Validation of Novel Indirect Calorimetry System Based on Luminescence Quenching On-Airway Oxygen Sensor

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Background

Clinical Uses

Metabolic gas exchange monitors are frequently used in the intensive care unit to study the oxygen kinetics and appraise the nutritional requirements for acutely ill patients. In a method known as indirect calorimetry, energy expenditure information is obtained non-invasively by measuring the respiratory gases under resting conditions.[1-3] A modified Weir equation relates the oxygen consumption (VO_2) and the carbon dioxide production (VCO_2) to the caloric burn rate.[4] The resting energy expenditure (REE) represents approximately 70% of the total energy expenditure (TEE).[5]

Critical illness has been shown to alter metabolic rate and influence VO_2. Inflammation, sepsis, seizures, and weaning from ventilation increase the VO_2, while sedation, muscle paralysis, shock, and hypothermia decrease the VO_2. Since underfeeding a patient may increase catabolism and overfeeding is associated with hyperglycemia, increased ventilation requirements, and lipogenesis, it is imperative for the patient's recovery that the diet meets nutritional requirements.[6-8]

Application to Space

Orr et al (1989) described the need for a small, lightweight, and reliable instrument to measure VO_2 and VCO_2 aboard the Space Station. This would allow astronauts to monitor deconditioning associated with weightlessness and track the effectiveness of exercise countermeasures.[9]

Traditional method –Datex Deltatrac

In clinical practice, the Datex Deltatrac Metabolic Monitor (Datex-Instrumentarium, Helsinki, Finland) is a widely-accepted noninvasive metabolic monitor useful in determining the indirect calorimetry measurements.[10-13] A paramagnetic oxygen sensor is used to measure oxygen concentrations; carbon dioxide is analyzed using an infrared sensor. Gases are collected in a mixing chamber and then sampled at a fixed flow rate. After a stabilization period, the data is updated every minute.

However, factors such as the bulkiness of the gas mixing chamber, incompatibility with other instruments that provide physiological information, elapsed time required for the Deltatrac to reach a steady state, complicated interface, off-site equipment repairs, and the requirement of a skilled technician to analyze the results deter some from using the Deltatrac.[7, 12]

Novel Approach - $NICO_2$ Metabolic Monitor

For the reasons cited, Respironics developed the NICO2 Cardiopulmonary Management System (Respironics, Inc., Wallingford CT). The NICO2 is a compact metabolic device with a user friendly interface. In addition to standard flow and CO_2 sensors, a novel on-airway oxygen sensor using luminescence quenching technology has been developed to determine oxygen consumption. The benefits of this sensor are the real-time oxygen consumption analysis and the elimination of water condensation collecting in the hoses of the drawn sample.[14]

The oxygen sensor portion of the instrument consists of a light emitting diode which serves as the excitation source. A photosensitive detector is mounted in a position to respond to the filtered fluorescent radiation emerging from the exit optical filter. The oxygen sensor is comprised of a thin film of transparent material containing luminescent dye in which rapid diffusion of molecular oxygen from the airway gas environment takes place. Oxygen concentration is proportional to the amount of quenching observed when in the fluorescence, **Figure 1**. This oxygen signal is presently designed to give a simple oxygen waveform and measurement of inspired and expired oxygen with the existing flow signal to calculate oxygen uptake in resting patients. Bench simulations found that the new device measure oxygen consumption with an average difference of 0.3+-2.8% at inspired oxygen levels between 30%-50%.[15]

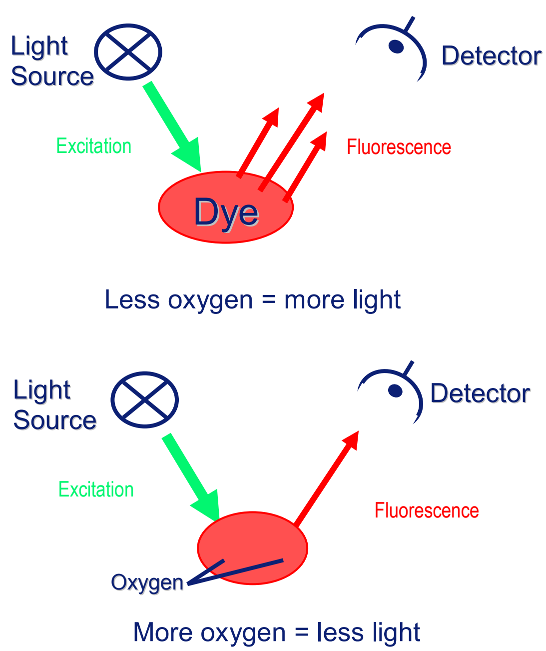

Figure 1 Schematic of luminescence quenching (a) when no oxygen is present the dye fluoresces; (b) oxygen molecules quench the fluorescence

