Non-invasive metabolic monitoring of patients under anaesthesia by continuous indirect calorimetry—an in vivo trial of a new method

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Background. Oxygen uptake is an important form of metabolic monitoring for patients under anaesthesia. In critically ill patients oxygen uptake has been shown to provide valuable clinical information in directed therapy and acts as a useful monitor of cardiovascular dysfunction. A new method of continuous real time monitoring of metabolic gas exchange was tested in patients during anaesthesia.

Methods. Using a standard anaesthetic machine with attached semi-closed circle absorber system, oxygen uptake was measured continuously throughout surgery in 30 patients undergoing cardiopulmonary bypass surgery and compared with paired measurements made with the reverse Fick method. The method is an indirect calorimetry technique which uses fresh gas rotameters for control, regulation and measurement of the gas flows into the system, with continuous sampling of mixed exhaust gas.

Results. When compared with the reverse Fick method the oxygen uptake showed a mean difference (and sd) of 20.7 ml min⁻¹ or 12.1% (25.3 ml min⁻¹) pre-bypass and 13.9 ml min⁻¹ or 8.1% (27.0 ml min⁻¹) post-bypass. This bias is consistent with previous studies comparing oxygen uptake measured at the mouth against oxygen uptake by reverse Fick, which have shown a difference of approximately 10–15% accounted for by the consumption of oxygen by lung tissue.

Conclusions. As the method allows continuous measurement of gas exchange and can be adapted to a modern anaesthetic workstation it is an attractive method for use in clinical setting.

Keywords: measurement techniques, Fick principle; monitoring, oxygen; metabolism, oxygen consumption

Accepted for publication: September 28, 2006

Measurement of oxygen uptake (VO₂) is an important form of metabolic monitoring for patients during anaesthesia and critical care. It provides an indicator of a patient’s metabolic status and oxygen delivery to the tissues, and of cardiorespiratory function. As with other vital physiological parameters, such as systemic blood pressure, continuous automated measurement of VO₂ permits early intervention by the physician when deterioration unexpectedly occurs.

A simple, continuous and non-invasive method of measurement of VO₂ would assist anaesthetists in monitoring patient stability intra-operatively. However, the measurement of VO₂ has traditionally been uncommon in the operating room. This is largely because of the difficulties of accurate and reproducible measurement of gas exchange, particularly at a high FIO₂ and in the presence of inhalational anaesthetic agents. Invasive techniques, such as the reverse Fick method, using a pulmonary artery catheter to measure mixed venous oxygen content and cardiac output, are rarely felt justified. For these reasons, measurement of VO₂ is not considered a part of common clinical anaesthetic practice.

Biro proposed a method for continuous VO₂ measurement in a breathing system, which was based on a formula by Foldes and colleagues. The Biro equation, which utilized...
We describe an approach which uses the fresh gas rotameters for control, regulation and measurement of the gas flows into a standard semi-closed breathing circuit, with continuous sampling of mixed exhaust gas instead. This method permits continuous real time monitoring of a lung gas exchange simulator by Stuart-Andrews and colleagues, who demonstrated a large mean bias in the calculated \( V_{O_2} \) relative to a precisely simulated value.

Methods

Theory

The method presented here is based on mass balance principles for \( O_2 \) and \( CO_2 \) within a breathing system attached to a patient breathing an air/\( O_2 \) mixture. For any given setting for fresh gas \( O_2 \) rotometer flow rate (\( V_{Frotair} \)) and air rotometer flow rate (\( V_{Frotair} \)), \( V_{O_2} \) is calculated from the following equation:

\[
V_{O_2} = V_{Frotair} + \frac{V_{FrotO_2}\left(0.2093 - \frac{F_{CO_2}}{F_{CO_2} - F_{CO_2}}\right)}{1 - \frac{F_{CO_2}}{F_{CO_2} - F_{CO_2}}},
\]

where \( F_{CO_2} \) and \( F_{CO_2} \) are mixed exhaust gas concentrations of \( O_2 \) and \( CO_2 \) respectively.

Equation (1) allows continuous monitoring of \( V_{O_2} \) from a measurement of mixed exhaust gas oxygen and \( CO_2 \) concentrations. We have termed this continuous indirect calorimetry. The derivation of the equation is given in the Appendix, but it should be noted that the presence of other gases in the inspired mixture is readily incorporated and their uptake can also be measured simultaneously. This includes \( CO_2 \) elimination although accurate measurement of \( V_{CO_2} \) is prevented in a circle absorber system by its uptake by soda lime.

