> max	Maximal Oxygen Consumption
W	Watt