Using the Deltatrac as a standard, the accuracy and precision of luminescence quenching oxygen sensor were evaluated in healthy volunteers.

Methods

Subjects

Twenty healthy volunteers between the ages of 18-60 were recruited to participate. Weight and height were measured on a Health O Meter Professional dial scale. Height of the volunteers was measured to the nearest inch. The characteristics of the volunteer group are presented in **Table 1**.

Table 1 Patient characteristics

Gender	10 F	10 M
Age (yr)	30±12.1	27.5±7.7
Weight (lbs)	145.2±-25.9	179±40.5
Height (inches)	66.9±2.1	72.2±1.4

M=male; F=female

Data presented as mean ± s.d

Design Protocol

Subjects were seated in a chair and instructed not to speak, minimize movements during the experiment, and breathe normally through a disposable mouthpiece to which the O_2, CO_2 and flow sensors were attached. A disposable nose clip was used to prevent breathing or leaking of gases through the nose.

The distal side of the sensor was connected to a valved T-piece such that all expired gas was diverted through a hose to the reference oxygen uptake analyzer. The one-way valves on the T-piece were replaced after each subject to prevent wear on the valve. Two mixing bags were connected to ensure homogeneous mixing of the inspired gas and to prevent forced airflow through the hose and across the sensor, **Figure 2.** The on airway oxygen sensor is labeled. **Figure 3** depicts the bulkiness of the Deltatrac mixing chambers.

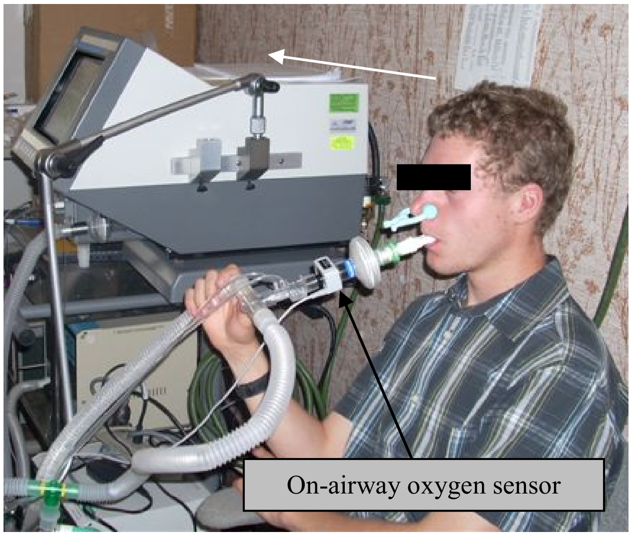

Figure 2 Volunteer study set-up

Figure 3 A size comparison of the $NICO_2$ (top) and Deltatrac (bottom) metabolic monitors

Measurement of Oxygen Consumption

Oxygen consumption was measured simultaneously using a Deltatrac II metabolic monitor and by the $NICO_2$ Cardiopulmonary Management System. Each morning, prior to use, the system was allowed a warm up period of 30 minutes, as recommended by the manufacturer. Prior to use, the system sensors were calibrated at two gas concentrations of 20% oxygen, 5% carbon dioxide balance nitrogen (Scott Medical Products, Plumsteadville, PA) and with 100% oxygen.

The systems were given a 10 minute stabilization period for each subject, and then VO_2 and VCO_2 from the Deltatrac and $NICO_2$ systems were recorded at 1 minute intervals and continuously, respectively. Breath data was collected for about 15 minutes. Following the first data collection of air, subjects were allowed to rest, and then the process was repeated with inspired gas of 40% oxygen and balance nitrogen.