Experimental protocol

Thirty patients undergoing cardiopulmonary bypass graft surgery at The Alfred hospital, Melbourne, Australia were recruited to the study. Ethical approval was obtained from the institution’s human research ethics committee and informed written consent was obtained from each patient at the time of surgical admission.

Before surgery patients were cannulated in accordance with routine anaesthetic management with a peripheral arterial line and pulmonary artery catheter (Edwards, Irvine, CA, USA). After a period of 1–2 min of pre-oxygenation, anaesthesia was induced with a mixture of fentanyl, a benzodiazepine, propofol and a neuromuscular blocker. Maintenance of anaesthesia was achieved using an infusion of propofol titrated according to the depth of anaesthesia with the assistance of bispectral index monitoring. After endotracheal intubation, controlled ventilation was initiated using a 7900 series ventilator (GE Healthcare, Helsinki, Finland) with tidal volumes of approximately 7–10 ml kg\(^{-1}\) at a rate of 9–12 bpm using a standard circle absorber breathing system. The fresh gas mixture was set to 5 litre min\(^{-1}\) (3 litre min\(^{-1}\) air and 2 litre min\(^{-1}\) \( O_2 \)) giving a fresh gas \( O_2 \) concentration of slightly more than 50%, although this was able to be increased by the anaesthetist if felt clinically indicated.

During surgery, simultaneous paired blood samples were drawn from the arterial line and the distal lumen of the pulmonary artery catheter. Blood samples were analysed immediately at point of contact for oxygen saturation, partial pressure and haemoglobin content on the operating suite’s blood gas analyser (Rapidlab 1265, Bayer Diagnostics, Sudbury, UK). During the measurement period a set of five cardiac output measurements were made by thermodilution using a 10 ml bolus of room temperature saline and the results averaged. Results were excluded if they were found to lie more than \( \pm 10\% \) outside of the mean value. Oxygen content of both the arterial and mixed venous samples were obtained by calculation using Equation (2) below. Values for saturation and partial pressure made by the blood gas analyser were corrected to 37°C before calculation of oxygen content was made

\[
CO_2 = 1.34\times[Hb\times\left(\frac{S_o}{100}\right) + (0.003\timesP_{O_2})],
\]

where \( CO_2 \) is the oxygen content of the sample (ml 100 ml\(^{-1}\)) being either mixed venous or arterial, 1.34 is Hufner’s constant, \( Hb \) is the haemoglobin content (g dl\(^{-1}\)), \( S_o \) is the measured percentage saturation of oxygen and \( P_{O_2} \) is the partial pressure of oxygen (mm Hg).

Using the cardiac output measurement in conjunction with the calculated arteriovenous oxygen content difference, oxygen uptake (\( V_{O_2}\text{Fick} \)) was determined by the reverse Fick method.

\[
V_{O_2}\text{Fick} = \left(\frac{C_{a,v}}{100} - C_{v}\right)\times\dot{Q}_\text{Thermo}\times1000,
\]

where \( C_{a,v} \) is the calculated arterial oxygen content of the sample, \( C_{v} \) is the mixed venous oxygen content and \( \dot{Q}_\text{Thermo} \) is the cardiac output measured by thermodilution.
Heart rate, mean arterial pressure, pulmonary capillary wedge pressure, end-tidal CO\textsubscript{2} concentration, room and patient temperature measured by nasopharyngeal probe were also noted at this time.

During this period measurements of oxygen uptake by continuous indirect calorimetry (\(V_{\text{O}2}\text{CIC}\)) were averaged over a 5 min period and corrected to STPD (standard temperature and pressure dry). This process was repeated at two discrete points during the operation, once pre-bypass and once post-bypass. The first measurement was made approximately 30 min post-sternotomy while the final measurement was made post-bypass immediately after sternal closure.

**Measurement system**

A standard anaesthetic delivery system was used consisting of an Excel 210SE anaesthetic machine (GE Healthcare, Helsinki, Finland) and semi-closed circle absorber system (Fig. 1). Fresh gas was obtained from an ‘E’ sized cylinder of medical air attached to the anaesthetic machine, instead of using the hospital’s wall supply, as this was found to vary significantly in pressure over a period of time, causing variation in fresh gas air flow rates. Cylinder air supply pressure however was monitored throughout the experimentation period and a correction for any change in supply pressure was made against a previously calibrated flow–pressure curve (obtained from the elapse time taken to fill a 1 litre dry gas syringe). The observed variance of the bottle supply pressure was 0.5 kPa, giving very stable flow measurement. The oxygen supply was connected directly into the wall. There was only a small variation in oxygen supply pressure but in any case this change did not result in a change in oxygen flow across the rotameters as oxygen supply pressure to the anaesthetic machine is regulated in a two-stage process resulting in a constant oxygen flow.

Values for fresh gas flow were set visually on the flow control valves and the read value entered on the computer. The rotameters used were standard design bobbin rotameters incorporated into the anaesthesia workstation and had been initially calibrated by the manufacturer for individual gas species at 20°C and 101.3 kPa. To ensure their linearity over a range of delivered flows we performed a further calibration using a 1 litre dry gas syringe. From this a correction (<1%) was applied to this value in software using the calculated calibration curve.

Gas concentrations were measured by side-stream sampling by a Capnomac Ultima rapid gas analyser (GE Healthcare, Helsinki, Finland). Analogue data from the analyser was downloaded to a desktop computer via an analogue to a digital converter card. The rapid gas analyser measured \(O_2\) concentration paramagnetically, with an observed SD under steady-state conditions of 0.1%. \(CO_2\) was measured by infrared spectroscopy, and \(N_2\) concentration calculated by subtraction of all other gases from 100%. Analogue data were downloaded from the analyser and pressure transducers to the computer every 100 ms via the analogue-digital converter card (12-bit Burr-Brown, AZ, USA). This sampling rate provided more than adequate precision of measurement of raw data, given that stable concentrations of mixed gases were being sampled. Computations were made in real time using Borland C++ operating on a personal desktop computer. Gas concentration samples were averaged and reported \(V_{O2}\) updates every 15 s.

Periodic (half hourly) recalibration of the system was performed by brief sampling of fresh gas, as follows. The fresh gas \(O_2\) concentration calculated from the rotometer flow of air and oxygen was compared with an average value measured by the analyser over a period of 15 s at the beginning of the measurement process and again after each automatic recalibration (or ‘zero’) of the analyser which occurred every half hour. The measured difference (\(\Delta V_{O2}\)) was used to correct all subsequent \(F_{XO2}\) measurements until the next recalibration. This effectively calibrated the \(O_2\) concentrations measured by the analyser against the rotometer settings. The gas analyser continuously sampled exhaust gas at all other times, between recalibrations.

This system had been previously validated against a laboratory benchtop lung simulator. The system was checked for leaks using a static pneumatic compression manoeuvre, and found to lose not more than 10 ml min\(^{-1}\) under average operating circuit pressures. Before each operation a dynamic system calibration was performed by ventilation of a pair of silicone bags of suitable compliance in place of the patient in the circuit in order to determine the value of any significant zero offset for \(V_{O2}\) in the system. This was generally found to be approximately –10 ml min\(^{-1}\). This value was used to correct all measurements made during the operation.

The measurement of agreement between simultaneous paired measurements of \(V_{O2}\) measured by continuous indirect calorimetry using Equation (1) (\(V_{O2}\text{CIC}\)) and \(V_{O2}\text{Fick}\) was done by the method of Bland and Altman, calculating mean difference (bias being \(V_{O2}\text{CIC}–V_{O2}\text{Fick}\)) and the SD of the difference and limits of agreement [bias ± 2 SD]. The Pearson correlation coefficient \(r\) and its statistical significance were also determined.

**Results**

Data were collected from all 30 patients whose average age was 69 yr. Twenty-two patients were undergoing coronary artery bypass graft surgery, four were undergoing a valve replacement whilst the remaining four patients were undergoing both bypass graft surgery and valve replacement. Further patient characteristics and type of surgery are shown in Table 1. Perioperative haemodynamic data showed that cardiac output was higher post-bypass, accompanied by a lower haemoglobin concentration attributable to haemodilution during cardiopulmonary bypass (Table 2). Mean \(V_{O2}\text{Fick}\) pre-bypass was 139 ml min\(^{-1}\) and rose to
160 ml min\(^{-1}\) post-bypass (\(P=0.02\) on an unpaired \(t\)-test) (Table 3). These values are quite typical of elderly anaesthetized patients, who were all under mild to moderate hypothermia, as is typical anaesthetic practice in the pre-bypass period. Despite the higher hypothermia, as is typical anaesthetic practice in the pre-bypass patients, who were all under mild to moderate (Table 3). These values are quite typical of elderly anaesthetic practice in the pre-bypass period. Despite the higher hypothermia, as is typical anaesthetic practice in the pre-bypass period. Despite the higher hypothermia, as is typical anaesthetic practice in the pre-bypass period.