The resting metabolic rate (RMR) was calculated using the abbreviated Weir equation:

$$RMR = [(3.941 * VO_2) + (1.106 * VCO_2)]*1.440$$

where VO_2 and VCO_2 are measured in liters per day (ml/min) and RMR in kilocalories per day (Kcal).

Metabolic measurements are determined by integrating the product of the flow and oxygen signals over the entire breath.

Statistical analysis

Reproducibility and agreement between the Deltatrac and $NICO_2$ RMR were assessed as outlined by the Bland-Altman limits of agreement testing. All statistical analyses were performed using Excel 2002 for Windows.

Results

Data was collected from 20 healthy volunteers using the Deltatrac system and $NICO_2$ system. Although some volunteers expressed discomfort, no-one was unable to complete the study. Previous studies have shown the canopy gas collection method to be preferred over the mouthpiece. One volunteer had a moderate gas leak around the mouthpiece, which was quickly corrected. A few volunteers appeared to be restless. All volunteer data was included in the statistical analysis.

The difference between VO_2 measured by the Deltatrac and $NICO_2$ had a mean and standard deviation of -5.5 ±10.2 (-2.09 ±3.86%) and 5.1 ±18.1 (1.77 ±6.29%) ml/min for 21% and 40% oxygen, respectively **(Table 2).** The $NICO_2$ measurements were lower than the Deltatrac at oxygen levels of 21%, but $NICO_2$ measurements were higher at 40% oxygen.

Table 2 Measurement differences for $NICO_2$™ vs. Deltatrac™(n=20), O_2 Consumption (VO_2), CO_2 production (VCO_2), and RQ mean and s.d.

Mean Difference*	21% Oxygen	40% Oxygen
VO_2 (ml/min)	-5.5 ±10.2	5.1 ±18.1
VCO_2 (ml/min)	3.9±10.4	4.6±10.5
RQ	-0.1±0.08	-0.1±0.07
REE (kcal/day)	-25±74.4	36.27±119.4
Percent Difference**	**21% Oxygen**	**40% Oxygen**
VO_2	-2.09 ±3.86%	1.77 ±6.29%
VCO_2	1.63±4.41%	2.05±4.69%
RQ	-11.44±9.31%	-15.21±8.66%

*Data presented as mean ± s.d.

**Data presented as mean % diff ± % s.d.

A linear comparison of the VO_2 for the Deltatrac and $NICO_2$ is shown in **Figure 4.**The correlation coefficients for as shown: for r^2= 0.9735 for 21% oxygen, and r^2 = 0.9164 for 40% oxygen.

Figure 5 and **Figure 6** shows Bland-Altman difference and limits of agreement for VO_2.[16] Two standard deviations are shown by the dotted green line.

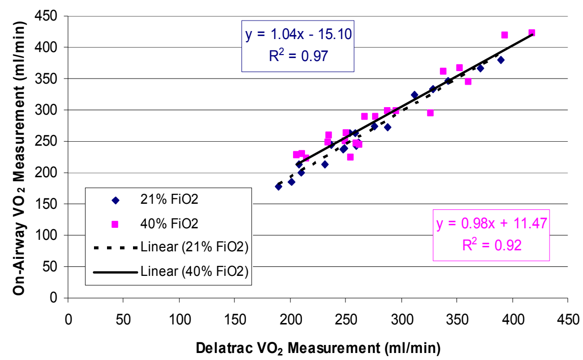

Figure 4 Linear X-Y the plot of NICO2 vs. Deltatrac at 21% and 40% oxygen

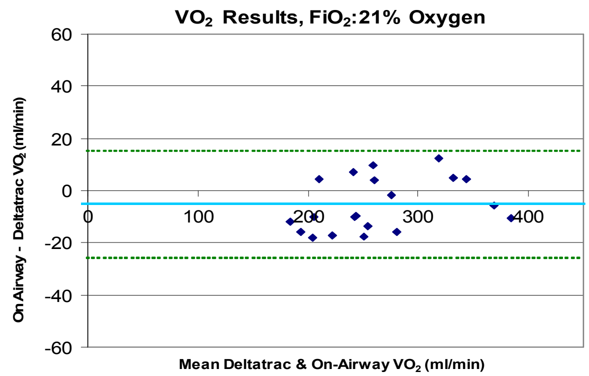

Figure 5 Bland-Altman difference -5.9 ± 10.4 ml/min (-2.2 ±4.4%) and the limits of agreement at 21% FiO_2