Comparison of \(V_O_2\) Fick against \(V_O_2\) CIC from Equation (1) are shown for both pre- and post-bypass results in Table 3. Results are reported as mean value [SD (median (inter-quartile range)])]. Overall the mean bias was found to be 17.2 ml min\(^{-1}\) (10.5% of the mean), with a SE of 2.4 ml min\(^{-1}\) and a SD of 26.1 ml min\(^{-1}\). This gives a 95% confidence limit for the mean bias of \(\pm 4.9\) ml min\(^{-1}\).

Figure 2 shows a Bland and Altman plot of these data, which distinguishes pre- and post-bypass measurements. The mean bias (and SD) pre-bypass was 20.7 ml min\(^{-1}\) (25.3 ml min\(^{-1}\)) while post-bypass it was 13.9 ml min\(^{-1}\) (2.70 ml min\(^{-1}\)). Correlation between the two methods was good (\(r=0.72\), \(P<0.01\) overall) given the relatively narrow range of oxygen uptake among the patient population.

The continuous nature of the method is demonstrated by data collected from one patient in the study. Figure 3 shows continuous measurement of \(V_O_2\) in a 71-yr-old female.

**Table 1** Characteristics of 30 patients undergoing cardiac surgery and the type of operation. Values are expressed as mean [std(range)].

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>69 [8 (80–49)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>20/10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78 [14 (104–48)]</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 [9 (184–146)]</td>
</tr>
<tr>
<td>Body surface area (m(^2))</td>
<td>1.91 [0.19 (2.26–1.45)]</td>
</tr>
<tr>
<td>Type of operation (CABGS/valve repair or replacement/both combined)</td>
<td>22/4/4</td>
</tr>
</tbody>
</table>

**Table 2** Perioperative haemodynamic and respiratory data in 30 patients before and after cardiopulmonary bypass. Values are expressed as mean [SD (median (inter-quartile range)]).

<table>
<thead>
<tr>
<th>Pre-bypass</th>
<th>Post-bypass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (litre min(^{-1}))</td>
<td>4.3 [1.1 (4.6 (3.3–5.1)])</td>
</tr>
<tr>
<td>Cardiac index (litre min(^{-1}) m(^{-2}))</td>
<td>2.2 [0.6 (2.3 (1.8–2.5)])</td>
</tr>
<tr>
<td>Haemoglobin (g 100 ml(^{-1}))</td>
<td>12.3 [1.8 (12.3 (11.0–13.4)])</td>
</tr>
<tr>
<td>Arterial oxygen saturation (%)</td>
<td>97.7 [1.1 (97.8 (97.2–98.8)])</td>
</tr>
<tr>
<td>Mixed venous oxygen saturation (%)</td>
<td>76.5 [5.9 (77.7 (72.0–79.9)])</td>
</tr>
<tr>
<td>Arterial oxygen tension (mm Hg)</td>
<td>176 [65 (163 (136–209))]</td>
</tr>
<tr>
<td>Mixed venous oxygen tension (mm Hg)</td>
<td>42 [6 (41 (37–44))]</td>
</tr>
<tr>
<td>Calculated oxygen delivery (ml min(^{-1}))</td>
<td>70 [19 (65 (54–91))]</td>
</tr>
</tbody>
</table>

**Table 3** Table comparing \(V_O_2\) Fick (‘reverse Fick’ method) against \(V_O_2\) CIC (\(V_O_2\) by continuous indirect calorimetry) at STPD. The results are reported as mean [SD (median (inter-quartile range)])]. Measurements made pre- and post-bypass and overall are shown. Statistical significance of the measured mean bias is given using a Student’s \(t\)-test for paired data.

<table>
<thead>
<tr>
<th>Pre-bypass</th>
<th>Post-bypass</th>
</tr>
</thead>
<tbody>
<tr>
<td>(V_O_2) Fick (ml min(^{-1}))</td>
<td>139 [27 (142 (119–153))]</td>
</tr>
<tr>
<td>(V_O_2) CIC (ml min(^{-1}))</td>
<td>160 [27 (158 (152–172))]</td>
</tr>
<tr>
<td>Difference (V_O_2) CIC−(V_O_2) Fick (ml min(^{-1}))</td>
<td>21 [25 (21 (3–41))]</td>
</tr>
<tr>
<td>(P)-value</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Discussion**

Non-invasive measurement of \(V_O_2\) can be made in a variety of different ways,\(^\text{11–15}\) in a fully closed breathing system, a patient’s oxygen uptake can be determined from the flow rate of oxygen required to maintain a constant volume, pressure and oxygen concentration inside the breathing circuit, but such approaches are not practical for routine use.\(^\text{16}\) Measurement of gas exchange inside a semi-closed breathing circuit has generally been performed by measurement of gas concentration and flow both into and out of the circuit. The change in total flow between these two points can be determined from the measured or calculated concentrations of an insoluble marker gas such as nitrogen (\(N_2\)) in fresh gas and mixed exhaust gas (the Haldane transformation) when the total inflow rate of \(N_2\) is known.\(^\text{17}\) At these points, thorough mixing will ensure stable gas concentrations in the face of tidal fluctuations in concentration at the mouthpiece, which improves accuracy and precision of the measurement. Indirect calorimetric methods such as this can be automated to provide ongoing measurement,\(^\text{18}\) but need repeated switching of gas sampling to achieve this,
which limits the frequency of measurement and precludes truly continuous gas exchange monitoring.

The continuous method tested here is an adaptation of the Haldane transformation and requires the presence of some $N_2$ in the exhaust gas flow in order to compute Equation (1). The results of this study demonstrate that the accuracy and precision of the Haldane approach of measuring gas exchange are retained, while permitting continuous monitoring to occur. Measurement of gas uptake from the breathing circuit after maximal gas mixing improves measurement stability. Furthermore, the continuous sampling allowed data averaging and smoothing to be done while maintaining the frequency of $V_{O2}\text{CIC}$ calculation at four times per minute.
The ‘reverse Fick’ method is a commonly used physiological standard against which calorimetric methods have been compared but it has its limitations. While measurement of cardiac output by thermodilution is traditionally assumed to be accurate to within ±10% of the true value, poorer agreement than this has been demonstrated against gold standards such as indwelling flow probes in animals. Overestimation of low cardiac output values in humans has also been shown. During a complete ‘reverse Fick’ calculation, propagation of random measurement errors throughout the calculation process has been shown previously. Conservative estimates of error in measured input variables produce errors of almost 20% in calculated \( \dot{V}O_2 \). This has prompted some commentators to suggest that indirect calorimetry is a more accurate technique. This is interesting, as there are relatively few examples in clinical measurement where a less invasive approach proves to be more reliable than its invasive alternative.

These concerns about reproducibility and precision of individual measurements with the reverse Fick method may explain much of the random scatter in agreement with continuous calorimetry we encountered. Similar levels of scatter in agreement between indirect calorimetry and the reverse Fick method were found by Walsh and colleagues and Marson and colleagues in intensive care patients. Previous laboratory validation of our measurement system using a lung gas uptake simulator showed only a \(-1.3 \text{ ml min}^{-1}\) mean bias with a SD of 6.5 ml min\(^{-1}\) in agreement with the target simulated \( \dot{V}O_2 \). Nevertheless, despite this, the reverse Fick method does provide a useful standard to assess the presence of bias in a comparator method, provided a large enough series of data is collected to reduce the standard error of the mean, and allowance is made for the presence of lung tissue \( O_2 \) uptake, which is not measured by the reverse Fick approach. Several previous studies have demonstrated this to be in the order of 10–15% of \( \dot{V}O_2 \) measured at the mouth, in patients undergoing cardiac surgery. The mean bias of 10.5% found in this study is consistent with this. Because its calculation shares no input variables with Equation (1), the reverse Fick method avoids the potential for artifactual correlation with calorimetry because of mathematical coupling.