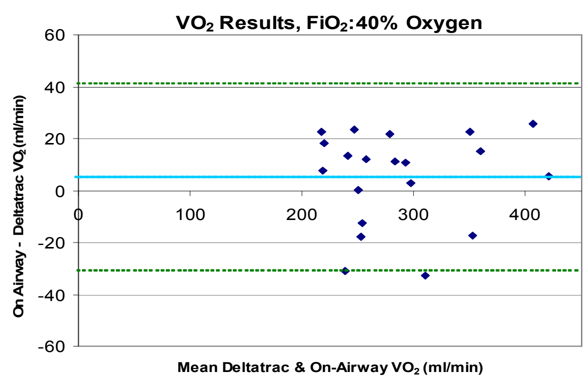

Figure 6 Bland-Altman difference 5.1 ± 18.1 ml/min (1.8 ± 6.3%) and the limits of agreement at 40% FiO_2

Discussion

The main aim of this study was to assess the validity of the new $NICO_2$ luminescent quenching oxygen sensor by comparing it to the clinical "gold standard" the Datex Deltatrac.[17]

On average the oxygen consumption measured by the $NICO_2$ was less than 5% higher than that measured by the Deltatrac at 21% oxygen. This difference was shown to be dependent on the oxygen level. Validity tests on the Med Gem, a handheld metabolic monitor, reported a 10% higher oxygen consumption reading over the Deltatrac. The Med Gem showed no significant differences in the measurement of VO_2 and RMR in healthy subjects. In the validation, Neieman *et al* (2003) evaluated a Body Gem metabolic monitor against the Douglas bag technique and found the correlation coefficients for oxygen consumption ranged 0.81 to 0.87.[13, 18] In our study of the $NICO_2$ and the Deltatrac, correlations ranged from 0.9164 to 0.9735.

The M-COVX, another compact and compatible metabolic monitor, measures VO_2 and VCO_2 on a breath to breath basis, similar to the $NICO_2$. Furthermore, it also uses a mathematical algorithm in order to provide data continuously. When compared to the Deltatrac, McLellan *et all* (2002) found that the M-COVX performed better than the Deltatrac at high Fi_{O2}.[19] It was found to be adequate when measuring respiratory gas exchange in ventilated critically ill patients.

Both systems were easily calibrated and the data collection was straight forward. Although both machines could require off-site equipment repairs, the compact $NICO_2$ is more easily transported than the Deltatrac cart, which hogs 6.6 squared feet of floor space and 3.4 feet vertical space. This also increases accessibility in tight spaces, such as the ICU. The $NICO_2$ oxygen sensor has a relatively short lifetime of ~4 days, but it is easily detached and replaced. This lifetime is adequate for a typical stay in the ICU.

This study had several limitations that should be considered. First, our goal was to validate the NICO2 oxygen sensor, thus repeated measure of the Deltatrac RMR was not taken. Previous research has fully established this indirect calorimeter to be within 5% for repeated measures.[20] Second, stabilization of the Deltatrac at steady state did not always occur after the prescribed warm up period. The protocol allowed for 15 minutes of data collection, a time that could be increased, but would cause an increased restlessness in the volunteers. Third, time and limited funding provided for only 20 volunteers. A larger, more diverse sample size would strengthen the study. To obtain an accurate RMR measurement by indirect calorimetry, factors such as recent physical activity, fasting and resting time must also be taken into consideration.[21] Further research is needed before the $NICO_2$ could replace the Deltatrac in clinical applications.

Conclusions

Determining an accurate RMR/REE is important when assessing the nutritional requirements of healthy and sick individuals. Clinicians, nutrition specialists, and even athletes use this crucial information when establishing individual-specific energy needs. This information is especially vital when caring for patients who are critically ill because overfeeding/underfeeding can have diverse affects on a patient's recovery. Indirect calorimetry is a reliable, non-invasive method for assessing the RMR/REE. The results of this trial reveal the on-airway luminescence quenching oxygen sensor VO_2 measurements were replicable and are feasible for use in an ICU setting..

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