The method is designed to provide continuous \( \dot{V}O_2 \) monitoring, which has been demonstrated in a previous in vitro study. This study was designed to validate its accuracy under clinical conditions against an independent standard. However, the continuous nature of the method is demonstrated by data in Figure 3, collected from one patient in the study during the onset of rapid AF. The likely acute reduction in cardiac output suggested by the decrease in blood pressure accompanying the AF would be expected to cause a transient decrease in \( \dot{V}O_2 \). Therefore, the sudden and sustained increase in \( \dot{V}O_2 \) we found was an interesting observation; clinical and laboratory studies have shown that AF reduces myocardial efficiency while increasing myocardial \( O_2 \) consumption. This anecdote demonstrates that routine measurement of metabolic gas exchange
may provide deeper insights into the physiological changes occurring in patients during surgery than are currently available to us.

While providing continuous monitoring of \( V_{O_2} \), the method tested here has the disadvantage of a delayed response time in its measurement with recirculating systems such as circle absorber systems, which have relatively high circuit volumes. This is attributable to the wash to the third end of the circuit. This is also seen with changes to the fresh gas concentration or flow rates, which require time for washthrough. We minimized this delay by using a relatively high fresh gas flow rate, having previously demonstrated in vitro that our system would still retain sufficient precision of measurement at higher flow rates, despite the consequent reduction in the fresh gas to exhaust gas \( O_2 \) concentration gradient.\(^5\) This delay is minimal with partial rebreathing systems, such as the Mapleson D (Bain circuit), or with non-rebreathing systems, such as are used with the Manley ventilator. The disadvantage of these high flow systems is poorer economy of gas usage. In addition we found that fresh gas oxygen concentrations up to 80% still provided sufficient accuracy in \( V_{O_2} \) measurements.

The advantage of the method lies in its adaptability. We have demonstrated the accuracy and practicability of the method by setting and reading fresh gas bobbin flowmeters and might use electronic flowmeters, such as are found as standard equipment on modern anaesthetic delivery workstations. This avoids the need to manually enter the selected standard equipment on modern anaesthetic delivery workstations. This project was supported financially by a research grant provided by GE Healthcare and the Australian Society of Anaesthetists.

**Non-invasive metabolic monitoring**

**Acknowledgements**

This project was supported financially by a research grant provided by GE Healthcare and the Australian Society of Anaesthetists.

**Appendix**

**Derivation of Equation (1).**

Based on mass balance principles, in a patient receiving an \( O_2 \)-air mixture, attached to a breathing system with total fresh gas flow \( V_{FT} \), the total flow of mixed exhaust gas at the point of gas concentration sampling (\( V_XT \)) is

\[
V_XT = V_{FT} - V_{O_2} + V_XCO_2, \tag{A1}
\]

where \( V_XCO_2 \), the flow of \( CO_2 \) in mixed exhaust gas, is the same as \( V_{CO_2} \) if there is no soda lime present and if there are no leaks in the system.

If \( FCO_2 \) is the fractional mixed exhaust concentration of \( CO_2 \)

\[
V_XCO_2 = V_XT \cdot FCO_2, \tag{A2}
\]

Substituting in (A1) and transposing

\[
V_XT = \frac{V_{FT} - V_{O_2}}{1 - FCO_2}. \tag{A3}
\]

Now, if \( V_{FO_2} \) is the total fresh gas flow of \( O_2 \) (from both air and \( O_2 \) rotameters) and \( FCO_2 \) is its mixed exhaust concentration

\[
V_{O_2} = V_{FO_2} - V_{FT} \cdot FCO_2, \tag{A4}
\]

Substituting from (3)

\[
V_{O_2} = V_{FO_2} - \frac{V_{FT} - V_{O_2}}{1 - FCO_2}. \tag{A5}
\]

Transposing

\[
V_{O_2} = \frac{V_{FO_2} - V_{FT} \cdot FCO_2}{1 - FCO_2}. \tag{A6}
\]

Given that the fresh gas air rotameter delivers 20.93% \( O_2 \), and that \( V_{FT} \) is the sum of the fresh gas \( O_2 \) rotometer flow rate (\( V_{Frot_{O_2}} \)) and the air rotometer flow rate (\( V_{Frot_{air}} \))

\[
V_{O_2} = V_{Frot_{air}} + \frac{V_{Frot_{O_2}} \cdot (0.2093 - FCO_2)}{1 - FCO_2}, \tag{A7}
\]

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51


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